**Excluded after the first screening:**

(2015). "Asian Pacific Digestive Week 2015." Journal of Gastroenterology and Hepatology (Australia) 30.

The proceedings contain 1058 papers. The topics discussed include: long-term prognosis of patients who underwent endoscopic resection for esophageal squamous cell carcinoma reaching or invading beyond the muscularis mucosae; corpus-predominant gastritis index can be a marker earlier than intestinal metaplasia to screen out the helicobacter pylori-infected non-ulcer dyspepsia patients at risks of gastric cancer; helicobacter pylori infection induces DNA damage repair deficiency via attenuating autophagy; the influence of efflux pump on the antibiotic resistance of helicobacter pylori to clarithromycin and moxifloxacin; risk factors influencing the outcome of peptic ulcer bleeding in chronic kidney disease after initial endoscopic hemostasis: nation-wide cohort study; upregulations of gastric TRPV receptors and decreased serum concentration of BDNF in patients with functional dyspepsia (FD); and cat dander sensitization: the link between irritable bowel syndrome and asthma.

(2018). "Long-term outcome of group D patients with negative serum anti-Helicobacter pylori antibody and positive serum pepsinogen test in healthy Koreans." Journal of Digestive Diseases 19(9): 529‐539.

Abadir, A., et al. (2012). "Intestinal metaplasia and the risk of gastric cancer in an immigrant asian population." Clinical Medicine Insights: Gastroenterology 5: 43-50.

The development of intestinal metaplasia (IM) has been purported to be a critical step in the pathogenesis of gastric cancer. However, the natural history of IM in migrant human populations has not been well elucidated. The purpose of this study was to determine the risk of gastric cancer posed by IM in Asian immigrants undergoing gastric cancer screening. A retrospective review of Asian immigrants found to have IM during screening was conducted over an 18-month period. In total, 222 patients were found to have IM. Altogether, 24% had a history of smoking, 48% had a family history of gastric cancer, and 52% had a history of Helicobacter pylori (H. pylori) infection with a 96% eradication rate. Patients with stable IM (SIM) were then compared with those who developed high risk pathology (HRP), specifically dysplasia and/or adenocarcinoma. Thirty-five patients (16%) were included in the HRP group, 31 with dysplasia (14%) and 4 with adenocarcinoma (2%). Of those with dysplasia, 55% demonstrated regression to IM over the course of follow-up. Patients in the SIM group were more likely to be female (60% vs. 31%, P = 0.002) and more likely to have had a normal biopsy during follow-up (32% vs. 9%, P = 0.005). Odds ratios for IM stability were 3.3 (95% CI 1.5-7.0) and 5.0 (95% CI 1.5-17.1) for female gender and presence of a normal biopsy, respectively. Intestinal metaplasia in immigrant Asian populations is predominantly a stable histologic finding associated with a low rate of persistent dysplasia and adenocarcinoma.

Adgey, C., et al. (2015). "Follow up of gastric intestinal metaplasia." Irish Journal of Medical Science 184(2): S32-S33.

Introduction: Gastric intestinal metaplasia (GIM) is considered a risk factor for gastric cancer however the management and follow up for these patients is uncertain. New consensus guidelines published January 2012, state patients with extensive IM should be offered endoscopic surveillance every 3 years. This study looked to assess the outcomes for a cohort of patients with GIM followed up in a district general hospital. Method: Patients were recruited to the study using a database of patients found to have GIM accumulated by one consultant. Retrospective chart review was undertaken for all patients in this database. Data was collected including patient's age, sex, certain assumed risk factors (smoking, alcohol intake and Helicobacter pylori), relevant medications and presence of Barrett's oesophagus. The follow up pathology was then analysed looking for progression (focal IMextensive IM-dysplasia), regression or no change. Results: There were 28 patients on the database, 43 % were male. Age ranged from 34 to 79 (mean 62). Patients had been on the database between 6 months and 9 years (median 4 years). 24 patients had been rescoped annually (86 %). Of these patients 29.2 % had no change in their pathology, 50 % had regressed to no IM, 8.3 % regressed from extensive to focal IM and 12.5 % progressed from focal to extensive IM. No patients developed gastric cancer in our follow up time. Conclusion: Although the majority of patients did not progress (or did in fact regress) a proportion of patients did progress in the extent of GIM and therefore we support follow up surveillance of this group of patients.

Agoston, A. T., et al. (2011). "Pit dysplasia of the stomach: A clinicopathologic, immunohistochemical, and outcome study." Gastroenterology 140(5): S676.

BACKGROUND: Intestinal-type gastric cancer is believed to develop via an intestinal metaplasia- dysplasia-carcinoma pathway. Previously, we reported that dysplasia-like atypia may be limited to the deep pit epithelium, without surface epithelium involvement, [Pit Dysplasia (PD)] in a study of patients with resected gastric cancer, and suggested that PD may represent an early form of gastric intestinal-type dysplasia. The aim of this biopsy study was to evaluate the prevalence, clinicopathologic, immunohistochemical profile, and outcome of PD in a consecutive group of patients with chronic gastritis and intestinal metaplasia (IM). DESIGN: Routinely processed mucosal biopsies from 166 patients with chronic gastritis and IM collected between the years 1991-2001 were evaluated for the presence or absence of PD, and a wide variety of clinical and pathologic features including age, gender, type of gastritis and activity, presence of H. pylori, and atrophy. A subset of 48 cases, in which tissue was available, was immunostained for Ki67, E-Cadherin, p53, MUC1, 2, 5, 6, and CDX2. Follow up biopsies were available for 82 patients. RESULTS: Twenty-four of 166 cases (14%) originally diagnosed as IM were reclassified as PD based on previously described criteria. There were no significant differences in the age, gender, type of gastritis and activity, or presence of H. pylori between patients with PD versus IM. However, cases with PD showed significantly increased atrophy (63%) versus IM (31%) (p<0.01). PD revealed significantly increased MUC6 expression (p=0.04), and there was a trend towards increased p53 expression (p=0.13), but the expression of Ki67, E-Cadherin, MUC1, 2, 5, and CDX2 were not significantly different between PD and IM. Upon follow up (mean follow up: 3.7 years), 4 of 73 patients (5.5%) with IM showed neoplastic progression, whereas 2 of 9 patients (22%) with PD showed progression to low grade dysplasia (p=0.069). CONCLUSION: The prevalence of PD in our consecutive series of patients with chronic gastritis and IM was 14%. Dysplasialike changes limited to the deep portions of the pits, without surface epithelium involvement (PD), probably represents an important histologically identifiable precursor to gastric cancer. There may be an increased rate of neoplastic progression associated with PD, but this needs to be confirmed and tested in a large number of patients.

Agoston, A. T. and R. D. Odze (2014). "Evidence that gastric pit dysplasia-like atypia is a neoplastic precursor lesion." Human Pathology 45(3): 446-455.

Most gastric cancers develop via an intestinal metaplasia (IM)-dysplasia-carcinogenic pathway. We have noted that some patients with chronic gastritis have dysplasia-like atypia (DLA) limited to the pit epithelium but without involvement of the surface epithelium. We performed this study to determine the clinical and biological characteristics and outcome of DLA, to gain insight into its role in the pathogenesis of gastric cancer. The study consisted of 102 consecutive patients with resected gastric cancer, a separate cohort of patients (n = 166) with chronic gastritis and IM in their index gastric biopsies, and 44 controls. All specimens were evaluated for clinical and pathologic features of the cancer (in the resection cohort) and background mucosa. Of 102 patients with gastric cancer, 50 (49%) had DLA in areas of mucosa adjacent to or near either conventional dysplasia or cancer. This value was significantly higher than controls (DLA 6.8%; P < .0001). Gastric cancer patients with DLA showed a significantly higher age at presentation; intestinal-type adenocarcinoma; low-grade differentiation; stage 1 tumors; and a higher rate of chronic gastritis, IM, atrophy, and conventional dysplasia in the background mucosa compared to patients without DLA. DLA showed intestinal-type differentiation, and a higher Ki-67 rate and MUC6 positivity compared with IM. Of the 166 patients with biopsies, DLA was identified in 24 (14%). Upon follow-up, 38% of positive cases showed persistent DLA, whereas 25% progressed to conventional low-grade dysplasia. Based on these results, we conclude that DLA represents an important precursor lesion in gastric carcinogenesis and supports its interpretation as a neoplastic lesion.

Akalın, Ç. and Ö. Özdemir (2019). "Evalution of the Patients with Colon Polyps in Terms of Helicobacter pylori with Sydney Criteria." Turkish Journal of Colorectal Disease 29(3): 111-117.

Aim: Colorectal cancer (CRC) is one of the leading three cancers with high mortality. Colon polyps are precursors for CRC development. Helicobacter pylori is known to increase the risk of gastric cancer by intestinal metaplasia (IM) and glandular atrophy (GA), there are studies suggesting that it increases the risk of CRC by various mechanisms. Sydney criteria have been developed to provide a standardized approach to histopathological changes in gastric mucosa caused by H. pylori. The aim of this study was to evaluate H. pylori according to the Sydney criteria in patients with colon polyps and to contribute to the literature. Method: The study cohort included a control group (n=231) with normal colonoscopy findings and a patient group (n=600) who underwent upper gastrointestinal endoscopy and colonoscopy on the same day and had hyperplastic polyps, adenomatous polyps and malignant polyps. Age, gender, complications during endoscopy, number and localization of polyps, and histopathological results of gastric and colon biopsies were analyzed. The relationship between H. pylori, IM and GA and colon polyps were investigated with logistic regression model. Results: H. pylori was present in 609 (73.3%) of 831 patients. There was no statistically significant relationship between coexistence of H. pylori + IM and hyperplastic polyp and adenomatous polyp (p>0.05). It was found that IM did not increase the risk of CRC without H. pylori (p=0.15). There was a statistically significant relationship between CRC and H. pylori + IM (p=0.03). GA was detected in 70 patients (8.4%), and there was a statistically significant relationship between the presence of GA and CRC, regardless of the presence of H. pylori (p<0.05). Conclusion: The results of the study showed that the coexistence of H. pylori and IM did not increase the risk of colon hyperplastic polyps, adenomatous polyps, but increased the risk of malignant polyps. There was also a statistically significant relationship between colon malignant polyps in the presence of GA regardless of the presence of H. pylori. In the light of the data obtained in the study, patients with H. pylori and IM and patients with GA should be followed up more closely for malignant colon polyps.

Akbari, M., et al. (2019). "Gastric cancer in patients with gastric atrophy and intestinal metaplasia: A systematic review and meta-analysis." PloS One 14(7): e0219865.

AIM: Intestinal metaplasia (IM) and gastric atrophy (GA) are precancerous lesions in the stomach. There is a large debate on natural course of these lesions and surveillance strategy in these patients. This meta-analysis was aimed to find the most appropriate follow up and the rate of progression from IM and GA to GC. METHODS: This meta-analysis is followed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Electronic databases including EMBASE, PubMed, Web of Science databases, Scopus, and the Cochrane Library were searched until July 2018. Cochran's Q test and I-square (I2) test were used to examine heterogeneity across included studies. We pooled data using random-effect or fixed effect models indicated as incidence rate or proportion with 95% confidence intervals (CI). The variables of study included demographic data, endoscopy interval, follow up interval and time, GA and IM type and GC stage. Moreover, incidence rate of GC and progress rate, regress and persistence proportion in both GA and IM patients were assessed. RESULTS: Overall, 68 original articles out of 32981 citations were included in our meta-analysis. The pooled GC incidence rate in patients with GA was 1.24 (95% CI, 0.80, 1.76; I2: 83.6%) cases per 1,000 person-years. The rates of later diagnosis of IM and gastric dysplasia in patients with GA were estimated as 41.42 (95% CI, 3.11, 64.45; I2: 95.6%) and 6.23 (95% CI, 2.34, 11.46; I2: 83.0%) cases per 1,000 person-years, respectively. The pooled regressed proportion was 32.23 (95% CI, 18.07-48.02; I2: 94.0%) and the persistence proportion was 38.83 (95% CI, 20.20-59.13; I2: 97.0%) per 100 observations in GA patients. In IM studies, the pooled incidence rate of GC was 3.38 (95% CI, 2.13, 4.85; I2: 93.4%) cases per 1,000 person-years. The progressed rate to dysplasia in IM patient was estimated to be 12.51 (95% CI, 5.45, 22.03; I2: 95.1%) cases per 1,000 person-years. The pooled regressed proportion was 31.83 (95% CI, 25.48-38.51; I2: 91.0%) and the persistence proportion was 43.46 (95% CI, 32.52-54.71; I2: 96.0%) per 100 observations in IM patients. CONCLUSION: Overall, the incidence of GC in patients with IM and GA are low but there is heterogeneity in data with the highest rate in Asian, males with those with incomplete IM. There is probability of regression or persistence without progression in patients with IM and GA who receive appropriate management.

Alhomsi, M. F. and E. O. Adeyemi (1996). "Grading Helicobacter pylori gastritis in dyspeptic patients." Comparative Immunology, Microbiology and Infectious Diseases 19(2): 147-154.

Helicobacter pylori-like organisms (Hp) and polymorphonuclear leucocytes (PMNs) in 2614 gastroduodenal biopsies from 602 patients with dyspepsia, in Al Ain, United Arab Emirates, between October 1990 and October 1992, were histologically graded to determine the prevalence of Hp gastritis and their utilization in the evaluation of treatment efficacy in these patients. Symptoms of functional dyspepsia included, in order of frequency, abdominal pain or discomfort, flatulence, burning sensation, regurgitation, fullness, nausea, vomiting, bloating and belching. The biopsies were paraffin embedded, sectioned and stained with hematoxylin and eosin (H and E) to grade the inflammation. In addition to H and E, several special stains including modified Giemsa (MG), Wharthin-Starry silver and cold Ziehl-Neelsen stains were utilized to clearly identify Hp organisms. Giemsa method was found to be superior to other special stains in visualizing the Hp organisms in paraffin sections, and was utilized in every case. Two immunohistochemical markers for B cells (CD20) and T cells (CD45RO) were utilized for labeling lymphocytes infiltrating the lamina propria of the gastroduodenal biopsies in formalin-fixed paraffin-embedded sections. H and E and MG stained sections were utilized to count PMNs and Hp, and were graded 0, 1, 2, and 3, corresponding to none, mild, moderate, and severe grades of the Sydney system for classification of gastritis, respectively. Of the total initial 2318 endoscopic biopsies, 98.8% of the patients had suitable biopsies for histologic evaluation. Unsuitable biopsies were recovered from patients with gastric carcinoma. Inflammation was seen in 98.5% of 595 patients with suitable biopsies. In 74.5% of these patients the inflammation was active; 37.5, 32.5 and 4.5% had mild, moderate and severe active inflammation, respectively. In the remaining 24% of the 595 patients, the gastritis was chronic without activity or atrophic changes. As many as 73.6% of the patients with suitable biopsies were Hp positive; 39.8, 29.1 and 4.7% had grades 1, 2 and 3 Hp, respectively. Intestinal metaplasia was found in 28.9% of the 602 patients, and was seen more often in Hp positive than Hp negative patients (34.5 vs 14%, P < 0.005, for d.f. = 1; chi 2 = 10.35). Of the Hp positive patients, 172 and 46 patients attended the first and second follow-up endoscopy visits, respectively. The triple treatment was composed of one dose of tinidazole (2gm), doxycycline, 200 mg initial dose and 100 mg daily for two weeks, and bismuth subcitrate (Gist-Brocades nv, Delft, The Netherlands), 2 tablets twice daily for 4 weeks. After triple drug treatment, eradication of Hp was accomplished, histologically, in 38.4 and 45.7% of the patients on first and second follow-up visits, respectively. Thus, the Sydney system-based grading scale provides an objective histological evaluation of Hp gastritis for accurate prevalence studies, and may prove to be of value in estimating treatment efficacy.

Almehdi, R., et al. (2019). "Value of peri-operative histopathology in sleeve gastrectomy at a major centre in Oman; adding evidence supporting pre and post-operative gastroscopy?" Obesity Surgery 29(5): 857.

Introduction: Obesity is a major Health challenge in Oman. The country also has one of the highest prevalences of Gastric cancer in the Middle East. Bariatric services at the Royal Hospital of Muscat started in 2012. Objectives: To consolidate evidence for pre-operative endoscopy in light of endemic Gastric cancer and prevalence of H.Pylori and to check if any of the pre-op and operative histology findings would warrant subsequent follow up endoscopy. Methods: Retrospective analysis from a prospective database, of Bariatric patients undergoing Sleeve gastrectomy, between Jan 2012 and Jan 2017. Results: Of 237 patients operated in this period, pre-op OGD was done in 220(92%). In the latter, 130(59%) biopsies were done. Abnormalities were in 166 episodes. Including Esophagitis in 35(27%), Gastritis in 115 (88.4%),Intestinal Metaplasia (IM) in 7(5%) and Helicobacter pylori (H.P) in 95(73%) (compared to 94% by CLO test). Post operative histopathology done in all 237(100%) specimens, showed Gastritis in 199(84%), IM in a different 8(3.4%) patients and H.Pylori in 11(4.6%). Incidental GIST was noted in 3(1.2%). Conclusion: Preoperative endoscopy showed significant H.pylori infection and Chronic gastritis. This obliged a management “pause” and prior course of medical treatment, leading to significant positive effect on the HP infection yet not so for Gastritis. Having IM in a total of 15 cases is by itself an indicator for endoscopic Gastric surveillance postoperatively. Similarly Esophagitis in a third of pre-op cases set a low threshold for operative Hiatal repair as well as suggesting selective follow up-endoscopy protocol in these cases.

Anand, N., et al. (2012). "Natural history of gastric intestinal metaplasia in an urban patient population." Gastroenterology 142(5): S633-S634.

Purpose: To determine the prevalence of gastric intestinal metaplasia (GIM) in GI subspecialty patients receiving upper endoscopy (EGD) in an urban patient population, and identify the risk of gastric cancer (GC) distal to the cardia. Methods: We retrospectively reviewed all EGDs (n=5,157) done over a five-year period at Kings County Hospital Center, in Brooklyn, NY. From this group we identified all EGDs performed with biopsy (n=2,799) and identified all patients found to have gastric pre-malignant and malignant lesions. The latter group makes up our study subset. Clinical and demographic data, including age, ethnicity, gender, H. pylori status, and endoscopic findings were recorded. Patients under the age of 18, and those in whom biopsy samples could not be obtained were excluded from the study. Results: A total of 294 patients were found to have GIM (10.5% of those biopsied), of these 54 (18.4%) had at least one repeat EGD. Of all African-American (AA) patients who had EGD with biopsy, 14.2% had GIM, 6.3% of Asians had GIM, 25.0% of Caucasians had GIM, 10.7% of Hispanics had GIM, and 19.0% of Middle Eastern patients had GIM. The mean age of patients with GIM was 63.2 +/- 0.73 (+/- SEM), whereas in patients without GIM it was 54.7 +/- 0.29 (p<0.01). The mean age of the entire cohort was 56.07 +/- 0.21. 53% of the GIM patients were male compared to 36.2% in the non-GIM group (p<0.01). 46.9% of the GIM patients had H. pylori, while only 27.1% of patients without GIM had it (p<0.01). Of the 294 patients with GIM, 2.7% (n=8) were found to have gastric cancer. Using a logistic regression model with a step-wise approach we assessed the risk of gastric cancer in patients with GIM; the odds ratio (OR) was 2.47 (1.08-5.7) (95% CI) after adjusting for age, sex, and endoscopic findings such as gastropathy, erosions, nodules, ulcers, etc. In our model, risk factors for cancer included age OR=1.04 (1.02-1.06), male sex OR=1.68 (1.03-2.74), and endoscopic evidence of gastropathy OR=4.07 (2.22-7.44). Conclusion: GIM predicts the risk of gastric cancer with age, male sex, and patients with endoscopic evidence of gastropathy, being the highest risk categories. Patients with GIM were older, more likely to be male, and more likely to have H. pylori, compared to patients without GIM. Further risk factors for gastric cancer in patients with GIM must be identified, and surveillance EGDs should be considered in groups at higher risk.

Araujo Castillo, R., et al. (2005). "[New ultrashort scheme for helicobacter pylori infection eradication using tetracyline, furazolidone and colloidal bismuth subcitrate in dyspeptic patients with or without peptic ulceration in the National Hospital Cayetano Heredia]." Revista de Gastroenterología del Perú 25(1): 23-41.

BACKGROUND: Helicobacter pylori (Hp) infection has been associated with the presence of duodenal ulcer, gastric ulcer and chronic active gastritis. It is also speculated that Hp may have a major role in gastric cancer development. Due to rising antibiotic resistance, probably lack of compliance and the expense of the currently used antimicrobial regimens, it's important to develop efficacious, short-duration and low cost therapies, especially for the treatment of low-income populations from underdeveloped countries. The goal of the present study is to asses the efficacy of two ultrashort antibiotic schemes against Hp infection. METHODS: Patients with diagnosis of Hp infection, found in antral gastric biopsies, were included. They were randomly assigned to receive one of the following therapeutic schemes: tetracycline 500 mg qid, furazolidone 100 mg qid and colloidal bismuth subcitrate 120 mg qid for 3 days (Scheme I) or 4 days (Scheme II). Patients were instructed to come back for follow-up at least 8 weeks after starting medication. At the control visit, an upper endoscopy was performed and an average of 3 antral biopsies was taken. Biopsies were stained with hematoxylin-eosin for histological assessment and with Warthin-Starry silver staining for Hp diagnosis. A single experienced pathologist read all biopsies. In both, the initial biopsy and the control one, we evaluated: presence of Hp; presence, depth and grade of chronic gastritis; presence and grade of inflammatory activity; presence, grade and extent of mucinous damage; presence of glandular atrophy, intestinal metaplasia and lymphoid follicles. We also evaluated dyspeptic symptoms prior and after the treatment, and the presence of adverse events. RESULTS: 80 patients were enrolled, 2 were excluded because of intense nausea and vomits, 4 patients didn't follow the indications properly and 8 patients couldn't be contacted for the control visit. From the remaining 66 patients, 32 were assigned to Scheme I and 34 to Scheme II, both groups were comparable. Eradication rate was 68.8% (22/32) (CI = 52.1% - 82.7%) for Scheme I and 88.2% (30/34) (CI = 74.9% - 96.2%), significant higher, for Scheme II. There was decrease of dyspeptic symptoms and significant improvement of the histological pattern for both groups, except for presence of chronic gastritis, intestinal metaplasia, glandular atrophy and lymphoid follicles. Hp eradication was associated with significant symptoms decrease, normal endoscopy raising and improvement of all the histological parameters, except for presence of intestinal metaplasia and glandular atrophy. Treatment was well tolerated, 57.6% of the patients reported only mild adverse events, nausea was the most frequent (19.7%) and there was no difference between schemes. CONCLUSIONS: The triple ultrashort duration scheme including tetracycline, furazolidone and bismuth for 4 days is efficacious against Hp, with a high eradication rate (88.2%). The Hp disappearance is followed by improvement in every histological parameter that we evaluated, except for glandular atrophy and intestinal metaplasia; and it's also accompanied by a decrease in dyspeptic symptoms.

Archampong, T. N., et al. (2019). "Gastro-duodenal disease in Africa: Literature review and clinical data from Accra, Ghana." World Journal of Gastroenterology 25(26): 3344-3358.

Gastroduodenal disease (GDD) was initially thought to be uncommon in Africa. Amongst others, lack of access to optimal health infrastructure and suspicion of conventional medicine resulted in the reported prevalence of GDD being significantly lower than that in other areas of the world. Following the increasing availability of flexible upper gastro-intestinal endoscopy, it has now become apparent that GDD, especially peptic ulcer disease (PUD), is prevalent across the continent of Africa. Recognised risk factors for gastric cancer (GCA) include Helicobater pylori (H. pylori), diet, Epstein-Barr virus infection and industrial chemical exposure, while those for PUD are H. pylori, non-steroidal anti-inflammatory drug (NSAID)-use, smoking and alcohol consumption. Of these, H. pylori is generally accepted to be causally related to the development of atrophic gastritis (AG), intestinal metaplasia (IM), PUD and distal GCA. Here, we perform a systematic review of the patterns of GDD across Africa obtained with endoscopy, and complement the analysis with new data obtained on pre-malignant gastric his-topathological lesions in Accra, Ghana which was compared with previous data from Maputo, Mozambique. As there is a general lack of structured cohort studies in Africa, we also considered endoscopy-based hospital or tertiary centre studies of symptomatic individuals. In Africa, there is considerable heterogeneity in the prevalence of PUD with no clear geographical patterns. Furthermore, there are differences in PUD within-country despite universally endemic H. pylori infection. PUD is not uncommon in Africa. Most of the African tertiary-centre studies had higher prevalence of PUD when compared with similar studies in western countries. An additional intriguing observation is a recent, ongoing decline in PUD in some African countries where H. pylori infection is still high. One possible reason for the high, sustained prevalence of PUD may be the significant use of NSAIDs in local or over-the-counter preparations. The prevalence of AG and IM, were similar or modestly higher over rates in western countries but lower than those seen in Asia. . In our new data, sampling of 136 patients in Accra detected evidence of pre-malignant lesions (AG and/or IM) in 20 individuals (14.7%). Likewise, the prevalence of pre-malignant lesions, in a sample of 109 patients from Maputo, were 8.3% AG and 8.3% IM. While H. pylori is endemic in Africa, the observed prevalence for GCA is rather low. However, cancer data is drawn from country cancer registries that are not comprehensive due to considerable variation in the availability of efficient local cancer reporting systems, diagnostic health facilities and expertise. Validation of cases and their source as well as specificity of outcome definitions are not explicit in most studies further contributing to uncertainty about the precise incidence rates of GCA on the continent. We conclude that evidence is still lacking to support (or not) the African enigma theory due to inconsistencies in the data that indicate a particularly low incidence of GDD in African countries.

Areia, M., et al. (2013). "Screening for gastric cancer and surveillance of premalignant lesions: a systematic review of cost-effectiveness studies." Helicobacter 18(5): 325-337.

BACKGROUND: Cost-effectiveness studies are highly dependent on the models, settings, and variables used and should be based on systematic reviews. We systematically reviewed cost-effectiveness studies that address screening for gastric cancer and/or surveillance of precancerous conditions and lesions. MATERIALS AND METHODS: A systematic review of cost-effectiveness studies was performed by conducting a sensitive search in seven databases (PubMed, Scopus, Web of Science, Current Contents Connect, Centre for Reviews and Dissemination, Academic Search Complete, and CINAHL Plus), independently evaluated by two investigators. Articles were evaluated for type of study, perspective, model, intervention, incremental cost-effectiveness ratio, clinical or cost variables, and quality, according to published guidelines. RESULTS: From 2395 abstracts, 23 articles were included: 19 concerning population screening and 4 on following up premalignant lesions. Studies on Helicobacter pylori screening concluded that serology was cost-effective, depending on cancer incidence and endoscopy cost (incremental cost-effectiveness ratio: 6264-25,881), and eradication after endoscopic resection was also cost-effective (dominant) based on one study. Studies on imaging screening concluded that endoscopy was more cost-effective than no screening (incremental cost-effectiveness ratio: 3376-26,836). Articles on follow-up of premalignant lesions reported conflicting results (incremental cost-effectiveness ratio: 1868-72,519 for intestinal metaplasia; 18,600-39,800 for dysplasia). Quality assessment revealed a unanimous lack of a detailed systematic review and fulfillment of a median number of 23 items (20-26) of 35 possible ones. CONCLUSIONS: The available evidence shows that Helicobacter pylori serology or endoscopic population screening is cost-effective, while endoscopic surveillance of premalignant gastric lesions presents conflicting results. Better implementation of published guidelines and accomplishment of systematic detailed reviews are needed.

Areia, M., et al. (2014). "Cost-utility analysis of endoscopic surveillance of patients with gastric premalignant conditions." Helicobacter 19(6): 425-436.

BACKGROUND: Progression of extensive gastric premalignant conditions to cancer might warrant surveillance programms. Recent guidelines suggest a 3-yearly endoscopic follow-up for these patients. Our aim was to determine the cost utility of endoscopic surveillance of patients with extensive gastric premalignant conditions such as extensive atrophy or intestinal metaplasia. MATERIALS AND METHODS: A cost-utility economic analysis was performed from a societal perspective in Portugal using a Markov model to compare two strategies: surveillance versus no surveillance. Clinical data were collected from a systematic review of the literature, costs from published national data, and community utilities derived from a population study by the EuroQol questionnaire in terms of quality-adjusted life years (QALY). Population started at age 50, for a time horizon of 25 years and an annual discount rate of 3% was used for cost and effectiveness. Primary outcome was the incremental cost-effectiveness ratio (ICER) of a 3-yearly endoscopic surveillance versus no surveillance for a base case scenario and in deterministic and probabilistic sensitivity analysis. Secondary outcomes were ICER of 5- and 10-yearly endoscopic surveillance versus no surveillance. RESULTS: Endoscopic surveillance every 3 years provided an ICER of € 18,336, below the adopted threshold of € 36,575 which corresponds to the proposed guideline limit of USD 50,000 and this strategy dominated surveillance every 5 or 10 years. Utilities for endoscopic treatment were relevant in deterministic analysis, while probabilistic analysis showed that in 78% of cases the model was cost-effective. CONCLUSIONS: Endoscopic surveillance every 3 years of patients with premalignant conditions is cost-effective.

Azócar Bizama, C., et al. (2019). "Indications and results of the resective gastric bypass in selected patients with obesity." Obesity Surgery 29(5): 213.

Introduction: The history of a first degree relative with gastric cancer (GC) and/or the presence of preneoplastic lesions during preoperative endoscopic evaluation in patients with obesity seeking bariatric surgery, identifies a group of patients in which is possible to consider a roux-en-Y- gastric bypass with resection of the distal stomach (R-RYGB). Objectives: To evaluate the indications and perioperative results of patients with obesity who underwent a R-RYGB. Methods: Retrospective cohort of all patients with obesity submitted to a primary or revisional R-RYGB between the years 2004-2018. There are no exclusion criteria. Data was obtained from electronic clinical record and prospective database. Clavien-Dindo ≥III complications were reported. Results: A total of 65 R-RYGB were performed, of which 7.7%(n=5) were revisional due to GERD or weight regain. 69.2%(n=45) was female with an age and BMI of 46.8(± 8.93) years and 38.3(± 4.5)kg/m2. The operative time was 151.8(±51.1)minutes and hospital stay 3.4(±1.5)days. Clavien-Dindo morbidity ≥III was 3.1%(n=2), both required reoperation. There were no conversions or mortality. The three more frequent indication were intestinal metaplasia (IM) 46.2%(n=30), history of GC in a first degree family of 32.3%(n=21), and polyps 21,5%(n=14). The most common finding on histological analysis were chronic gastritis 72.3%(n=47) with 29.2%(n=19) of atrophy and IM in 32.3%(n=21). Conclusion: The lower correlation between endoscopic findings and histological analysis in a significant proportion of patients highlights the importance of using a optimized algorithm to minimize this difference. Due to its low morbidity rate, R-RYGB could be considered safe for a selected group of patients.

Bae, D. H., et al. (2021). "STK31 upregulation is associated with chromatin remodeling in gastric cancer and induction of tumorigenicity in a xenograft mouse model." Oncology Reports 45(4).

Pathological changes in the epigenetic landscape of chromatin are hallmarks of cancer. Our previous study showed that global methylation of promoters may increase or decrease during the transition from gastric mucosa to intestinal metaplasia (IM) to gastric cancer (GC). Here, CpG hypomethylation of the serine/threonine kinase STK31 promoter in IM and GC was detected in a reduced representation bisulfite sequencing database. STK31 hypomethylation, which resulted in its upregulation in 120 cases of primary GC, was confirmed. Using public genome‑wide histone modification data, upregulation of STK31 promoter activity was detected in primary GC but not in normal mucosae, suggesting that STK31 may be repressed in gastric mucosa but activated in GC as a consequence of hypomethylation‑associated chromatin remodeling. STK31 knockdown suppressed the proliferation, colony formation and migration activities of GC cells in vitro, whereas stable overexpression of STK31 promoted the proliferation, colony formation, and migration activities of GC cells in vitro and tumorigenesis in nude mice. Patients with GC in which STK31 was upregulated exhibited significantly shorter survival times in a combined cohort. Thus, activation of STK31 by chromatin remodeling may be associated with gastric carcinogenesis and also may help predict GC prognosis.

Baiocchi, G., et al. (2007). "Metachronous occurrence of gastric carcinoma after gastric stromal tumor. Considerations on therapeutic strategy." Annali Italiani di Chirurgia 78(4): 319-321.

INTRODUCTION: To our knowledge, the metachronous occurrence of a stromal and epithelial gastric tumour has not been previously reported in the Literature. CASE REPORT: A 73-year-old man underwent open resection of a gastric stromal tumour located in the posterior antrum wall. The maximum size of the tumour was 5 cm, and final histological examination diagnosed it as a primary gastrointestinal autonomic nerve tumour (the so-called GAN tumour); mitotic index was intermediate (10 x 50 HPF). Twelve months later, during endoscopic follow-up, a small ulcerated adenocarcinoma was found at the gastric angulus and subtotal gastrectomy with D2 lymphadenectomy was performed. Final pathological stadiation was T1smN0. The patient is alive and disease free 50 months later. Since he has had two tumours, it would appear that this patient has a tendency to develop neoplasia. However, no risk factor was found being consistent with an aetiological role in both tumours, if we exclude the presence of chronic atrophic gastritis with intestinal metaplasia in the gastric mucosa around both tumours. CONCLUSIONS: In those cases of gastric stromal tumours, of intermediate size and mitotic index, in whom a wedge gastric resection may be proposed, a radical gastrectomy should be considered as a valid alternative, especially when, as in the described patient, chronic atrophic gastritis with intestinal metaplasia is associated.

Barbosa, J., et al. (2003). "Use of Helicobacter pylori-specific antibodies in the evaluation of intestinal metaplasia and gastric dysplasia." British Journal of Biomedical Science 60(4): 175-179.

It is believed that Helicobacter pylori acts mainly during the initial phases of gastric carcinogenesis. Therefore, this study aims to assess the usefulness of H. pylori diagnosis in patients with chronic gastritis (CG), intestinal metaplasia (IM) and dysplasia--conditions that are associated with gastric cancer. A cross-sectional study of 94 patients was performed, which involved endoscopic biopsy and determination of specific serum anti-H. pylori antibodies (IgA, IgG and IgM) by enzyme-linked immunosorbent assay (ELISA). Biopsies were taken from the gastric antrum and corpus, and from endoscopic lesions. Two specimens per patient were used for bacterial culture. H. pylori infection status, used as the gold standard, was based on culture results. Validity measures were determined and receiver operating curve (ROC) was used to determine the best cut-off for serum antibody levels. Histopathological evaluation (n = 160) was performed independently by two pathologists. Lesions consistent with CG were found in 86 patients (91%), consistent with IM in 69 patients (73%) and with dysplasia in five patients (5%). In the 86 patients with CG, 38 (44%) were infected by H. pylori, as were 26 (38%) and one (20%) with IM and dysplasia, respectively (P=0.039). Area under the curve (AUC) was 0.40 (95% confidence interval [CI]: 0.28-0.51) for IgM, 0.69 (0.58-0.80) for IgA and 0.83 (0.74-0.92) for IgG for the diagnosis of H. pylori infection. Best cut-off was 41 u/mL for IgG, with a sensitivity (95% CI) of 90% (84-96%) and a negative predictive value (NPV) of 91% (85-97%). For IgA the results were 22 u/mL, 74% (65-83%) and 77% (68-86%), respectively. Prevalence of H. pylori appeared to decrease with increasing severity of the gastric lesion. In conclusion, it is suggested that non-invasive serological evaluation of anti-H. pylori (IgG) status after eradication therapy for peptic ulcer disease could be extended, after proper assessment of cut-off values and their validation, to the follow-up of patients with CG and IM.

Bartelli, T. F., et al. (2020). "Unravelling the gastric microbiome in health and disease: Gastric cancer beyond Helicobacter pylori in a Brazilian cohort." Cancer Research 80(8).

Although numerous studies have shown the relevance of the gut microbiome in several diseases, underlying questions remain concerning the stomach microbiome and the establishment of a causal link between the microbiota and the development of gastric diseases, much beyond Helicobacter pylori and Epstein Barr virus. In this study, we aimed to characterize the bacterial composition of the stomach of subjects undergoing upper endoscopy, including gastric cancer (GC) individuals, aiming to identify fluctuations in bacterial populations that might be associated with stomach health. During endoscopic examination at A.C. Camargo Cancer Center (Sao Paulo, Brazil), gastric fluids (GF) were recovered from either GC patients (113) or individuals with gastric-related complaints, such as superficial gastritis (SG; 79), atrophic gastritis (AG; 12), and intestinal metaplasia (IM; 33). For eubacteria identification, the V3-V4 region of the 16S rRNA gene was amplified and paired-end sequenced (Illumina MiSeq). Analyses were carried out using Qiime2 and phyloseq packages. On average, we identified between 14 and 104 OTUs per subject, evidencing the potential of GFs for determining the stomach microbial composition and the interindividual variation. Testing of sample richness between GC and controls showed significant differences between the number of OTUs observed in each group (an average of 44 and 52 OTUs, respectively-Mann-Whitney test, p<0.05) and SG patients had a significantly increased alpha diversity (Shannon, p<0.05) as compared to AG, IM, and GC patients (both intestinal and diffuse subtypes), indicating dysbiosis already in early carcinogenesis steps. Additionally, the prolonged use of proton pump inhibitors or the presence of H. pylori (except for SG) did not seem to interfere with bacterial diversity. Specific genera are enriched in the sample subsets, including a lower presence of Corynebacterium and increased Streptococcus (Linear discriminant analysis Effect Size, LDA score >2) in AG samples as compared to SG patients, which are also increased in the IM, and GC. These results indicate these bacteria to be potentially associated with the stomach dysbiosis that may lead to the carcinogenesis cascade. Besides the regular turnover of the gastric epithelial tissue and pouring of cells onto the gastric cavity, GF certainly contains a high proportion of transient oral-derived bacteria, while stomach-resident microbiota is expected to be in close contact with the gastric epithelia. Preliminary data analyzing the bacterial content of the saliva x GF in a subset of patients showed no significant beta-diversity differences, but both fluids differ significantly from their biopsies' composition. We are currently performing culturomics and transcriptomics to identify bacteria that are alive in the stomach. As GC is a complex malignancy with limited treatment options, these results may contribute to developing new interventions to treat and to better understand this disease.

Bas, B. and B. Dinc (2020). "Helicobacter pylori-related precancerous lesions in Turkey: a retrospective endoscopic surveillance study." Croatian Medical Journal 61(4): 319-325.

AIM: To assess the relationship between Helicobacter pylori (H. pylori) infection and atrophic gastritis (AG) and intestinal metaplasia (IM) development and to assess the rate of dysplasia or gastric cancer development in patients with AG and/or IM. METHODS: This retrospective endoscopic follow-up study enrolled 2214 patients. The patients were followed for at least five years between 2007 and 2017 at the Department of Endoscopy at Antalya Ataturk Government Hospital. The results of third-year and five-year surveillance biopsy were assessed. RESULTS: The mean follow-up time was 7.77 ± 2.78 years. H. pylori was histologically assessed in 1417 (64.6%) patients. Of 198 patients with severe H. pylori infection, 32 (16%) and 139 (70.3%) developed extensive AG and extensive IM, respectively. There was a significant relationship between H. pylori density and AG and IM degrees. High grade dysplasia, early gastric cancer, and advanced gastric cancer were diagnosed in 73 patients with median age 58.2 (28-80) years, and the incidence rate was 3.29% (73/2214). The annual incidence of gastric neoplastic lesions was 0.46% in total, 0.08% for early GC, and 0.02% for advanced gastric cancer. CONCLUSIONS: H. pylori infection has an important role in the development of AG and IM. H. pylori density is directly related to atrophy and metaplasia degree.

Basu, P., et al. (2012). "Prevalence of Recurrence of Helicobacter pylori (HP) infection in a special population in the community. Herroic study: Helicobacter pylori recurrence resistance or re-infections in a special population base community: An observational study." American Journal of Gastroenterology 107: S49-S50.

Purpose: WHO states that HP is a global epidemic with significant morbidities and gastric cancer. HP is ubiquitous with diverse genetic polymorphism and infective and oncogenic potentials. The clinical morbidities, non ulcer dyspepsia, peptic ulcers, atrophic gastritis, intestinal metaplasia, low grade gastric lymphoma to adenocarcinoma. True resistance or recurrence has not yet been properly described due to paucity of available biogenetic assay. Clinical eradication has been accepted by stool antigen, stool PCR, and breath testing. Recurrence or reinfection stands a clinical dilemma. Recently recurrence rates vary in countries. Recrudescence and retention to therapy or neo infection by a new strain and rapidly developing drug resistance is becoming (Table presented) a challenge. This study demonstrates the prevalence of reinfection in a specific subpopulation. Methods: Seven hundred and thirty (n=730) patients were evaluated from 2003 till 2011 with HP infection treated with multiple regimen of antibiotics for at least 7 days. One hundred sixty-eight (n=168) were recruited from the medical profession with successful eradication. Group A (n=42): dental technicians, Group B (n=40): emergency room (17/40) and operating room nurses (23/40). Group C (n=40): endoscopy nurses (19/40) and technicians (21/40). Group D (n=48) Control: [medical office clerks (12/48), managers (10/48), radiology technicians (8/48) and front desk personnel (18/48)]. All underwent upper endoscopy with four quadrant antro-gastric biopsies with proven HP post eradication follow-up revealed 33/168 (19.6%) HP infection with further confirmation with breath and stool antigen testing. Group A: 17/42(40%), Group B: 2/40(5%), Group C: 13/38(32%) and Group D: 2/48(4%) had the HP infection. Results: See Table. Conclusion: Prevalence and recurrence rate of HP infection is most common among dental technicians in certain communities. 40% subjects in Group A HP positive had travelled abroad. 1/18(5.5%) from Dominican Republic acquired recurrence or reinfection in five year interval compared to control {2/48(4%)}. We postulate that amongst all profession dental technicians have the highest prevalence of reinfection and recurrence. A larger multicenter trial is needed to validate these findings.

Bataga, S., et al. (2019). "Prevention of gastric cancer and preneoplastic lesions." Journal of Gastrointestinal and Liver Diseases 28: 13.

In spite of its declining incidence in the last years, gastric cancer (GC) is still the fifth most common cancer in the world, after lung, breast, colorectal and prostate cancer. However, GC is the third worldwide cause of mortality among all malignant diseases. The prevention of GC includes the primary prevention: eradication of Helicobacter pylori (HP) and secondary prevention: detection, surveillance and/or treatment of the preneoplastic lesions. In Romania we have no screening programme for HP, but it has been organized an important public awareness campaign. The entire community of gastroenterologists, internal medicine specialists and general practitioners are now involved in detecting and treating HP infection. Secondary gastric cancer prevention program is addressing to the patients with severe preneoplastic changes in the stomach. Population-based screening by endoscopy for detection of these preneoplastic lesions is implemented only in countries with a high incidence of gastric cancer, such as Japan and Korea. In the European countries, regular endoscopic follow-up is offered to patients with endoscopically visible preneoplastic lesions according to the MAPS recommendations. Identifying and surveillance of patients with gastric preneoplastic lesions leads to early diagnosis of gastric cancer, treatment options and an improvement in the survival rate. The non-invasive screening is also possible with tests such as pepsinogen test (GastroPanel®). In our experience in the First Gastroenterology Clinic from Târgu Mureş, between 2014-2018, 12,541 patients underwent upper digestive endoscopy. Patients with gastric cancer were excluded from the study. In all the patients, gastric biopsies and histopatological examination were made, and the OLGA classification was used. The histopathology examination revealed: in 5.55% atrophic gastritis, in 7.30% intestinal metaplasia and in 0.11% dysplasia. In 0.81% of the patients, polyps were detected and extirpated. Active gastritis/pangastrits with HP infection was identified in 59.3% of the patients. The premalignant lesions were present mostly in the patients between 60 and 70 years, males and females being equally affected. In summary, Helicobacter pylori infection was identified in more than half of our patients, indicating that it still has a high incidence in Romania. Women are as much exposed as men to present premalignant gastric lesions after 60 years. After the age of 60, it is worthy to screen the patients by endoscopy or to perform at least one non-invasive test such as pepsinogen (GastroPanel®), even in the regions with a low incidence of gastric cancer.

Beyer, B. C. M., et al. (2006). "Urokinase system expression in gastric carcinoma: Prognostic impact in an independent patient series and first evidence of predictive value in preoperative biopsy and intestinal metaplasia specimens." Cancer 106(5): 1026-1035.

BACKGROUND. The prognostic relevance of urokinase-type plasminogen activator (u-PA), u-PA receptor (u-PAR), and plasminogen activator inhibitor 1 (PAI-1) in gastric carcinoma was demonstrated in an independent patient series. To the authors' knowledge, the roles of these activators as predictors of aggressive phenotypes in preoperative biopsies, Helicobacter pylori infection, and intestinal metaplasia have to date not been investigated simultaneously in resected tumors. The objectives of the current study were 1) to demonstrate the prognostic relevance of u-PA, u-PAR, and PAI-1 in an independent series; 2) to evaluate u-PA system expression in preoperative biopsy specimens compared with resected tumors; and 3) to evaluate u-PA system expression in intestinal metaplasias and samples with H. pylori infection. METHODS. In 104 patients with gastric carcinoma (median follow-up, 68 mos), u-PA, u-PAR, and PAI-1 in tumors and metaplasias were evaluated immunohistochemically. Preoperative biopsies were evaluated in a subset of patients. Patients were screened for H. pylori (urease) and tumor cells in bone marrow (u-PAR/CK18). RESULTS. u-PA and PAI-1 were confirmed as independent prognostic parameters, and u-PAR was associated with a trend toward a poor prognosis. u-PA system tumor expression was found to be correlated significantly with u-PAR in disseminated tumor cells and H. pylori-infected tumors, implicating a role of H. pylori in protease induction. There was a significant correlation noted between u-PA system staining between preoperative biopsies and the results in resected tumors. The expression of u-PAR and PAI-1 in intestinal metaplasias was found to be associated significantly with advanced tumor stage (depth of invasion; pathologic tumor status) and lymph node involvement (pathologic lymph node status) and was correlated significantly with u-PA system expression in tumors. CONCLUSIONS. To the author's know the current study is the first to date to demonstrate that u-PA system expression may serve as a predictor of risk in intestinal metaplasias and preoperative biopsies, implicating consequences for neoadjuvant therapy. The independent impact on recurrence and survival and a correlation with u-PAR-expression of minimal residual disease were identified in this independent series. © 2006 American Cancer Society.

Bianchi, A., et al. (1998). "Upper digestive tract dyspepsia and early gastric cancer." Revista Española de Enfermedades Digestivas 90(9): 639-645.

AIM: The study of the frequency and evolution of upper digestive tract dyspepsia in a group of patients operated for early gastric cancer (EGC) and to perform a strategy of diagnosis for the patients with long term upper digestive tract dyspepsia. METHODS: Clinical data of 35 patients operated for EGC were retrospectively evaluated. The frequency, characteristics and evolution time of upper digestive tract dyspepsia, main when it began more than 6 months before surgery, were analyzed. Radiologic and endoscopic exams carried out for diagnosis were also evaluated. Histological diagnosis of surgical specimens were considered, looking for the presence of chronic atrophic gastritis, intestinal metaplasia, and peptic gastric ulcer. RESULTS: Long-term upper digestive tract dyspepsia was present in 27 patients (mean evolution time of 43.4 months). Clinical changes of previous symptoms that suggested gastric carcinoma were not found in 15 patients. Concurrent peptic gastric carcinoma were not found in 15 patients. Concurrent peptic gastric ulcer along with EGC was diagnosed by histology in 11 patients, and chronic atrophic gastritis and intestinal metaplasia were both present in the non-tumoral gastric mucosa in all cases. CONCLUSIONS: 1) Unspecific upper digestive tract dyspepsia is frequently found in patients with EGC. 2) Endoscopy should be the first exam performed in patients with upper digestive tract dyspepsia. 3) The patients with gastric ulcer, chronic atrophic gastritis or intestinal metaplasia must be submitted to sequential endoscopic follow-up.

Bleibel, W., et al. (2013). "Intestinal metaplasia of the stomach is associated with an increased risk of gastric cancer in a western population ACG governors award for excellence in clinical research." American Journal of Gastroenterology 108: S48.

Purpose: Gastric carcinoma (GCA) is believed to arise via a process that includes chronic inflammation, atrophy, intestinal metaplasia, and finally dysplasia. Aim: To study the natural history of intestinal metaplasia of the stomach (IMS) and its associated risk of GCA in a Western population. Methods: A hospital database and electronic medical records were used to select adult patients who had EGD with gastric biopsy showing IMS from 1993 to 2012 at an academic tertiary-care center in Virginia. Patients with preexisting GCA and those diagnosed with GCA within 6 months following the index EGD were excluded. A control group included patients who had EGD with a normal gastric biopsy from 2002 to 2012. Pathology reports of all patients were reviewed. Patient demographics and H. pylori infection status were collected. ICD-9 codes from an institutional database were used to diagnose development of GCA. Last follow-up was either the last encounter at our institution or date of documented death. Results: Fourteen of 675 patients (2.1%) in the IMS group developed GCA, as compared to one patient of 1,273 (0.1%) in the control group (p<0.0001; Tables 1 and 2). Patients with IMS were older (61 vs. 44 years) and had longer follow-up (5.3 vs. 3.1 years). Only 17.5% of IMS patients had H. pylori on biopsy. On univariate analysis both IMS (HR 15.7;; 95% CI 2.00-122.81; p<0.009) and H. pylori infection (HR 3.4; 95% CI 1.02-1.099; p<0.05) were associated with increased risk for GCA. On multivariate analysis, of these factors: IMS, H. pylori, age, sex, and race, only IMS was associated with an increased risk for GCA (HR 11.23; 95% CI 1.35-93.40; p<0.025; Figure 1). The mean time interval between diagnoses of IMS and GCA was 4 years (SD 3.5 years). Conclusion: Western patients with IMS are at increased risk for GCA, and this risk may be increased by 11-fold in those with IMS. Given the relatively short time in which GCA develops in these patients following diagnosis of IMS, EGD for GCA surveillance at regular intervals should be considered. (Figure presented).

Boregowda, U., et al. (2020). "NARROWBAND IMAGING VERSUS WHITE LIGHT ENDOSCOPY IN DETECTION OF GASTRIC INTESTINAL METAPLASIA: A META-ANALYSIS AND SYSTEMATIC REVIEW." Gastrointestinal Endoscopy 91(6): AB620.

Background: Gastric cancer is the 6th leading cause of cancer-related death worldwide. Gastric intestinal metaplasia (GIM) is a premalignant condition that can lead to gastric adenocarcinoma. However, GIM continues to be challenging to diagnose, and random gastric biopsies can often miss GIM. Narrowband imaging (NBI) has shown potential in the detection of GIM, but pooled estimates are not known compared to standard white light endoscopy (WLE). Methods: Electronic literature search (Medline, Embase, and Cochran database) was performed for studies of NBI for the detection of GIM compared to WLE. Studies in abstract form only, case series, case reports, editorials, and review articles were excluded. The primary outcome was the pooled detection rate of GIM when NBI was used compared to WLE. The gold standard for the primary outcome was the detection of GIM on histopathology. Pooled estimates using proportions from each group were compared using a random-effects model with odds ratio (OR) and 95% CI. Publication bias was examined using funnel plot asymmetry. Results: A total of 595 articles were reviewed, and seven studies were found eligible. There were two prospective randomized, blinded crossover studies, two prospective blinded studies, two prospective unblinded studies, and one retrospective cohort study. A total of 1,008 subjects underwent upper endoscopy for various indications including reflux symptoms (12.3%), dyspepsia (8.4%), abdominal pain (8%), postprandial fullness (5.5%), and anemia (2.9%). The average age was 55.3 years and 54.6% were males. There were 300 (29.7%) subjects who were found to have GIM. NBI was able to detect GIM in 23% additional subjects that were not detected by WLE alone. Pooled OR was 0.52 (95% CI 0.20-0.83; p<0.01) suggestive that NBI was better at the detection of GIM compared to WLE [Figure 1]. Only four patients needed to undergo NBI to find 1 GIM compared to WLE. There was moderate heterogeneity in outcomes (I2 34%). There was no evidence of publication bias (Figure 2). Conclusion: Narrow band imaging could detect more patients with GIM as compared to WLE alone. Findings suggest that NBI should be employed in clinical practice during upper endoscopy to guide targeted sampling given its effectiveness in improving the detection of gastric intestinal metaplasia. [Formula presented] [Formula presented]

Boreiri, M., et al. (2013). "Gastric cancer mortality in a high incidence area: Long- term follow-up of helicobacter pylori-related precancerous lesions in the general population." Archives of Iranian Medicine 16(6): 343-347.

BACKGROUND: Due to a lack of clear criteria for recognizing subjects at risk of progression to gastric cancer (GC), this cohort study seeks to identify predictors of GC death in a high-risk population. METHODS: During 2000-2001, 1011 randomly selected residents of Ardabil, Iran without a history of gastrointestinal diseases, underwent upper endoscopy with targeted biopsy sampling. Until 2013, cancer mortality data were obtained using cancer and death registry data and verbal autopsy reports. Cox regression was used to estimate hazard ratios (HR). RESULTS: A total of 3.95% of the participants [mean age: 53.1 ± 9.9 years, 49.8% males, and 88.2% Helicobacter pylori (H. pylori-positive)] died of GC. In the multivariate model, precancerous lesions at the beginning of follow-up were associated with increased GC mortality. The HR [95% confidence interval (CI)] was 7.4 (1.6-33.8) for atrophic gastritis (AG) and 23.6 (5.5-102.3) for intestinal metaplasia (IM). Age over 50 (HR = 4.4; 1.3-14.2), family history of GC (HR = 6.8; 3.3-13.8), smoking (HR = 7.4; 3.2-17.3), and endoscopically confirmed gastric ulcer (GU, HR = 6.5; 2.5-16.4) were independently associated with GC mortality. The concomitant presence of a precancerous lesion increased the HR to 46.5 (10.8-198.6) for a family history of GC, 27.6 (6.5-116.4) for smoking, and 25.1 (6.3-105.3) for age >50 years. CONCLUSIONS: In this population with a high rate of H. pylori infection, age over 50 years, smoking, family history of GC, IM, AG, and in particular, an undiagnosed GU were significant independent risk factors for mortality due to GC. The assessment of a combination of these risk factors might identify individuals at risk of GC who could possibly benefit from regular surveillance.

Borg, D., et al. (2016). "Expression of IFITM1 as a prognostic biomarker in resected gastric and esophageal adenocarcinoma." Biomark Res 4: 10.

BACKGROUND: There is an increasing amount of reports on IFITM1 (interferon-inducible transmembrane protein 1) in various malignancies. The aim of this study was to examine the expression of IFITM1 and its prognostic significance in gastroesophageal adenocarcinoma. METHODS: Tissue samples were obtained from a consecutive cohort of 174 patients surgically treated between 2006 and 2010 for gastroesophageal (gastric, gastroesophageal junction and esophageal) adenocarcinoma, not subjected to neoadjuvant therapy. Expression of IFITM1 was examined using immunohistochemistry on tissue microarrays of primary tumors and paired samples of adjacent normal epithelium, intestinal metaplasia and lymph node metastases. RESULTS: Expression of IFITM1 was significantly elevated in primary tumors and lymph node metastases compared to adjacent normal epithelium and intestinal metaplasia, regardless of tumor location. Overexpression of IFITM1 was associated with M0-disease (no distant metastases). In gastric cancer IFITM1 expression was significantly associated with improved TTR (time to recurrence) in Kaplan-Meier analysis and Cox regression, both in the unadjusted analysis (HR 0.33, 95 % CI 0.12-0.88) and in the adjusted analysis (HR 0.32, 95 % CI 0.12-0.87) but there was no significant impact on OS (overall survival). In esophageal adenocarcinoma expression of IFITM1 had no impact on TTR or OS in Kaplan-Meier-analyses, but in the adjusted Cox regression IFITM1 expression had a negative impact on both TTR (HR 3.05, 95 % CI 1.09-8.53) and OS (HR 2.71, 95 % CI 1.11-6.67). CONCLUSIONS: IFITM1 was overexpressed in gastroesophageal adenocarcinoma and associated with M0-disease. In gastric cancer IFITM1 expression had a positive impact on TTR but in esophageal cancer it seemed to have an adverse impact on survival. The reason for the diverging prognostic impact of IFITM1 in esophageal and gastric cancer is unclear and warrants further studies.

Borg, D., et al. (2016). "Expression of podocalyxin-like protein is an independent prognostic biomarker in resected esophageal and gastric adenocarcinoma." BMC Clinical Pathology 16: 13.

BACKGROUND: Podocalyxin-like protein (PODXL) is a cell surface transmembrane glycoprotein, the expression of which has been associated with poor prognosis in a range of malignancies. The aim of this study was to investigate the impact of PODXL expression on survival in esophageal and gastric adenocarcinoma. METHODS: The study cohort consists of a consecutive series of 174 patients with esophageal (including the gastroesophageal junction) or gastric adenocarcinoma, surgically treated between 2006 and 2010 and not subjected to neoadjuvant treatment. Immunohistochemical expression of PODXL was assessed in tissue microarrays with cores from primary tumors, lymph node metastases, intestinal metaplasia and adjacent normal epithelium. Survival analyses were performed on patients with no distant metastases and no macroscopic residual tumor. RESULTS: In the majority of cases, expression of PODXL was significantly higher in cancer cells compared to normal epithelial cells and was significantly associated with lymph node metastases and high grade tumors. In esophageal adenocarcinoma, Kaplan-Meier analyses revealed that patients with PODXL negative tumors had a superior time to recurrence (TTR) and overall survival (OS) compared to patients with PODXL positive tumors. In gastric adenocarcinoma, patients with PODXL negative tumors had a superior TTR and a trend towards an improved OS. In esophageal and gastric adenocarcinoma combined, the prognostic significance of PODXL expression on TTR was confirmed in unadjusted Cox regression analysis (HR = 5.36, 95 % CI 1.68-17.06, p = 0.005) and remained significant in the adjusted model (HR = 3.39, 95 % CI 1.01-11.35, p = 0.048). Moreover, the impact of PODXL expression on OS was also confirmed in unadjusted analysis (HR = 2.52, 95 % CI 1.31-4.85, p = 0.006) and remained significant in the adjusted model (HR = 2.03, 95 % CI 1.04-3.98, p = 0.039). CONCLUSIONS: In esophageal and gastric adenocarcinoma, PODXL expression is an independent prognostic biomarker for reduced time to recurrence and poor overall survival. This is the first report on the prognostic role of PODXL in esophageal adenocarcinoma and validates recent findings in gastric cancer.

Botezatu, A. and N. Bodrug (2021). "Chronic atrophic gastritis: an update on diagnosis." Med Pharm Rep 94(1): 7-14.

BACKGROUND AND AIM: Atrophic gastritis is a precancerous gastric lesion, therefore its early detection is a priority in preventing gastric cancer. The aim of the present paper is to develop a narrative synthesis of the present knowledge on diagnostic methods of chronic atrophic gastritis. METHODS: A literature search was carried out on main databases: PubMed, Hinari, SpringerLink and Scopus (Elsevier) for the period 2000-2020. The searched keywords were: chronic atrophic gastritis, intestinal metaplasia and dysplasia + diagnosis. Inclusion criteria were focused on the articles about the invasive and non-invasive diagnosis of chronic atrophic gastritis and of precancerous gastric lesions, intestinal metaplasia and dysplasia; exclusion criteria were articles published before 2000 and those that did not include the proposed theme. RESULTS: The search returned 575 papers addressing the topic of precancerous lesions. From these, 60 articles were qualified representative for the materials published on the topic of this synthesis article, being those that met the inclusion criteria. The data emphasize the need to use upper digestive endoscopy with biopsies for the diagnosis of chronic atrophic gastritis. However serological diagnosis is available as alternative mainly recommended in follow up. CONCLUSIONS: There are two main methodological approaches for the evaluation of chronic atrophic gastritis as a precancerous gastric lesions: invasive examination, which requires histological analysis of biopsy samples taken during upper digestive endoscopy, being the "gold standard" for diagnosis, and non-invasive serological examination using markers of gastric function.

Boura, H., et al. (2018). "Prevalence of H. pylori infection and precancerous gastric lesions in Moroccan population." Helicobacter 23: 60.

Helicobacter pylori (H. pylori) present a serious public health problem. This pathogen is closely associated with various gastric diseases, including premalignant, and malignant lesions such as chronic gastritis, atrophic gastritis, intestinal metaplasia, and gastric adenocarcinoma. The aim of this study was to assess the prevalence of H. pylori infection in Moroccan population and the risk to develop gastric precancerous lesions and gastric cancer. Totally, 298 patients were enrolled in the present study, divided to 68 of asymptomatic sub-jects and 230 of patients with gastric diseases. Histological examination was carried out to classify gastric lesions and to detect H. pylori. ELISA was used also to determine H. pylori status of patients. The prevalence of H. pylori was observed to be higher (90%) withinasymptomatic and symptomatic subjects. A significant relationship was detected between H. pylori infection and the risk of gastric dis-eases (P-value < 0.0001). A meaningful association between gastric lesions increasing and age was observed (P-value = 0.03). The risk to develop gastric cancer among infected patients was observed elevated with rate of 9%. Our results showed a high prevalence of H. pylori infection in both Asymptomatic and Symptomatic subjects. We noticed that chronic gastric lesions increase with age. We remarked also that the risk to develop gastric cancer among infected patients was elevated in our population. Therefore, it is necessary to update the recommendations regarding diagnosis, treatment of H. pylori infection, and follow-up of the patients, to avoid the evolution of a simple chronic gastritis to gastric cancer.

Brito-Gonçalves, G., et al. (2020). "Clinicopathologic Characteristics of Patients with Gastric Superficial Neoplasia and Risk Factors for Multiple Lesions after Endoscopic Submucosal Dissection in a Western Country." GE Port J Gastroenterol 27(2): 76-89.

BACKGROUND: Endoscopic submucosal dissection (ESD) is a treatment for early gastric neoplasms that preserves the stomach. However, the risk of multiple lesions persists. OBJECTIVES: To assess clinicopathologic characteristics of patients with early gastric neoplasms in a Western country and evaluate risk factors for multiple gastric lesions, synchronous, or metachronous. METHODS: A retrospective cohort of 230 consecutive patients who underwent ESD for primary neoplasms from 2012 to 2017 (median follow-up: 33 months) was assessed to determine the clinicopathologic characteristics and risk factors for multiple lesions. RESULTS: The mean age was 68 years, and 53.9% were male. Current/former smoking status was present in 40.4%, and 29.5% had family history of gastric cancer. A third of the patients had only focal gastric atrophy/metaplasia (operative link on gastritis assessment/operative link on gastric intestinal metaplasia assessment [OLGA/OLGIM] I/II; endoscopic grading of gastric intestinal metaplasia [EGGIM] 1-4). Synchronous and me-tachronous lesions occurred in 14.3 and 8.6% of patients, respectively. There was a trend for higher risk of multiple lesions in smokers and patients with extensive metaplasia (EGGIM >4), but only older age was an independent risk factor (OR 3.30; 95% CI 1.05-10.34). Age >60 years (OR 10.10, 95% CI 1.40-88.04), current/former smoking status (OR 3.64, 95% CI 1.07-12.40), and OLGIM III/IV (OR 3.07, 95% CI 1.01-9.36) were independent risk factors for synchronous lesions. No risk factors for metachronous lesions were found. CONCLUSIONS: Surveillance limited to patients with advanced stages of gastritis may miss some primary superficial neoplasms. Although older age increases the risk of multiple lesions, no risk factors were found for metachronous lesions. Therefore, endoscopic surveillance after ESD should be done equally in all patients.

Bukin, Y. V., et al. (1997). "Decrease of ornithine decarboxylase activity in premalignant gastric mucosa and regression of small intestinal metaplasia in patients supplemented with high doses of vitamin E." Cancer Epidemiology, Biomarkers and Prevention 6(7): 543‐546.

Busuttil, R. A., et al. (2014). "Role of p53 in the progression of gastric cancer." Oncotarget 5(23): 12016-12026.

Intestinal metaplasia (IM) is a premalignant lesion associated with gastric cancer (GC) but is poorly described in terms of molecular changes. Here, we explored the role of TP53, a commonly mutated gene in GC, to determine if p53 protein expression and/or the presence of somatic mutations in TP53 can be used as a predictive marker for patients at risk of progressing to GC from IM. Immunohistochemistry and high resolution melting were used to determine p53 protein expression and TP53 mutation status respectively in normal gastric mucosa, IM without concurrent GC (IM-GC), IM with concurrent GC (IM+GC) and GC. This comparative study revealed an incremental increase in p53 expression levels with progression of disease from normal mucosa, via an IM intermediate to GC. TP53 mutations however, were not detected in IM but occurred frequently in GC. Further, we identified increased protein expression of Mdm2/x, both powerful regulators of p53, in 100% of the IM+GC cohort with these samples also exhibiting high levels of wild-type p53 protein. Our data suggests that TP53 mutations occur late in gastric carcinogenesis contributing to the final transition to cancer. We also demonstrated involvement of Mdmx in GC.

Caetano, A. C., et al. (2013). "Risk stratification using olgim system and modified vries risk score in a high risk population." United European Gastroenterology Journal 1(1): A23-A24.

INTRODUCTION: A cascade of premalignant gastric lesions such as atrophic gastritis (AG), intestinal metaplasia (IM) and dysplasia precedes intestinal-type adenocarcinoma. Other risk factors seem to be related with an increased risk of progression to gastric cancer (GC). It is consensual the need to identify subgroups of patients with higher risk of progression to GC. The Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM) was recently proposed with this purpose. AIMS&METHODS: Aims: To determine if GC risk stratification by OLGIM system can be applied in a high risk population and if its association with other factors can influence the selection and follow-up of patients with AG and IM. Methods: A prospective study included 84 patients with premalignant gastric lesions/conditions. An upper GI endoscopy was performed and extensive biopsy samples were obtained for OLGIM staging. Endoscopy surveillance indication and demographic data were collected. A modified Vries risk score was created by using family history of GC, alcohol use and III-IV OLGIM stages. RESULTS: From 84 patients (348/509, median age 59±12 years), 36 were classified as III-IV OLGIM stages and 48 patients were classified as 0-II OLGIM stages. An association between the III-IV OLGIM stages and the occurrence of dysplasia was not found (p = 0,14) as well as between a high modified Vries risk score and dysplasia (p = 0,26). In a multivariate analysis, high-risk OLGIM stages (III-IV) were associated with male sex (p=0,02). CONCLUSION: This population, known to benefit from long-lasting attentive endoscopic surveillance, should not rely only in OLGIM system to stratify future risk of GC. Other factors can have major influence in this area of high GC prevalence. Moreover, the proposed risk score (that incorporated OLGIM classification) can not at this time be recommended. These provocative results demand further efforts to improve the reproducibility of any staging criteria.

Capelle, L., et al. (2009). "Grading and staging gastritis with the olga system: Intestinal metaplasia as a reproduciblse alternative." Gastroenterology 136(5): A461.

Background: The recently proposed OLGA staging system (Gut 2007;56;631-636) is based on the extent and severity of atrophic gastritis (AG) and provides relevant clinical information regarding gastric cancer risk. However, AG is a difficult histopathological diagnosis of which the interobserver agreement is low. In contrast, intestinal metaplasia (IM) has better defined specific histopathological features and is associated with a much better interobserver agreement. The aim of this study was to evaluate interobserver agreement for AG, IM and dysplasia (DYS) and to assess whether a staging system based on IM instead of AG may be preferred to estimate gastric cancer risk. Methods: In a prospective multicenter study, patients with IM and DYS underwent surveillance endoscopy with extensive biopsy sampling. Three expert pathologists graded biopsy specimens according to the updated Sydney classification and the Vienna classification. Interobserver variation for these classifications was analysed by kappa (K) statistics. In the OLGA staging system AG was replaced by IM creating the IM staging system. Both classifications were evaluated for patient distribution and severe pre-malignant gastric lesions by stage. Results: In total, 125 patients (69 men and 56 women) with a mean (± SD) age of 61 ±11.7 years (range 23-81 years) were included in this study. DYS was diagnosed in 7 (6%) patients. For DYS interobserver variability was fair (K=0.4; low grade DYS K=0.2; and high grade DYS K=0.5). The interobserver agreement was moderate for AG (K=0.6), whereas agreement was almost perfect for IM (K=0.9). Overall, 83 (66%) patients were classified in stage I-IV according to the OLGA staging system (stage I n=23; stage II n=29; stage III n=23; stage IV n=8) and 80 (64%) patients were classified in stage I-IV according to the IM staging system (stage I n=24; stage II n=25; stage III n=22; stage IV n=9). Of the dysplasia patients, 5 (71%) patients clustered in stage III-IV in the OLGA system, whereas 6 (86%) patients clustered in III-IV of the IM staging system. Conclusions: Replacement of AG by IM in the staging and grading of gastritis increases interobserver agreement considerably. Moreover, the correlation with the severity of gastritis remains at least as effective as the OLGA classification. Therefore, the intestinal metaplasia staging may be preferred over the OLGA system for the prediction of gastric cancer risk in patients with pre-malignant gastric lesions. Further research is needed to evaluate the use of this system for the selection of a small category of patients for more intense follow-up.

Capelle, L. G., et al. (2012). "Premalignant gastric lesions in patients with gastric mucosa-associated lymphoid tissue lymphoma and metachronous gastric adenocarcinoma: a case-control study." European Journal of Gastroenterology and Hepatology 24(1): 42-47.

BACKGROUND: Patients with gastric mucosa-associated lymphoid tissue lymphoma or diffuse large B-cell lymphoma have an increased risk of developing gastric carcinoma (GC). Identifying patients at high GC risk may lead to improved survival and prognosis. The aim of this case-control study was to evaluate whether premalignant gastric lesions are more prevalent and severe in gastric lymphoma (GL) patients with a subsequent diagnosis of GC than in those without GC. METHODS: Patients with a first GL diagnosis from 1991-2008 were identified in the Dutch histopathology registry (PALGA). Cases were patients with a diagnosis of GL and a subsequent diagnosis of GC. Controls were patients with a diagnosis of GL without GC development. RESULTS: In total, eight cases (mean follow-up 5.5 years) and 31 controls (mean follow-up 5.3 years) were included (mean age 60 years). At lymphoma diagnosis, six (75%) cases were diagnosed with premalignant lesions, whereas in the control group, 21 (68%) had histological evidence for premalignant lesions (P=0.69). At GC diagnosis, five (63%) cases showed intestinal metaplasia in the surrounding gastric mucosa. In 22 (71%) controls premalignant lesions were present at the end of follow-up (P=0.47). CONCLUSION: No differences were demonstrated in the prevalence of premalignant lesions of cases and controls at GL diagnosis or the end of follow-up. As the prevalence of premalignant lesions is substantial in both the groups of patients, careful endoscopic surveillance of GL patients is warranted not only for recurrence of lymphoma, but also for progression to adenocarcinoma.

Cariani, S., et al. (2011). "An outlet for endoscopic access to the remnant does not reduce the effectiveness of gastric bypass: Long-term outcomes of a modified Roux-en-Y gastric bypass that allows traditional endoscopy of bypassed stomach." Obesity Surgery 21(8): 1000.

Background: Roux-en-Y Gastric Bypass (RYGB) is one of the most common operation performed worldwide as treatment for severe obesity. Patients who undergo this procedure need a periodic follow-up mainly radiological, but often endoscopic, in order to state the surgical long term outcome. These patients usually have a long life expectance, with the possibility to develop several pathologies also in the anatomically excluded stomach. In 2002, it has been introduced in bariatric surgery a modified gastric bypass, the Roux-en-Y Gastric Bypass on Vertical Banded Gastroplasty (RYGB-on-VBG), where traditional endoscopic study of the gastric remnant resulted to be feasible through a small passage between gastric pouch and excluded stomach that has been leaved. In the mid-term, RYGB-on-VBG obtained results in terms of weight loss and comorbidities resolution equivalent to those found after standard RYGB. Aim of our study is to verify the outcomes in the long-term. Methods: Between June 2002 and June 2010, 320 patients, with mean age 42.0±11.3 years, mean BMI 48.0±8.7 and mean EBW% 94.05±36.6 underwent modified RYGB via an open approach. The 37.5% of the patients were superobese. Preoperative comorbidities were hypertension (p.155, 48.4%), OSAS (p.79, 24.6%) and type II DM (p. 55, 17.1%). Results: Operative mortality was 0.6% (p.2) and early complications 1.9% (p.6). At 2 year of follow-up mean BMI and EWL% were 30.9±5.8 and 68.9±17.0 respectively. The average percentages of comorbidities resolution were: OSAS 90.1%; type II DM 83.5%; hypertension 47.5%; hyperlipidemia 30%. Early surgical complications were 4 (1.4%). At 8 year of follow-up, the mean BMI and EWL% were 34.0±7.7 and 63.4 ±18.5 respectively. Late specific complications were 8 (1.7%). For all the followed patients (95% of the patients) the modified RYGB enabled traditional endoscopic and radiologic evaluation of the gastric remnant. Our macroscopic and microscopic results were similar to other reports where Authors performed the gastric remnant exploration backward through the alimentary limb (Double Baloon Enteroscopy), with gastritis of various degree in 97% of cases and intestinal metaplasia in 15.8% of them. Conclusions: In the long-term, an outlet for access to the remnant did not reduce the effectiveness of gastric bypass. The modified RYGB outcomes in term of weight loss, resolution of comorbidities and surgical complications are comparable to those after standard RYGB as reported in literature. The frequent detection of altered mucosal surfaces, even in patients with normal preoperative endoscopic pattern, suggest for a systematic evaluation for all patients who underwent RYGB in the follow-up, to better define the nature of the lesions and how they respond to specific medications. In this series standard endoscopy was feasible in all patients who underwent RYGBon- VBG, and can be proposed as screening tool, specially in countries with high incidence of gastric cancer.

Cazzato, M., et al. (2020). "GASTRIC CANCER OCCURS AT 3-YEARS ENDOSCOPIC SURVEILLANCE IN LOW RISK ATROPHIC GASTRITIS PATIENTS." Digestive and Liver Disease 52: S52.

Background and aim: Patients with corpus atrophic gastritis (AG) or intestinal metaplasia (IM) are at risk for intestinal-type gastric cancer (GC) and type-1 gastric carcinoid (T1GC). The European MAPS II guidelines recommend for patients with advanced stage of AG, without other risks factors, surveillance with high quality endoscopy every 3 years. This study aimed to assess the occurrence of pre- and neoplastic lesions in AG patients at 3-years endoscopic and histological follow-up. Materials and methods: Prospective study (2011-2019) on consecutive patients with histological diagnosis of AG, included in a surveillance programme for early detection of neoplastic lesions, who performed endoscopic and histological follow-up at 3-years interval (± 6 months) were included. Exclusion criteria were: endoscopic follow-up and/or endoscopic polypectomy/intervention <3 years. Gastroscopy was first evaluated in high resolution white light endoscopy and then by Narrow Band Imaging (NBI). Histological examination was performed according to Updated Sydney System with neoplastic risk stratification by OLGA/OLGIM (operative link on gastric atrophy/metaplasia) scores. Results: Overall 128 patients (73% female, median age 63 yrs (31-83)) were included (46.9% patients with new AG diagnosis). The median endoscopic follow-up was 36 (30-42) months. At baseline, endoscopically visible elevated lesions were observed and removed in 10 (7.8%) patients. The histological finding were low grade dysplasia (LGD) adenoma in 1 patient (0.8%), TIGC in 3 (2.3%) patients and hyperplastic polyps in 6 (4.7%) patients. At 3-years follow-up, 16 (12.5%) patients presented 16 (12.5%) pre-neoplastic lesions, 14 endoscopically visible and 2 intramucosal. In detail, the endoscopically polypoid lesions were 3 (2.3%) GC, 3 (2.3%) T1GC, 1 (0.8%) LGD adenoma and 7 (5.5%) hyperplastic polyps. Intramucosal lesions were LGD, identified in biopsies of 2 (1.6%) patients. GC was diagnosed at 31/36/32 months with respect to previous upper endoscopy. In detail, the 3 patients with GC neither presented low grade of OLGA/OLGIM scores nor first-degree familiarity for GC nor H. pylori infection. All patients with GC are alive and they were treated by endoscopic (1 patient) and surgical treatment (2 patients). Conclusions: In AG patients, the 3-years endoscopic surveillance seems satisfactory to timely detect gastric neoplastic lesions. However 2 patients needed a surgical treatment. Likely, current criteria for early detection of neoplastic lesions should be better addressed.

Chacko, A., et al. (2010). "Narrow band imaging vs. white light gastroscopy in detecting gastric premalignant and early malignant lesions: A randomized prospective crossover study." Gastrointestinal Endoscopy 71(5): AB144-AB145.

Introduction: Narrow band imaging (NBI) detects mucosal surface details (pit pattern) as well as the microvasculature details of mucosa. In premalignant and early malignant conditions the pattern and regularity of pits and microvasculature are altered. Patients above 45 years of age with dyspeptic symptoms have higher risk of gastric malignancy than younger patients. Aims & Methods: We aimed to assess whether narrow band imaging is superior to conventional white light gastroscopy (WLG) in detecting gastric premalignant and early malignant lesions in patients above 45 years with dyspepsia. We conducted a randomized prospective crossover study from January 2009 to July 2009 at CMC, Vellore in India. Patients above 45 years of age with dyspepsia (ROME III criteria) in absence of alarm symptoms underwent gastric mucosal examination using WLG and NBI in same session by different endoscopists who were blinded to each others finding. Biopsy was taken if needed at the end of second scopy after a third observer reviewed report of both scopists. The sequence of scopies (WLG or NBI first) was determined by block randomization. The total yield of gastric premalignant lesions (atrophic gastritis, intestinal metaplasia, dysplasia, adenomatous polyp) and early malignancy was estimated for both. Comparison of sensitivities of the two screening tests was done using McNemar's test. Kappa test was done to assess agreement between the two tests. The study was approved by institute review board and ethics committee. Results: A total of 200 (Males-132) patients participated in the study after giving written informed consent. The mean age was 52.3 + 6.4 years. The total number of patients diagnosed to have premalignant lesions by any of the two modalities were 32. No patient had early gastric cancer. WLG detected lesions in 17 patients (atrophic gastritis in 12, intestinal metaplasia in7,) and NBI in 31 patients (atrophic gastritis in 22, intestinal metaplasis in 9). The sensitivity of lesion detection by NBI was significantly higher than WLG (p=0.001). The kappa value for agreement between the two tests was 0.63. As no prior prevalence data of gastric premalignant lesions in our population was available, we could not estimate a sample size prior to the study. However, post study analysis showed the power of study to be more than 90% indicating the sample studied was adequate. Conclusion: NBI is a promising new modality for detection of gastric premalignant lesions. To assess the impact of these results, long term follow up studies are required.

Chalise, S. and S. Pradhan (2020). "Gastric intestinal metaplasia: prevalence and distribution of Helicobacter pylori infection, dysplasia and carcinoma in its subtypes." Virchows Archiv 477(SUPPL 1): S181-S182.

Background & objectives: Gastric intestinal metaplasia is considered as a precursor lesion for gastric adenocarcinoma. The aim of this study was to evaluate the prevalence of gastric intestinal metaplasia and distribution of Helicobacter pylori infection, dysplasia and carcinoma in its subtypes. Methods: This prospective study was conducted at Kathmandu Medical College Teaching Hospital between December 2018 to December 2019. The endoscopic biopsies were evaluated for intestinal metaplasia and its subtyping was done with the help of periodic acid- Schiff/Alcian Blue and High Iron Diamine- Alcian Blue stain at pH 2.5. The biopsies were assessed for Helicobacter pylori, dysplasia and carcinoma. Results: Intestinal metaplasia was observed in 182 (13.5%) out of 1350 biopsies. Type III intestinal metaplasia was the most frequent subtype found in 48.3% of cases. Helicobacter pylori was positive in 74(40.6%) cases most commonly observed in type I subtype (69.2%) whereas dysplasia (2.7%) and carcinoma (13.7%) were commonly seen in type III subtype. Conclusion: Intestinal metaplasia is the common finding in endoscopic biopsies. Subtyping and long term follow-up studies is necessary with orwithout eradication of helicobacter pylori to clarify the natural history of intestinal metaplasia and also to define the value of type III intestinal metaplasia as a precursor lesion for gastric carcinoma.

Chang, W. L., et al. (2011). "Increased gastric osteopontin expression by Helicobacter pylori Infection can correlate with more severe gastric inflammation and intestinal metaplasia." Helicobacter 16(3): 217-224.

BACKGROUND: Osteopontin (OPN) is involved in the gastric cancer progression. The study validated whether OPN expressions correlate with Helicobacter pylori-related chronic gastric inflammation and the precancerous change as intestinal metaplasia (IM). METHODS: This study included 105 H. pylori-infected patients (63 without and 42 with IM) and 29 H. pylori-negative controls. In each subject, the gastric OPN expression intensity was evaluated by immunohistochemistry, and graded from 0 to 4 for the epithelium, lamina propria, and areas with IM, respectively. For the H. pylori-infected subjects, the gastric inflammation was assessed by the Updated Sydney System. Forty-nine patients received follow-up endoscopy to assess OPN change on gastric mucosa after H. pylori eradication. The in vitro cell-H. pylori coculture were performed to test the cell origin of OPN. RESULTS: The H. pylori-infected patients had higher gastric OPN expression than the noninfected controls (p < .001). For the H. pylori-infected patients, an increased OPN expression correlated with more severe chronic gastric inflammation (p < .001) and the presence of IM (OR: 2.6, 95% CI: 1.15-5.94, p = .02). Within the same gastric bits, lamina propria expressed OPN stronger than epithelium (p < .001), suggesting OPN predominantly originates from inflammatory cells. The in vitro assay confirmed H. pylori stimulate OPN expression in the monocytes, but not in the gastric epithelial cells. After H. pylori eradication, the gastric OPN expression could be decreased only in areas without IM (p < .05). CONCLUSIONS: Increased gastric OPN expression by H. pylori infection can correlate with a more severe gastric inflammation and the presence of IM.

Chang, Y. W., et al. (2015). "The incidence of synchronous and metachronous gastric cancer after endoscopic resection of early gastric cancer according to the degree of differentiation of the primary gastric cancer." United European Gastroenterology Journal 3(5): A549-A550.

Introduction: Endoscopic resection (ER) is widely used as a standard treatment for early gastric cancer (EGC) these days. However, gastric cancer can develop synchronously or metachronously after ER treatment. Aims & Methods: The aims of this study were to investigate the predictors of recurrence of EGC after ER, especially regarding to the degree of the differentiation of primary gastric cancer. We enrolled a total of 293 patients who met the extended criteria for ER and underwent this procedure from January 2007 to December 2012 at Kyung Hee University Hospital in Seoul, Korea. And, we retrospectively analyzed baseline characteristics and clinicopathological information about primary gastric cancer. Patients were classified into two groups, the differentiated group and the undifferentiated group. Annually, we followed up the patients with esophagogastroduodenoscopy (EGD) after ER. We excluded the patients whose follow up period was less than 6 months after ER. Synchronous gastric cancer (SGC) and metachronous gastric cancer (MGC) were counted in each group and then performed analysis which factor can influence the development of gastric cancer. Results: Of the 293 patients, SGC developed in 41 patients (15.2%) in the differentiated group and only one patients (4.2%) in the undifferentiated group (p=0.221). MGC developed in 19 patients (7.1%) in the differentiated group and none in the undifferentiated group (p=0.382). Intestinal metaplasia was seen in 91.5 % of the patients in the differentiated group and 58.3 % of the patients in the undifferentiated group (p=0.001). Although age was the only significant predictor of SGC in both univariate (p=0.047) and multivariate analysis (OR 3.193; p=0.010), it did not show significance in occurrence of MGC. Alcohol showed significant difference between the non-metachronous group and the metachronous group with p-value 0.036 in univariate analysis, but failed to show significant result in multivariate analysis (p=0.077). Other factors including sex, smoking, Helicobacter pylori infection and baseline gastric mucosal atrophy did not show any statistical significance. Conclusion: Differentiated type of gastric cancer may be a predictor of occurrence of SGC and MGC because of its high portion of intestinal metaplasia. We should consider the degree of differentiation of primary cancer, age and history of alcohol consumption together with scheduled follow-up EGD after ER. Furthermore, large scale, prospective, long-term follow-up study will be needed to validate our results.

Chang, Y. W., et al. (2015). "The incidence of synchronous and metachronous gastric cancer after endoscopic resection of early gastric cancer according to the degree of differentiation of the primary gastric cancer." Journal of Gastroenterology and Hepatology (Australia) 30: 270-271.

Introduction: Endoscopic resection (ER) is widely used as a standard treatment for early gastric cancer (EGC) these days. However, gastric cancer can develop synchronously or metachronously after ER treatment. Aims & Methods: The aims of this study were to investigate the predictors of recurrence of EGC after ER, especially regarding to the degree of the differentiation of primary gastric cancer. We enrolled a total of 293 patients who met the extended criteria for ER and underwent this procedure from January 2007 to December 2012 at KyungHee University Hospital in Seoul, Korea. And we retrospectively analyzed baseline characteristics and clinicopathological information about primary gastric cancer. Patients were classified into two groups, the differentiated group and the undifferentiated group. Annually, we followed up the patients with esophagogastroduodenoscopy (EGD) after ER. We excluded the patients whose follow-up period was less than 6months after ER. Synchronous gastric cancer (SGC) and metachronous gastric cancer (MGC) were counted in each group and then performed analysis which factor can influence the development of gastric cancer. Results: Of the 293 patients, SGC developed in 41 patients (15.2%) in the differentiated group and only one patients (4.2%) in the undifferentiated group (P = 0.221). MGC developed in 19 patients (7.1%) in the differentiated group and none in the undifferentiated group (P = 0.382). Intestinal metaplasia was seen in 91.5 % of the patients in the differentiated group and 58.3 % of the patients in the undifferentiated group (P = 0.001). Although age was the only significant predictor of SGC in both univariate (P = 0.047) and multivariate analysis (odds ratio 3.193; P = 0.010), it did not show significance in occurrence of MGC. Alcohol showed significant difference between the non-metachronous group and the metachronous group with P-value 0.036 in univariate analysis but failed to show significant result in multivariate analysis (P = 0.077). Other factors including sex, smoking, Helicobacter pylori infection, and baseline gastric mucosal atrophy did not show any statistical significance. Conclusions: Differentiated type of gastric cancer may be a predictor of occurrence of SGC and MGC because of its high portion of intestinal metaplasia. We should consider the degree of differentiation of primary cancer, age, and history of alcohol consumption together with scheduled follow-up EGD after ER. Furthermore, large scale, prospective, long-term follow-up study will be needed to validate our results.

Chapelle, N., et al. (2020). "Evaluation of a Phone Call Reminder Strategy in the Surveillance of Patients with Gastric Precancerous Lesions Lost to Follow-Up." Gastrointest Tumors 7(4): 110-116.

BACKGROUND: Surveillance of gastric precancerous lesions (GPL) may reduce gastric cancer (GC)-related mortality, but some patients with GPL are lost to follow-up. OBJECTIVE: The aim of this study was to evaluate the feasibility and efficacy of a "phone-call" strategy in surveillance of the lost to follow-up patients. PATIENTS AND METHODS: Among all the patients diagnosed with GPL (atrophic gastritis, intestinal metaplasia, low-grade dysplasia) between 2000 and 2015, we identified those who should undergo surveillance endoscopy according to the current guidelines. They were contacted by telephone and invited to undergo endoscopy with gastric biopsies for histological analysis. RESULTS: Among 535 patients with GPL, 134 were contacted. Sixty-two (46%) could not be joined, 36 did not have endoscopy for other reasons, and finally, 36 patients (22 males, median age 65 years) were included. After the median time interval of 57 months between 2 endoscopies, 18 patients showed stability, 11 regression, and 7 progression of GPL, including 1 patient who developed GC. CONCLUSION: Despite several telephone calls, only one-third of the contacted patients could be brought to surveillance endoscopy. Most of the patients showed stability of GPL, but 1 progressed to GC and could be successfully treated.

Chapelle, N., et al. (2019). "Evaluation of a ?phone call strategy? for the patients with gastric precancerous lesions lost for follow-up: A prospective study in a single center in France." United European Gastroenterology Journal 7(8): 1012.

Introduction: Early detection and adequate surveillance of gastric precancerous lesions (GPL) may prevent the development of gastric cancer (GC) and reduce GC-related mortality. However, some patients with GPL are lost for follow up. The aims of this prospective study were: 1) to evaluate the feasibility and efficacy of a ?phone-call? strategy to rescue the patients lost for follow-up, and 2) to assess the evolution of GPL in these patients. Aims &Methods: Among all the patients diagnosed with GPL (atrophic gastritis, AG, intestinal metaplasia, IM, low grade dysplasia, LGD) in our center between January 2000 and December 2015, we identified those who according to the European MAPS guidelines [1]should undergo a surveillance endoscopy, who were under the age of 80, and who had no severe comorbidities. They were all contacted by phone (three calls) by a medical doctor, and invited to undergo a surveillance endoscopy. In those who accepted, the upper endoscopy was performed during which 5 random gastric biopsies (2 from the antrum, 1 from the angulus, and 2 from the corpus) were obtained for histological analysis performed by an expert pathologist with the evaluation of the presence of GPL and their severity. The results were compared to those of the initial endoscopy. Results: Among the 535 patients with a GPL,134 fulfilled the inclusion criteria and were contacted by telephone. Among them, 62 could not be joined, 16 were followed in another center, 8 agreed to participate but never came, 8 refused endoscopy, and 3 had endoscopy but without biopsies. Thus finally, 36 patients (27%) were included in the analysis. There were 22 males (61%), the mean age was 57 years at index endoscopy and 63 years at inclusion, and the mean duration of follow up was 65 months. At index endoscopy, 3 patients had AG, 27 IM, and 6 LGD. Nine patients (25%) were H. pylori positive and in all of them the bacterium was successfully eradicated. During the follow up, 7 patients (19%) showed a progression of GPL [(1 from AG to IM, 4 from antrum- or corpus-limited IM to pangastric IM, 1 from IM to LGD, and 1 from extensive IM to GC which could be treated curatively (pT2pN0)]. Eleven patients (31%) showed regression of GPL (1 from AG to normal mucosa, 6 from IM to normal mucosa, 1 from pangastric- to corpus limited-IM, 3 from LGD to IM), and 18 patients (50%) showed stability of the lesions. Conclusion: This study shows that: 1) despite several phone calls, a follow-up endoscopy could only be performed in a quarter of patients who had indication for control endoscopy according to the current guidelines, and 2) most of the patients showed stability of the GPL, but one patient progressed to GC and thanks to this strategy, he could be diagnosed on time and successfully treated.

Chapelle, N., et al. (2020). "Prevalence, Characteristics and Endoscopic Management of Gastric Premalignant Lesions in France." Digestive Diseases 38(4): 286-292.

INTRODUCTION: Surveillance of gastric precancerous lesions (GPL) is recommended, but the data on their clinical and endoscopic management in a "real-life" practice are limited. Our aim was to study the modalities of endoscopic management of patients with GPL in France. DESIGN: All the patients diagnosed with GPL in our center between 2000 and 2015 were grouped and analyzed according to the most severe GPL found, in the following order: atrophic gastritis only (AG), intestinal metaplasia (IM), low grade dysplasia (LGD), high grade dysplasia (HGD). RESULTS: Out of 16,764 patients having undergone upper endoscopy with gastric biopsies, 507 were identified with GPL (detection rate 3.2%). Overall, Helicobacter pylori infection was found in 41% of patients. IM was by far the most frequently found lesion (79%), followed by LGD (17%), HGD (2%), and AG only (2%). H. pylori infection rate was decreasing, while the age of the patients was increasing, together with the increasing severity of GPL (p = 0.005). Only 28% of the patients had at least one follow-up endoscopy. No correlation was found between the endoscopist's appreciation of the mucosa and histological results. CONCLUSION: In France, GPL can be expected in about 3% of patients undergoing upper endoscopy with gastric biopsies for any reason. The correlation between the endoscopic evaluation and histology is poor. Spreading of published guidelines should improve the management of patients with GPL in the future.

Chen, D., et al. (2016). "Hypomethylation of repetitive elements in blood leukocyte DNA and risk of gastric lesions in a Chinese population." Cancer Epidemiology 41: 122-128.

BACKGROUND: To explore the association between hypomethylation of repetitive elements (LINE-1, Sat2, and ALU) in blood leukocyte DNA and risks of gastric lesions, and development of gastric cancer (GC), a population-based study was conducted in a high-risk area of GC in China. MATERIALS: Methylation levels were determined by MethyLight in 902 subjects with various gastric lesions from two cohort studies at baseline and 276 subjects with long-term follow-up data. RESULTS: The frequency of LINE-1 or Sat2 hypomethylation was significantly increased in subjects with dysplasia (DYS) compared with superficial gastritis/chronic atrophic gastritis. The odds ratios (ORs) were 2.22 [95% confidence interval (CI): 1.45-3.40] for LINE-1 and 1.58 (95% CI: 1.14-2.21) for Sat2. A dose-response pattern was found for the risk of DYS and LINE-1 hypomethylation (P-trend<0.001). Further stratified analysis indicated that the frequency of LINE-1 or Sat2 hypomethylation was higher in subjects with Helicobacter pylori infection. The ORs were 1.83 (95% CI: 1.12-2.99) for LINE-1 and 1.44 (95% CI: 1.01-2.05) for Sat2. The follow-up data indicated that the risk of progression to GC was increased in intestinal metaplasia (IM) subjects with LINE-1 hypomethylation (OR=2.82; 95% CI: 1.17-6.77) or Sat2 hypomethylation (OR=2.78; 95% CI: 1.15-6.74). The risk of progression to GC was also increased in DYS subjects with Sat2 hypomethylation (OR=5.24; 95% CI: 2.00-13.74). CONCLUSIONS: These findings suggest that hypomethylation of repetitive elements in blood leukocytes is associated with the risks of advanced gastric lesions and development of GC.

Chen, S. J., et al. (2015). "Long term surveillance among patients with H.pylori negative intestinal metaplasia by endoscopic marking target biopsy." Journal of Gastroenterology and Hepatology (Australia) 30: 32.

Background: Intestinal metaplasia lesions was regarded as a risk factor of gastric carcinogenesis. However, the development of patients with intestinal metaplasia without H. pylori infection were not determined. We have previously demonstrated that Marking target biopsy (MTB) technique, which simultaneously combines tattoo marking and obtaining biopsy of gastric lesions, could help more concise surveillance of gastric lesions. We aim to evaluate the outcome of patients with H. pylori negative intestinal metaplasia by applying MTB-guided surveillance program in long-term follow-up. Method: Participants were enrolled after initially confirmed with intestinal metaplasia lesion and eradication with H. pylori from Jun 2006 to Dec 2013 in a single clinical center. Patients were followed up with MTB-guide endoscopic surveillance program every one year . Marking target biopsy was performed by injected diluted Indian ink into the gastric wall of the five points of gastric mucosa including angulus, small curvature and large curvature of body, small curvature and large curvature of antrum. Patients were received with chemoprevention trial with teprenone alone or combined with folic acid. Primary outcome was the proportion of the biopsies that demonstrated histologic improvement of gastric intestinal metaplasia at final compared to index endoscopy. Result: 123 of 156 enrolled patients completed the surveillance program with mean follow up of 4.2+1.6 years. At the endpoint examination, the proportion of gastric biopsies that demonstrated histologic improvement of intestinal metaplasia in five points of gastric mucosa were 60.44%, 51.33%, 83.33%, 56.25%, 45.13%, respectively, which at larger curvature of the antrum, lesser curvature of the antrum, larger curvature of the body, lesser curvature of the body, and angulus. 4.07% patients (5/123) developed low-grade dysplasia and none of the patients developed gastric carcinoma. 7 of 8 patients (88%) who had gastric dysplasia when enrolled had complete histologic resolution of dysplasia at final endoscopy. Conclusion: Long-term surveillance demonstrated that high rate of histologic improvement of gastric intestinal metaplasia when they were H. pylori negative by applying MTB. Results indicate that eradication with H. Pylori and chemoprevention may contribute to the histologic resolution of intestinal metaplasia. However, future large studies still need to be implemented to validate this.

Chen, S. J., et al. (2015). "Long-term surveillance among patients with H. pylori -negative intestinal metaplasia by endoscopic marking target biopsy." Journal of Digestive Diseases 16: 44.

Objective Intestinal metaplasia (IM) is regarded as a risk factor of gastric carcinogenesis. However, the development of gastric carcinogenesis in patients with IM without Helicobacter pylori (H. pylori) infection was not determined. We have previously demonstrated that marking target biopsy (MTB) technique, which simultaneously combines tattoo marking and obtaining biopsy of gastric lesions, could help for the concise surveillance of gastric lesions. We aimed to evaluate the outcome of patients with H. pylori -negative IM by applying MTB-guided surveillance program in long-term follow-up. Methods Participants were enrolled after initially confirmed with IM and H. pylori eradication from June 2006 to December 2013 in a single clinical center. Patients were followed up with MTB-guide endoscopic surveillance program every year. Marking target biopsy was performed by injecting diluted Indian ink into the gastric wall of the five points of gastric mucosa including angulus, small curvature and large curvature of body, small curvature and large curvature of antrum. Patients received chemoprevention trial with teprenone alone or combined with folic acid. Primary outcome was the proportion of the biopsies that demonstrated histological improvement of gastric IM at final compared to index endoscopy. Results A total of 123 of 156 enrolled patients completed the surveillance program with a mean follow-up of 4.2 ± 1.6 years. At the endpoint examination, the proportion of gastric biopsies that demonstrated histologic improvement of IM in five points of gastric mucosa were 60.44%, 51.33%, 83.33%, 56.25% and 45.13%, respectively, which located at the larger curvature of the antrum, lesser curvature of the antrum, larger curvature of the body, lesser curvature of the body, and angulus. Five of 123 (4.07%) patients developed low-grade dysplasia and none of the patients developed gastric carcinoma. Seven of 8 patients (87.5%) who had gastric dysplasia when enrolled had complete histologic resolution of dysplasia at final endoscopy. Conclusions Long-term surveillance demonstrated that high rate of histologic improvement of gastric IM when they were H. pylori - negative by applying MTB. H. pylori eradication and chemoprevention may contribute to the histologic resolution of IM. However, large studies still need to be implemented to validate this in the future.

Chen, T. and C. Chiu (2016). "Linked color imaging combine magnify endoscopy for helicobacter pylori infection and intestinal metaplasia: A pioneer study with preliminary result in Taiwan." United European Gastroenterology Journal 4(5): A342.

Introduction: LCI as a novel image-enhanced endoscopy has been reported usefully in H. pylori infection diagnosis. Since, H. pylori is one of the carcinogen of gastric cancer and also related to gastric or duodenal ulcer. We expect that LCI combine magnify endoscopy can increase diagnosis rate of H.pylori infection Aims & Methods: The aim of this study is to evaluate the usefulness of LCI combine magnify endoscopy for diagnosis of H. pylori infection. We conduct a prospective study enrolled 52 patients from June 2016 to April 2016 at Chang Gung Memorial Hospital, Linkou medical center, Taoyuan, Taiwan. We use at least 2 methods to make sure of H. pylori infection. The procedures were performed only by one experience endoscopist. The specimens are checked by two experience pathologist. Results: The accuracy diagnostic rate of H. pylori infection in LCI/Magnify endoscopy/Combine group were: 78.5%/83.6%/92.3%. The accuracy diagnostic rate of intestine metaplasia was 72.4% Conclusion: LCI is a useful tool for diagnosis of H. pylori infection and intestinal metaplasia when combine with magnify endoscopy. And, we can eradicate H. pylori as soon as possible once it was diagnosed. We also can arrange intensive follow up for those patients who have precancerous lesions.

Chen, Z., et al. (2020). "RISK FACTORS IN THE DEVELOPMENT OF GASTRIC ADENOCARCINOMA IN HIGH-RISK AREAS: THE WUWEI COHORT STUDY." Gastroenterology 158(6): S-1008.

Gastric adenocarcinoma (GAC) is the second leading cause of cancer-related deaths worldwide. Most GACs develop through a stepwise progression of histologic lesions, starting with chronic non-atrophic gastritis (CNAG), followed by chronic atrophic gastritis (CAG), intestinal metaplasia (IM), low grade dysplasia (LGD), high grade dysplasia (HGD), and eventually adenocarcinoma. Risk factors that have been identified for GAC, where the healthy population was always used as the reference, may have different impacts on each of progressions from CNAG to CAG, from CAG to IM, from IM to LGD, and from LGD to GAC/HGD. The aim of this study was to examine which groups of risk factors, and to what extent influence the disease stages of GAC in high-risk areas. We enrolled 1,739 patients with CNAG, 3,409 patients with CAG, 1,757 patients with IM, 2,239 patients with LGD, and 208 patients with HGD or intestinal-type GAC from the baseline data from the Wuwei Cohort, a population-based cohort study of gastric cancer in northwest area of China. Adjusted logistic regression was used to assess the baseline risk factors between each two consecutive stages from CNAG to GAC/HGD. Our results show that different groups of risk factors appear to be associated with different stages from CNAG to CAG in high-risk areas. Age, occupation of farmer, low annual family income, H. pylori infection, drinking, eating hot food and histories of gastritis and peptic ulcers were associated with the development of CAG from CNAG. Age, illiteracy, H. pylori infection, smoking, eating hot food, eating quickly, histories of gastritis and gallbladder diseases were associated with the progression to IM from CAG. Male gender, occupation of farmer and history of peptic ulcers were associated with the development of LGD from IM. Age, male gender and history of polyps were the only three risk factors associated with the development of GAC/HGD from LGD. In total, it seems that most risk factors, such as H. pylori infection, smoking, drinking, eating hot food, eating quickly, histories of gastritis and peptic ulcer, function more as a set of switches that initiated the GAC carcinogenesis and play a pivotal role before developing IM, and intervention for the risk factors of GAC should be conducted before the stage of IM in high-risk areas.

Cheng, H. C., et al. (2017). "The corpus-predominant gastritis index can be an early and reversible marker to identify the gastric cancer risk of Helicobacter pylori-infected nonulcer dyspepsia." Helicobacter 22(4).

BACKGROUND: Corpus-predominant gastritis index (CGI) is an early histological marker to identify Helicobacter pylori-infected gastric cancer relatives at risk of cancer. This study validated whether CGI is more prevalent in H. pylori-infected nonulcer dyspepsia (NUD) subjects than in duodenal ulcer (DU) controls and whether it is reversible after H. pylori eradication or is correlated with noninvasive biomarkers. MATERIALS AND METHODS: In this longitudinal cohort study, 573 H. pylori-infected subjects were enrolled, including 349 NUD and 224 DU. Gastric specimens were provided to assess CGI, spasmolyic polypeptide-expressing metaplasia (SPEM), and Operative Link on Gastric Intestinal Metaplasia assessment (OLGIM). Serum pepsinogen I and II levels were assessed using enzyme-linked immunosorbent assay. CGI subjected were followed up at least 1 year after H. pylori eradication. RESULTS: NUD subjects had higher prevalence rates of CGI (47.0% vs 29.9%, P<.001) and OLGIM stages III-IV (24.1% vs 15.2%, P=.01) than controls. CGI was highly prevalent in NUD subjects after the age of 40, which was 10 years earlier than atrophic gastritis and intestinal metaplasia. NUD subjects with CGI had higher risk of SPEM (OR 2.86, P<.001) and lower serum pepsinogen I/II ratios (P<.001) than those without CGI. Serum pepsinogen I/II ratios <9 could predict CGI modestly (AUROC 0.69, 95% CI: 0.63-0.74). CGI was regressed after eradication (P<.001). CONCLUSIONS: CGI was more prevalent in H. pylori-infected NUD subjects than in controls, was correlated with SPEM, and may serve as a marker earlier than OLGIM to indicate risk of gastric cancer. Moreover, CGI could be regressed after eradication.

Cheung, K. S. and W. K. Leung (2018). "Risk of gastric cancer development after eradication of Helicobacter pylori." World Journal of Gastrointestinal Oncology 10(5): 115-123.

Helicobacter pylori (H. pylori) infection is the most important risk factor for gastric cancer (GC) development through the Correa's gastric carcinogenesis cascade. However, H. pylori eradication alone does not eliminate GC, as pre-neoplastic lesions (atrophic gastritis, intestinal metaplasia and dysplasia) may have already developed in some patients. It is therefore necessary to identify patients at high-risk for gastric cancer after H. pylori eradication to streamline the management plan. If the patients have not undergone endoscopy with histologic assessment, the identification of certain clinical risk factors and non-invasive testing (serum pepsinogen) can predict the risk of atrophic gastritis. For those with suspected atrophic gastritis, further risk stratification by endoscopy with histologic assessment according to validated histologic staging systems would be advisable. Patients with higher stages may require long-term endoscopic surveillance. Apart from secondary prevention to reduce deaths by diagnosing GC at an early stage, identifying medications that could potentially modify the GC risk would be desirable. The potential roles of a number of medications have been suggested by various studies, including proton pump inhibitors (PPIs), aspirin, statins and metformin. However, there are currently no randomized clinical trials to address the impact of these medications on GC risk after H. pylori eradication. In addition, most of these studies failed to adjust for the effect of concurrent medications on GC risk. Recently, large population-based retrospective cohort studies have shown that PPIs were associated with an increased GC risk after H. pylori eradication, while aspirin was associated with a lower risk. The roles of other agents in reducing GC risk after H. pylori eradication remain to be determined.

Cheung, T. K. and B. C. Y. Wong (2008). "Treatment of Helicobacter pylori and prevention of gastric cancer." Journal of Digestive Diseases 9(1): 8-13.

Gastric cancer is the second commonest fatal malignancy in the world with a high incidence in China. Helicobacter pylori infection is an important factor in the pathogenesis of gastric cancer. Epidemiological studies have shown a strong causal relationship between H. pylori infection and gastric cancer. Animal studies also show that eradication of H. pylori infection, especially at the early stage, is effective in preventing H. pylori-related gastric carcinogenesis. H. pylori eradication leads to regression and prevents the progression of gastric precancerous lesions, but only in a minority of cases. H. pylori eradication appears to be the most promising approach in gastric cancer prevention. The current available data in human studies showed that H. pylori eradication can reduce the risk of developing gastric cancer and this strategy is more useful in patients without atrophic gastritis or intestinal metaplasia. A longer follow-up and additional studies are needed for better understanding this issue. © Journal compilation © 2008 Chinese Medical Association Shanghai Branch, Chinese Society of Gastroenterology and Blackwell Publishing Asia Pty Ltd.

Cheung, T. K., et al. (2007). "Helicobacter pylori eradication for gastric cancer prevention." Journal of Gastroenterology 42(SUPPL.17): 10-15.

Gastric cancer is the second most common fatal malignancy in the world. Its incidence is high in East Asia. Helicobacter pylori infection is an important factor in the pathogenesis of gastric cancer. Epidemiological studies have established a strong causal relationship between H. pylori infection and gastric cancer. H. pylori eradication is therefore likely to be one of the most promising approaches to gastric cancer prevention. Animal studies have shown that eradication of H. pylori infection, especially at the early stage, is effective in preventing H. pylori-related gastric carcinogenesis. However, the available data from human studies show that H. pylori eradication does not completely prevent gastric cancer and that it might be useful only in patients without atrophic gastritis or intestinal metaplasia at baseline. Longer follow-up and additional studies are needed to clarify this issue. © Springer-Verlag Tokyo 2007.

Chiang, T. H., et al. (2021). "Mass eradication of Helicobacter pylori to reduce gastric cancer incidence and mortality: A long-term cohort study on Matsu Islands." Gut 70(2): 243-250.

Objective Although mass eradication of Helicobacter pylori has been proposed as a means to eliminate gastric cancer, its long-term effects remain unclear. Design Mass eradication of H. pylori infection was launched in 2004 and continued until 2018 for a high-risk Taiwanese population aged 30 years or older dwelling on Matsu Islands with prevalent H. pylori infection. Test positives for the 13 C-urea breath test underwent eradication therapy. We evaluated the effectiveness of the mass eradication in reducing two main outcomes, incidence and mortality rates of gastric cancer, until the end of 2016 and 2018, respectively. Results After six rounds of mass screening and eradication, the coverage rate reached 85.5% (6512/7616). The referral rate for treatment was 93.5% (4286/4584). The prevalence rates of H. pylori fell from 64.2% to 15.0% with reinfection rates of less than 1% per person-year. The presence and severity of atrophic gastritis and intestinal metaplasia also decreased with time. Compared with the historical control period from 1995 to 2003, the effectiveness in reducing gastric cancer incidence and mortality during the chemoprevention period was 53% (95% CI 30% to 69%, p<0.001) and 25% (95% CI-14% to 51%, p=0.18), respectively. No significant changes were noted in the incidence rates of other digestive tract cancers or the antibiotic resistance rate of H. pylori. Conclusion Population-based eradication of H. pylori has significantly reduced gastric cancer incidence with no increase in the likelihood of adverse consequences. A significant reduction in mortality is likely to be achieved with a longer follow-up period. Trial registration number NCT00155389

Chirinos, J. A. and J. L. Gomez (2018). "Screening gastric lesions using systematic endoscopy with blue laser imaging and magnifying chromoendoscopy in symptomatic patients." Gastrointestinal Endoscopy 87(6): AB415.

Background: Currently, cancer is one of the main causes of mortality worldwide. In Peru, gastric cancer is one of the most aggressive and frequent entities, with a higher mortality rate in the highlands. Eight out of 10 cases of gastric cancer are detected in advanced stages. Therefore, we looked for detection of early gastric cancer or possible precancerous lesions with the use of a new technology. Gastric intestinal metaplasia (IM) and Gastric Atrophy (GA) are considered precancerous lesions for gastric cancer. Using conventional endoscopy, IM or GAn be very difficult to identify, furthermore random biopsies could lead to sampling errors. A systematic endoscopic approach helps to have a full evaluation of the gastric surface. Blue Laser Imaging Magnification chromoendoscopy (M-BLI) allows optical interrogation of microvasculature and microsurface of abnormal areas, being able to target biopsies appropriately. Methods: This is a retrospective study of upper endoscopies performed using EG-L590ZW Lasereo (Fujifilm Co., Tokyo, Japan) from April 2016 to April 2017 in symptomatic patients. We determined prevalence of IM using a systematic endoscopy approach with at least 28 pictures. We also determined sensitivity, specificity, positive predictive value, negative predictive value and kappa index of M-BLI compared to histopathological findings of targeted and Sydney protocol biopsies. Results: A total of 300 patients were included, average age was 53 y.o (range 23-87), 60.3% females. IM and GA prevalence were 20.7% and 1%, respectively. 93.7% of the patients presented superficial chronic gastritis and 11.3% patients were positive for H. pylori. The sensitivity, specificity, positive predictive value, negative predictive value and kappa index of IM determined by M-BLI were 79%, 91%, 69%, 94% and 0.66. There was no concordance of GA determined by MBLI. We did not find a statistically significant relationship between IM and age, sex or prevalence of Hp. Conclusions: A systematic endoscopy approach combined with MBLI allows an accurate detection and prediction of IM. This might help early gastric detection on follow up. Further studies should be done testing this promising technology and endoscopic systematic approach.

Chiu, P. W. Y., et al. (2012). "Endoscopic submucosal dissection (ESD) compared with gastrectomy for treatment of early gastric neoplasia: A retrospective cohort study." Surgical Endoscopy 26(12): 3584-3591.

Introduction: This study aims to compare perioperative outcomes and oncological clearance of endoscopic submucosal dissection (ESD) versus gastrectomy for treatment of early gastric cancer (EGC). Methods: This is a retrospective cohort study including all cases of EGC or severe dysplasia treated at a universityaffiliated hospital from 1993 to 2010. Preoperative endoscopic ultrasound and image-enhanced endoscopy were employed to determine depth of invasion. Clinical outcomes including baseline demographics, pathology, postoperative complication, and hospital stay, as well as 3-year survival were compared. Results: From 1993 to 2010, 114 patients with severe dysplasia or EGC were treated: 40 of them received gastrectomy, while 74 received ESD. There was no difference in age, gender, comorbidity or American Society of Anesthesiologists grade between the two groups. Of patients in the gastrectomy group, 92.5 % presented with symptoms as compared with 27.0 % of those treated by ESD (p < 0.001). More patients in the ESD group had atrophic gastritis (31.1 vs 10 %; p = 0.009) and intestinal metaplasia (68.9 vs 55.0 %; p = 0.04). Patients treated by gastrectomy sustained longer operative time [265 (150-360) min] when compared with ESD [89.6 (45-360) min; p < 0.001]. They also had longer median hospital stay [9.9 (6-26) days vs 3.0 (2-10) days; p < 0.001]. There was no perioperative mortality, but the overall complication rate was significantly higher in the gastrectomy group. The 3-year survival rate was 94.6 % for ESD and 89.7 % for gastrectomy group (log-rank test, p = 0.44). Conclusions: ESD achieved similar oncological outcomes when compared with radical gastrectomy for treatment of EGC. Patients receiving ESD had better perioperative outcomes in terms of operative time, complication rate, and hospital stay. © Springer Science+Business Media, LLC 2012.

Cho, H., et al. (2021). "Gastric cancer is highly prevalent in Lynch syndrome patients with atrophic gastritis." Gastric Cancer 24(2): 283-291.

BACKGROUND: Although gastric cancer is one of the Lynch syndrome (LS)-related tumors, the clinicopathological features of gastric cancer in patients with LS remain uncertain. To investigate the incidence risk and clinicopathological features of gastric neoplasms in LS, we conducted a retrospective cohort study in Japanese LS patients. METHODS: LS patients with pathogenic mismatch repair (MMR) gene variants were extracted from the LS registry of the National Cancer Center Hospital, Japan. Cumulative risks of gastric neoplasm, including dysplasia and cancer, were estimated using the Kaplan-Meier method. Gastric atrophy was evaluated endoscopically and/or histologically. Immunohistochemical staining for MMR proteins was performed for all available specimens. RESULTS: Of 118 eligible patients, 26 patients were diagnosed with 58 gastric neoplasms. The cumulative incidence of gastric neoplasm was 41.0% (95% confidence interval, 26.9-55.0) at the age of 70. Of these, 13 (50%) patients developed synchronous and/or metachronous multiple gastric neoplasms. Among the 49 gastric neoplasms available for detailed pathological evaluation, all were associated with intestinal metaplasia. Immunohistochemically, 42 (86%) were MMR-deficient. The individuals with gastric atrophy had a significantly higher risk of developing gastric neoplasms compared with those without gastric atrophy (26 cases/54 individuals vs. 0 cases/53 individuals) (P = 0.026). CONCLUSION: LS patients, particularly those with atrophic gastritis, are at high risk of gastric neoplasm and often develop multiple tumors. Endoscopic surveillance for gastric cancer is recommended for LS patients, especially those with atrophic gastritis.

Cho, S. J., et al. (2013). "Randomised clinical trial: the effects of Helicobacter pylori eradication on glandular atrophy and intestinal metaplasia after subtotal gastrectomy for gastric cancer." Alimentary Pharmacology and Therapeutics 38(5): 477‐489.

Choe, Y. G., et al. (2012). "Characteristics of synchronous and metachronous neoplasm in adenoma or EGC patients after gastric ESD." Gastroenterological Endoscopy 54: 1126.

Background & aims: Since endoscopic submucosal dissection (ESD) have been actively performed and made it possible to preserving most of the stomach, the occurrence of synchronous and metachronous lesion should be monitored thoroughly. We investigated the risk factors for the occurrence of synchronous neoplasm (SN) or metachronous neoplasm (MN) after gastric ESD. Methods: A total of 111 patients with gastric adenoma or early gastric cancer(EGC) who had undergone ESD and scheduled endoscopic surveillance for 12 months or longer from January 2006 to May 2009 were enrolled retrospectively. The incidence. duration and risk factors for SN and MN were assessed Results: The incidences of SN and MN were 4.5% (n = 5) and 9% (n = 10) respectively. The median periods of endoscopic follow up were 7.4 months (SN, range 3-11 months) and 27 months (MN. range 13-40 months). Most common location of SN or MN was lesser curvature and posterior wall of low body to antrum. Annual incidence rate of MN was approximately 2.5% The incidence of SN or MN was significantly increased in atrophic gastritis (p = 0.035) and intestinal metaplasia (p = 0.049) of initial endoscopic finding, Age, status of Helicobacter pylori, procedure time and gross finding had no significant relationship with SN or MN occurrence. Conclusions: We should examine more carefully the patients who have atrophic gastritis or intestinal metaplasia and the blind spots located in lesser curvature and posterior wall of low body to antrum after successful ESD.

Choi, J., et al. (2014). "Eradication of Helicobacter pylori after endoscopic resection of gastric tumors does not reduce incidence of metachronous gastric carcinoma." Clinical Gastroenterology and Hepatology 12(5): 793‐800.

Choi, S. R. and J. S. Jang (2013). "Risk factors associated with multiple and missed gastric neoplastic lesions after endoscopic resection; prospective study at a single institution in south korea (when do we perform follow up endoscopy after endoscopic resection of gastric neoplastic lesion?)." Gastrointestinal Endoscopy 77(5): AB269.

Introduction: Because only a small part of the gastric mucosa containing the visible lesion can be removed by endoscopic resection, accurate detection of multiple lesions is important. This study was aimed to identify the incidence rate and associated risk factors of multiple and missed gastric lesions, and proper timing of follow up endoscopy within one year after endoscopic resection. Methods: The patients, who had gastric neoplastic lesion and scheduled to undergo endoscopic resection, were prospectively enrolled. Intensively endoscopic surveillance was performed on 1 week, and 1, 6, 12 months after endoscopic resection. All multiple gastric lesions were divided into main and accessory lesion, and accessory lesions were subdivided into detected and missed lesion. Results: A total 250 lesions of 215 patients were analyzed, and there were 81 of early gastric cancer, 50 of high grade dysplasias and 119 of low grade dysplasias. The overall incidence rate of synchronous gastric cancer was 5.3%. And a total 30(14%) of 215 patients had multiple gastric neoplastic lesions, either adenoma or cancer, within 1 year follow up after endoscopic resection. In univariate and multivariate analysis, old age (odds ratio 1.063, 95% CI 1.009- 1.121), men (odds ratio 3.412, 95% CI 0.095-0.907) and severe intestinal metaplasia (odds ratio 3.268, 95% CI 0.129-0.728) were independent risk factors of multiple gastric lesions. Of 35 accessory lesions in 30 patients, 25 lesions in 21 patients (25/35, 71.4%) were detected at preoperative endoscopic examination, and 10 accessory lesions in 9 patients were missed (10/35, 28.6%). Small size (>1cm) and flat morphology were major risk factors for missed lesion by endoscopy (p=0.047, p=0.027). Among 10 missed lesions, 9 (90%) lesions could be detected within 6 month after endoscopic resection. Conclusion: We should keep in mind the fact that old age, men and severe intestinal metaplasia were risk factors for multiple gastric lesions after endoscopic resection, and multiple gastric lesions can often be missed at the time of treatment. Therefore, to reduce a missing of multiple gastric lesions, the entire stomach should be carefully examined, and follow up endoscopy might be necessary at least one time within six month after endoscopic resection.

Chu, L., et al. (2021). "Confocal laser endomicroscopy under propofol‐based sedation for early gastric cancer and pre‐cancerous lesions is associated with better diagnostic accuracy: a retrospective cohort study in China." BMC Anesthesiology 21(1).

Background: Confocal laser endomicroscopy (CLE) has advantages in detecting gastric neoplastic lesions, meanwhile it requires strict patient cooperation. Sedation could improve patient cooperation and quality of endoscopy. However, sedation is still not very popular in some resource-limited countries and regions. The purpose of this study was to compare propofol-based sedated versus un-sedated CLE in the value of diagnosing early gastric cancer (EGC) and precancerous lesions. Methods: A retrospective, cohort, single center study of 226 patients who underwent CLE between January 1, 2015 and December 31, 2017 was performed. Patients enrolled were allocated into the propofol-based sedated group (n = 126) and the un-sedated group (n = 100). The comparison of validity and reliability of CLE for identifying EGC and precancerous lesions between the two groups was performed through analyzing CLE diagnosis and pathological diagnosis. Reporting followed the STROBE guidelines. Results: The area under receiver operating characteristic curve (AUROC) of diagnosing EGC in the sedated group was 0.97 (95 % CI: 0.95 to 0.99), which was higher than that in the un-sedated group (0.88 (95 % CI: 0.80 to 0.97), P = 0.0407). CLE with sedation performed better than without sedation in diagnosing intraepithelial neoplasia and intestinal metaplasia (P = 0.0008 and P = 0.0001, respectively). For patients considered as high-grade intraepithelial neoplasia or EGC by endoscopists, they would not get biopsy during CLE but receive endoscopic submucosal dissection (ESD) subsequently, and the misdiagnosis rate of CLE was 0 % in the sedated group and 27.59 % (95 % CI: 10.30–44.91 %) in the un-sedated group (P = 0.006). Conclusions: Propofol based sedation was associated with improved diagnostic value of CLE for detecting EGC as well as precancerous lesions (intraepithelial neoplasia OR intestinal metaplasia).

Ciok, J., et al. (1997). "Helicobacter pylori eradication and antral intestinal metaplasia--two years follow-up study." Journal of Physiology and Pharmacology 48 Suppl 4: 115-122.

Intestinal metaplasia (IM) appears to be an important stage in the pathogenesis of intestinal type of gastric cancer. The purpose of the study was to evaluate how H. pylori eradication modifies IM in gastric antrum. 35 patients (19 M + 16 F) with peptic ulcer (28 duodenal ulcer +7 gastric ulcer) and antral IM with accompanying H. pylori infection proven by urease test and histological examination were followed-up after healing an ulcer achieved by 14 days treatment with 40 mg/d omeprazole and 2 g/d amoxicillin. Endoscopy examination was done every 4 months during 2 years after eradication. At least two antral biopsies were taken during each endoscopy. H. pylori eradication was achieved in 23 patients (66%). No reinfection was observed during the time of observation. The medium grade of intestinal metaplasia after eradication of H. pylori declined from 1.76 to 0.57 over the period of follow-up (p < 0.01). The difference became statistically significant from the 12 months after eradication. No significant change was seen in the group of non-eradicators (1.83 at the beginning of observation and 1.91 at the end point). Statistical difference between eradicators and non-eradicators was stated from the 12th month after eradication. Total regression of intestinal metaplasia was observed in 30% cases after one year and 61% cases after two years after H. pylori eradication. The cure of H. pylori infection significantly reduces the presence of antral IM. Regression of IM appears to be a long-term process taking many months after H. pylori eradication.

Ciok, J., et al. (2006). "Regression of antral intestinal metaplasia after Helicobacter pylori eradication - Nine year follow-up study." Gastroenterologia Polska 13(4): 241-245.

Introduction: Intestinal metaplasia (IM) appears to be an important stage in the cascade of pathogenesis of intestinal type of gastric cancer. Aim of study: The purpose of the study was to evaluate how Helicobacter pylori (H.p.) eradication modifies the severity of gastritis and IM in gastric antrum in long-term (9 year) observation. Material and methods: A group of patients with ulcer disease successfully eradicated in 1994 were followed-up prospectively. In 23 cases (10 F + 13 M) antral IM was diagnosed before the eradication treatment. In this group of patients 3 and 9 years after eradication upper endoscopy was done and at least two antral biopsies were taken. Severity of gastritis and IM was graded according to Sydney classification of gastritis (scale of 0-3). Results: No reinfection of H.p. was observed during the time of observation. Total regression of IM was observed in 61% of patients 3 years after H.p. eradication and in the same 61% of pts 9 years after eradication. Mean intensity of antral IM was 1.87±0.69 at the start point, 0.65±0.93 after 3 years and 0.56±0.79 after 9 years after eradication. Statistical difference of mean value of IM between eradicators and non-eradicators was stated (p<0.001). The mean grade of antral gastritis intensity declined from 2.61±0.66 to 1.48±0.66 after 3 years and 1.35±0.50 during the time of observation. The mean grade of activity of gastritis decreased from 2.52±0.73 at the start to 1.39±0.66 after 3 years and 1.30±0.56 after 9 years. The mean grade of atrophy decreased from 2.17±0.72 at the start to 1.65±0.78 after 3 years and 1.43±0.73 after 9 years after eradication. All of these differences in comparison to the results obtained before eradication were statistically significant. Conclusions: In the group of patients with antral intestinal metaplasia during long-term observation (9 years) after successful H.p. eradication in part of the cases (61%) total regression of antral IM was seen and in the remaining patients no progression of IM was observed. Stable reduction of antral gastritis was achieved. Copyright © 2006 Cornetis.

Coker, O. O., et al. (2019). "Microbial compositional and ecological dysbiosis in gastric carcinogenesis." Digestion 99(1): 108.

Introduction: Gut microbiota dysbiosis is associated with gastrointestinal diseases. We aimed to characterize microbial compositional and ecological changes associated with progressive histological stages of gastric tumorigenesis. Methods: We performed 16S rRNA gene analysis of gastric mucosal samples from 81 cases including superficial gastritis (SG), atrophic gastritis (AG), intestinal metaplasia (IM) and gastric cancer (GC) from Xi'an, China, to determine mucosal microbiome dysbiosis across stages of GC. We validated the results in mucosal samples of 126 cases from Inner Mongolia, China. Result: We observed significant mucosa microbial dysbiosis in IM and GC subjects, with significant enrichment of 21 and depletion of 10 bacterial taxa in GC compared to SG (q < 0.05). Microbial network analysis showed increasing correlation strengths among them with disease progression (p < 0.001). Five GC-enriched bacterial taxa whose species identifications correspond to Peptostreptococcus stomatis, Streptococcus anginosus, Parvimonas micra, Slackia exigua and Dialister pneumosintes had significant centralities in the GC ecological network (p < 0.05) and classified GC from SG with an area under the receiver-operating curve (AUC) of 0.82. Moreover, stronger interactions among gastric microbes were observed in Helicobacter pylori-negative samples compared to H. pylori-positive samples in SG and IM. Metagenomics functional prediction showed that nucleotide metabolism, peptidoglycan biosynthesis and carbohydrate digestion and absorption were significantly higher in GC microbiota, while proteins associated with host bacterial recognition were depleted. The GC-associated microbial functional changes, fold changes of selected bacteria and strengths of their interactions were successfully validated in the Inner Mongolian cohort, in which the five bacterial markers distinguished GC from SG with an AUC of 0.81. Conclusion: In addition to microbial compositional and functional changes, we identified differences in bacterial interactions across stages of gastric carcinogenesis. The significant enrichments and network centralities suggest the potentially important roles of P. stomatis, D. pneumosintes, S. exigua, P. micra and S. anginosus in GC progression.

Coker, O. O., et al. (2017). "Mucosal microbiota dysbiosis across stages of gastric carcinogenesis." Gastroenterology 152(5): S1011.

BACKGROUND & AIMS: Helicobacter pylori infection is an important risk factor for gastric cancer (GC). However, other members of gastric microbiota could also contribute to the development of GC. In this study, we aimed to determine the mucosal microbiota dysbiosis associated with GC. METHODS: A total of 205 gastric biopsy tissues from 21 superficial gastritis (SG), 23 atrophic gastritis (AG), 17 intestinal metaplasia (IM) and 20 GC subjects were obtained from Xian, China for discovery cohort analysis. Additional 126 gastric biopsy tissues from 56 SG, 51 AG and 19 GC subjects from Inner Mongolia, China were used for validation. V4 regions of 16S ribosomal rRNA genes from the samples were sequenced and analyzed using Mothur pipeline. Bacterial abundances were adjusted for age, gender, tissue position and H. pylori-status. Differentially abundant bacteria were selected using modelfree feature screening and logistic regression. SparCC algorithm was used to infer sparsitycorrected correlations and node centralities were estimated by weighted node connectivity scores. An adjusted p-value < 0.05 was considered significant. RESULTS: Significant decreases in microbial richness were observed in IM (p = 0.045) and GC (p = 0.041) compared to SG samples, indicating the association of microbiota dysbiosis with gastric carcinogenesis. Compared to SG, 21 bacteria were enriched in GC (p < 0.05) while 10 bacteria were depleted in GC (p < 0.05); the fold changes were validated in Inner Mongolian cohort (p = 0.0044). Co-occurrence and co-exclusion interactions among the 31 selected bacteria were stronger in AG than in SG (p=0.0001), in IM than in SG (p=1.08 x 10-12) and in GC than in IM (p < 1.00 x 10-16), AG (p < 1.00 x 10-16) and SG (p < 1.00 x 10-16). A subset of five GCenriched bacteria, namely Peptostreptococcus stomatis, Streptococcus anginosus, Parvimonas micra, Slackia exigua and Dialister pneumosintes had significant node centralities in the GC microbial interaction network (p = 0.00038, 0.012, 0.029, 0.0046, 0.038 respectively). These five markers could distinguish GC from SG with areas under the receiver-operating curve (AUC) of 0.82 in Xian cohort; which was validated in Inner Mongolian cohort with AUC of 0.81. All five bacteria are members of oral pathogenic taxa. Furthermore, the association of H. pylori infection with microbiota alterations was evaluated. We observed significantly weaker interactions among the 31 bacteria in H. pylori-positive samples compared to -negative samples in SG (p = 0.013) and IM (p = 2.46 × 10-9), but not in AG and GC. CONCLUSIONS: Mucosal dysbiosis was identified across stages of gastric carcinogenesis. The significant enrichments and centralities of P. stomatis, D. pneumosintes, S. exigua, P. micra and S. anginosus might play roles in the development of gastric cancer. (Figure presented).

Coker, O. O., et al. (2018). "Mucosal microbiome dysbiosis in gastric carcinogenesis." Gut 67(6): 1024-1032.

OBJECTIVES: We aimed to characterise the microbial changes associated with histological stages of gastric tumourigenesis. DESIGN: We performed 16S rRNA gene analysis of gastric mucosal samples from 81 cases including superficial gastritis (SG), atrophic gastritis (AG), intestinal metaplasia (IM) and gastric cancer (GC) from Xi'an, China, to determine mucosal microbiome dysbiosis across stages of GC. We validated the results in mucosal samples of 126 cases from Inner Mongolia, China. RESULTS: We observed significant mucosa microbial dysbiosis in IM and GC subjects, with significant enrichment of 21 and depletion of 10 bacterial taxa in GC compared with SG (q<0.05). Microbial network analysis showed increasing correlation strengths among them with disease progression (p<0.001). Five GC-enriched bacterial taxa whose species identifications correspond to Peptostreptococcus stomatis, Streptococcus anginosus, Parvimonas micra, Slackia exigua and Dialister pneumosintes had significant centralities in the GC ecological network (p<0.05) and classified GC from SG with an area under the receiver-operating curve (AUC) of 0.82. Moreover, stronger interactions among gastric microbes were observed in Helicobacter pylori-negative samples compared with H. pylori-positive samples in SG and IM. The fold changes of selected bacteria, and strengths of their interactions were successfully validated in the Inner Mongolian cohort, in which the five bacterial markers distinguished GC from SG with an AUC of 0.81. CONCLUSIONS: In addition to microbial compositional changes, we identified differences in bacterial interactions across stages of gastric carcinogenesis. The significant enrichments and network centralities suggest potentially important roles of P. stomatis, D. pneumosintes, S. exigua, P. micra and S. anginosus in GC progression.

Compare, D., et al. (2011). "Global DNA hypomethylation is an early event in Helicobacter pylori-related gastric carcinogenesis." Journal of Clinical Pathology 64(8): 677-682.

AIM: Cancer, particularly gastric cancer (GC), is prevalently an epigenetic phenomenon that is dependent on an altered DNA methylation pattern. In gastric carcinogenesis, many genes show aberrant methylation; however, none of them may be used as a biomarker of cancer risk and progression. The authors aimed to evaluate the global DNA methylation of gastric mucosa in Helicobacter pylori (Hp)-related chronic gastritis, in GC and in 10 patients with preneoplastic lesions (ie, atrophy and intestinal metaplasia) followed up for 10 years. METHODS: The authors analysed 93 dyspeptic patients who underwent upper endoscopy, 41 surgical GC samples and 10 patients with preneoplastic gastric lesions followed up for 10 years after successful Hp eradication therapy. Global DNA methylation status and surrogate markers of cell proliferation and apoptosis were evaluated by immunohistochemistry using the anti-5-methylcytosine (5-MC), anti-Ki-67 and anti-p53 (anti-apoptotic marker)-specific antibodies, respectively. RESULTS: Global DNA methylation of gastric mucosa gradually decreased from normal mucosa to Hp-positive gastritis, Hp-positive chronic atrophic gastritis, independent of Cag-A status and GC; however, the variation was significant (p<0.05) only between Hp-negative subjects and Hp-positive chronic gastritis. Interestingly, the 5-MC immunostaining was absent in areas of intestinal metaplasia. In the 10 patients with preneoplastic lesions, global DNA methylation decreased over time despite the eradication of Hp infection, but reached significance only at 10 years versus baseline. The 5-MC immunostaining negatively correlated with Ki-67 and p53 expression in all groups. CONCLUSION: Global DNA hypomethylation is an early molecular event in Hp-related gastric carcinogenesis. Further studies with more cases and a longer follow-up are needed to establish the potential GC predictive role of DNA hypomethylation.

Compare, D., et al. (2010). "Risk factors in gastric cancer." European Review for Medical and Pharmacological Sciences 14(4): 302-308.

STATE OF THE ART: Gastric cancer (GC) is still a major health problem worldwide due to its frequency, poor prognosis and limited treatment options. At present prevention is likely to be the most effective means of reducing the incidence and mortality from this disease. The most important etiological factors implicated in gastric carcinogenesis are diet and Helicobacter pylori (H. pylori) infection. High intake of salted, pickled or smoked foods, as well as dried fish and meat and refined carbohydrates significantly increased the risk of developing GC while fibers, fresh vegetables and fruit were found to be inversely associated with GC risk. Epidemiological investigations (retrospective, case-control and prospective) and several meta-analyses have demonstrated that concurrent or previous H. pylori infection is associated with an increased risk of GC in respect to uninfected people. H. pylori colonizes gastric mucosa where it induces a complex inflammatory and immune reaction that on time leads to a severe mucosal damage i.e., atrophy, intestinal metaplasia (IM) and dysplasia. The risk of GC is closely related to the grade and extension of gastric atrophy, IM and dysplasia. PERSPECTIVES AND CONCLUSIONS: Today a plausible program for GC prevention means: (1) a correct dietary habit since childhood increasing vegetables and fruit intake, (2) a decrease of H. pylori spread improving family and community sanitation and hygiene, (3) a search and treat H. pylori strategy in offspring of GC, (4) a search and treat H. pylori strategy in patients with chronic atrophic gastritis and intestinal metaplasia (IM), (5) a careful endoscopic and histologic follow-up if precancerous lesions persist irrespective of H. pylori eradication.

Correa, P., et al. (1990). "Gastric precancerous process in a high risk population: cohort follow-up." Cancer Research 50(15): 4737-4740.

In an attempt to characterize the natural history of the gastric precancerous process, 1422 residents of a high risk area of Nariño, Columbia, have been followed from 3-16 years (average 5.1) with repeated gastric biopsies, for a total of 7290 person-years. The original cohort consisted of 1788 individuals yielding a successful completion rate of 79.5%. Comparison of initial and subsequent biopsies revealed a very complex dynamic flow of both progressive and regressive events, suggesting sporadic environmental forces of modulation. One-time measurement of gastric juice, pH, and nitrite failed to predict future events in the gastric mucosa. The net loss of individuals whose gastric mucosa initially showed normal histology or superficial gastritis was 3.3%/year, representing a net gain of 1.7% for chronic atrophic gastritis, 0.9% for intestinal metaplasia, and 0.7% for dysplasia. The incidence rate of gastric cancer in this population was 0.16/100 person-years. The net rates of progression were higher and those of regression lower in older compared to younger individuals. The general pattern detected is that of a slow forward movement in the previously described hierarchical organization of precursor lesions. The presence of progressive as well as regressive changes and the slow pace of change offer special opportunities to inhibit progression through intervention strategies targeting previously identified etiological factors. The difficulties and opportunities offered by the long term follow-up studies as well as the congruency of the findings with current etiological hypotheses are discussed.

Correa, P., et al. (1990). "Gastric precancerous process in a high risk population: cross-sectional studies." Cancer Research 50(15): 4731-4736.

The gastric precancerous process is evaluated in 1788 participants in a gastroscopy survey in the population of Nariño, Colombia, which has one of the highest gastric cancer incidence rates on record. A detailed histological classification is used, and a hierarchical distribution of lesions is described with the main stages being gland neck hyperplasia, atrophy (gland loss), intestinal metaplasia and dysplasia. Acute inflammation was not found to be a specific stage in the sequence but rather a common finding in all stages of the precancerous spectrum. Indices of disease progression for the different steps are calculated and found to increase with gastric pH and nitrate and nitrite content of the gastric juice. The effects of high pH and nitrite content are intimately correlated. Relative risks of specific lesions, namely, hyperplasia, atrophy, metaplasia, and dysplasia, increase linearly with higher pH, nitrate, and nitrite values in the gastric juice. The severity of atrophy correlates with the prevalence of metaplasia, suggesting a sequential relationship between the described stages, a finding supported by all parameters examined. The model of progression described may serve as a basis for comparisons with populations at different levels of gastric cancer risk but it fails to provide information concerning the time required for each change, which should be provided by follow-up (cohort) studies.

Cortés, P., et al. (2017). "Magnifying image-enhanced endoscopy for diagnosis of gastric atrophy and H. pylori infection in a amerindian population with a high-risk of gastric cancer." Gastrointestinal Endoscopy 85(5): AB446.

To improve detection of early gastric cancer (GC), patients with premalignant lesions should be identified on every diagnostic upper GI endoscopy (UGIE) (opportunistic screening) and included in a follow-up endoscopic program. Diagnostic performance of white-light endoscopy (WLE) to detect gastric atrophy (GA), intestinal metaplasia (IM) and H. pylori (Hp) infection has been disappointing in the West and histological assessment is recommended, which adds cost and risks to the standard UGIE. We aim to evaluate the diagnostic performance of Image-Enhanced Magnifying Endoscopy (IEE) in a selected population with high GC risk. Methods: To reduce the waiting list for UGIE in a rural region of central-southern Chile, with predominantly native Amerindian population (Mapuche) and high GC risk, 40 endoscopists, nurses and technicians performed 715 UGIE in 5 weeks. The aim was to detect GC and to identify patients with gastric premalignant lesions, deserving endoscopic follow-up. Gastric biopsies were obtained according to the updated Sydney Protocol and patients categorized according to the Operative Link for Gastric Assessment (OLGA) system. A proportion of the studies (n = 139) were performed with magnifying high-resolution endoscopes with blue laser imaging (BLI) (Fujifilm EG-L590 ZW). Supraangular gastric mucosa was probed with IEE and classified according to modified Yagi classification (Kawamura et al. J Gastroenterol Hepatol 2011;26:477-483) as B=0 (normal), B=1-3 (suggestive of Hp gastritis) or A=1-2 (suggestive of MI or GA). Because most endoscopists had no previous experience with IEE, one training session was assembled at the beginning of the operation to teach them the basic principles and Yagi classification. Diagnostic performance of WLE and IEE was compared with OLGA system for detection of GA, and IEE was compared to histology and/or rapid urease test (RUT) for detection of Hp infection. Results: 139 patients, with a mean age of 57,2 years, and Female in 71% were included. Histology detected some grade of GA in 71% (OLGA 0: 29%; I-II 51%; III-IV 20%). WLE suggested GA in 25% and IEE in 32% (p<0.05 against histology). Diagnostic performance of IEE compared to histology is shown in the table. Conclusion: Histology confirmed a high prevalence of GA in this high-risk population. WLE markedly subdiagnoses GA, supporting the recommendation to perform gastric biopsies even in apparently normal UGIE in high-risk population. IEE is promising, because evaluating only corpus mucosa is able to detect most cases of Hp infection and severe GA (OLGA III-IV), but low specificity undermine severely its diagnostic accuracy. Better training on the method and/or refinement of endoscopic diagnoses to include antral mucosa might improve these results. (Table presented).

Courillon-Mallet, A. (2014). "[Follow-up of patients after Helicobacter pylori eradication]." Revue du Praticien 64(2): 211-214.

After Helicobacter pylori eradication, the risk of new contamination in adulthood is very low and there is no need for further microbiological surveillance. Helicobacter pylori infection induces alteration of the gastric mucosa, beginning with chronic active gastritis and leading to atrophy, intestinal metaplasia and dysplasia. Chronic active gastritis disappears completely a few months after bacterial eradication while atrophy, intestinal metaplasia or dysplasia remain. Mucosal atrophy and intestinal metaplasia confer a high risk for the development of gastric cancer. The risk of cancer occurring on these premalignant lesions depends on their extension, topography and severity. So their diagnosis and grading is important for cancer prevention and implies that antral and fundic biopsies are systematically done even on endoscopically normal mucosa. Low grade atrophy or intestinal metaplasia limited to the antrum do not require further surveillance. For high grade or fundic lesions reassessment of endoscopic and histologic lesions is recommended every three years. Dysplasia should undergo specialized management.

Crespi, M., et al. (1978). "Results and prospectives of a mass-screening for gastric cancer and precancerous lesions of the stomach." Acta Endoscopica 8(2): 73-85.

Selection and follow-up of 'high-risk' population groups must be considered as the first step in cancer control. A project for mass-screening for gastric cancer has been in process since 1968 by the Gastroenterology Unit of the Regina Elena Institute for Cancer Research. For the stomach, chronic gastritis with atrophic changes and intestinal metaplasia have shown a statistically significant association with cancer and represent, from a biological viewpoint, an almost mandatory step in carcinogenesis. 26.712 asymptomatic subjects were tested for stomach acidity in our Unit by simple laboratory examinations, and 4.432 who evidenced impaired acid secretions were submitted to blind abrasive gastric cytology by a special retractable nylon brush. Following the special parameters used for cytology, 709 of these subjects were classified as 'high-risk'. Endoscopic examinations performed on this latter group permitted us to show a very significant gastric pathology in comparison with the control group, including 8 cases of early gastric cancer, and one 'in situ' carcinoma. Besides this, the clinical, radiological and endoscopical examinations performed on a population group of symptomatic subjects allowed us to diagnose 80 gastric cancers, 28 gastric ulcers, 15 cases of polyposis and 3 cases of Menetriere's disease. The kind of mass-screening that we perform, clearly appears to give valuable results for early diagnosis of gastric cancer and for selection of 'high-risk' subjects.

De Idiáquez, D., et al. (1999). "[HELICOBACTER PYLORI INFECTION ERRADICATION IN DISPEPTIC PATIENTS WITH AND WITHOUT PEPTIC ULCER]." Revista de Gastroenterología del Perú 19(3): 179-194.

BACKGROUND: Helicobacter pylori (HP) infection is very prevalent worldwide, and has been associated with the presence of duodenal ulcer, gastric ulcer and chronic active gastritis. It is also speculated that HP may have a role in gastric cancer development. Triple drug schemes have been shown to be the most effective approach to erradicate HP infection. Nevetheless, high rates of resistance against some antibiotics as well as high costs affect the effectiveness of these therapies. The goal of the present study is to assess the effectiveness of the combination of tetracycline, furazolidone and bismuth in erradicating HP, as well as the changes in the histology.METHODS: Patients with diagnosis of HP infection, found in their antral gastric biopsies (hematoxylin and eosin staining (H-E)), were included. They received the following scheme for 10 days: tetracycline 500 mg qid., furazolidone 100 mg qid., and colloidal bismuth subcitrate 120 mg qid. Patients were instructed to come back for follow-up 6 to 8 weeks after starting the therapy. At that time a control upper endoscopy was performed and 3 antral biopsies were taken. Biopsies were stained with H-E and read by experienced pathologists. In both, the biopsy before treatment and the control biopsy, the following parameters were looked for: presence and density of HP; presence, depth and grade of chronic gastritis (lymphoplasmocytic infiltrate); presence and grade of inflammatory activity (polymorphonuclear inflitrate); presence of glandular atrophy; presence, grade (partial or total) and extent (focal or multifocal) of mucinous damage (epithelial damage); presence of intestinal metaplasia; and presence of lymphoid follicles.RESULTS: Fifty-nine patients (30 men and 29 women) completed per protocol. Mean age was 43 +/- 18 (range: 14-73). HP erradication was achieved in 54 patients (91.5%). Control biopsies showed improvement in the following parameters: presence and density of HP (p<0.001); presence, depth and grade of chronic gastritis (p<0.001); presence and grade of inflammatory activity (p<0.001); presence, grade and extent of mucinous damage (p<0.001); and presence of lymphoid follicles (p<0.001). Neither the presence of glandular atrophy nor the presence of intestinal metaplasia showed any significant change. Patients who did not erradicate HP showed no significant difference in any of the parameters.CONCLUSIONS: The triple drug scheme including tetracycline, furazolidone and bismuth is effective in HP erradication. Erradication of HP is followed by an improvement in the following histologic parameters: presence, depth and grade of chronic gastritis (LMN infiltrate); presence and grade of inflammatory activity (PMN infiltrate); presence, grade and extent of mucinous damage; and presence of lymphoid follicles. This scheme is a cost-effective alternative for the therapy of HP infection in low income populations with a high prevalence of infection with this bacteria.

De Martel, C., et al. (2010). "Comparison of polymerase chain reaction and histopathology for the detection of Helicobacter pylori in gastric biopsies." International Journal of Cancer 126(8): 1992-1996.

Using data from a Venezuelan cohort of 1,948 adults, the gastric detection of Helicobacter pylori (H. pylori) by polymerase chain reaction (PCR) of the vacA gene in 1 antral biopsy was compared to the detection of H. pylori by hlstopathotogy (hematoxylln-eosin and Giemsa staining) in 5 biopsies (antrum and corpus). Overall, H. pylori was detected in 85% and 95% of the subjects by PCR and hlstopathology, respectively. When results were analyzed by severity of precancerous lesions, PCR on 1 biopsy detected the bacteria less often than hlstopathology on 5 biopsies in subjects with normal gastric mucosa and non-atrophlc gastritis. However, in subjects with the most severe lesions (intestinal metaplasia type III and dysplasia), PCR on 1 biopsy detected H. pylori as often as hlstopathology on 5 biopsies, and significantly more often than hlstopathology on a single biopsy. In conclusion, these findings confirm that hlstopathology on 5 biopsies is an accurate tool for H. pylori detection in most subjects, compared to the PCR method on 1 biopsy. Nevertheless, the elevated sensitivity of PCR for detecting the bacteria In advanced precancerous lesions, and the possibility to use PCR to distinguish between cagA-positlve and cagA-negative strains, makes the PCR technique especially useful in studies of stomach cancer. © 2009 UICC.

de Vries, A. C., et al. (2009). "The use of clinical, histologic, and serologic parameters to predict the intragastric extent of intestinal metaplasia: a recommendation for routine practice." Gastrointestinal Endoscopy 70(1): 18-25.

BACKGROUND: Surveillance of intestinal metaplasia (IM) of the gastric mucosa should be limited to patients at high risk of gastric cancer. Patients with extensive IM are at increased cancer risk; however, the intragastric extent of IM is usually unknown at the time of the initial diagnosis. OBJECTIVE: To assess the predictive value of clinical, histologic, and serologic parameters for the intragastric extent of IM. DESIGN AND SETTING: Prospective, multicenter study. PATIENTS: Eighty-eight patients with a previous diagnosis of IM of the gastric mucosa. INTERVENTION: Surveillance gastroscopy with extensive random biopsy sampling. MAIN OUTCOME MEASUREMENTS: Biopsy specimens were evaluated according to the Sydney classification system. In addition, serologic testing of Helicobacter pylori and cagA status, pepsinogens I and II, gastrin, and intrinsic factor antibodies was performed. The association between the available parameters and extensive IM was evaluated with logistic regression analysis. RESULTS: In 51 patients (58%), IM was present in the biopsy specimens from at least 2 intragastric locations. The most important predictors of extensive IM were a family history of gastric cancer, alcohol use > or = 1 unit/d (1 glass, approximately 10 mL or 8 g ethanol), moderate or marked IM of the index biopsy specimen, and a pepsinogen I to II ratio < 3.0. A simple risk score based on these factors could identify extensive IM in 24 of 25 patients (sensitivity 96%). LIMITATION: A prospective cohort study should confirm the proposed risk stratification. CONCLUSIONS: A risk score of clinical, histologic, and serologic parameters can predict extensive intragastric IM and may serve as a practical tool to select patients for surveillance endoscopy in routine clinical practice.

de Vries, A. C., et al. (2007). "The detection, surveillance and treatment of premalignant gastric lesions related to Helicobacter pylori infection." Helicobacter 12(1): 1-15.

Gastric cancer is an important worldwide health problem and causes considerable morbidity and mortality. It represents the second leading cause of cancer-related death worldwide. A cascade of recognizable precursor lesions precedes most distal gastric carcinomas. In this multistep model of gastric carcinogenesis, Helicobacter pylori causes chronic active inflammation of the gastric mucosa, which slowly progresses through the premalignant stages of atrophic gastritis, intestinal metaplasia and dysplasia to gastric carcinoma. Detection and treatment of premalignant lesions may thus provide a basis for gastric cancer prevention. However, at present, premalignant changes of the gastric mucosa are frequently disregarded in clinical practice or result in widely varying follow-up frequency or treatment. This review provides an overview of current knowledge on detection, surveillance and treatment of patients with premalignant gastric lesions, and identifies the uncertainties that require further research.

De Vries, A. C., et al. (2012). "Cochrane review: Helicobacter pylori eradication for pre-malignant lesions of the gastric mucosa." Gastroenterology 142(5): S633.

Background: Helicobacter pylori infection is a major risk factor for gastric cancer development. However, the effect of eradication for prevention of gastric cancer is still controversial, in particular in patients with pre-malignant gastric lesions. This systematic literature Cochrane review was performed to assess the effect of H. pylori eradication therapy on different stages of pre-malignant lesions of the gastric mucosa, i.e. atrophic gastritis, intestinal metaplasia and dysplasia. Methods: Randomized controlled trials comparing H. pylori eradication therapy with placebo or symptomatic treatment in patients with pre-malignant gastric lesions were included. The trials were identified through electronic searches of the Cochrane Library, MEDLINE and EMBASE databases, using appropriate subject headings and keywords. Data were collected on histological changes of the gastric mucosa and functional parameters of gastric mucosal condition. Results: Nineteen randomized controlled trials were included, with a total of 5.087 patients (range 20 to 1.630 patients per study). These trials compared H. pylori eradication therapy (n=2.604) with placebo or no treatment (n=1.764), or acid suppressive therapy (n=719). The effect of H. pylori eradication on gastric mucosal changes was evaluated after 8 weeks to 12 years follow-up (2 studies with follow-up ≤ 3 months; 7 studies ≤ 12 months; 5 studies ≤ 2 years; 5 studies 3 to 9 years). In 17 studies details on the effect of H. pylori eradication on atrophic gastritis were reported, of these 10 studies demonstrated less progression or even regression of atrophic gastritis (total n= 2.237; followup range 1 to 9 years), whereas 7 studies reported no beneficial effect (total n= 904; followup range 8 weeks to 1 year). Fourteen studies reported on the effect on intestinal metaplasia, of these four studies showed significant less progression (total n= 1.119; follow-up range 1 to 6 years), however, this finding was not confirmed by the reports of ten studies (total n= 1.822; follow-up range 1 to 9 years). The effect on the progression of dysplasia was only reported in three trials, one study showed a significant reduction of the progression of dysplasia after 9 years follow-up in a study population of 567 patients, whereas two studies showed no significant effect after 5 and 6 years of follow-up in a total of 824 patients. Since outcome measures varied between studies using non-interchangeable parameters, quantification of outcomes was not performed. Conclusion: Clinical evidence for the prevention of carcinogenic progression in patients with atrophic gastritis is highly suggestive, whereas the evidence in patients with intestinal metaplasia and dysplasia is conflicting. Therefore, H. pylori eradication may be insufficient to halt gastric carcinogenesis in patients with intestinal metaplasia and dysplasia.

De Vries, A. C., et al. (2009). "Helicobacter pylori eradication and gastric cancer: When is the horse out of the barn." American Journal of Gastroenterology 104(6): 1342-1345.

Helicobacter pylori infection is a major risk factor for gastric cancer development. Therefore, H. pylori eradication may be an important approach in the prevention of gastric cancer. However, long-term data proving the efficacy of this approach are lacking. This report describes two patients who developed gastric cancer at, respectively, 4 and 14 years after H. pylori eradication therapy. These patients were included in a study cohort of H. pylori-infected subjects who received anti-H. pylori therapy during the early years of development of H. pylori eradication therapy and underwent strict endoscopic follow-up for several years. In both patients, gastric ulcer disease and premalignant gastric lesions, i.e., intestinal metaplasia at baseline and dysplasia during follow-up, were diagnosed before gastric cancer development. These case reports demonstrate that H. pylori eradication does not prevent gastric cancer development in all infected patients after long-term follow-up. In patients with premalignant gastric lesions, in particular in patients with a history of gastric ulcer disease, adequate endoscopic follow-up is essential for early detection of gastric neoplasia. © 2009 by the American College of Gastroenterology.

De Vries, A. C., et al. (2007). "Epidemiological trends of pre-malignant gastric lesions: A long-term nationwide study in the Netherlands." Gut 56(12): 1665-1670.

Background: The pre-malignant gastric lesions atrophic gastritis (AG), intestinal metaplasia (IM) and dysplasia (DYS) have long been identified as principal risk factors for gastric cancer. Objective: To evaluate epidemiological time trends of pre-malignant gastric lesions in the Netherlands. Methods: Patients with a first diagnosis of AG, IM or DYS between 1991 and 2005 were identified in the Dutch nationwide histopathology registry. The number of new diagnoses per year were evaluated relative to the total number of patients with a first gastric biopsy. Time trends were evaluated with age-period-cohort models using logistic regression analysis. Results: In total, 23 278 patients were newly diagnosed with AG, 65 937 patients with IM, and 8517 patients with DYS. The incidence of AG declined similarly in men and women with 8.2% per year [95% CI 7.9% to 8.6%], and DYS with 8.1% per year [95% CI 7.5% to 8.6%]. The proportional number of new IM cases declined with 2.9% per year [95% CI 2.7% to 3.1%] in men and 2.4% [95% CI 2.2% to 2.6%] in women. With age-period-cohort models a cohort phenomenon was demonstrated for all categories of pre-malignant gastric lesions in men and in women with IM and DYS. Period phenomena with a larger decline in number of diagnoses after 1996 were also demonstrated for AG and IM. Conclusions: The incidence of pre-malignant gastric lesions is declining. Period and cohort phenomena were demonstrated for diagnoses of AG and IM. These findings imply that a further decrease of at least 24% in the incidence of gastric cancer in the coming decade may be anticipated in Western countries without specific intervention.

de Vries, A. C., et al. (2008). "Gastric Cancer Risk in Patients With Premalignant Gastric Lesions: A Nationwide Cohort Study in the Netherlands." Gastroenterology 134(4): 945-952.

Background & Aims: A cascade of precursor lesions (eg, atrophic gastritis, intestinal metaplasia, and dysplasia) precedes most gastric adenocarcinomas. Quantification of gastric cancer risk in patients with premalignant gastric lesions is unclear, however. Consequently, endoscopic surveillance is controversial, especially in Western populations. Methods: To analyze current surveillance practice and gastric cancer risk in patients with premalignant gastric lesions, all patients with a first diagnosis between 1991 and 2004 were identified in the Dutch nationwide histopathology registry (PALGA); follow-up data were evaluated until December 2005. Results: In total, 22,365 (24%) patients were diagnosed with atrophic gastritis, 61,707 (67%) with intestinal metaplasia, 7616 (8%) with mild-to-moderate dysplasia, and 562 (0.6%) with severe dysplasia. Patients with a diagnosis of atrophic gastritis, intestinal metaplasia, or mild-to-moderate dysplasia received re-evaluation in 26%, 28%, and 38% of cases, respectively, compared with 61% after a diagnosis of severe dysplasia (P < .001). The annual incidence of gastric cancer was 0.1% for patients with atrophic gastritis, 0.25% for intestinal metaplasia, 0.6% for mild-to-moderate dysplasia, and 6% for severe dysplasia within 5 years after diagnosis. Risk factors for gastric cancer development were increasing severity of premalignant gastric lesions at initial diagnosis (eg, severe dysplasia, hazard ratio 40.14, 95% confidence interval 32.2-50.1), increased age (eg, 75-84 years, hazard ratio 3.75, 95% confidence interval 2.8-5.1), and male gender (hazard ratio 1.50, 95% CI 1.3-1.7). Conclusions: Patients with premalignant gastric lesions are at considerable risk of gastric cancer. As current surveillance of these patients is inconsistent with their cancer risk, development of guidelines is indicated. © 2008 AGA Institute.

Delchier, J. C. (2014). "[Natural history of gastric cancer linked to Helicobacter pylori]." Revue du Praticien 64(2): 195-198.

Gastric carcinogenesis is related to inflammatory reaction induced by Helicobacter pylori infection. Infection is involved in pathogenesis of both histological types of gastric cancer, intestinal or diffuse. In the first type, cancer is the last step of successive alterations of the gastric mucosa (atrophy, intestinal metaplasia, dysplasia). In the second type, cancer occurs faster due to chromosomic alterations related to oxidative stress. Inflammation and consequently cancer risk are modulated by bacterial virulence and by the immunologica responsiveness of the host. Helicobacter pylori eradication should be proposed to high risk patients: first degree relatives of patients having gastric cancer, patients with preneoplastic lesions. Cancer prevention is more effective when eradication is performed before occurrence of preneoplastic lesions. When preneoplastic lesions are present, eradication decreases but not suppresses the risk of cancer. Therefore periodic follow up with gastroscopy and biopsies should be planned in these patients.

Den Hoed, C. M., et al. (2010). "Premalignant gastric lesions in patients with gastric MALT and diffuse large B-cell lymphoma and metachronous gastric carcinoma: A case-control study." Gastroenterology 138(5): S442.

Background: Patients with low grade gastric MALT lymphoma (gMALT) and diffuse large B-cell lymphoma (DLBCL), formerly high grade gastric MALT lymphoma, have an increased risk of developing gastric carcinoma (GC). Identifying gMALT and DLBCL patients at high GC risk may allow early endoscopic intervention, and thus lead to an improved survival and prognosis. The strength of the association with premalignant gastric lesions, as well as their progression rate are however unknown. Aim: To evaluate whether premalignant gastric lesions (PM): atrophic gastritis (AG), intestinal metaplasia (IM) and dysplasia (DYS), can be identified in gMALT or DLBCL patients and whether these lesions are more severe in gMALT or DLBCL patients with a subsequent diagnosis of GC. Methods: Patients with a first diagnosis of gMALT or DLBCL between 1991 and 2006 were identified in a nationwide histopathology registry (PALGA). Cases were patients with a diagnosis of gMALT or DLBCL and a subsequent diagnosis of GC. Controls, without a diagnosis of GC during follow-up (FU), were matched to cases by age and years of FU. The histopathology was evaluated by an expert GI pathologist who was blinded for the case/control status. AG and IM were scored according to the updated Sydney classification, DYS according to the revised Vienna Classification. Results: 8 cases (M/F 3/5) and 31 controls (M/F 19/12) with a mean age of 60 yrs (18-86 yrs) were included. 6 cases (M/F 3/3) demonstrated gMALT and 2 cases (M/F 0/2) DLBCL. 26 controls were diagnosed with gMALT (M/F 16/10) and 5 (M/F 3/2) with DLBCL. In the cases with gMALT GC developed within 6.2 yrs, the controls had a mean FU of 5.2 yrs. For DLBCL patients GC developed after a mean period of 3.6 yrs, the controls had a mean FU of 5.7 yrs. In cases gMALT/DLBCL 75% demonstrated PM; 1 AG, 3 IM, and 2 DYS as most severe diagnosis. 67% of the controls demonstrated PM; 7 AG, 11 IM and 3 DYS (p=0.638). 10 controls with gMALT/DLBCL (32%) demonstrated progression of PM after a mean Fu of 5.3 years. Conclusions: The majority of patients with gastric MALT lymphoma also have premalignant gastric lesions (in particular atrophic gastritis and intestinal metaplasia). Given this high prevalence, there are no specific parameters which enable early differentiation between those who are likely to progress to cancer, and those who do not. The prevalence of severe PM (DYS) is high in both groups of patients, warranting careful surveillance of PM in gMALT and DLBCL patients to avoid gastric cancer development.

Den Hoed, C. M., et al. (2010). "Premalignant gastric lesions in patients with gastric MALT lymphoma and metachronous gastric carcinoma: A case-control study." Helicobacter 15(4): 385.

Patients with low grade gastric MALT lymphoma (gMALT) and diffuse large B-cell lymphoma (DLBCL), have an increased risk of developing gastric carcinoma (GC). Identifying gMALT/ DLBCL patients at high GC risk may allow early endoscopic intervention; lead to improved survival and prognosis. Can we identify premalignant gastric lesions (PM): atrophic gastritis (AG), intestinal metaplasia (IM) and dysplasia (DYS), in gMALT/DLBCL patients and demonstrate whether these lesions are more severe in gMALT/DLBCL patients with subsequent GC? Patients with a first diagnosis of gMALT/DLBCL 1991-2006 in a nationwide histopathology registry (PALGA); Cases: patients with a diagnosis of gMALT/DLBCL and subsequent GC. Controls: no GC during follow-up (FU), matched by age and FU. Histopathology evaluated by a pathologist, blinded for case/ control status. 8 cases (M/F 3/5) and 31 controls (M/F 19/12), mean age 60 yrs (18-86 yrs).Cases with gMALT developed GC within 6.2 yrs, controls had a mean FU of 5.2 yrs. DLBCL patients GC after a mean of 3.6 yrs, controls had a mean FU of 5.7 yrs. Cases gMALT/DLBCL 75% PM; 1 AG, 3 IM, and 2 DYS as most severe diagnosis. 67% of controls PM; 7 AG, 11 IM and 3 DYS (p = 0.638). 10 controls (32%) demonstrated progression of PM after a mean of 5.3 years. The majority of patients with gMALT have premalignant gastric lesions. No specific parameters which enable early identification of those likely to progress to cancer. The prevalence of severe PM (DYS) is high in both groups of patients, warranting careful surveillance of PM in gMALT/DLBCL patients.

Den Hoed, C. M., et al. (2010). "Prevalence of premalignant changes in the stomach of patients undergoing routine colonoscopy; A cohort study." Helicobacter 15(4): 321.

H. pylori (Hp) initiates the pathway of gastric carcinogenesis which follows from gastritis through atrophic gastritis (AG), to intestinal metaplasia (IM), dysplasia (DYS) and malignancy. The presence of these lesions in the general population is a predictor for gastric cancer incidence in the coming decades. Most subjects with Hp infection and premalignant gastric lesions are asymptomatic. Prevalence data are mostly obtained from endoscopy data in symptomatic patients or serology. Therefore a need exists for histological prevalence data in asymptomatic subjects. 383 patients, (F/M: 192 /191; mean age 53.1; range 17-86) undergoing routine, colonoscopy, underwent esophagogastroduodenoscopy prior to colonoscopy. Biopsies were taken from the antrum and corpus and visible abnormalities. Hp infection was present in 22%, ranging from 14% in subjects <40 to 33% in subjects >50 yrs. Non-Caucasian subjects had a higher rate of Hp infection 54% vs. 22% (p < 0.001). AG and IM and DYS were found in 9.3% of subjects; 0.8% had AG, 7.1% IM and 1.4% had DYS. Subjects with Hp infection or AG, IM or DYS were significantly older than subjects with normal gastric mucosa; mean age 53.1 yrs in normal gastric mucosa vs 56.1 yrs in Hp (p = 0.025), mean age 60 yrs in AG, IM or DYS (p = 0.03). No association was found between gender, GI symptoms, lifestyle and medication use between subjects with or without premalignant gastric lesions or Hp. There is a considerable prevalence of premalignant gastric lesions in asymptomatic subjects. This means that gastric cancer will remain a prevalent disease in western countries.

den Hoed, C. M., et al. (2013). "Follow-up of premalignant lesions in patients at risk for progression to gastric cancer." Endoscopy 45(4): 249-256.

BACKGROUND AND STUDY AIMS: A recent international guideline recommends surveillance of premalignant gastric lesions for patients at risk of progression to gastric cancer. The aim of this study was to identify the role of the distribution and severity of premalignant lesions in risk categorization. PATIENTS AND METHODS: Patients with a previous diagnosis of atrophic gastritis, intestinal metaplasia, or low grade dysplasia were invited for surveillance endoscopy with non-targeted biopsy sampling. Biopsy specimens were evaluated by pathologists (four general and one expert) using the Sydney and the operative link for gastric intestinal metaplasia (OLGIM) systems, and scores were compared using kappa statistics. RESULTS: 140 patients were included. In 37 % (95 % confidence interval [CI] 29 % - 45 %) the severity of premalignant lesions was less than at baseline, while 6 % (95 %CI 2 % - 10 %) showed progression to more severe lesions. Intestinal metaplasia in the corpus was most likely to progress to more than one location (57 %; 95 %CI 36 % - 76 %). The proportion of patients with multilocated premalignant lesions increased from 24 % at baseline to 31 % at surveillance (P = 0.014). Intestinal metaplasia was the premalignant lesion most frequently identified in subsequent endoscopies. Intestinal metaplasia regressed in 27 % compared with 44 % for atrophic gastritis and 100 % for low grade dysplasia. Interobserver agreement was excellent for intestinal metaplasia (k = 0.81), moderate for dysplasia (k = 0.42), and poor for atrophic gastritis (k < 0). CONCLUSIONS: Premalignant gastric lesions found in the corpus have the highest risk of progression, especially intestinal metaplasia, which has excellent interobserver agreement. This supports the importance of intestinal metaplasia as marker for follow-up in patients with premalignant gastric lesions.

Den Hoed, C. M., et al. (2012). "The topography, severity and extent of premalignant lesions in patients at risk for progression to gastric cancer." Gastroenterology 142(5): S427-S428.

Background: Recent international guidelines (Endoscopy 2012; in press) recommend surveillance of premalignant gastric lesions for patients at risk of progression to gastric cancer. However, clear risk categorization systems are lacking. The severity and extent as well as the localization of the premalignant lesions (PM) likely give an indication of the risk of progression to cancer. Aim: To study the role of the distribution and severity of premalignant lesions in risk categorization. Methods: Patients with a previous diagnosis of atrophic gastritis (AG), intestinal metaplasia (IM) or low grade dysplasia (LGD) within the past 6 years were invited for surveillance endoscopy with extensive random biopsy sampling of antrum and corpus. Biopsy specimens were evaluated by a local and an expert pathologist and scored using the Sydney system and the OLGIM score (GI endoscopy 2010). The association with risk factors was evaluated with logistic regression analysis. Results: 140 Patients were included (M/F: 72/68, mean age 63.0 yrs, range 31.8-81.3). At baseline 8% of patients were diagnosed with AG, 76% with IM and 16% with LGD. 59% had PM in the antrum only, 16% in the corpus only and 24% had PM in more than one location. In 37% (95%CI: 29-45%) the severity of PMs was less than at baseline, while 6% (95%CI: 2-10%) showed progression to more severe lesions. Most lesions were localized in the antrum (47%). Lesions in the corpus were most likely to extend to more than one location (57%; 95%CI: 36-76%), this increase was significantly higher (p 0.014) than the increase of intragastric extent found in patients with only IM in the antrum or angulus at inclusion (22.9%; 95%CI: 13.9-31.9%). The proportion of patients with multi-located PM increased from 24.% at baseline to 44% at surveillance (p 0.014). Using the OLGIM classification, 19% of patients scored grade III to IV. No correlations could be found between sex, PPI or NSAID use, interval between baseline and surveillance endoscopy, and progression or regression of the severity and extent or OLGIM score. Current or past Hp infection was identified in 46% and was correlated with a more severe PM at surveillance (R2 0.166 p 0.05). IM was the PM mostly identified in subsequent endoscopies (Regression in 27% vs 44% in AG and 100% in LGD). Conclusion: Premalignant gastric lesions found in the corpus have the highest risk of progression during surveillance. Past or current Hp infection is correlated with progression of extent and severity of PM. This study demonstrates the importance of IM as marker for follow-up instead of AG or LGD.

Den Hoed, C. M., et al. (2010). "Prevalence of premalignant changes in the stomach of patients undergoing routine colonoscopy: A cohort study." Gastroenterology 138(5): S728.

Background: Gastric cancer is the 4th most common cancer and 2nd leading cause of cancerrelated mortality worldwide. There is a cascade of gastric mucosal changes in the pathway of gastric carcinogenesis. Helicobacter pylori(Hp) initiates the cascade which follows from gastritis through atrophic gastritis(AG), intestinal metaplasia(IM), dysplasia(DYS) to malignancy. The presence of these lesions in the general population is a predictor for gastric cancer incidence in the coming two decades. Most subjects with Hp infection and premalignant gastric lesions are asymptomatic and prevalence data are mostly obtained from serological studies with limited sensivity and specificity and from endoscopy data in symptomatic patients. A need exists for histological prevalence data in asymptomatic subjects. Aims: Investigate the age-related prevalence of Hp infection and its related gastric changes in asymptomatic subjects. Methods: 383 patients (F/M: 192/191; mean age 53.1; 17-86 yrs) undergoing routine, non-urgent colonoscopy were included. Patients with informed consent and IRB approval underwent upper GI endoscopy prior to colonoscopy and completed the Gastrointestinal Symptom Rating Scale (GSRS). Biopsies were taken from the antrum (n=2) and corpus (n=2) and scored for Hp, IM and AG and DYS. Additional biopsies were taken of any visible abnormality or lesion. Results: Hp infection was present in 22% (95%CI 18- 26%) of subjects. This prevalence ranged from 14% in subjects <40 to 28% in subjects >50 yrs. Non-Caucasian subjects had a significantly higher rate of Hp infection 54% vs 22% (p <0.001). AG, IM, and DYS were found in 8.9% of subjects; 0.2% had AG, 7,2% IM and 1.4% had DYS as most severe lesion. Subjects with Hp gastritis, AG, IM or DYS were significantly older than subjects with normal gastric mucosa; mean age 53.1 yrs in normal mucosa vs 56.1 yrs in Hp gastritis (p=0.025), and mean age 60 yrs in subjects with AG, IM or DYS (p=0.003). The more severe the gastric lesion observed, the more significant the age association p= 0.025 in Hp infection, p=0.03 in AG and p=0.002 in IM and DYS, respectively. No association was demonstrated between gender, presence and severity of GI symptoms as scored by GSRS, lifestyle and medication use between subjects with or without premalignant gastric lesions or Hp infection. Conclusions: The prevalence of premaligant gastric lesions, particularly intestinal metaplasia, is considerable in a general Western population. In most subjects, this is not associated with specific upper gastrointestinal symptoms. Our findings imply that gastric cancer will remain a prevalent disease in Western countries for the coming 2 decades.

den Hollander, W. J., et al. (2019). "Surveillance of premalignant gastric lesions: a multicentre prospective cohort study from low incidence regions." Gut 68(4): 585-593.

OBJECTIVE: International guidelines recommend endoscopic surveillance of premalignant gastric lesions. However, the diagnostic yield and preventive effect require further study. We therefore aimed to assess the incidence of neoplastic progression and to assess the ability of various tests to identify patients most at risk for progression. DESIGN: Patients from the Netherlands and Norway with a previous diagnosis of atrophic gastritis (AG), intestinal metaplasia (IM) or dysplasia were offered endoscopic surveillance. All histological specimens were assessed according to the updated Sydney classification and the operative link on gastric intestinal metaplasia (OLGIM) system. In addition, we measured serum pepsinogens (PG) and gastrin-17. RESULTS: 279 (mean age 57.9 years, SD 11.4, male/female 137/142) patients were included and underwent at least one surveillance endoscopy during follow-up. The mean follow-up time was 57 months (SD 36). Four subjects (1.4%) were diagnosed with high-grade adenoma/dysplasia or invasive neoplasia (ie, gastric cancer) during follow-up. Two of these patients were successfully treated with endoscopic submucosal dissection, while the other two underwent a total gastrectomy. Compared with patients with extended AG/IM (PGI/II≤3 and/or OGLIM stage III-IV), patients with limited AG/IM (PG I/II>3 and OLGIM stage 0-II) did not develop high-grade adenoma/dysplasia or invasive neoplasia during follow-up (p=0.02). CONCLUSION: In a low gastric cancer incidence area, a surveillance programme can detect gastric cancer at an early curable stage with an overall risk of neoplastic progression of 0.3% per year. Use of serological markers in endoscopic surveillance programmes may improve risk stratification.

Deng, J., et al. (2017). "Prognostic value of the cancer oncogene Kelch-like 6 in gastric cancer." British Journal of Surgery 104(13): 1847-1856.

BACKGROUND: Kelch-like 6 (KLHL6) is a cancer oncogene previously associated with specific human cancers, such as chronic lymphocytic leukaemia. Here, the mechanisms of KLHL6 function were explored in gastric cancer (GC) cells, in an in vivo experimental tumour model, and the prognostic value of KLHL6 analysis in GC tissue evaluated in a cohort of patients with GC. METHODS: Associations between clinicopathological and survival data and KLHL6 expression in GC tissues were analysed. The effects of downregulation of KLHL6 in GC cells was investigated using proliferation, invasion, apoptosis and lymphangiogenesis assays, and analysis of tumour growth in an in vivo experimental model. RESULTS: KLHL6 was upregulated in 43 per cent of GC tissues compared with 5 per cent of paired non-tumour tissues from 84 patients. KLHL6 protein expression in GC tissues was much higher than that in atrophic gastritis, intestinal metaplasia and dysplasia tissues from benign gastric disease samples. KLHL6 expression was positively related to the intestinal Laurén classification in GC tissues. Downregulated expression of KLHL6 in MGC-803 GC cells reduced colony formation, proliferation, viability, migration and invasion, enhanced apoptosis and inhibited the cell cycle in the G1 phase. Downregulated expression of KLHL6 also suppressed tumour growth in mice. Furthermore, downregulated expression of KLHL6 mRNA reduced the expression of nuclear-associated antigen Ki-67, vascular endothelial growth factor C, hepatocyte growth factor and matrix metalloproteinase 2 in vitro, and KLHL6 protein in tumour tissue of mice. CONCLUSION: Abnormal expression of the KLHL6 oncogene promoted GC progression in vitro and in vivo, and its expression level in tumour tissue was found to be of prognostic value.

Dhingra, R., et al. (2020). "Increased Risk of Progression to Gastric Adenocarcinoma in Patients with Non-dysplastic Gastric Intestinal Metaplasia Versus a Control Population." Digestive Diseases and Sciences 65(11): 3316-3323.

AIM: In previous studies, the 5-year progression rate of gastric intestinal metaplasia to gastric adenocarcinoma has varied substantially. We investigated the incidence rate of dysplasia and gastric adenocarcinoma and the rate of progression among a cohort of patients with non-dysplastic gastric intestinal metaplasia. METHODS: This is a single-center, single-cohort retrospective study. Patients who had undergone an EGD with biopsies from 01/01/1993 to 12/31/2013 were included. The primary outcome of interest was the composite of low-grade dysplasia, high-grade dysplasia, or adenocarcinoma. Time to progression and risk factor subgroup analyses were performed. RESULTS: A total of 1628 subjects were screened, of whom 358 met the inclusion criteria. A total of 21 first-time events were recorded. The annual incidence rate of low-grade dysplasia was 2.1 (95% CI 1.3-3.5) cases per 1000 person-years, 0.5 (95% 0.2-1.3) per 1000 person-years for high-grade dysplasia, and 0.8 (95% CI 0.3-1.6) cases per 1000 person-years for gastric adenocarcinoma. The historical control group had an annual adenocarcinoma incidence rate of 0.07 per 1000 person-years. The event rate in Asians was also noted to be significantly higher between years 0-8 as compared with patients of non-Asian race, and extensive intestinal metaplasia was an independent risk factor (HR = 4.06 (95% CI 1.45-11.34), p = 0.007). CONCLUSIONS: Patients with non-dysplastic gastric intestinal metaplasia may progress to dysplasia and gastric adenocarcinoma. The incidence rate of gastric adenocarcinoma is higher than that of the historical control population (0.07 per 1000 person-years). The presence of extensive intestinal metaplasia was a risk factor for progression of disease. Triennial EGD may be warranted in patients with non-dysplastic gastric intestinal metaplasia.

Dhingra, R., et al. (2017). "Assessing the rate of progression of non-dysplastic gastric intestinal metaplasia in a high-risk population." Gastrointestinal Endoscopy 85(5): AB75.

Background: Gastric cancer is a major cause of cancer-related mortality in the world and results in over 10,000 deaths per year in the United States (US). Risk factors such as family history, smoking, high salt intake, and Helicobacter pylori (HP) infection have been well established. Atrophic gastritis, gastric intestinal metaplasia (GIM), and dysplasia are known precursor lesions to gastric adenocarcinoma (ADCA). The rate of progression to ADCA, however, is not known, and no surveillance guidelines exist in the US. The aim of this study is to determine the rate of progression of GIM to LGD, HGD, and ADCA in an urban, predominantly Asian American population. Methods: We conducted a retrospective review of patients 18 years and older at a tertiary academic medical center who underwent an upper endoscopy with biopsies and were diagnosed with non-dysplastic GIM of the corpus, antrum, or both. Cases with dysplasia and/or ADCA at the time of the index procedure were excluded, as were patients with no repeat endoscopy. Subjects were followed until the development of an event, defined as LGD, HGD, ADCA, or date of last endoscopy. Age, gender, ethnicity, HP status, smoking status, family history of gastric ADCA, presence of concurrent Barrett's esophagus, presence of mucosal atrophy, mean number of endoscopies performed, and the location of the GIM were collected. Proportions and means were used to describe the demographic and clinical characteristics of the participants. Mean length of follow-up and time to progression were calculated in months. A Kaplan-Meier plot was used to estimate the percentage of patients with an event at 12, 36, and 60 months. Results: 116 patients were included, of which 51.7% were male. The mean age was 58.4 years (± SD 12.5), and the racial breakdown was as follows: 59.5% Asian, 29.3% Caucasian, 6.0% Black, and 5.2% Hispanic. HP infection was found in 34.5%, 46.6% were current or former smokers, 19.8% had concurrent Barrett's esophagus, 15.5% had a positive family history for gastric ADCA, and mucosal atrophy was present in 30.2%. GIM was discovered in the antrum in 79.3%, in the corpus in 5.2%, and in both locations in 15.5%. Mean follow-up and number of upper endoscopies were 53.0 months and 4, respectively. 14 patients experienced an event. There were 10 cases of LGD, 1 case of HGD, and 3 cases of ADCA. Mean time to progression to LGD was 23.9 months, one case progressed to HGD in 24.0 months, and progression to ADCA was seen in a mean of 69.7 months. 5.6% of patients experienced an event at 12 months (95% CI 2.6-12.1%), 13.0% at 36 months (95% CI 7.2-22.7%), and 16.9% (95% CI 9.9-28.0%) at 60 months. Conclusion: There is significant risk of progression of non-dysplastic GIM in this high-risk population. A surveillance interval of 36 months is reasonable given that over 10% of subjects experienced an event in that time period. (Figure Presented).

Dias, A., et al. (2011). "Gastric juice prostaglandins and peptide growth factors as potential markers of chronic atrophic gastritis, intestinal metaplasia and gastric cancer: their potential clinical implications based on this pilot study." Digestive Diseases and Sciences 56(11): 3220-3225.

BACKGROUND: Gastric secretion can provide valuable information especially when Helicobacter pylori (Hp) infection results in chronic atrophic gastritis (CAG) and intestinal metaplasia (IM) preceding adenocarcinoma (AdCa). AIMS: Looking for a potential biomarker of malignant transformation in the setting of chronic inflammation we studied the levels of prostaglandin E2 (PGE(2)), as well as peptide growth factors [epidermal growth factor (EGF) and transforming growth factor α (TGFα)], harbingers of injury and repair, in gastric juice aspirated at endoscopy from patients with CAG, CAG/IM, AdCa, and controls. METHODS: The PGE(2), EGF and TGFα concentrations in the gastric juice were measured using radioimmunoassays (RIAs). RESULTS: In patients with AdCa gastric juice PGE(2) increased fivefold versus controls (P < 0.01) and almost threefold versus patients with CAG (P < 0.05). The EGF levels in patients with AdCa were fourfold higher versus controls (P < 0.001) and almost threefold higher versus CAG (P < 0.05). In patients with CAG/IM the EGF levels were also almost 3 times higher versus controls. The TGFα levels in patients with AdCa were half the value of controls and CAG (P < 0.05). In patients with CAG/IM the levels were as low as 1/5 of controls or CAG (P < 0.05). CONCLUSIONS: Testing the gastric juice for PGE(2), EGF, and TGFα in patients with endoscopy and biopsy proven CAG, may be helpful in follow up of patients who may potentially progress to IM and ultimately AdCa. This could be considered as an adjunct to histologic assessment especially that even the best surveillance biopsy specimen regimens are inherited with sampling errors.

Diffalha, S. A. L., et al. (2016). "Cd133 protein expression as a biomarker for early detection of gastric cancer." Gastroenterology 150(4): S874-S875.

Background: Gastric cancer remains the second most common cause of cancer deaths worldwide, yet specific biomarkers for early detection remain elusive. The present work proposes CD133 as a marker for disease progression in gastric cancer. We hypothesize that CD133+ expression may increase during the progression from normal gastric mucosa to metaplasia, dysplasia and carcinoma. Design: Using gastric samples from a cohort of 111 patients we measure variations in CD133 expression from normal gastric mucosa (NM) to inflammation/intestinal metaplasia (IM) to dysplasia (DS) and finally gastric adenocarcinoma (GCA). Samples were divided as follows: 21 NM, 26 IM, 19 DS and 45 GCA. All cases were stained for CD133 using the Ventana automated immunostainer Discovery XT (Ventana, Tucson, AZ). Scoring was conducted using the Allred scoring system featuring a proportion score and an intensity score to give a total score between 0 and 8. Results: A significant increase in CD133 expression was observed during all three progression stages. From NM to IM total positivity score increased 54%(P value:0.001), from IM to DS this increase was 38% (P value:2.2E07) and from DS to GCA 15%(P value:1.8E09)(Fig 1) Conclusion: CD133 expression may represent a biomarker for early detection of gastric cancer. (Figure presented).

Dilaghi, E., et al. (2018). "In atrophic gastritis 3-years endoscopic surveillance according to maps (management of precancerous conditions and lesions in the stomach) guidelines seems satisfactory to early detect potential neoplastic lesions." United European Gastroenterology Journal 6(8): A107.

Introduction: Atrophic gastritis (AG) is associated with gastric cancer (GC) and type I gastric carcinoid (TIGC). Current European MAPS guidelines (1), recommend for AG patients with extensive atrophy and/or intestinal metaplasia endoscopic follow-up every 3-years after diagnosis. OLGA/OLGIM (operative link on gastric atrophy/metaplasia) assessment was proposed for staging of gastritis and stratifying neoplastic risk (2,3). Prospective studies evaluating whether 3- years follow-up interval is appropriate in terms of early detection of gastric neoplastic lesions are lacking. Aims and Methods: This study aimed to evaluate the occurrence of gastric neoplastic and preneoplastic lesions and changes of OLGA/OLGIM scores in AG patients at 3-years endoscopic-histological follow-up. A total of 80 consecutive, newly diagnosed AG patients (77.5% F, median age 64.5 (29-87) years) followed-up 3 years after diagnosis were included. Each patient underwent gastroscopy with biopsies (Sydney System) at baseline and at 3-years follow-up. Among them, 25 (31.1%) were cured from H. pylori. At baseline OLGA scores 0, I, II, III, IV were observed in 0, 9 (11.3%), 58 (72.5%), 10 (12.5%), 3 (3.7%) patients, respectively; OLGIM scores 0, I, II, III, IV were observed in 11 (13.8%), 22 (27.5%), 43 (53.7%), 4 (5%), 0 patients, respectively. Extensive atrophy/intestinal metaplasia was present in 21 (26.3%) patients. At baseline 7 (8.7%) patients presented polypoid neoplastic lesions, all removed by snare polypectomy: 3 low-grade dysplasia (LGD) adenomas and 4 TIGC. The number of gastroscopies needed to be performed (NNS) to detect 1 case of gastric neoplastic lesion was expressed as the number of 3-years surveillance endoscopies by the number of detected neoplastic lesions. Results: At 3-years follow-up overall 6 (7.5%) neoplastic lesions were detected: 2 (2.5%) LGD adenomas in 2 patients, 4 (5%) carcinoids in 4 patients (in 2 of them recurrent), no GC. The NNS was 13.3. OLGA and OLGIM scores were unchanged, increased and decreased in 58 (72.5%) and 49 (61.2%), 9 (11.3%) and 15 (18.8%), and 13 (16.2%) and 16 (20%) patients, respectively. The occurrence of gastric neoplastic lesions in patients with or without extensive atrophy/intestinal metaplasia was not different (p=0.943 by chi-square test). When only the 21 (26.3%) patients with extensive atrophy/intestinal metaplasia at baseline would have been considered eligible for surveillance, at 3-years followup only 1 LGD adenoma would have been detected, as the other neoplastic lesions 4 TIGC and the other LGD adenoma occurred in patients without extensive atrophy/intestinal metaplasia at baseline. Conclusion: In AG patients, the 3-years endoscopic surveillance as proposed by MAPS seems satisfactory to early detect potential gastric neoplastic lesions. An increase of OLGA/OLGIM scores is observed in a low proportion of patients (10% and 18%). Extensive atrophy/intestinal metaplasia as eligibility criteria to offer surveillance in AG patients may be restrictive.

Dinis-Ribeiro, M., et al. (2003). "Magnification chromoendoscopy for the diagnosis of gastric intestinal metaplasia and dysplasia." Gastrointestinal Endoscopy 57(4): 498-504.

BACKGROUND: The aim of this study was to define the reproducibility and accuracy of magnification chromoendoscopy for the diagnosis of lesions associated with gastric cancer (intestinal metaplasia and dysplasia). METHODS: A total of 136 patients with previously diagnosed lesions and 5 gastrectomy specimens were studied. Endoscopic examination was performed with a magnification endoscope after methylene blue (1%) spraying. According to differences in color and mucosal pattern, groups and subgroups of endoscopic images were defined, and biopsies taken (n = 462). Five endoscopists were asked to classify individually 2 endoscopic images per subgroup on 2 separate occasions. RESULTS: Three groups of endoscopic images were defined: nonmetaplastic, nondysplastic mucosa (I); metaplastic mucosa (II); and dysplastic mucosa (III). Ten subgroups were defined according to pit pattern: round small (IA), round and tubular small (IB), coarse round (IC), and course round pits with a straight pit (ID); blue irregular marks (IIA), blue round and tubular pits (IIB), blue villi (IIC), and blue small pits (IID); and loss of clear pattern, with depression (IIIA) or with slight elevation (IIIB). The kappa statistic for intraobserver agreement on the classification of endoscopic images in groups was 0.86; for interobserver agreement, it was 0.74. For classification into subgroups, kappa values ranged from 0.48 to 0.78. For 85% of the areas classified endoscopically as Group I (n = 146), no mucosal lesions or gastritis was described at histologic examination; for 83% of those in Group II (n = 198), intestinal metaplasia was found. Subgroups IIA and IIB were more often associated with complete intestinal metaplasia (62%), and IIC and IID with incomplete metaplasia (67%); in Group III (n = 118), dysplasia was diagnosed histopathologically in 33%. For the diagnosis of dysplasia, specificity was 81% (95% CI [77%, 85%]) and negative predictive value 99% (95% CI [99%, 100%]). CONCLUSIONS: Gastric endoscopic patterns with chromoendoscopy and magnification seem reproducible and valid for the diagnosis of lesions associated with gastric cancer. This procedure may improve the follow-up of individuals at high-risk of gastric cancer, at least for the exclusion of severe lesions.

Dinis-Ribeiro, M., et al. (2007). "Feasibility and cost-effectiveness of using magnification chromoendoscopy and pepsinogen serum levels for the follow-up of patients with atrophic chronic gastritis and intestinal metaplasia." Journal of Gastroenterology and Hepatology 22(10): 1594-1604.

BACKGROUND: The follow-up of patients with atrophic chronic gastritis or intestinal metaplasia may lead to early diagnosis of gastric cancer. However, to-date no cost-effective model has been proposed. Improved endoscopic examination using magnification chromoendoscopy together with non-invasive functional assessment with pepsinogen serum levels are accurate in the diagnosis of intestinal metaplasia (extension) and minute dysplastic lesions. The aim of this study was to assess the feasibility and cost-effectiveness of a follow-up model for patients with atrophic chronic gastritis and intestinal metaplasia based on gastric mucosal status using magnification chromoendoscopy and pepsinogen. METHODS: A cohort of patients with lesions as severe as atrophic chronic gastritis were followed-up according to a standardized protocol using magnification chromoendoscopy with methylene blue and measurement of serum pepsinogen I and II levels. A single node decision tree and Markov chain modeling were used to define cost-effectiveness of this follow-up model versus its absence. Transition rates were considered time-independent and calculated using primary data following cohort data analysis. Costs, quality of life and survival were estimated based on published data and extensive sensitivity analysis was performed. RESULTS: A total of 100 patients were successfully followed-up over 3 years. Seven cases of dysplasia were diagnosed during follow-up, all among patients with incomplete intestinal metaplasia at baseline, six of whom had extensive (pepsinogen I to II ratio <3) incomplete intestinal metaplasia. For those individuals with atrophic chronic gastritis or complete intestinal metaplasia, a yearly measurement of pepsinogen levels or an endoscopic examination on a 3-yearly basis would cost 455 euros per quality-adjusted life year (QALY) gain. Endoscopic examination and pepsinogen serum level measurement on a yearly basis would cost 1868 euros per QALY for patients with extensive intestinal metaplasia. CONCLUSIONS: The follow-up of patients with atrophic chronic gastritis or intestinal metaplasia is both feasible and cost-effective if improved accurate endoscopic examination of gastric mucosa together with non-invasive assessment of gastric mucosal status are used to identify individuals at high-risk for development of gastric cancer.

Dittmar, Y., et al. (2016). "[Extended Pathohistological Criteria for Assessment of the Long-Term Prognosis of Gastric Cancer]." Zentralblatt für Chirurgie 141(4): 433-441.

BACKGROUND: Gastric cancer is one of the most frequent tumour diseases worldwide. Despite numerous innovations in the diagnostic procedures and treatment the prognosis remains poor as the detection of the disease depends on tumour-associated symptoms which develop rather late in the majority of cases. The treatment outcomes may be improved by a more differentiated and individualised evaluation of the tumour biology. We present a detailed analysis of potentially relevant factors. MATERIAL AND METHODS: From 1995 to 2011, data from 923 patients with gastric cancer have been collected in a prospective tumour database. We performed monovariate and multivariate analyses of factors. For the statistical analyses, SPSS software version 19.0 was used. The literature research was performed with Medline. RESULTS: 748 patients underwent surgical exploration. The resection rate was 87 % with a morbidity and mortality of 27 and 9 % (2004 to 2001: 13 and 5 %), respectively. 36 and 29 % of patients survived 5 years or 10 years, respectively. The 5-year and 10-year survival after curative resection was 58 and 46 %, respectively. TNM-associated criteria, tumour size, histological growth pattern, intestinal metaplasia, location of the tumour and classification according to Lauren were of significant influence in the monovariate analyses. In the multivariate analysis, tumour size, curative resection and lymph node involvement were independent prognostic factors. 90 % of the tumour recurrences developed within five years. The median recurrence-free interval was 16 months. Depending on the type of tumour, different survival times were identified. The 228 patients with node-negative curatively resected gastric cancer had a markedly better long-term prognosis. Diffuse type according to Lauren, tumour size, non-tubular histological growth pattern, female sex and proof of serosa infiltration from the primary tumour were prognostic factors in the monovariate analysis. In the multivariate analysis, tumour size was an independent significant prognostic factor (p = 0.05). CONCLUSION: The data analyses showed that the evaluation of gastric cancer may be extended in a sensitive way by factors that have not been previously established. The benefit of an individualised structured treatment and follow-up on the basis of extended criteria should be investigated in future studies.

Dittmar, Y., et al. (2017). "Extended pathohistological criteria for assessment of the long-term prognosis of gastric cancer." Tumor Diagnostik und Therapie 38(8): 515-525.

Background Gastric cancer is one of the most frequent tumour diseases worldwide. Despite numerous innovations in the diagnostic procedures and treatment the prognosis remains poor as the detection of the disease depends on tumour-associated symptoms which develop rather late in the majority of cases. The treatment outcomes may be improved by a more differentiated and individualised evaluation of the tumour biology. We present a detailed analysis of potentially relevant factors. Material and Methods From 1995 to 2011, data from 923 patients with gastric cancer have been collected in a prospective tumour database. We performed monovariate and multivariate analyses of factors. For the statistical analyses, SPSS software version 19.0 was used. The literature research was performed with Medline. Results 748 patients underwent surgical exploration. The resection rate was 87% with a morbidity and mortality of 27 and 9% (2004 to 2001: 13 and 5%), respectively. 36 and 29% of patients survived 5 years or 10 years, respectively. The 5-year and 10-year survival after curative resection was 58 and 46%, respectively. TNM-associated criteria, tumour size, histological growth pattern, intestinal metaplasia, location of the tumour and classification according to Lauren were of significant influence in the monovariate analyses. In the multivariate analysis, tumour size, curative resection and lymph node involvement were independent prognostic factors. 90% of the tumour recurrences developed within five years. The median recurrence-free interval was 16 months. Depending on the type of tumour, different survival times were identified. The 228 patients with node-negative curatively resected gastric cancer had a markedly better long-term prognosis. Diffuse type according to Lauren, tumour size, non-tubular histological growth pattern, female sex and proof of serosa infiltration from the primary tumour were prognostic factors in the monovariate analysis. In the multivariate analysis, tumour size was an independent significant prognostic factor (p=0.05). Conclusion The data analyses showed that the evaluation of gastric cancer may be extended in a sensitive way by factors that have not been previously established. The benefit of an individualised structured treatment and follow-up on the basis of extended criteria should be investigated in future studies.

Dohi, O., et al. (2019). "Blue laser imaging-bright improves the real-time detection rate of early gastric cancer: a randomized controlled study." Gastrointestinal Endoscopy 89(1): 47-57.

BACKGROUND AND AIMS: Blue laser imaging-bright (BLI-bright) has shown promise as a more useful tool for detection of early gastric cancer (EGC) than white-light imaging (WLI). However, the diagnostic performance of BLI-bright in the detection of EGC has not been investigated. We aimed to compare real-time detection rates of WLI with that of BLI-bright for EGC. METHODS: This was a prospective, randomized, controlled study in 2 Japanese academic centers. We investigated 629 patients undergoing follow-up endoscopy for atrophic gastritis with intestinal metaplasia or surveillance after endoscopic resection of EGC. Patients were randomly assigned to receive primary WLI followed by BLI-bright or primary BLI-bright followed by WLI. The real-time detection rates of EGC were compared between primary WLI and primary BLI-bright. RESULTS: There were 298 patients in each group. The real-time detection rate of EGC with primary BLI-bright was significantly greater than that with primary WLI (93.1% vs 50.0%; P = .001). Primary BLI-bright had a significantly greater ability to detect EGCs in patients with a history of endoscopic resection for EGC, no Helicobacter pylori infection in the stomach after eradication therapy, lesions with an open-type atrophic border, lesions in the lower third of the stomach, depressed-type lesions, small lesions measuring <10 mm and 10 to 20 mm in diameter, reddish lesions, well-differentiated adenocarcinomas, and lesions with a depth of invasion of T1a. CONCLUSIONS: BLI-bright has a higher real-time detection rate for EGC than WLI. BLI-bright should be performed during surveillance endoscopy in patients at high risk for EGC. (Clinical trial registration number: UMIN000011324.).

Dong, E., et al. (2019). "GASTRIC CANCER SCREENING AT 2 U.S. MEDICAL CENTERS." Gastroenterology 156(6): S-1073.

Background: Gastric cancer (GC) screening is limited in the US due to overall low incidence; it remains unclear who would benefit from screening. We conducted a pilot prospective screening program of patients with a first-degree family history of GC to evaluate the prevalence of precursor lesions such as extensive intestinal metaplasia (IM) or dysplasia on biopsy, as well as evaluate feasibility of implementation of standardized endoscopic screening protocol in a community-based setting. Methods: We conducted a prospective screening study of patients beginning in 3/2017 to present date at 2 high-volume endoscopy centers in southern California. Patients were identified through a current registry of health plan members with either a family history of GC in the electronic health record, or family history obtained through medical provider interview. Patients could also be referred through their primary care physician for screening. Patients were contacted if they were active health plan members, and at least 40 years of age, or within 10 years of age prior to diagnosis of GC in their first-degree relative. Patients with symptoms, hereditary cancer syndromes, or a personal history of GC were excluded. Patients were offered a screening upper endoscopy exam with mapping biopsy protocol. Biopsies were obtained from the lesser and greater curvatures of both body and antrum, and sampling from the incisura. All specimens were placed in separate containers. Extensive IM was defined as IM detected in two or more regions of the stomach. Those with IM or dysplasia were notified, and these patients were then placed on a follow-up schedule for surveillance exams based on their pathology. Results: 43 patients completed a screening upper endoscopy with mapping biopsy protocol. Average age was 59.7 years at time of screening exam with 23 (53.4%) females. Non- Hispanic Asians comprised 27 (62.8%) patients of the screening cohort, followed by Hispanics with 11 (25.6%), and non-Hispanic whites with 5 (11.6%). Nine (21%) patients had a history of H. pylori infection, all 9 (100%) were treated. Nine (21%) patients had smoking history, with 14 (32.6%) reporting alcohol history. With our mapping biopsy protocol, 19 (44.2%) patients were found with gastric IM, with 16 (37.2%) cases of extensive IM and 3 (7%) cases of focal IM. One (2.3%) case of low-grade dysplasia was detected. All patients were willing to participate in continued surveillance. There were no adverse events in performing the upper endoscopy exams. Mapping protocol was found feasible to be implemented in a standard upper endoscopy procedure. Conclusion: From our pilot prospective screening program, prevalence of gastric intestinal metaplasia was 44%, with dysplasia prevalence of 2.3%. Endoscopic screening appears safe and feasible for detection of potential precursor lesions at baseline.

Dong, E. and B. U. Wu (2017). "Prevalence of intestinal metaplasia in patients with family history of gastric cancer living in the United States." Gastroenterology 152(5): S259.

Background Intestinal metaplasia is a precancerous lesion in the gastric cancer carcinogenesis pathway. Recent guidelines in the U.S. have recommended that patients who are at high risk for developing gastric cancer should be considered for screening. The objective of this study was to determine prevalence and characteristics of intestinal metaplasia in a crosssection of patients with family history of gastric cancer. Methods Weconducted a retrospective cross-sectional study of patients with a family history of gastric cancer (ICD-9 code V16.0) seen at a tertiary medical center in Southern California. We used manual chart review to determine whether patients underwent screening esophagogastroduodenoscopy (EGD) for a family history of gastric cancer. If biopsies were taken, pathology was reviewed to evaluate the location and extent of gastric intestinal metaplasia. Results 258 patients were determined to be high risk for gastric cancer based on reported family history. Median age was 55 years. 170 (66%) of 258 were female. Of the 258 patients, 139 (53.9%) had undergone screening endoscopy for family history of gastric cancer and other causes such as reflux disease, gastrointestinal bleeding. Of those who underwent EGD, 107 (77%) had biopsies taken during index exam. Two patients were diagnosed with gastric cancer. There were 24 (22.4%) cases of gastric intestinal metaplasia (GIM) among those biopsied identified during crosssectional analysis. Eight of 24 (33.3%) cases of GIM were extensive involvement: two or more locations of GIM found on pathology specimens. Involvement of the antrum was seen in 22 of 24 (91.7%) of GIM cases. 183 (70.9%) patients were found to need either screening EGD, repeat EGD with dedicated GIM mapping, or follow up EGD for GIM. Discussion Among patients with family history that had endoscopic biopsy obtained in routine care, the prevalence of extensive GIM was high, as was the rate of gastric cancer. Application of a standardized sampling protocol based on family history as well as other high-risk features may inform future approaches to screening for gastric cancer in low prevalence regions such as the United States.

Dougherty, M., et al. (2018). "Characteristics of Patients with Advanced Gastric Premalignant Lesions at a Southeastern U.S. Medical Center." Gastroenterology 154(6): S-512-S-513.

BACKGROUND: Gastric adenocarcinoma develops from a cascade of premalignant lesions, from atrophic gastritis (AG) to gastric intestinal metaplasia (GIM) to dysplasia and carcinoma. Surveillance of premalignant lesions in low-incidence regions is challenging, as many patients have small areas of GIM/AG on biopsies performed for symptomatic complaints, but few progress to cancer. The population of the southeastern U.S. has evolved over recent decades to one of more varied ethnic and exposure backgrounds, for which the epidemiology of gastric premalignant lesions is not well-described. Specifically, since increasing severity and extension of GIM and AG contribute to greater risk of malignant progression and may warrant surveillance (Dinis-Ribeiro 2012), an improved understanding of which patients have the severe spectrum of these lesions is needed. METHODS: We performed a descriptive epidemiological study of 261 adult patients from an academic medical center in the southeastern U.S., who had either GIM, AG, dysplasia, or adenocarcinoma on a gastric biopsy specimen between March 2014 and November 2016. The cohort was identified using our institutional pathology database, with demographic characteristics abstracted from the electronic medical record. “Advanced” premalignant lesions were defined as either AG or GIM that the pathologist specifically called “moderate,” “severe,” or “extensive.” “Limited” premaligant lesions were described as “mild,” “focal,” “minimal,” or “sparse.” Using multivariable logistic regression we examined the association of age, sex, race, ethnicity, preferred language (surrogate for non-U.S. place of birth), H. pylori infection, tobacco and alcohol use with the presence of “advanced” histology within the group of non-cancer, premalignant lesions. RESULTS: We identified 233 patients with AG or GIM, plus 28 cases of adenocarcinoma. Of the premalignant lesions, 34 were advanced. There was no association between advanced lesions and lifestyle factors, sex, race, ethnicity, or language. Increasing age was strongly associated with advanced lesions in multivariable analysis, with an age >65 years increasing the odds of an advanced premalignant lesion by 3.4 (95% CI 1.6-7.2). We did not find any signal of association with H. pylori infection, whether active, prior, or any. CONCLUSION: Increasing severity of GIM and AG is associated with increasing age but not with other gastric cancer risk factors such as tobacco and H. pylori in this U.S. population. It is possible that these other risk factors contribute more to initial development of premalignant lesions, but that progression is more of a time-dependent phenomenon mediated by yet-to-be-determined host and environmental factors. The <15% of premalignant lesions with advanced histology are the most appropriate for surveillance, so these lesions should be sought in patients >65. [Table Presented]

Draşovean, S. C., et al. (2018). "Optical biopsy strategy for the assessment of atrophic gastritis, intestinal metaplasia, and dysplasia." Romanian Journal of Morphology and Embryology 59(2): 505-512.

BACKGROUND AND AIMS: The pathogenesis of gastric cancer involves premalignant changes of the gastric mucosa. An accurate estimation of the topography and severity of these lesions represents an important step in detecting premalignant lesions, thereby classifying patients into low or high risk of developing gastric cancer. We prospectively analyzed the diagnostic performance of narrow-band imaging with magnification endoscopy (NBI-ME) for assessing premalignant gastric lesions during real-time examination. PATIENTS, MATERIALS AND METHODS: A total number of 59 patients were examined by NBI-ME and target biopsies of the antrum, corporeal, and incisura angularis levels. Modified endoscopic patterns were classified into three groups: type A [tubulo-villous mucosal pattern with regular microvessels, or the light blue crest (LBC) sign], type B [disappearance of normal subepithelial capillary network (SECN) pattern], and type C [irregular mucosal pattern (IMP) and∕or irregular vascular pattern (IVP)]. The endoscopic diagnosis was compared to histological findings (the gold standard). The NBI-ME results were assessed for accuracy, sensitivity, specificity, and negative and positive predictive values in detecting intestinal metaplasia, atrophic gastritis and dysplasia. RESULTS: Analysis of endoscopic patterns showed a good correlation with premalignant lesions (p<0.05). Type A pattern showed 80.2% accuracy, 80.43% sensitivity and 80% specificity [area under receiver operating characteristic (AUROC) of 0.8] in detecting intestinal metaplasia. Diagnostic performance for assessment of atrophic gastritis was not ideal (69.5% accuracy, 83.72% sensitivity, 56.04% specificity, AUROC 0.69). Pattern C represents a reliable endoscopic marker for the diagnosis of dysplasia (91.1% accuracy, 83.3% sensitivity, 91.81% specificity, AUROC 0.87). The extension of precancerous lesions was estimated during endoscopic examination. CONCLUSIONS: NBI-ME represents a valuable tool in the assessment of premalignant gastric lesions, thereby categorizing patients into low and high risks of developing gastric cancer. The applicability of the method in routine practice is promising, as it helps shape the follow up protocol of patients with premalignant lesions of the stomach. It is worth mentioning that, this method requires standardization, additional training, and expertise.

Duncan, D. L., et al. (2016). "Carcinoma-related mutation detected in 23% of macrodissected premalignant gastric mucosal lesions." Journal of Molecular Diagnostics 18(6): 1014-1015.

Introduction: Premalignant epithelial lesions are commonly diagnosed yet current medical practice is limited in its ability to stratify them for risk of progression to carcinoma. We cataloged the genomic mutation spectrum in lesions adjacent to invasive gastric adenocarcinoma to explore how frequently premalignant lesions shared mutation signatures in common with those found in the malignancy. Methods: Macrodissected cancers and 30 premalignant lesions from 25 gastric carcinoma patients' paraffin embedded tissue weresequenced across hotspots in 26 human cancer genes (Illumina TruSight Tumor 26 reagents on a MiSeq). Also sequenced were an additional 4 premalignant gastric lesions from 4 patients without subsequent cancer on long-term follow-up. Non-synonymous mutations and small indels at allele frequency >5% with population frequency < 1% were cataloged. Results: 24/25 invasive carcinomas had a detectable mutation (range 1 to 4 mutations per tumor) in TP53, KRAS, APC, PIK3CA, FBXW7, CDH1, SMAD4, PTEN, MSH6, MET, or ALK. All 30 dissected premalignant lesions yielded adequate read depth (>500x) for interpretation of hotspot mutations. Whereas 23 premalignant lesions had no detectable mutation, 7 (23%) had at least one mutation (range 1 to 2 mutations of TP53, APC, MET, or CDH1) that nearly always matched mutation(s) present in the adjacent invasive cancer. Average mutant allele fraction in these 7 premalignant lesions was 31 (range 8 to 53%). In two patients there was evidence of clonal evolution whereby the premalignant lesion harbored only one of two mutations detected in the carcinoma. Only 1/30 premalignant lesions had a mutation that was absent in the matched cancer, suggesting that variants in these 26 cancer-related genes may be uncommon unless the patient has cancer or cancer precursor lesions. A non-canonical NRASmutation was also identified in an intestinal metaplasia (IM) lesion from one of four IM patients who did not progress to cancer on long term follow-up. Conclusion: Successful sequencing of dissected premalignant mucosal lesions is feasible. Genomic findings reflect intrinsic biology of precursor lesions and suggest they can be clonally related to cancer tissue of the same patient. The findings promote surveillance studies to explore indicators of risk of progression to cancer and to consider potential cancer prevention strategies.

Dursun, N., et al. (2017). "Epstein Barr virus infection in gastritis with benign lymphoid infiltration." Virchows Archiv 471(1): S188.

Objective: The association of Epstein Barr virus (EBV) with gastric malignancies has been proven in many studies in the literature. However, information about EBV associated inflamation/gastritis is remains limited. Method: 119 gastritis cases with Wotherspoon Grade 2-3 inflammation but without H. Pylori were included the study. Chromogenic in situ hybridization (EBER) and immnunhistochemistry (LMP-1 antibody) were performed. The prevelance of EBV and its relationship with age, intestinal metaplasia and atrophy were analyzed. Results: 14 cases showed positive staining for EBV. EBV positivity was seen mostly in the lymphoid tissue (13 cases), but it was also detected at the gastric epithelium (7 cases). The mean age of the patients was 44, which is slightly younger than the EBV negative cases (48). Intestinal metaplasia was detected 7 % of the cases. Interestingly, EBV positive cases had higher incidence of atrophy (21 % vs 3.8 % without EBV ) . Conclusion: EBV can be detected in 12 % of the gastritis cases without H. Pylori infection. It is very close to the incidence of EBV associated gastric carcinoma (10 % in the literature). Endoscopic follow-up may be appropriate for gastritis cases which are EBV-positive.

Dutta, A. K., et al. (2013). "Narrow band imaging versus white light gastroscopy in detecting potentially premalignant gastric lesions: a randomized prospective crossover study." Indian Journal of Gastroenterology 32(1): 37‐42.

El-Zimaity, H. M. T., et al. (2001). "Gastric intestinal metaplasia: Subtypes and natural history." Journal of Clinical Pathology 54(9): 679-683.

Background - It has been suggested that the subtyping of intestinal metaplasia in the stomach is useful in stratifying patients with regard to risk of developing gastric cancer. Aim - To determine whether subtyping intestinal metaplasia provided useful information regarding the natural history of intestinal metaplasia. Methods - The study used large cup gastric biopsy specimens from predetermined locations (gastric mapping). Follow up biopsies were obtained at one, two, and/or nine years. Biopsies with intestinal metaplasia were stained with high iron diamine/Alcian blue (HID/AB) to determine whether they expressed neutral mucins, sialomucins, or sulphomucins. Results - Seventy nine patients with intestinal metaplasia were studied and characterised with regard to the most advanced subtype of intestinal metaplasia. The most severe type of intestinal metaplasia was type II in 33 patients and type III in 34 patients. Helicobacter pylori was cured in 67 patients. Follow up showed that changes in type of metaplasia (apparent regression or progression) occurred in both directions and were independent of H pylori status. For example, biopsy sites with "loss" of metaplasia at a follow up visit might have it"reappear" at a subsequent visit. During follow up, no patient developed gastric dysplasia or died from gastric cancer. Conclusion - HID subtyping did not provide useful information to the clinician or the pathologist. The data are consistent with the notion that the pattern, extent, and severity of atrophy with/without intestinal metaplasia is a far more important predictor of increased cancer risk than intestinal metaplasia subtype.

Ende, A. R., et al. (2016). "Gastric intestinal metaplasia, dysplasia, and gastric cancer in a U.S. tertiary care population-who's at risk?" Gastrointestinal Endoscopy 83(5): AB459.

Introduction: Gastric cancer is the fifth most common cancer worldwide. Although the incidence in the U.S. is low (24,950 new cases in 2015), it is actually higher than the incidence of esophageal cancer (16,980 new cases in 2015). Gastric intestinal metaplasia (GIM) is known to be a precancerous condition, analogous to Barrett's esophagus, and may increase a patient's risk of gastric cancer more than 10-fold. GIM in the U.S. has not been well studied, however, and consensus guidelines for surveillance strategies in the U.S. are lacking. In order to establish guidelines for screening and surveillance in the U.S., the risk factors for developing GIM, dysplasia, and gastric cancer in U.S. patients must be better understood. The aims of this study are to determine risk factors for GIM, dysplasia, and gastric cancer by comparing these patients to the entire cohort of patients who have had endoscopy at our institution. Methods: This was a retrospective, case-control analysis of patients with GIM, dysplasia and cancer in a large, tertiary care center between 1999 and 2014. IRB approval was obtained prior to the initiation of the study. Results: 36,799 patients hadEGD's in our system between 1999 and 2014. Of these, 2,225 (6.0%) of patients had biopsies with GIM, dysplasia or cancer. Of these 2,225 patients, 2083 (93%) had GIM, 24 (1.1%) had low-grade dysplasia, 19 (0.85%) had high-grade dysplasia and 100 (4.5%) had gastric cancer. Of the patients with GIM, 1,046 were male and 1036 were female. The mean age in this group was 60.2 compared to a mean age of 50.3 in the control group (p<.0001). The most common indication for EGD in the GIM group was abdominal pain (23%) followed by GERD/dyspepsia (19%). GIM screening or surveillance accounted for 2.7% of cases. There was a statistically significant difference in the prevalence of ethnicities in the GIM group compared to the control group (Figure 1), with Asian/Pacific Islander patients accounting for 29% of the GIM group compared to 8% of the control group (p< .0001). The odds ratios for certain ethnicities being a risk factor for GIM are presented in table 1. Asian/Pacific Islander patients also accounted for 38.2% of gastric cancers in our study. H Pylori was positive in 579 out of 2218 cases (26%). GIM surveillance was recommended in 19.7% of cases with GIM and performed in 21.2% of cases. Conclusions: Gastric intestinal metaplasia may be more common than previously recognized in certain groups of patients. In our study, there was a statistically significant difference in prevalence of ethnicities in patients with GIM compared to controls, with the most striking difference being among Asian/Pacific Islander patients. Further study is needed to evaluate the risk of progression to gastric cancer in this population. (Table presented).

Esposito, G., et al. (2017). "Preliminary results of 3 years follow-up according to maps guidelines in atrophic gastritis patients." Digestive and Liver Disease 49: e218.

Background and aim: Atrophic gastritis and intestinal metaplasia are considered to be precancerous conditions as they constitute the background in which dysplasia and intestinal-type gastric adenocarcinoma may develop. European guidelines (MAPS) recommend a scheduled 3 years surveillance for those patients who have extensive, that is both, gastric antrum and body, atrophic gastritis or intestinal metaplasia. This time interval still needs validation. The aim of the study was to assess progression of gastric histological changes at 3 years follow-up in atrophic gastritis patients. Material and methods: 29 pts (female 72.4%; median age 66, range 46-83 years; median BMI 26.4, range 20.3-41.9 m2/kg; 1st degree family history of gastric cancer 3.4%; 12 pts successfully eradicated) with previously diagnosed atrophic gastritis, consecutively followed-up for gastric neoplasia surveillance at 3 years time interval after diagnosis, were considered. During gastroscopy a standard bioptic mapping was performed and biopsies were analyzed by a dedicated pathologist who expressed a report according to operative link on gastritis assessment/operative link on intestinal metaplasia assessment (OLGA/OLGIM) classification. Pts with OLGA/OLGIM between 0 and 2 (metaplasia/atrophy only located at the body) and OLGA/OLGIM 3-4 (extensive metaplasia/atrophy) were considered as separate groups. Results: At baseline, 23 (79.3%) pts had OLGIM 0-2 (OLGIM 0, 1, 2 in 3 (13.0%), 8 (34.8%), 12 (52.2%), while 6 (20.7%) pts had OLGIM 3. At 3 years follow-up, pts with OLGIM 0 and 1 decreased to 1 (4.3%) and 4 (17.4%), those with OLGIM 2 increased to 14 (60.9%), and 4 (17.4%) pts progressed to OLGIM 3. In the OLGIM 3 group, 5 (83.3%) pts remained stable and 1 (16.7%) progressed to OLGIM 4. At baseline, 23 (79.3%) pts had OLGA 1-2 (OLGA 1 and 2 in 2 (8.7%) and 21 (91.3%), while 6 pts (20.7%) had OLGA 3. At 3 years follow-up, the 2 OLGA 1 pts remained stable, pts with OLGA 2 decreased to 17 (73.9%) and in 3 (13.0%) pts progression to OLGA 3 and 1 (4.3%) to OLGA 4 was observed. In the OLGA 3 group, 5 (83.3%) pts remained stable and 1 (16.7%) progressed to OLGA 4. No gastric adenocarcinoma, dysplasia or carcinoids were detected in the two groups. Conclusions: Endoscopic-histological surveillance at 3 years seems to be a safe time interval in atrophic gastritis pts. Progression of OLGIM scores is observed not only in the group of pts with extensive metaplasia, but also in those with corpus-restricted metaplasia.

Estevens, J., et al. (1993). "Anti-Helicobacter pylori antibodies prevalence and gastric adenocarcinoma in Portugal: report of a case-control study." European Journal of Cancer Prevention 2(5): 377-380.

Evidence from large cohort studies has established an increased risk of gastric cancer for individuals infected with Helicobacter pylori (HP). In low incidence countries, like the United Kingdom and Sweden, case-control studies suggested that the prevalence of anti-HP antibodies in gastric cancer patients (at the time of cancer diagnosis) is greater than in control populations. We present results from a case-control study of the prevalence of IgG anti-HP antibodies in gastric cancer patients and a control population in a country with a high incidence of gastric cancer. Sera were studied from 80 gastric cancer patients (GC group) admitted consecutively to our department in 1990/91, and from 80 controls (CT group) matched by age and sex. IgG anti-HP was determined by ELISA. Patients' files were reviewed for evidence of previous diagnosis of peptic ulcer, gastric surgery, tumor localization and histopathological classification. Controls were submitted to a questionnaire for past history of peptic ulcer and gastric surgery. Positive results for anti-HP were: gastric cancer patients, 70.0%; control group, 81.5% (NS). However, the median optical densities (OD, a measure of antibody concentration) were significantly lower in the gastric cancer group than in controls: gastric cancer patients, 0.720 +/- 0.424 OD; control group, 0.906 +/- 0.443 OD (P = 0.004). There were no differences concerning past history of peptic ulcer or surgery. The proportion of positives for cancer of the cardia (66.7%) was lower than for the other tumour localizations (70.4%) (NS). Anti-HP positivity was lower in patients with gastric cancer associated with intestinal metaplasia than in controls (P = 0.14).(ABSTRACT TRUNCATED AT 250 WORDS)

Euctr, E. S. (2012). "First-line eradication treatment of Helicobacter pylori infection: clinical trial without placebo, randomized, multi-center and three parallel treatment groups comparing classic triple therapy versus modified sequential therapy and other concomitant therapy." http://www.who.int/trialsearch/Trial2.aspx?TrialID=EUCTR2011-006258-99-ES.

Fang, C. (2014). "Risk factors of proximal gastric carcinoma in 438 Chinese patients." Journal of Digestive Diseases 15: 38.

Background In recent years in China, a decreasing trend in incidence of distal gastric carcinoma (DGC) is observed because of effective treatment of H. pylori (Hp) infection, in contrast to a rising incidence of proximal gastric carcinoma (PGC) with unknown mechanisms. Herein we presented epidemiologic evidence on clinical risk factors of early PGC in patients treated at a single highvolume medical center in Nanjing, China. Methods Electronic pathology records stored in Department of Pathology of Nanjing Drum Tower Hospital were retrospectively reviewed for surgical resections of early gastric cancer diagnosed with the 2010 WHO criteria over the period from January 2005 to December 2012. All patients were telephone interviewed and their clinical medical records were investigated for survival and risk factors, such as demographics, elder age (over 50 years), overweight and obesity (defined as body-mass index over 24 and 28), salty food (SF), history of exposure to industrial toxins(EIT), temperament, family history of cancer (FC), personal history of cancer (PC), HP infection, gastroesophageal reflux disease (GERD), hiatal hernia, columnar-lined esophagus, tobacco-alcohol abuse, non-steroids, fruit and vegetable intakes, hypertension, diabetes, intestinal metaplasia and atrophy, etc. which were compared between PGC and DGC with the Cox logistic regression analysis. P < 0.05 was defined as statistically significant. Results Among 438 qualified cases, 131 (30%) were PGC and the rest (307, 70%) were DGC. The average patient age were older in PGC (64.1 years) than in DGC (58.9, P = 0.402). The M/F ratio was 2.6 in PGC, slightly higher than that (2.1) of DGC. 58 (13.2%) cases are lost to follow-up. 25 cases were die of cancer. Average month after surgery of DGC is 48.3 ± 27.5, PGC is 43.2 ± 23.6. ( P = 0.814) Univariate logistic regression analyses: significant risk factors in PGC, compared to DGC, in elderly age ( P < 0.001), overweight and obesity ( P < 0.001), GERD ( P < 0.001), and EIT ( P < 0.01) but less Hp ( P < 0.001), FC ( P = 0.016), and SF ( P < 0.001); no differences in other factors. Multivariate logistic regression analyses shows that elderly age (OR = 11.907, P < 0.001), overweight (OR = 8.166, P = 0.012), obesity (OR = 8.037, P = 0.025), GERD (OR = 1.840, P = 0.044) and EIT (OR = 2.645, P < 0.001) are independent risk factor (IRF) for PGC; SF (OR = 2.697, P < 0.001), HP (OR = 3.327, P < 0.001), and FC (OR = 2.485, P < 0.01), are IRF for DGC. Cox regression analysis shows that PC (OR = 3.474, P = 0.028) was poor prognostic risk factors for DGC. In contrast, No Epidemiological Risk Factor is related to survival prediction. And the survival rate has no difference between early PGC and early DGC. Conclusion In Chinese patients, elderly age, GERD, obesity, and EIT were significant risk factors for PGC, while Hp, FC, and SF were risk factors for DGC, which has significant difference with PGC. The results support the classification of PGC as a separate gastric cancer entity.

Fann, J. C. Y., et al. (2018). "Personalized risk assessment for dynamic transition of gastric neoplasms." Journal of Biomedical Science 25(1).

Background: To develop an individually-tailored dynamic risk assessment model following a multistep, multifactorial process of the Correa's gastric cancer model. Methods: First, we estimated the state-to-state transition rates following Correa's five-step carcinogenic model and assessed the effect of risk factors, including Helicobacter pylori infection, history of upper gastrointestinal disease, lifestyle, and dietary habits, on the step-by-step transition rates using data from a high-risk population in Matsu Islands, Taiwan. Second, we incorporated information on the gastric cancer carcinogenesis affected by genomic risk factors (including inherited susceptibility and irreversible genomic changes) based on literature to generate a genetic and epigenetic risk assessment model by using a simulated cohort identical to the Matsu population. The combination of conventional and genomic risk factors enables us to develop the personalized transition risk scores and composite scores. Results: The state-by-state transition rates per year were 0.0053, 0.7523, 0.1750, and 0.0121 per year from normal mucosa to chronic active gastritis, chronic active gastritis to atrophic gastritis, atrophic gastritis to intestinal metaplasia, and intestinal metaplasia to gastric cancer, respectively. Compared with the median risk group, the most risky decile had a 5.22-fold risk of developing gastric cancer, and the least risky decile around one-twelfth of the risk. The median 10-year risk for gastric cancer incidence was 0.77%. The median lifetime risk for gastric cancer incidence was 5.43%. By decile, the 10-year risk ranged from 0.06 to 4.04% and the lifetime risk ranged from 0.42 to 21.04%. Conclusions: We demonstrate how to develop a personalized dynamic risk assessment model with the underpinning of Correa's cascade to stratify the population according to their risk for progression to gastric cancer. Such a risk assessment model not only facilitates the development of an individually-tailored preventive strategy with treatment for H. pylori infection and endoscopic screening but also provides short-term and long-term indicators to evaluate the program effectiveness.

Fedeli, G., et al. (1990). "Increased prevalence of intestinal metaplasia in the gastric mucosa of the elderly: clinical implications." Annali Italiani di Medicina Interna 5(1): 26-30.

Evidence which suggests a close relationship between intestinal-type gastric carcinoma (IGC) and intestinal metaplasia (IM) associated with chronic atrophic gastritis (CAG) has accumulated in the literature. The aim of this study has been to analyze retrospectively the prevalence of IM in patients with bioptically-proven chronic gastritis, as well as its age-specific distribution. A series of 230 patients, comprising 162 cases of CAG with IM (70.5%) and 68 cases of gastritis without IM (29.5%-57 superficial type, 11 CAG) was reviewed. All patients underwent upper gastrointestinal endoscopy one or more times, during which multiple biopsies were taken from the gastric mucosa. Moreover, patients were divided into two age-groups: over and under 65 years old. Three features were also investigated: location, endoscopic appearance and clinical manifestations. In agreement with other Authors, our findings showed: 1) predominance of the antral location (B-type gastritis); 2) a close relationship between prevalence of IM and increasing age, with an upward age-related trend. A statistically significant difference was noted between patients with IM and those without the lesion, emerging in the VII decade, with a further rise in the succeeding decade. In line with the literature, these findings emphasize the importance of endoscopic-bioptic follow-up, which takes on even greater significance in elderly patients, in whom an increased incidence of IGC has been reported.

Feng, G. S., et al. (2008). "Celecoxib-related gastroduodenal ulcer and cardiovascular events in a randomized trial for gastric cancer prevention." World Journal of Gastroenterology 14(28): 4535‐4539.

Feng, Z., et al. (2015). "Identification of individuals at high risk of gastric cancer for targeted endoscopic screening." Gastroenterology 148(4): S762.

Background: Endoscopic screening for gastric cancer is useful for the detection of early gastric neoplasia; however there is scant data to guide the selection of individuals at increased risk. The Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP) is a prospective multicentre study initialized in 2004 with the aims of identifying predictive risk factors for gastric cancer in the Singapore Chinese population. The study was presented atDDW2013 (Lim et al, Gastroenterology 2013;144(5):S-95-S-96). Objectives: To identify individuals at high risk of gastric cancer in the Singapore Chinese population. Method: Chinese subjects aged >50 years were recruited into this cohort study and endoscopy surveillance was offered for a minimum of 5 years. All subjects gave informed consent. Approval from institutional review boards was obtained. The main outcome measure is the detection of early gastric neoplasia (EGN), including high grade dysplasia or adenocarcinoma. Risk factors (RF) were identified by univariate analysis, and those satisfying p<0.15 were entered in backward regression model. Receiver operating characteristic (ROC) analysis was performed for the risk prediction model. Results: 3033 Chinese with mean age 59±7 years were recruited. The study is still in progress and will be completed by 2015. So far, 21 cases of de novo EGN have been detected during prospective surveillance. 2649 subjects with complete data results were analysed. Eight risk factors including age, education, smoking, alcohol consumption, Helicobacter pylori (Hp) seropositivity, serum pepsinogen index (PGI), atrophic gastritis, and intestinal metaplasia (IM) were selected for backward regression analysis. The most parsimonious model in risk prediction included four RF, age >70, smoking, serum PGI and IM with adjusted odds ratios (95%CI) of 3.17 (1.19-8.47), 3.49 (1.45-8.41), 3.80 (1.33-10.91), 4.167 (1.20-14.50) respectively. The area under curve (AUC) in identifying EGN was 0.76 (95%CI 0.64-0.87). 64% of the cohort and 91% of EGN had at least one of these 4 RF. The cohort was grouped into high risk (HR), moderate risk (MR) and average risk (AR) based on RF >2, 1 and 0 respectively. The prevalence of EGN in the HR, MR and AR groups was 2.3%, 0.5% and 0.2% respectively. The subjects in the HR group had 11.33- fold (95%CI 2.55-50.40) increased prevalence of EGN compared to those with no RF. Conclusions: In our study, individuals with >2 of 4 RF (age >70, smoking, serum PGI, IM) comprised 19% of the cohort and were at 11-fold increased risk of EGN. These criteria could be useful to risk-stratify high risk individuals for endoscopic surveillance to detect EGN. (Table Presented).

Fernandes, S., et al. (2015). "High prevalence of Inflammatory Bowel Disease like findings in endoscopic and pathological samples of patients with common variable immunodeficiency." Journal of Crohn's and Colitis 9: S142.

Background: Common variable immunodeficiency (CVID) is an immunological disorder characterized by a primary deficiency in antibody production. Patients are at risk for recurrent infections but paradoxically may present with autoimmune manifestations some resembling inflammatory bowel disease (IBD). Our aim was to review endoscopic and pathologic findings in patients with CVID and determine the prevalence of IBD like findings. Methods: We reviewed patients with CVID followed in our institution. Reasons for endoscopy included dyspepsia (37.0%) and diarrhea (34.2%) and for colonoscopy diarrhea (55.2%) and suspicion of IBD (20.7%). Results: Out of 82 patients with CVID, 35 (65.7% males, age 43.2 ± 15.2 years) were reviewed including 86 endoscopies and 50 colonoscopies. Biopsies were taken from the esophagus (8), stomach (52), duodenum (48), ileum (14) and colon (25). Endoscopy was normal in 20.9%. Findings included esophageal candidiasis (5), esophagitis (7), varices (5), gastric polyps (12), ulcers (4) and hypere-mia (37), duodenal ulcers (11) and atrophy (10). Pathology revealed chronic gastritis in most patients (48), with Helicobacter pylori being frequent (21.2%). Atrophic gastritis (17), complete intestinal metaplasia (20) and lymphoid aggregates (14) were common findings. 2 patients lacked plasmocytes and 3 resembled lympho-cytic gastritis. Gastric carcinoma was diagnosed in 5 patients. CMV inclusions were found in 4 patients. Duodenal specimens showed villous atrophy or irregularity (10), chronic duodenitis (22), crypti-tis (7), intraepithelial lymphocytosis (13) and lymphoid aggregates (9). 9 patients lacked plasma cells and 4 patients revealed Giardia infection. Colonoscopy showed ileum (5) and colon ulceration (10), diminished vascular pattern (6) and polyps (8). Ileum showed architectural distortion (16), chronic ileitis (13) and focal cryptitis (5). 2 patients had paucity of plasma cells, 3 granulomas and 2 a collagen-ous and lymphocytic pattern. Giardia and CMV were detected in 1 patient. Colon samples revealed chronic inflammation (24), reaching the submucosa in 5. Crypt distortion was present in 18 patients with cryptitis in 17. A paucity of plasma and goblet cells were found in 7 and 4 patients respectively. Lymphoid aggregates were frequent (11). 2 patients showed a lymphocytic and 1 a collagenous colitis pattern. Paneth cell metaplasia was found in 5 patients and adenocarcinoma in 2. CMV was detected in 2 patients. Conclusions: CVID may present with a wide spectrum of both endo-scopic and pathologic findings. In our series, up to 30% had findings resembling IBD. This has important implications in both therapy, follow-up and cancer surveillance. We alert to the high incidence of gastrointestinal neoplasia in these patients.

Ferrero Celemín, E., et al. (2019). "Gastrectomy and gastric bypass as a treatment of morbid obesity with gastric intestinal metaplasia." Obesity Surgery 29(5): 1196.

Background: The annual gross incidence of gastric cancer for patients with intestinal metaplasia is 129 × 10 (-5), compared with 20 ×10 (-5) in patients with normal mucosa. It has also been shown that in 20 years 1 out of 39 patients with intestinal metaplasia will develop gastric cancer compared to 1 in every 256 patients with normal mucosa. Objectives: It's important to perform preoperative endoscopy in patients who are going to undergo a gastric bypass because its result can change the surgical technique. Methods: The clinical case is about a female, 61 years old, with sleep apnea syndrome, GERD, anxiety depressive syndrome, dyslipidemia and knee osteoarthritis. The patient BMI is 46.7, therefore it's a morbid obesity with indication of bariatric surgery. Preoperative gastroscopy is performed: Hiatal hernia. Non-erosive gastropathy. Endoscopic biopsy: Gastric antrum mucosa with chronic atrophic gastritis with intestinal metaplasia. No signs of dysplasia are observed. Results: Since the patient has GERD, the proposal for bariatric surgery would be a gastric bypass. With this technique, endoscopic follow-up of intestinal metaplasia in the excluded stomach cannot be done. So it was decided to complete the gastric bypass with gastrectomy of the remnant stomach. The definitive histology report describes: Chronic moderate atrophic gastritis. Moderate multifocal intestinal metaplasia. No dysplasia in the included material. Conclusion: The resection of the gastric remnant if there are potentially malignant histological alterations in the preoperative biopsy, should be considered before performing a gastric bypass, since this technique avoids the endoscopic control of the excluded stomach.

Filipe, M. I., et al. (1993). "Assessment of proliferating cell nuclear antigen expression in precursor stages of gastric carcinoma using the PC10 antibody in PCNA." Histopathology 22(4): 349-354.

Immunohistochemistry using the PC10 antibody to proliferating cell nuclear antigen (PCNA) was applied to archival material from mucosa adjacent to gastric carcinoma ('normal', hyperplasia, complete and incomplete intestinal metaplasia and dysplasia) and non-cancer controls (normal and complete intestinal metaplasia). Overall, increased PCNA indices, with expansion and altered location of the proliferative zones, were observed in carcinoma fields and compared with controls (P < 0.001). These differences were particularly significant in 'normal' mucosa far from carcinoma as compared with normal in controls (P < 0.001). In carcinoma 'fields' distinct patterns of PCNA expression were noted in complete and incomplete intestinal metaplasia. Similarly, in dysplastic lesions high PCNA indices were present either throughout the gland or found predominantly in the upper compartment. We conclude that these differences in PCNA index and staining patterns might prove useful in monitoring the evolution of the disease in the follow-up of patients at risk of developing gastric cancer.

Filomena, A., et al. (2011). "Gastric cancer surveillance in a high-risk population in tuscany (Central Italy): preliminary results." Digestion 84(1): 70-77.

BACKGROUND/AIMS: The surveillance of subjects at high risk for developing gastric cancer (GC) may represent an effective strategy for reducing specific morbidity and mortality. The aim of this study was to identify GC at its initial phase and to identify precancerous lesions in a group of GC high-risk subjects. METHODS: We enrolled first-degree relatives of patients affected by GC who resided in a GC high-risk area (Tuscany, Central Italy). The study's protocol included the collection of several individual measurements, including a blood sample for the determination of specific biomarkers, an upper digestive tract endoscopy with detailed gastric biopsies and Helicobacter pylori (Hp) treatment followed by a specific check. RESULTS: We enrolled 167 subjects who were members of 128 different familial groups with GC history. We identified 1 case of initial-phase GC, 1 gastric dysplasia type II, 32 intestinal metaplasia, 10 gastric atrophy, and 21 atrophic chronic gastritis. 81 subjects were Hp-positive and underwent eradication therapy. CONCLUSION: This study of a GC high-risk Italian population reveals positive results in terms of population compliance, the identification of specific gastric lesions requiring close follow-up and successful therapy for Hp infection. To define future surveillance strategies, a longer follow-up of these patients is necessary.

Finch, P. J., et al. (1986). "Beta-glucuronidase, LDH and LDH isoenzyme levels and screening for gastric cancer." European Journal of Surgical Oncology 12(3): 253-256.

Lactic dehydrogenase (LDH) and beta-glucuronidase (bGLU) levels are elevated in the gastric juice of patients with gastric cancer, and these enzymes have been used as a screening test for gastric cancer. False positives are common, however, and we have measured enzyme levels, including LDH isoenzyme fraction, in tissue homogenates from resected stomach specimens and compared these with histological features. Increases in bGLU were found in carcinoma and chronic gastritis, an increase in LDH was found in carcinoma, whilst mLDH fraction was increased in chronic gastritis, carcinoma and intestinal metaplasia, particularly the sulphomucin variant. These findings indicate the basis for the screening test, and also the reason for the false positives. An elevated mLDH fraction may be a useful marker of a group at increased risk of developing gastric cancer, and worthy of long-term follow-up.

Forbes, G. M., et al. (1996). "Long-term follow-up of gastric histology after Helicobacter pylori eradication." Journal of Gastroenterology and Hepatology 11(7): 670-673.

Helicobacter pylori causes chronic active gastritis and is thought to be associated with the development of gastric atrophy, intestinal metaplasia and carcinoma. As the effect of H. pylori eradication on this process is poorly understood, we sought to determine the long-term effects of H. pylori eradication on gastric histology. Fifty-four patients with duodenal ulceration associated with H. pylori infection received H. pylori eradication therapy in 1985/86 and either remained infected (n = 22) or had the infection eradicated (n = 32); patients were followed up by endoscopy with gastric antral biopsy for 7.1 years (mean). Histopathological analysis of gastric antral mucosa from patients rendered H. pylori-negative revealed a marked decrease in both inflammatory cells within the lamina propria and intraepithelial neutrophils and an increase in epithelial mucinogenesis. Gland atrophy remained unchanged in both H. pylori-positive and -negative patients. When examined for the presence and severity of intestinal metaplasia, there was neither a difference between the two patient groups nor a change with time. These data demonstrate that significant long-term improvements in gastric histology accompany H. pylori eradication when compared with histology in patients with persistent infection. Whether this confers a protective effect by reducing the risk of gastric carcinoma remains unknown.

Forbes, G. M., et al. (1996). "Long-term follow-up of gastric histology after Helicobacter pylori eradication." Journal of Gastroenterology and Hepatology (Australia) 11(7): 670-673.

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Fuccio, L., et al. (2009). "Meta-analysis: can Helicobacter pylori eradication treatment reduce the risk for gastric cancer?" Annals of Internal Medicine 151(2): 121‐128.

Garai, J., et al. (2014). "The homing receptor CD44 is involved in the evolution to more advanced gastric lesions overtime in subjects infected with helicobacter pylori and development of mucous metaplasia in mice." Gastroenterology 146(5): S-504.

BACKGROUND: Gastric cancer is one of the most common cancers worldwide. Infection with Helicobacter pylori (H. pylori) is the main factor associated with the development of intestinal-type gastric cancer. The infection induces a cascade of inflammatory events leading to non-atrophic gastritis, multifocal atrophic gastritis, intestinal metaplasia, dysplasia and cancer. The molecular events controlling the dynamic of these lesions are not fully understood. Inflammation is initiated by the migration of inflammatory cells into the infected mucosa. This migration is mediated, among other molecules, by CD44. However, the role of this molecule in progression of precancerous lesions over time has not been documented. METHODS: gene expression arrays were used to compare gene profiles in human gastric mucosa at baseline and 6 years of follow-up and real-time PCR and immunohistochemistry to confirm the microarray results. Mouse models of CD44-/- were used to investigate the role of CD44 in the development of H. pylori-induced gastric lesions. RESULTS: using baseline expression levels as reference we found that individuals who progressed to more advanced gastric lesions over a six year period, had increased levels of CD44. These results were confirmed by real-time PCR. In addition, in vitro experiments showed that CD44 was induced in response to H. pylori infection. Immunohistochemical analysis showed increased expression of the variant 4 of the CD44 (CD44v4). CD44-/- mice infected with H. pylori over a period of seven months developed less mucous metaplasia when compared to wild type controls, suggesting a major role of CD44 in the development of advanced gastric lesions. CONCLUSIONS: our data indicate that CD44 expression is crucial for the development of precancerous gastric lesions both in humans and mice. The identification of specific variants may lead to the identification of early biomarkers of disease and to devise of therapeutic strategies to block the progression of the gastric inflammatory cascade that leads to cancer.

Garcia, T. V., et al. (2012). "The clonal origins of gastric adenocarcinoma." Gastroenterology 142(5): S643.

We have previously shown that entire fields of dysplasia in the human stomach are derived from a single mutated, metaplastic gland[1]. This suggests that intestinal metaplasia (IM) can be considered a field defect amongst which dysplasia can arise and this would indicate that adenocarcinomas derived from such dysplasia would also be clonal. Recent work published by our laboratory has indicated that familial adenomatous polyposis-associated colorectal adenomas as well as some sporadic lesions[2] and dysplasia within Barrett's oesophagus[3] are polyclonal. There is therefore a need to ascertain the clonality of gastric adenocarcinomas (GA). Here we screened a large cohort of GA patients for mutations in genes accounting for nearly 90% of reported mutations in GA in order assess mutation frequencies. The screening was then followed by laser capture microdissection PCR sequencing and loss of heterozygosity (LOH) analysis of the mutated specimens in order to assess clonality of GA from dysplasia and IM. From the 51 patients cohort we have found 18 patients (35.3%) presenting mutations, but only 1 out of the 51 patients (1.9%) presented two independent mutations in a single cancer. We found 3 mutations in APC (6.3%), 1 in CDKN2A (2.2%), 13 in TP53 (27.7%), 1 in CTNNB1 (2.2%) and 1 in K-RAS (2.4%), but none in PIK3CA or PTEN. Our mutation frequencies are comparable to previous reports, however we observed that most functional mutations occurred as a single event despite screening multiple genes. Current data seems to show that GA have a monoclonal origin but are comprised by genetically diverse populations of cells. Analysis of multiple laser capture microdissected areas of 6 patients revealed multiple genotypes within the same cancer. However, LOH data in the patient presenting two independent mutations (TP53 and CTNNB1) shows loss of heterozygosity in 17q throughout the cancer in all different genotypes. This suggests that 17q LOH might have been the first hit mutation followed by subsequent mutations in TP53 exon 7 and then in CTNNB1. This data suggests that GA cells might become genetically diverse as the cells evolve in the tumour and IM is likely to represent a field defect for gastric cancer.

Garrido, M., et al. (2020). "Natural history of autoimmune atrophic gastritis: A retrospective, tertiary centre experience from a high-risk area for gastric cancer." United European Gastroenterology Journal 8(8 SUPPL): 149-150.

Introduction: Autoimmune atrophic gastritis (AAG) is a chronic inflammatory condition that results in a progressive replacement of the corpus parietal cell mass by atrophic and metaplastic mucosa. It is considered a pre-malignant condition due to increased risk of gastric neuroendocrine neoplasms (g-NENs) and gastric adenocarcinomas. Hence, endoscopic surveillance is recommended every 3 to 5 years. However, data on clinical outcomes in histologically confirmed AAG is scarce, particularly in highrisk regions for gastric cancer, as the north of Portugal. Aims & Methods: To characterize the clinical, analytical, endoscopic and pathological phenotype of patients with AAG and to evaluate the risk of progression of pre-malignant gastric conditions and the occurrence of gastric neoplasia during the follow-up (f-up) by a retrospective identification of adult patients with positive anti-gastric parietal cell (anti-GPC) and/or anti-intrinsic factor (anti-IF) antibodies, from 01/2014 to 08/2019 (n=585) and inclusion of those with histologic findings consistent with AAG. Results: A total of 145 patients (pts) were included (71.7% female sex) with a mean age of 55.8±15.1 years. 27.6% had another autoimmune disease, 11.9% (14/117) reported a family history of gastric adenocarcinoma and 43.1% (59/137) infection with H. pylori. 70.3% showed anti-GPC (+) and 5.5% anti-IF positivity alone; 24.1% showed both autoantibodies (+). At diagnosis, 67.6% had anaemia, 62.8% vitamin B12 deficiency (19.2% PA) and 46.2% iron depletion. At the first endoscopic evaluation (T-0), gastric body biopsies revealed intestinal metaplasia (IM) in 79.7% and chronic atrophic gastritis (CAG) in the remaining. Antrum biopsies found premalignant conditions in 44.2% (23.9% CAG; 20.3% IM). Gastric dysplasia (g-DYS) was diagnosed in 5 (3.45%) pts (4 low-grade; 1 high-grade dysplasia; up to 22mm). Enterochromaffin like (ECL) cell hyperplasia was found in 9 (6.2%) and ECL dysplasia in 2 (1.4%) pts. 13 g-NENs were diagnosed in 11 (7.6%) pts (most up to 5mm (n=10), all grade 1 (G1) and stage I g-NENs, except for one 13mm g-NEN, G1, stage II, resected by endoscopic submucosal dissection). Pts had a mean clinical f-up time of 5.06±3.95 years. 84 pts were submitted to endoscopic f-up during a mean time of 4.24±2.87 years. During this period, a significant progression of gastric pre-malignant conditions was not found. No g-DYS or adenocarcinoma were detected. Overall, 18 g-NENs were detected (up to 7mm; 15 G1, 3 G2; all stage I) among 8 pts, including 13 g-NENs out of 5 patients with g-NEN at T-0. The mean time to g-NEN development was 44.8 months (maximum 81 months). The incidence rate of new g-NENs was 9.7 per 1000 person-years. 4 pts died, none related to AAG. In bivariate analysis, both ECL hyperplasia (28.6% vs 7.6%, p=0.012) and dysplasia (100% vs 7.1%, p< 0.001) were associated with g-NETs. Pts with ECL hyperplasia had a 4.84 higher OR of developing g-NENs [CI 95% 1.28- 18.24]. Male gender (9.8% vs 1.9%, p=0.033) and H. pylori infection (8.5% vs 1.3%, p=0.042) were associated with g-DYS. Conclusion: ECL hyperplasia and dysplasia were associated with the development of g-NETs, whereas male gender and H. pylori infection were associated with gastric dysplasia. Overall, 14.5% of AAG pts developed gastric neoplasms (g-NEN 9.66%; g-DYS 3.45%). All g-NENs and gastric dysplasia were early lesions amenable to endoscopic management. There was no AAG related mortality during the median 5-year f-up time, confirming the overall benign disease course when support treatment and endoscopic follow-up are offered.

Gavric, A., et al. (2019). "Survival in patients with missed upper gastrointestinal cancer during oesophagogastroduodenoscopy." United European Gastroenterology Journal 7(8): 524.

Introduction: According to a recent meta-analysis the rate of missed gastric cancer during upper endoscopy is approximately 10% (1). While risk factors for missed upper gastrointestinal cancer have been identified in retrospective studies, the effect of missed upper gastrointestinal cancer on long-term survival is not clearly documented. Aims & Methods : We aimed to identify risk factors associated with missed upper gastrointestinal cancer and to compare survival between missed and non-missed upper gastrointestinal cancer. This is a single centre, retrospective cohort study. All upper endoscopies performed at our department between January 2007 and December 2015 were included in the study. The endoscopy database was cross-referenced with the Slovenian Cancer Registry Database. Missed cancers were defined as those diagnosed within 36 months since the last upper endoscopy. We excluded patients with a history of previous upper gastrointestinal cancer and those who were in surveillance program due to high risk conditions for the cancer development (Barrett's oesophagus, intestinal metaplasia with OLGIM stage ≥ 3). The association of demographic and endoscopic characteristics was analysed with multivariable logistic regression, categorical data were compared using the chi-squared test. Survival analysis was performed with the Kaplan-Meier method. Results: During the study period 29,617 upper endoscopies were performed and 663 upper gastrointestinal cancers were diagnosed; 164 (24.7%) patients were excluded because of previous upper gastrointestinal cancer, further 10 (1.5%) were excluded because their cancer was diagnosed during surveillance for precancerous conditions. In the final cohort of 489 upper gastrointestinal cancers, 37 were missed (7.6 %; esophagus: 3.8%; gastric: 8.0%; duodenum: 23%) (Table 1). Conclusion: Median survival of patients with missed upper gastrointestinal cancer during upper endoscopy was shorter compared to non-missed upper gastrointestinal cancer. (Table Presented) .

Gemignani, L., et al. (2014). "Changes in gastric intestinal metaplasia extension in annually followed-up patients: 1-year results of a study performed by means of narrow band imaging with magnification endoscopy." United European Gastroenterology Journal 2(1): A325.

INTRODUCTION: Gastric Intestinal Metaplasia (GIM) is a precancerous condition potentially leading to gastric cancer. However, this occurs in a limited number of cases and, therefore, the need of endoscopic surveillance and follow-up is controversial. Moreover, there is no universal consensus regarding which patients should be better investigated and followed-up in the long-term period. Most of the experts among pathologists and gastroenterologists recommend to perform an upper endoscopy with multiple biopsies every three-year only in patients with extensive GIM, but no studies have validated the effectiveness of this protocol, so far. AIMS & METHODS: Our aim was to investigate whether changes in extension and/or progression of GIM occur during a strict yearly endoscopic follow-up program. Between November 2011 and December 2013, we prospectively evaluated consecutive patients with an histologically defined diagnosis of GIM by means of Narrow Band Imaging with Magnification Endoscopy (NBI-ME) and multiples gastric biopsies (2 antrum +1 angulus +2 corpus). Helicabacter pylori infection was excluded. Patients with a GIM extension higher than 20% were offered to repeat the endoscopic examinations every year and, to date, 20 out of 121 accepted and were included in the follow-up program. Endoscopic examinations have been performed by experienced endoscopists (each of them with more than 1000 NBI-MEs performed). Biopsies were taken at sites suggestive for GIM based on NBI-ME appearance (i.e. presence of light blue crests on the surface of gastric mucosa) or randomly if no evident mucosal alterations were seen. Biopsies were assessed by two expert and blinded pathologists, who evaluated the percentage of extension of GIM at both times. RESULTS: The median time between the two observations was 13 months (range 11-18). As shown in the Table, patients were divided in three categories, according to the changes in GIM extension, which was considered stable if there were tiny variations (0-5%) between the two observations, or raised/lowered otherwise. At 1-year, in all patients, the second evaluation confirmed the presence of GIM. In patients with worsened extension, the mean percentage of GIM increase was 20%, whereas the mean percentage of GIM lowering was 26%in patients with a reduced GIM extension. CONCLUSION: Our results demonstrate that already at 1-year the extension of GIM and, therefore, the risk of developing a gastric cancer GIM-related, worsens in about 45% of the patients. Thus, these data seem to support a more close follow-up in patients with a GIM extension higher than 20% at histologic assessment. (Table Presented).

Genta, R. M. and A. Sonnenberg (2015). "Characteristics of the gastric mucosa in patients with intestinal metaplasia." American Journal of Surgical Pathology 39(5): 700-704.

Gastric intestinal metaplasia (IM) occurs in response to different injuries, some of which involve increased risk for gastric cancer, whereas others may not. The background in which IM arises has not been systematically investigated. This study was designed to determine the relative prevalence of the histopathologic conditions of the gastric mucosa associated with IM in a large cohort. We extracted from a database patients who had undergone esophagogastroduodenoscopy with gastric biopsies between January 2008 and December 2013 in endoscopy centers throughout the United States. For each subject we recorded demographic, clinical, and histopathologic information. We stratified patients according to the presence of IM and compared the prevalence of Helicobacter pylori infection, reactive gastropathy, minimal inflammatory and gastropathy changes, mucosal atrophy, gastric polyps, cancer, and lymphoma in the 2 groups. IM, present in 8.4% of the 810,821 unique patients, increased with age and was more common in male than in female individuals. Compared with other Americans, East Asian ancestry was associated with a 5-fold risk for IM. Helicobacter gastritis and its sequelae were present in 42.2% of patients with IM, and reactive gastropathy in 17.3%. In >50% of patients under the age of 30 and in 26% of older adults, foci of IM occurred in an almost normal gastric mucosa. Thus, approximately half of the patients with IM had no histopathologic evidence of current or previous Helicobacter gastritis, whereas almost one fifth had a background of reactive gastropathy. Longitudinal studies are needed to determine the relative risk for gastric cancer in patients with IM associated and not with Helicobacter infection.

Gisbert, J. P. (2012). "[Helicobacter pylori-related diseases]." Gastroenterología y Hepatologia 35 Suppl 1: 12-25.

This article summarizes the main conclusions drawn from the studies presented in Digestive Disease Week in 2012 on Helicobacter pylori infection. In developed countries, the prevalence of this infection has decreased, although it continues to be high. The prevalence in Spain is high (50%) and does not seem to be decreasing. There is an increase in antibiotic resistance, which is correlated with the frequency of prior antibiotic prescription. H. pylori eradication improves the symptoms of "epigastric pain syndrome" in functional dyspepsia. The frequency of idiopathic peptic ulcers seems to be increasing. To prevent the development of gastric cancer, eradication therapy should be administered early (before intestinal metaplasia develops). H. pylori eradication in patients undergoing early endoscopic resection of gastric cancer reduces the incidence of metachronous tumors, although endoscopic follow-up should be performed periodically. H. pylori eradication induces MALT lymphoma regression in most patients and tumoral recurrence in the long term is exceptional; radiotherapy is an excellent second-line option; a watch and wait approach to histologic recurrence after initial MALT lymphoma remission is a reasonable alternative. Idiopathic thrombocytopenic purpura is an indication for eradication therapy in children as well as adults. There are several diagnostic innovations, such as high-resolution endoscopy, narrow-band imaging, a method based on the electrochemical properties of H. pylori, and the cytosponge. Quadruple therapy with bismuth is at least as effective as standard triple therapy. The superiority of "sequential" therapy over standard triple therapy should be confirmed in distinct settings. The efficacy of "concomitant" therapy is similar -or even better- than that of "sequential" therapy, but has the advantage of being simpler. A hybrid sequential-concomitant therapy is highly effective. In patients allergic to beta-lactams, the efficacy of treatment with a proton pump inhibitor-clarithromycin-metronidazole is insufficient. When standard triple therapy fails, the second-line option of a 10-day course of levofloxacin is effective and is simpler and better tolerated than quadruple therapy. Triple therapy with levofloxacin is also a promising alternative after failure of "sequential" and "concomitant" therapy. New-generation quinolones, such as moxifloxacin and sitafloxacin, could be useful as eradication therapy, especially as rescue therapy. When two eradication therapies have failed, empirical administration of a third (e.g. levofloxacin) is a valid option. Even after three eradication therapies have failed, an empirical rescue therapy (with rifabutin) can be effective. H. pylori reinfection is highly frequent in developing countries, probably due to intrafamilial transmission.

Giuliani, A., et al. (2003). "Cancer precursor lesions in intact stomach Helicobacter pylori gastritis and in resected stomach gastritis." Journal of Experimental and Clinical Cancer Research 22(3): 371-378.

Hemigastrectomy for benign disease and Helicobacter pylori infection are risk conditions for the development of gastric cancer. Aim of the study was to compare gastric histology and precursor lesions of malignancy in these two conditions. The hemigastrectomy group included 351 consecutively endoscoped subjects operated for gastroduodenal benign disease. Six to ten biopsy specimens were routinely taken from the residual gastric mucosa. The intact stomach group included 2097 consecutively endoscoped symptomatic subjects, who did not receive eradication therapy against H. pylori. The histological findings were classified as normal mucosa (NM), chronic non atrophic gastritis (CNAG), chronic atrophic gastritis (CAG), intestinal metaplasia (IM) and dysplasia (DYS). One thousand and three intact stomachs were H. pylori negative, and 1094 showed H. pylori colonization. The age over fifty was a significant risk factor for the occurrence of IM (OR 2.52, P < or = 0.001) and DYS (OR 3.46, P < or = 0.001), while Hp-positivity was a risk factor for CNAG (OR 1.81, P < or = 0.001) and CAG (OR 3.88, P < or = 0.001). Gastroresection was associated to higher risk for CNAG (OR 1.53, P < or = 0.001) and DYS (OR 4.31, P < or = 0.001) and to a lower risk of CAG (OR 0.49, P < or = 0.001). Both in males and females the risk for CNAG was significantly higher in Hp-positive (males OR 1.92, P=0.000; females OR 1.70, P=0.000) and gastrectomized subjects (males OR 2.06, P=0.000; females OR 2.43, P=0.000). Gastrectomized males, furthermore, showed an increased risk for DYS (OR 5.82, P=0.000). The aged Hp-negative and Hp-positive subjects evidenced a significant risk for IM (respectively OR's 3.42, P=0.000 and 4.85, P=0.000); the risk for DYS was significant in aged Hp-negative subjects (OR 4.09 P < or = 0.020). The Hp-positive individuals evidenced a significant risk for metaplastic mucosal changes (OR 38.17, P=0.000). Subjects aged over forty at the time of surgery and those with a longer postoperative follow up endoscopy presented an increased risk for CNAG of the residual mucosa (respectively OR's 2.75, P=0.000 and 5.25, P=0.000). CNAG and IM were the most frequently observed mucosal lesions both in subjects operated for duodenal and gastric ulcer (respectively OR's 4.02, P=0.000 and 3.00, P=0.000). Our data support that hemigastrectomy for benign disease and H. pylori infection may induce an increased incidence for histological precursor lesions for gastric malignancy and suggest that carcinogenesis in a resected stomach may be different from that in the intact stomach.

Gomez, J. M., et al. (2013). "The presence of gastric intestinal metaplasia in patients undergoing EGD with biopsy is associated with a family history of gastric cancer in the United States." Journal of Gastroenterology and Hepatology Research 2(8): 726-729.

Aim: Gastric intestinal metaplasia (IM) is a pre-malignant lesion that can develop into adenocarcinoma through a sequential cascade involving non-atrophic gastritis, atrophic gastritis, IM, gastric dysplasia, and ultimately carcinoma. To estimate the prevalence of gastric IM in patients undergoing EGD with biopsy at an academic medical center; and determine what clinical factors might be associated with gastric IM. Methods: Three hundred consecutive patients presenting for EGD with biopsy at a tertiary-care medical center were enrolled in a retrospective single-center cohort study. Results: Gastric biopsies found H. pylori infection in 2% (n=6), chronic gastritis in 20% (n=61), and gastric IM in 5% (n=15) of patients. A first-degree family history of gastric cancer was a risk factor for having gastric IM (OR 8.51, 95% CI: 1.52-40.22, P=0.018) on age-adjusted multivariate analysis. Uninsured patients (OR 5.1, 95% CI: 2.4-11.2, P<0.001) and those with Medicaid (OR 3.6, 95% CI: 1.3-9.7, P=0.014) were more likely to have chronic gastritis as compared to those with private insurance on age-adjusted multivariate analysis. Conclusion: A family history of gastric cancer significantly increased the odds of having gastric IM. Uninsured patients and those with Medicaid were at increased risk of having chronic gastritis and trended towards having IM on gastric biopsies. As guidelines regarding the screening and surveillance of premalignant gastric lesions emerge, attention should be paid to patients with a family history of gastric cancer, and possibly those with lower socioeconomic status who might be at increased risk for gastric IM. © 2013 ACT.

Gomez, J. M., et al. (2017). "Gastric intestinal metaplasia is associated with gastric dysplasia but is inversely correlated with esophageal dysplasia." World Journal of Gastrointestinal Endoscopy 9(2): 61-69.

AIM: To determine which clinical factors might be associated with gastric intestinal metaplasia (IM) in a North American population. METHODS: Pathology and endoscopy databases at an academic medical center were reviewed to identify patients with and without gastric IM on biopsies for a retrospective cohort study. Patient demographics, insurance status, and other clinical factors were reviewed. RESULTS: Four hundred and sixty-eight patients with gastric IM (mean age: 61.0 years ± 14.4 years, 55.5% female) and 171 without gastric IM (mean age: 48.8 years ± 20.8 years, 55.0% female) were compared. The endoscopic appearance of atrophic gastritis correlated with finding gastric IM on histopathology (OR = 2.05, P = 0.051). Gastric IM was associated with histologic findings of chronic gastritis (OR = 2.56, P < 0.001), gastric ulcer (OR = 6.97, P = 0.015), gastric dysplasia (OR = 6.11, P = 0.038), and gastric cancer (OR = 6.53, P = 0.027). Histologic findings of Barrett's esophagus (OR = 0.28, P = 0.003) and esophageal dysplasia (OR = 0.11, P = 0.014) were inversely associated with gastric IM. Tobacco use (OR = 1.73, P = 0.005) was associated with gastric IM. CONCLUSION: Patients who smoke or have the endoscopic finding of atrophic gastritis are more likely to have gastric IM and should have screening gastric biopsies during esophagogastroduodenoscopy (EGD). Patients with gastric IM are at increased risk for having gastric dysplasia and cancer, and surveillance EGD with gastric biopsies in these patients might be reasonable.

Gomez, J. M., et al. (2013). "Gastric intestinal metaplasia is associated with gastric abnormalities but is inversely correlated with esophageal abnormalities on endoscopy and histopathology." Gastrointestinal Endoscopy 77(5): AB261.

Background: Gastric intestinal metaplasia (IM) is a precursor to gastric adenocarcinoma. Despite recent European/ESGE guidelines (Endoscopy 2012;44: 74-94), there are no North American consensus recommendations as to which patients might benefit from EGD with biopsy for screening or surveillance for gastric IM. Aim: To determine what clinical factors might be associated with gastric IM so as to identify potential indications for screening and/or surveillance with gastric biopsies. Methods: Pathology and endoscopy databases at a tertiarycare academic medical center were reviewed to identify patients with and without gastric IM on biopsies for a retrospective cohort study. Patient demographics, insurance status, and other clinical factors were retrieved from electronic medical records. Fisher's exact test and age-adjusted exact logistic regression were performed. Results: 746 patients were included: 483 with gastric IM (median age: 63 years, range: 3-92 years, 55.1% female) and 285 without gastric IM (median age: 53 years, range: 1-91 years, 54.7% female). The most frequent indication for EGD was abdominal pain (gastric IM group: 42.3%, no gastric IM group: 48.4%, P=0.81). Among indications for procedures, weight loss (OR 1.69 [0.99-2.96], P=0.055) trended towards an association with gastric IM, whereas dysphagia (OR 0.63 [0.41-0.97], P=0.04) and history of Barrett's (OR 0.17 [0.08-0.32], P<0.001) were inversely associated with finding gastric IM on biopsies. Tobacco use was not associated with gastric IM, but alcohol use was inversely associated with gastric IM (OR 0.52 [0.37-0.74], P < 0.001). Family history of gastric cancer was associated with gastric IM (OR 2.97 [1.25-8.0], P=0.01), and trended towards significance when adjusted for age (OR 1.91 [0.79- 5.28], P=0.16). Significant associations among gastric IM and endoscopic findings are reported in Table 1. Significant associations among gastric IM and histopathological diagnoses found on biopsies are reported in Table 2. These tables show that many commonly encountered gastric diagnoses were associated with gastric IM; whereas, Barrett's and other esophageal irregularities inversely correlated with gastric IM. Conclusions: Patients with biopsy-proven gastric IM were significantly more likely to have endoscopic findings of gastritis, atrophic gastritis, gastric erosions, ulcers, and masses, and these findings should prompt screening gastric biopsies during EGD. Patients with gastric IM were associated with increased odds of having gastric dysplasia and cancer, and a program of surveillance biopsies in these patients may be reasonable. Patients with gastric IM were more likely to have H. pylori infection and atrophic gastritis, which typically correlate with lower gastric acid output, and might explain the inverse relationship among gastric IM and Barrett's esophagus and esophageal dysplasia. (Table Presented).

Gong, C., et al. (1999). "KRAS mutations predict progression of preneoplastic gastric lesions." Cancer Epidemiology, Biomarkers and Prevention 8(2): 167‐171.

Kang, S. J., et al. (2015). "Pepsinogen and incident chronic atrophic gastritis and intestinal metaplasia: A longitudinal study." United European Gastroenterology Journal 3(5): A14.

Introduction: Pepsinogen (PG) I and II are the two main precursors of pepsin, and are both produced by chief cells and mucous neck cells of the stomach.[1, 2] PG II is also produced by pyloric gland cells. When atrophic mucosal change develops, the chief cells are replaced by pyloric glands, leading to a decrease in PGI. However, PG II decreases in very small amount.[2] Thus, low serum PG I level and low PG I/II ratio are well known to be serological markers of gastric atrophy. Aims & Methods: This study was performed to investigate association between serum pepsinogen (PG) level and incidence of chronic atrophic gastritis (CAG) and intestinal metaplasia (IM). This is a retrospective cohort study. Our data were composed of 3,927 participants (over 30 years of age) who underwent upper endoscopy and serum PG test between March 2008 and December 2009 whose baseline endoscopy showed no evidence of CAG and IM. Of these, 2,166 participants underwent follow-up endoscopy after at least 1 year. Thus, the final study subjects consisted of 2,166 adults with follow-up data. Structured questionnaires were reviewed about purported risk factors for CAG and IM such as family history of gastric cancer, current smoking, and alcohol consumption. Serum PG I and PG II were measured by a latex-enhanced turbidimetric Immunoassay. Serum anti-Helicobacter pylori (H. pylori) IgG was detected by enzyme-linked immunosorbent assay. Follow-up endoscopy was performed either at 1-year or 2-year intervals by taking into account factors such as age, family history of gastric cancer, and patients' preference. CAG and IM were diagnosed endoscopically by experienced board-certified endoscopists. Results: Median follow-up in the 2,166 participants was 1490.5 days (interquartile range, 772.8-1898.0). There were a total of 783 patients with CAG and 166 patients with IM during the follow-up. Subjects with a PG I/II ratio of≤3.0 showed higher incidence of CAG and IM compared with those with a PG I/II ratio of>3.0 by using log-rank test (p<0.001, both for CAG and IM). The results of Cox's regression analysis confirmed that the PG I/II ratio was significantly inversely associated with incident CAG (HR, 0.86; 95% CI, 0.82- 0.90; p<0.001) after full adjustment for risk factors. The PG I/II ratio was also significantly inversely associated with incident IM (HR, 0.76; 95% CI, 0.68- 0.85; p<0.001). To test diagnostic performance of the PG I/II ratio for incident CAG, we performed a receiver-operating curve analysis. The cutoff value that is farthest from the line of equality was PG ratio of 4.6, with modest sensitivity (54.5%; 95% CI, 51.0%>58.1%) and specificity (66.1%; 95% CI, 63.5%>68.6%). Conclusion: The PG I/II ratio was found to be significantly inversely associated with development of CAG and IM in asymptomatic population without CAG and/or IM at baseline.

Karita, M., et al. (2004). "Atrophic progression induced by H. pylori infection is correlated with a changing pepsinogen I value and associated with the development of gastric cancer." Digestive Diseases and Sciences 49(10): 1615-1620.

It is well known that H. pylori infection induces gastric mucosal atrophy, and patients with gastric cancer, which is often complicated by H. pylori infection, possess gastric mucosal atrophy including intestinal metaplasia as a background. One hundred forty-seven patients with dyspeptic symptom and without gastric cancer diagnosed at first endoscopy have been prospectively studied to detect early gastric cancer every year by endoscopy for approximately 6 years. The status of H. pylori infection was detected by histology and ELISA, the value of pepsinogen I (PGI) determined by ELISA, and atrophic pattern determined by the histology of multiple specimens. After the follow-up period (mean, 6.1 years), 6 early gastric cancers had developed in the 49 H. pylori-positive patients with transformation of the atrophic pattern, and no cancer had developed in either the 48 H. pylori-positive patients without transformation of the atrophic pattern or the 50 H. pylori-negative patients. There is a significant relationship between the incidence of transformation of the atrophic pattern and that of the development of gastric cancer in the H. pylori-positive patients. PGI per year in the H. pylori-positive group with transformation of the atrophic pattern was significantly decreased compared with that in the other two groups. Gastric cancers have a background of progressive atrophy, and PGI per year can be a good marker to detect gastric cancer at early stages which is developing or has developed on the background of atrophic progression.

Kashiwagi, H. (2003). "Ulcers and gastritis." Endoscopy 35(1): 9-14.

This article reviews recently published literature regarding ulcers and gastritis. Although endoscopy is the most useful procedure for diagnosis in the upper gastrointestinal tract, complications do occur, and procedure-related costs are significant. The appropriate indication for endoscopy has recently been debated. Helicobacter pylori is known to be an important pathogen involved in gastric and duodenal inflammation. Peptic ulcer disease and severe gastric mucosal injury are caused by virulent strains, and many reports have focused on CagA. Follow-up studies on surveillance endoscopy in patients with peptic ulcer or gastritis report that patients with atrophic gastritis and intestinal metaplasia are at significantly higher risk for gastric cancer. H. pylori eradication sometimes causes gastroduodenal erosion and reflux esophagitis, and the mechanisms involved have been revealed. Proton-pump inhibitors are useful in the treatment of ulcers caused by nonsteroidal anti-inflammatory drugs (NSAIDs), reflux esophagitis, and for preventing rebleeding after endoscopic hemostasis, but the effect of long-term acid suppression on the gastric mucosa is still a matter of debate. H. pylori infection and NSAID intake are both risk factors for peptic ulcer disease, and are important aspects in this field.

Katelaris, P. H., et al. (2012). "A prospective evaluation of levofloxacxin based triple therapy for refractory H. pylori infection in a large Australian cohort." Journal of Gastroenterology and Hepatology 27: 16.

First line Helicobacter pylori eradication failure is a common and challenging problem. Salvage treatments may be hampered by antibiotic resistance (repeat clarithromycin therapies), difficult dosing schedules (quadruple therapy), adverse effects (rifabutin therapy), limited access to some antimicrobial agents and drug allergy. The aim of this study was to assess the efficacy of salvage levofloxacin triple therapy in unselected patients in clinical practice in Australia (where primary levofloxacin resistance is low). Methods: Prospective patients referred after prior treatment failure(s) were prescribed esomeprazole 40 mg, amoxicillin 1 g and levofloxacin 500 mg each twice daily for ten days. All patients received detailed written and verbal compliance support. Clinical and demographic data, including prior treatment number and type, compliance and adverse effects were recorded. Those with a history of penicillin allergy were tested immunologically and treated if amoxicillin was considered safe to use (20 patients). Outcome assessment was by 13C-urea breath test and/or histology and urease test. Results: In 150 evaluable patients (66% female, mean age 54 ± 14 years; 6 smokers), the main indications for treatment were peptic ulcer disease (17%), increased gastric cancer risk (family history or intestinal metaplasia, 20%), symptoms (35%) and other risk reduction (28%). The median number of previous treatments was 2 (range 1-7). Eradication of H. pylori was achieved in 90% of patients (ITT) and 90.6% (PP). The eradication rate did not differ according to the type or number of prior treatments: 92% when -2 (n = 106) compared with 83% when > 2 prior treatments, (n = 42; p = 0.13) or with age, ethnicity or indication for treatment but it was higher in females (94% vs 86%, p = 0.04). Compliance was excellent (95%). No serious adverse effects were observed; mild adverse effects were reported in 11% (nausea, thrush, sore throat, constipation, muscle aches). Conclusion: The efficacy and safety of this levofloxacin based triple therapy suggests it should be the first choice salvage regimen in clinical practice in Australia. Randomised comparative trials are unlikely to be done but these data compare favourably with local data for other salvage therapies.

Katicić, M., et al. (2014). "[Croatian guidelines for gastric cancer prevention by eradication of Helicobacter pylori infection]." Lijecnicki Vjesnik 136(3-4): 59-68.

Gastric cancer is the fourth most common type of cancer and the second leading cause of cancer-related death in the world. Although gastric cancer has a multifactorial etiology, infection with Helicobacter pylori is highly associated with gastric carcinogenesis. Carcinogenesis is also influenced by some environmental factors and host genetic diversity, which engenders differential host inflammatory responses that can influence clinical outcome. Chronic gastritis induced by H. pylori is the strongest known risk factor for adenocarcinoma of the distal stomach, but the effects of bacterial eradication on carcinogenesis have remained unclear up to now. Although eradication of H. pylori infection appears to reduce the risk of gastric cancer, several recent controlled interventional trials by H. pylori eradication to prevent gastric cancer have yielded disappointing results. To clarify this problem in a high-risk population, the investigators conducted a prospective, randomized, double-blind, placebo-controlled, population-based studies. The results of previous studies highlight the importance of longer and careful follow-up after eradication therapy. It seems that eradication treatment is effective in preventing gastric cancer if it is given before preneoplastic conditions/lesions, gastric atrophy, metaplasia, and dysplasia, have had time to develop. Furthermore, the significant efficacy of treatment observed in younger patients suggests the need to eradicate H. pylori as early as possible. This consensus aimed to propose guidelines for the diagnosis, management and control of individuals with chronic gastritis, atrophy, intestinal metaplasia, or dysplasia.

Khadija, B., et al. (2014). "Autoimmune gastritis: OLGA/OLGIM staging." Virchows Archiv 465(1): S144.

Objective: Few studies are available on staging auto-immune gastritis (AG) using Operative Link for Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia (OLGIM). In Helicobacter pylori gastritis, studies supported the association between OLGA/OLGIM stages III-IV and gastric cancer risk. The aim of our study was to compare the OLGA and OLGIM staging systems in the assessment of High-risk stages in AG. Method: A series (spanning the years 2008-2014) of 30 patients with serologically confirmedAGunderwent Sydney classification grading and OLGA/OLGIM staging. Results: High-risk stages (III-IV) gastritis was observed in 26.6 % of patients by both OLGA and OLGIM staging, but OLGIM down-staged 13.33 % of patients and down-staged to low risk stage 3.3 % of patients. No cases staged as high-risk by OLGIM were down-staged when OLGA criteria were applied. Conclusion: Because of its clinical impact, the stage of gastritis should be included as a conclusive message in gastritis histology report. Since it focuses on intestinal metaplasia alone and disregards those atrophy phenotypes occurring specifically in AG, OLGIMstaging is less sensitive than OLGA staging in identification high-risk gastritis and this may result in the down-staging of patients who should be offered follow-up.

Khor, C., et al. (2013). "Systematic endoscopic surveillance is feasible for the detection of early gastric neoplasia." Journal of Gastroenterology and Hepatology 28: 503.

Objective: Gastric cancer is a curable disease if detected early. Endoscopy surveillance is the only way to detect gastric cancer in the early stages. More targeted screening and surveillance is required in countries with intermediate incidence rate of gastric cancer. The Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP), initialized in 2004, is a prospective multicentre study with the ultimate goal of developing an optimal approach and cost-effective algorithm for targeted screening for gastric cancer in the Singapore Chinese population. We aim to determine whether systematic prospective endoscopic surveillance is feasible for the detection of early gastric cancer in Singapore Chinese cohort. Methods: Chinese subjects aged 50 years and above were recruited from gastroenterology clinics of four major public hospitals in Singapore from 2004-2010. Endoscopy surveillance was offered for a minimum of 5 years. Informed consent was obtained from all subjects and the study was approved by the institutional review boards. The main outcome measurement is the number of subjects who develop high grade dysplasia or gastric adenocarcinoma. Results: 3033 subjects with mean age 59 ± 7 years were recruited. 51% were male, 16% had family history of gastric cancer and 30% had H. pylori infection history based on their medical records. The prevalence of chronic gastritis, current H. pylori infection, atrophic gastritis and intestinal metaplasia at baseline were 81%, 20%, 19% and 44% respectively. The study is in progress, 1,300 have completed 5 years surveillance and the rest will complete by 2015.18 high grade dysplasia or early gastric cancers were detected so far after an average follow up period of 3 years. 12 of those cases were high grade dysplasia or intramucosal carcinoma and 6 were invasive cancers in stage 1A or 1B. The interval between the most recent endoscopy with no abnormal findings and the endoscopy where cancer was diagnosed is 4-25 months. Conclusion: Endoscopic surveillance is effective, and has already detected high grade dysplasia or early gastric cancer in a high risk Singaporean Chinese population.

Kim, G. H., et al. (2016). "Screening and surveillance for gastric cancer in the United States: Is it needed?" Gastrointestinal Endoscopy 84(1): 18-28.

BACKGROUND AND AIMS: Although the incidence of gastric cancer in the United States is relatively low, the incidence of gastric cancer is higher than for esophageal cancer, for which clear guidelines for screening and surveillance exist. With the increasing availability of endoscopic therapy, such as endoscopic submucosal dissection, for treating advanced dysplasia and early gastric cancer, establishing guidelines for screening and surveillance of patients who are at high risk of developing gastric cancer has the potential to diagnose and treat gastric cancer at an earlier stage and improve mortality from gastric cancer. The aims of this article were to review the data regarding the risk factors for developing gastric cancer, methods for gastric cancer screening, and results of national screening programs. METHODS: A review of the existing literature related to the aims was performed. RESULTS: Risk factors for gastric cancer that were identified include race/ethnicity (East Asian, Russian, or South American), first-degree relative diagnosed with gastric cancer, positive Helicobacter pylori status, and presence of atrophic gastritis or intestinal metaplasia. Endoscopy has the highest rate of detecting gastric cancer compared with other gastric cancer screening methods. The national screening program in Japan has demonstrated a mortality reduction from gastric cancer based on cohort data. CONCLUSIONS: Gastric cancer screening with endoscopy should be considered in individuals who are immigrants from regions associated with a high risk of gastric cancer (East Asia, Russia, or South America) or who have a family history of gastric cancer. Those with findings of atrophic gastritis or intestinal metaplasia on screening endoscopy should undergo surveillance endoscopy every 1 to 2 years. Large prospective multicenter studies are needed to further identify additional risk factors for developing gastric cancer and to assess whether gastric cancer screening programs for high-risk populations in the United States would result in improved mortality.

Kim, H., et al. (2017). "Risk factor of metachronous recurrence after endoscopic submucosal dissection for gastric epithelial neoplasm." Helicobacter 22: 70-71.

Background: Eradication of H. pylori after endoscopic submucosal dis-section of early gastric cancer is recommended to prevent metachro-nous recurrence of gastric neoplasm. However, the H. pylori infection does not seem to be significantly related to metachronous tumors in some other studies. Therefore, we conducted study to evaluate the association between H. pylori infection and recurrence of metachronous tumor after ESD. Method: A total of 176 patients with gastric neoplasm who had underwent ESD without Helicobacter eradication were included and the follow-up data were analyzed retrospectively. Result: 101 patients (57.4%) showed H. pylori infection (confirmed by CLO test). Metachronous gastric neoplasms developed in 26 (25.7%) in the CLO positive group and 16 (21.3%) in CLO negative group and there was no significant difference (P=.496). Pathologically confirmed mucosal atrophy (P=<.001) and intestinal metaplasia (IM) (P<.001) showed statistically significant association with metachronous recur-rence. In multivariate analysis, atrophy and IM were statistically associated with metachronous recurrence (P=.005 and 0.011, respectively). Among patients with H. pylori infection, metachronous recurrence was associated with atrophy (P=.052) or IM (P=.015). Similarly, in patients without H. pylori infection, there was significant relationship between metachronous recurrence and atrophy (P=.003) or IM (P<.001). In subgroup analysis of patients without significant IM (n=40), there was no significant association between H. pylori status and metachronous recurrence (P=.202). Conclusion: In context of metachronous recurrence after ESD of gastric neoplasm, mucosal atrophy and IM showed more significant rela-tionship than H. pylori infection status.

Kim, H. J., et al. (2008). "[The prevalence of atrophic gastritis and intestinal metaplasia according to gender, age and Helicobacter pylori infection in a rural population]." Journal of Preventive Medicine and Public Health. Yebang Uihakhoe Chi 41(6): 373-379.

OBJECTIVES: The objective of this study was to evaluate the prevalence of atrophic gastritis and intestinal metaplasia according to gender, age and Helicobacter pylori infection in a rural population in Korea. METHODS: Between April 2003 and January 2007, 713 subjects (298 men and 415 women, age range: 18-85) among the 2,161 adults who participated in a population-based survey received gastrointestinal endoscopy. All the subjects provided informed consent. Multiple biopsy specimens were evaluated for the presence of atrophic gastritis and intestinal metaplasia. The presence of Helicobacter pylori was determined using CLO and histology testing. RESULTS: The age-adjusted prevalence of atrophic gastritis was 42.7% for men and 38.1% for women and the prevalence of intestinal metaplasia was 42.5% for men and 32.7% for women. The prevalence of atrophic gastritis and intestinal metaplasia increased significantly with age for both men and women (p for trend<0.001). The age-adjusted prevalence of Helicobacter pylori was similar for men (59.0%) and women (56.7%). The subjects with Helicobacter pylori infection showed a significantly higher prevalence of intestinal metaplasia (44.3%) compared with that (26.8%) of the noninfected subjects (p<0.001). However, the prevalence of atrophic gastritis was not statistically different between the Helicobacter pylori-infected subjects and the noninfected individuals. CONCLUSIONS: Our findings suggest that the prevalence of atrophic gastritis and intestinal metaplasia is higher for a Korean rural population than that for a Western population; this may be related to the high incidence of gastric cancer in Koreans. Especially, the prevalence of intestinal metaplasia was high for the subjects with Helicobacter pylori infection. The multistep process of gastric carcinogenesis and the various factors contributing to each step of this process need to be determined by conducting future follow-up studies.

Kim, H. S., et al. (2012). "Heterotopic gastric mucosa with focal intestinal metaplasia and squamous epithelium in the rectum." Digestive Endoscopy 24(1): 46-48.

Heterotopic gastric mucosa has been described in all levels of the gastrointestinal tract. However, gastric heterotopia of the rectum is a rare finding. It is usually reported along with polyp located in the rectum between 5 and 8 cm from the anal verge. The most common symptom is painless rectal bleeding, and non-specific gastrointestinal symptoms may also be presented. We report an incidentally found case of a 46-year-old man without any gastrointestinal symptoms. The pathology showed gastric mucosa and squamous epithelium and focal intestinal metaplasia. This finding could be a clue as to the origins of the heterotopic gastric mucosa. Although there are no guidelines for treatment or the follow-up period, regular endoscopic surveillance is necessary for gastric cancer screening.

Kim, J. L., et al. (2020). "Long-term natural history after endoscopic resection for gastric dysplasia." Surgical Endoscopy.

BACKGROUND AND STUDY AIMS: Natural history after endoscopic resection (ER) for gastric dysplasia is still unclear. The aim of this study was to evaluate the long-term clinical outcomes and risk factors after ER for gastric dysplasia between control and cases with synchronous or metachronous gastric neoplasm. METHODS: A total of 1090 patients who had undergone ER for gastric dysplasia and been followed up for at least one year from December 2002 to December 2013 were finally analyzed. Risk factors affecting the development of synchronous or metachronous neoplasm (SMN) and long-term clinical outcomes after ER for gastric dysplasia were evaluated. RESULTS: Synchronous and metachronous neoplasms had developed in 126 (11.6%) and 133 patients (12.2%) during the mean follow-up duration of 63.6 months, respectively. Five-year and 10-year risk of metachronous neoplasm were 9.8% and 27.2%, respectively. Median duration to the development of metachronous neoplasm was 103.1 months. While age (P < 0.001) and mucosal atrophy (P = 0.09) of index cases were associated with the development of synchronous neoplasm, age (P = 0.017), incomplete resection (P = 0.025), and intestinal metaplasia (P = 0.017) of background mucosa of index cases were significantly related to the development of metachronous neoplasm in multivariate analysis. Cumulative incidence of SMN was not significantly different among H. pylori negative, eradicated, and persistent group. CONCLUSIONS: Age, incomplete ER, and background intestinal metaplasia of index gastric dysplasia were significantly associated with metachronous recurrence. Endoscopic surveillance for metachronous recurrence after ER for gastric dysplasia is mandatory for longer than 10 years.

Kim, J. W., et al. (2020). "METACHRONOUS CANCER AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WITH UNDIFFERENTIATED HISTOLOGY: A RETROSPECTIVE ANALYSIS." Gastrointestinal Endoscopy 91(6): AB601-AB602.

Background: Endoscopic submucosal dissection (ESD) has become a widely accepted as a standard treatment for early gastric cancer (EGC) with differentiated histology. However, therapeutic outcome of ESD for undifferentiated cancer is still controversial. As ESD is a technique that leaves the at-risk native stomach, patients with EGC who have previously underwent ESD have the potential to develop metachronous gastric cancer (MGC). Given evidence has demonstrated that the cumulative incidence of MGC after endoscopic resection is not negligibly low. This study evaluated the incidence of MGC after complete endoscopic resection for EGC with undifferentiated histology. Methods: We retrospectively analyzed a prospectively collected registry (KHU-ESD registry) of clinical, endoscopic, and pathologic results of patients who underwent ESD for EGC. The study included 573 consecutive patients (465 differentiated and 108 undifferentiated carcinomas) who underwent complete endoscopic resection and followed more than 1 year. They were generally followed by annual esophagogastroduodenoscopy. Compared with differentiated carcinoma (DC group), we investigated the incidence of MGC in EGCs with undifferentiated histology (UDC group). Also, the risk factors for MGC were assessed over the follow-up period. Results: The median follow-up duration was 4.2 (2.1-7.0) years in DC group and 4.8 (2.5-6.0) years in UDC group (P = 0.683). Younger and female patients were more common in the UDC group compared to the DC group (all P < 0.001). Whereas, patients with both atrophy and intestinal metaplasia (IM) were more common in the DC group than in the UDC group. Cumulative incidence of MGC was significantly higher in the DC group than in the UDC group (2.5% vs. 0.7% per person year, P = 0.011) (Fig. 1). In logistic regression analysis, undifferentiated histology was not associated with the development of MGC (OR 0.428, 95% CI 0.149-1.229, P = 0.115) and presence of synchronous cancer was a significant risk factor (OR 2.335, 95% CI 1.345-4.052, P = 0.003). Meanwhile, atrophy, IM, and Helicobacter pylori infection were not associated. Conclusions: In analysis of large number of EGCs with undifferentiated histology, the incidence of MGC after complete resection by ESD was lower than that of differentiated cancer. Therefore, if complete resection is expected, ESD can be considered as initial therapeutic modality for undifferentiated type EGC in term of metachronous recurrence. [Formula presented]

Kim, K., et al. (2019). "Body Mass Index and Risk of Intestinal Metaplasia: A Cohort Study." Cancer Epidemiology, Biomarkers and Prevention 28(4): 789-797.

BACKGROUND: We examined the association between body mass index (BMI) and development of endoscopic intestinal metaplasia. METHODS: This retrospective cohort study included 142,832 Korean adults free of endoscopic intestinal metaplasia and atrophic gastritis who underwent upper endoscopy at baseline and subsequent visits and were followed for up to 5 years. A parametric proportional hazards model was used to estimate the adjusted HR with 95% confidence interval (CI) for incident intestinal metaplasia. RESULTS: In more than 444,719.1 person-years of follow-up, 2,281 participants developed endoscopic intestinal metaplasia (incidence rate, 5.1 per 1,000 person-years). Increased BMI categories were associated with increased risk of new-onset intestinal metaplasia in a dose-response manner. After adjustment for age, sex, center, year of screening exam, smoking status, alcohol intake, exercise, total calorie intake, history of diabetes and hypertension, and history of Helicobacter pylori infection, the multivariable adjusted HRs (95% CIs) for incident intestinal metaplasia comparing BMIs of <18.5, 23-24.9, 25.0-29.9, and >30 kg/m(2) with a BMI of 18.5-22.9 kg/m(2) were 0.84 (0.64-1.09), 1.03 (0.93-1.16), 1.07 (0.96-1.20), and 1.48 (1.20-1.83), respectively. These associations did not differ by clinically relevant subgroups. Risk of endoscopic atrophic gastritis also increased as the baseline BMI category increased. CONCLUSIONS: In a large cohort of Korean men and women, obesity was independently associated with increased incidence of endoscopic atrophic gastritis and intestinal metaplasia. IMPACT: Excessive adiposity appears to play a role in development of stomach precursor lesions of stomach cancer, requiring further studies to determine whether strategies to reduce obesity will also help reduce precancerous lesions and, in turn, gastric cancer.

Kim, K., et al. (2019). "Smoking and Urinary Cotinine Levels Are Predictors of Increased Risk for Gastric Intestinal Metaplasia." Cancer Research 79(3): 676-684.

Studies on a longitudinal relationship between smoking status and intestinal metaplasia (IM), a premalignant lesion of stomach cancer, are limited. Here we examined the association of smoking status and urinary cotinine levels, an objective measure of smoking, with the development of endoscopic IM. This cohort study included 199,235 Korean adults free of endoscopic IM who underwent upper endoscopy at baseline and subsequent visits and who were followed for up to 6.8 years (median, 3.7 years). Former and current smoking status and pack-years based on self-reports were associated with an increased risk of new-onset IM in men but not in women. However, urinary cotinine levels were positively associated with incident IM in a dose-response manner in both men and women. For men, the multivariable-adjusted HR [95% confidence interval (CI)] for incident IM comparing the urinary cotinine levels of 50 to 99 ng/mL, 100 to 499 ng/mL, and ≥500 ng/mL with <50 ng/mL were 1.20 (0.94-1.55), 1.26 (1.14-1.40), and 1.54 (1.44-1.64), respectively, whereas for women, corresponding HR (95% CI) were 0.75 (0.19-2.99), 1.86 (1.20-2.88), and 1.57 (1.07-2.30), respectively. These associations were observed when changes in smoking status and other confounders were updated during follow-up as time-varying covariates. In this large cohort of young and middle-aged men and women, urinary cotinine levels were independently associated with an increased incidence of endoscopic IM in a dose-response manner. Collectively, these data confirm smoking as an independent risk factor for the development of gastric IM, a precursor lesion of stomach cancer. SIGNIFICANCE: A large-scale cohort study of nearly 200,000 adults associates smoking with increased risk for gastric intestinal metaplasia, a precursor lesion of stomach cancer.

Kim, K., et al. (2020). "Low Levels of Alcohol Consumption and Risk of Intestinal Metaplasia: A Cohort Study." Cancer Epidemiology, Biomarkers and Prevention 29(12): 2633-2641.

BACKGROUND: The impact of alcohol drinking on gastric precancerous lesions remains unclear. We investigated the relationship of alcohol intake with risk of atrophic gastritis (AG) and intestinal metaplasia (IM). METHODS: This study included 202,675 Korean adults free from AG and IM on their initial endoscopy who were followed with repeated endoscopic examinations. A parametric proportional hazards model was used to estimate the adjusted HR (aHR) with 95% confidence interval (CI) for incident AG and IM based on endoscopic diagnosis. RESULTS: During a mean follow-up of 4.7 years, 64,853 incident AG cases and 4,536 IM cases were identified. Alcohol consumption including drinking frequency, quantity, and binge drinking were consistently associated with increased risk of both AG and IM in a dose-response manner. After adjustment for confounders, the multivariable aHRs (95% CIs) for incident IM comparing average alcohol intake of <10, 10-<20, 20-<40, and ≥40 g/day with lifetime abstainers were 1.27 (1.02-1.56), 1.34 (1.07-1.66), 1.50 (1.20-1.86), and 1.54 (1.23-1.93), respectively. Former drinkers were also at a higher risk for AG and IM compared with lifetime abstainers. These associations were consistently observed in never smokers and in time-dependent analyses. CONCLUSIONS: In a large cohort of Korean individuals, alcohol intake even at low levels was independently associated with increased risk of developing endoscopic AG and IM, supporting a role of alcohol consumption in the pathogenesis of AG and IM, the precursor lesions of stomach cancer. IMPACT: Alcohol consumption from low-level drinking may contribute to gastric carcinogenesis.

Kim, M. S., et al. (2013). "Long-term follow up Helicobacter Pylori reinfection rate after second-line treatment: bismuth-containing quadruple therapy versus moxifloxacin-based triple therapy." BMC Gastroenterology 13: 138.

Kim, N. (2019). "Chemoprevention of gastric cancer by Helicobacter pylori eradication and its underlying mechanism." Journal of Gastroenterology and Hepatology 34(8): 1287-1295.

The cascade of gastric cancer, a leading cause of cancer incidence and mortality, is multifactorial. Helicobacter pylori (HP) infection plays a major role in gastric cancer (GC), and there has been an accumulation of data regarding the chemopreventive effect of HP eradication. However, it remains unclear how HP infection causes GC and how HP eradication prevents GC. To clarify this issue, the following approaches were performed in this review article. First, how HP-induced atrophic gastritis (AG) and intestinal metaplasia (IM) provoke the development of GC is shown, followed by how long HP eradication takes to induce a reversible change in AG and IM. Second, epigenetic studies of PTPN6, MOS, DCC, CRK, and VAV1 were performed in noncancerous gastric specimens in terms of HP status. Among these genes, MOS was found to be a possible surrogate marker for GC development. HP eradication decreased aberrant DNA methylation in a gene-specific manner, and MOS played a role in metachronous gastric neoplasms. Third, transforming growth factor-β1 (TGF-β1) and TGF-β1-induced epithelial-mesenchymal transition (EMT) markers were investigated in gastric mucosa. HP infection triggered the TGF-β1-induced EMT pathway and caused the emergence of GC stem cells, such as CD44v8-10. When HP was eradicated, these two pathways were inhibited. Finally, a 2222 cohort study showed that HP eradication significantly decreased the risk of noncardiac GC. Taken together, HP eradication is effective as a primary GC prevention method, and its underlying mechanism includes reversibility of AG and IM, methylation, EMT, and stem cells.

Kim, N., et al. (2009). "[Diagnosis and treatment guidelines for Helicobacter pylori infection in Korea]." Korean Journal of Gastroenterology 54(5): 269-278.

Eleven years has passed since the guideline of the Korean College of Helicobacter and Upper Gastrointestinal Research group for H. pylori infection was produced in 1998. During this period the research for H. pylori has much progressed that H. pylori is now regarded as the major cause of gastric cancer. The seroprevalence of H. pylori in Korea was found to be decreased especially below the age of 40s and in the area of Seoul-Gyeonggi province, and annual reinfection rate of H. pylori has decreased up to 2.94%. In the aspect of diagnostic tests of H. pylori the biopsy is recommended in the body instead of antrum in the subjects with atrophic gastritis and/or intestinal metaplasia for the modified Giemsa staining or Warthin Starry silver staining. The urea breath test is the test of choice to confirm eradication when follow-up endoscopy is not necessary. Definite indication for H. pylori eradication is early gastric cancer in addition to the previous indications of peptic ulcer including scar and Marginal zone B cell lymphoma (MALT type). Treatment is also recommended for the relatives of gastric cancer patient, unexplained iron deficiency anemia, and chronic idiopathic thrombocytopenic purpura. One or two week treatment of proton pump inhibitor (PPI) based triple therapy consisting of one PPI and two antibiotics, clarithromycin and amoxicillin, is recommended as the first line treatment regimen. In the case of treatment failure, one or two weeks of quadruple therapy (PPI+metronidazole+tetracycline+bismuth) is recommended. Herein, Korean College of Helicobacter and Upper Gastrointestinal Research proposes a diagnostic and treatment guideline based on currently available evidence.

Kim, N., et al. (2008). "Helicobacter pylori infection and development of gastric cancer in Korea: long-term follow-up." Journal of Clinical Gastroenterology 42(5): 448-454.

BACKGROUND AND AIM: Infection of Helicobacter pylori is viewed as a major driver of progression to the precancerous state or to gastric cancer. This study was performed to investigate the effect of H. pylori infection on gastric cancer development and to determine to what extent H. pylori eradication is likely to reduce the prevalence of gastric cancer. METHODS: Gastric cancer development was investigated in 1790 Korean subjects who underwent gastroscopy and H. pylori testing between 1992 and 1998. The effects of H. pylori-positive and eradicated states on gastric cancer development were analyzed. RESULTS: Gastric cancer developed in 5 of the study cohort during a mean follow-up period of 9.4 years. All of these patients were positive for H. pylori infection, and 4 of the 5 had antral intestinal metaplasia (IM) at the time of study enrollment. One of these 5 patients was in an eradicated state when the gastric cancer was diagnosed, and had histologic IM before eradication therapy was performed. Gastric cancer was found to develop 10.9 times more frequently in the presence of IM than in its absence. CONCLUSIONS: The present study shows a close relationship between H. pylori infection and IM, and between IM and the development of gastric cancer. In addition, our finding suggests that chronic H. pylori infection looks like an important risk factor for the development of gastric cancer in Korea, where the prevalence of H. pylori remains high. This study indicates that to prevent gastric cancer H. pylori eradication is best performed before the development of IM.

Kim, N., et al. (2008). "Prevalence and risk factors of atrophic gastritis and intestinal metaplasia in a Korean population without significant gastroduodenal disease." Helicobacter 13(4): 245-255.

BACKGROUND AND AIM: The prevalence of gastric cancer and Helicobacter pylori infection is unacceptably high in Korea. This study was performed to evaluate the prevalence of atrophic gastritis (AG) and intestinal metaplasia (IM) and to identify their risk factors with respect to H. pylori virulence factors, and environmental and host factors, in Korean population without significant gastroduodenal disease. METHODS: The study cohort consisted of 389 subjects (> or = 16 years). AG and IM were scored histologically using the Sydney classification in the antrum and body, respectively. Prevalences and bacterial factors (i.e. cagA, vacA m1, and oipA), environmental factors (i.e. smoking and alcohol), and host factors (i.e. genetic polymorphisms of IL-1B-511, IL-1RN, TNF-A-308, IL-10-592, IL-10-819, IL-10-1082, IL-8-251, IL-6-572, GSTP1, p53 codon 72, and ALDH2) were evaluated. RESULTS: Prevalences of AG in the antrum and body were 42.5% and 20.1%, and those of IM were 28.6% and 21.2%, respectively. The presences of AG and IM were significantly higher in H. pylori-positive than in the H. pylori-negative subjects. Multivariate analysis showed that the risk factors for AG were H. pylori infection, age > or = 61 years, and cagA and vacA m1 positivity. For IM the risk factors were H. pylori infection, age > or = 61 years, a smoking history (rather than current smoking), strong spicy food, occupation (unemployed or nonprofessional vs. professional), and the presence of IL10-592 C/A as opposed to A/A. In addition, IL6-572 G carrier was found to have a protective effect against IM development as compared with C/C. CONCLUSION: H. pylori infection was most important risk factor of AG and IM. Bacterial factors were found to be important risk factor for AG but environmental and host factors were more important for IM.

Kim, S. B., et al. (2016). "Association between Helicobacter pylori status and metachronous gastric cancer after endoscopic resection." World Journal of Gastroenterology 22(44): 9794-9802.

AIM: To investigate the effect of Helicobacter pylori (H. pylori) status test and H. pylori eradication on the occurrence of metachronous gastric cancer (MGC) after endoscopic submucosal dissection (ESD) of early gastric cancer (EGC) and risk factors of MGC. METHODS: The authors retrospectively reviewed the medical records of 433 patients (441 lesions) who underwent ESD for EGC from January 2005 to January 2015 in Yeungnam University Hospital. Patients were categorized into two groups; the H. pylori tested group (n = 257) and the H. pylori non-tested group (n = 176) based on performance of H. pylori status test after ESD of EGC. The H. pylori tested group was further categorized into three subgroups based on H. pylori status; the H. pylori-eradicated subgroup (n = 120), the H. pylori-persistent subgroup (n = 42), and the H. pylori-negative subgroup (n = 95). Incidences of MGC and risk factors of MGC were identified. RESULTS: Median follow-up duration after ESD was 30.00 mo (range, 6-107 mo). Total 15 patients developed MGC during follow-up. MGC developed in 11 patients of the H. pylori tested group (7 in the H. pylori-negative subgroup, 3 in the H. pylori-eradicated subgroup, and 1 in the H. pylori-persistent subgroup) and 4 patients of the H. pylori non-tested group (P > 0.05). The risk factors of MGC were endoscopic mucosal atrophy in the H. pylori tested group and intestinal metaplasia in all patients. CONCLUSION: H. pylori eradication and H. pylori status test seems to have no preventive effect on the development of MGC after ESD for EGC. The risk factors of MGC development were endoscopic mucosal atrophy in the H. pylori tested group alone and intestinal metaplasia in all patients.

Kim, Y. M., et al. (2019). "Sarcopenia and Sarcopenic Obesity as Novel Risk Factors for Gastric Carcinogenesis: A Health Checkup Cohort Study." Frontiers in Oncology 9: 1249.

Background: Insulin resistance, the primary mechanism of metabolic syndrome, promotes gastric carcinogenesis. Metabolic syndrome is associated with sarcopenia. We aimed to investigate the association between sarcopenia and gastric carcinogenesis, including precancerous conditions such as atrophic gastritis (AG), intestinal metaplasia (IM), and dysplasia. Methods: The study included adult patients who underwent gastroduodenoscopy at a checkup center. AG and IM were evaluated using endoscopy. Based on muscle mass, sarcopenia was defined as a skeletal muscle index <1 standard deviation below the sex-specific mean for healthy adults aged 20-39 years (cutoff point: 29.3% for males and 26.7% for females). Obesity was defined as a body mass index (BMI) ≥25 kg/m(2) according to the Asia-Pacific criteria. Sarcopenic obesity was defined as a combination of sarcopenia and obesity. The association between gastric carcinogenesis and sarcopenia was evaluated. Results: Among 8,356 enrolled participants, 0.14 and 42.5% were diagnosed with gastric cancer and precancerous conditions, respectively. Approximately 41.7% of gastric cancer patients and 16.9% of patients with precancerous conditions were diagnosed with sarcopenia. Both sarcopenic obesity (odds ratio [OR] = 4.139, P = 0.016) and diabetes mellitus (DM) (OR = 5.152, P = 0.005) were significantly associated with gastric cancer. Sarcopenia, DM, hypertension, dyslipidemia, Helicobacter pylori infection, smoking, and alcohol consumption were significantly associated with precancerous conditions. Conclusions: Sarcopenia and sarcopenic obesity were associated with gastric carcinogenesis and may be novel risk factors for gastric carcinogenesis.

Kim, Y. M., et al. (2019). "Association between sarcopenia and gastric carcinogenesis: A health check-up cohort study." Journal of Clinical Oncology 37.

Background: Insulin resistance which is a mechanism of metabolic syndrome has been known to promote carcinogenesis of various malignancies. In addition, metabolic syndrome is associated with sarcopenia. Thus, the aim was to investigate the association between sarcopenia and gastric carcinogenesis including precancerous conditions: atrophic gastritis (AG), intestinal metaplasia (IM), and gastric adenoma. Methods: The study subjects were an adult population who underwent gastroduodenoscopy at Gangnam Severance Check-up Center. AG and IM were evaluated by endoscopic findings. Sarcopenia based on muscle mass was defined as appendicular skeletal muscle (ASM) as a percentage of body weight that was less than 1 standard deviation below the sex-specific mean for healthy adults aged 20 to 39 years (cutoff point: 29.3% in male and 26.7% in female). Obesity was defined as body mass index (BMI) ≥ 25 kg/m2 according to the Asia-Pacific criteria. Sarcopenic obesity was a condition of combined sarcopenia and obesity. The association between sarcopenia and gastric lesions was evaluated. Results: 8,356 patients were enrolled this study. Among them, 12 (0.14%) and 3,552 (42.5%) patients were diagnosed as gastric cancer and precancerous conditions, respectively. 5 (41.7%) of 12 gastric cancer patients and 594 (16.9%) of 3.552 patients with gastric precancerous conditions were diagnosed with sarcopenia. Both diabetes mellitus (DM) (OR = 5.152, P = 0.005) and sarcopenic obesity (OR = 4.139, P = 0.016) were independent predictive factors for gastric cancer. And smoking, alcohol, DM, hypertension, dyslipidemia, Helicobacter pylori, and sarcopenia were significantly associated with gastric precancerous conditions. Conclusions: Sarcopenia and sarcopenic obesity were significantly associated with gastric carcinogenesis. Thus, sarcopenia may be one of the risk factors for gastric carcinogenesis.

Kim, Y. M., et al. (2019). "ASSOCIATION BETWEEN SARCOPENIA AND GASTRIC CARCINOGENESIS: A HEALTH CHECK-UP COHORT STUDY." Gastroenterology 156(6): S-677-S-678.

Background/Aims Insulin resistance which is a mechanism of metabolic syndrome has been known to promote carcinogenesis of various malignancies. In addition, metabolic syndrome is associated with sarcopenia. Thus, the aim was to investigate the association between sarcopenia and gastric carcinogenesis including precancerous conditions: atrophic gastritis (AG), intestinal metaplasia (IM), and gastric adenoma. Methods: The study subjects were an adult population who underwent gastroduodenoscopy at Gangnam Severance Check-up Center. AG and IM were evaluated by endoscopic findings. Sarcopenia based on muscle mass was defined as appendicular skeletal muscle (ASM) as a percentage of body weight that was less than 1 standard deviation below the sex-specific mean for healthy adults aged 20 to 39 years (cutoff point: 29.3% in male and 26.7% in female). Obesity was defined as body mass index (BMI) ≥25 kg/m2 according to the Asia-Pacific criteria. Sarcopenic obesity was a condition of combined sarcopenia and obesity. The association between sarcopenia and gastric lesions was evaluated. Results: 8,356 patients were enrolled this study. Among them, 12 (0.14%) and 3,552 (42.5%) patients were diagnosed as gastric cancer and precancerous conditions, respectively. 5 (41.7%) of 12 gastric cancer patients and 594 (16.9%) of 3.552 patients with gastric precancerous conditions were diagnosed with sarcopenia. Both diabetes mellitus (DM) (OR = 5.152, P = 0.005) and sarcopenic obesity (OR = 4.139, P = 0.016) were independent predictive factors for gastric cancer. And smoking, alcohol, DM, hypertension, dyslipidemia, Helicobacter pylori, and sarcopenia were significantly associated with gastric precancerous conditions. Conclusion: Sarcopenia and sarcopenic obesity were significantly associated with gastric carcinogenesis. Thus, sarcopenia may be one of the risk factors for gastric carcinogenesis.

Kodama, M., et al. (2012). "Ten-year prospective follow-up of histological changes at five points on the gastric mucosa as recommended by the updated Sydney system after Helicobacter pylori eradication." Journal of Gastroenterology 47(4): 394-403.

BACKGROUND: Atrophic gastritis and intestinal metaplasia (IM) are well known as precancerous lesions of gastric cancer. The present study evaluated the gastric mucosa for 10 years after H. pylori eradication at five points of the stomach as recommended by the updated Sydney system to clarify the relationship between H. pylori eradication and gastric cancer prevention. METHODS: Among the comprised 373 patients, 323 were H. pylori-positive while 50 patients were H. pylori-negative. Patients with successful eradication underwent follow-up endoscopic examination every year. Biopsy specimens were taken from five points of the stomach, as recommended by the updated Sydney system, and were evaluated for the degree of gastritis prospectively. RESULTS: Two hundred ninety-four out of the 323 H. pylori-positive patients successfully achieved eradication. Of the 197 patients on whom five-point biopsy was performed, the courses of 30 patients were able to be observed every year for 10 years after successful eradication. Inflammation, activity, and atrophy score at all five points were significantly reduced half a year to 6 years after eradication. IM scores fluctuated intensely up and down during all observation periods; however, IM score of the lesser curvature of the corpus continued decreasing gradually and showed a significant decrease 6 years after (0.97 ± 0.09 to 0.42 ± 0.17, P < 0.05). CONCLUSION: In 10 years after H. pylori eradication, atrophy at all sites and IM in the lesser curvature of the corpus gradually and significantly decreased. These results suggest that the improvement of gastric atrophy and IM might have association with the reduction of gastric cancer occurrence.

Kodama, M., et al. (2012). "Long term prospective follow-up of histological alteration at 5 points on the gastric mucosa recommended by the updated sydney system after helicobacter pylori eradication." Gastroenterology 142(5): S477.

Background: Atrophic gastritis and intestinal metaplasia (IM) are recognized as premalignant lesions of gastric cancer. Many studies which described the histological change after eradication showed disagreement. We prospectively evaluated the change of gastric mucosa for 10 years period after H. pylori eradication at 5 points of the stomach to clarify the association between H. pylori eradication and gastric carcinogenesis. Materials and Methods: Of the 373 patients, H. pylori positive were 323, on the other hand 50 patients were H. pylori-negative. Successful eradicated group underwent follow-up endoscopic examination every year. Biopsy specimens were taken from 5 points of the stomach, which recommended by updated Sydney system, and were evaluated gastritis status, that of inflammation, activity, atrophy, and intestinal metaplasia. Results: 294 out of the 323 H. pylori-positive patients achieved successfull eradication. Of the 197 patients on whom 5-point biopsy was performed, 30 patients were able to be observed every year for 10 years after successful eradication. Inflammation, activity, and atrophy score at all 5 points were significantly reduced half a year to 6 years after eradication. IM scores fluctuated intensely up and down during all observation periods, however, IM score of the lesser curvature of the corpus continued decreasing gradually and showed a significant decrease 6 years after (0.97±0.09 to 0.42±0.17, P<0.05). Conclusion: Atrophy at all sites and IM in the lesser curvature of the corpus gradually and significantly decreased in 10 years follow after H. pylori eradication. It is considered that these findings suggested the improvement of gastric atrophy and IM may have association with the reduction of gastric cancer.

Kodama, M., et al. (2021). "Gastric mucosal changes, and sex differences therein, after Helicobacter pylori eradication: A long-term prospective follow-up study." Journal of Gastroenterology and Hepatology.

BACKGROUND AND AIM: Improvement of atrophic gastritis and intestinal metaplasia (IM) is considered to reduce the gastric cancer risk, but whether it can be achieved by H. pylori eradication (HPE) remains controversial. To evaluate the effect of HPE, we observed the gastric mucosa for up to17 years after HPE and sex differences in gastric mucosa. METHODS: In total, 172 patients (94 males, 78 females) with HPE were enrolled. Annual histological evaluations were performed for up to 17 years. The grades of mononuclear cells, neutrophils, atrophy, IM in the antrum and corpus were evaluated using the updated Sydney system. RESULTS: Relative to the pre-HPE period, atrophy had improved significantly 1 year after HPE in the antrum (1.50 ± 0.75 vs. 1.21 ± 1.25, P < 0.01) and corpus (0.59 ± 0.75 vs. 0.18 ± 0.52, P < 0.05). IM showed no significant change during 17 years after HPE at either biopsy site. Atrophy scores did not differ significantly between males and females. IM scores were significantly higher in males than in females before eradication (antrum, 0.67 ± 0.94 vs. 0.44 ± 0.77, P = 0.003, corpus, 0.20 ± 0.62 vs. 0.047 ± 0.21, P = 0.0027) and at most observation timepoints. CONCLUSIONS: During 17 years after HPE, atrophy, but not IM, improved significantly at the greater curvatures of the antrum and corpus. IM was significantly more severe in males than in females. Careful follow-up after HPE based on sex differences in gastric mucosal characteristics is important.

Koh, C. J., et al. (2016). "Predicting gastric intestinal metaplasia and cancer using pre-endoscopic risk factors." Journal of Gastroenterology and Hepatology (Australia) 31: 93.

Background: Gastric intestinal metaplasia (IM) is a pre-malignant condition and early identification of individuals with intestinal metaplasia facilitates further endoscopic screening for gastric cancer. Objective: To assess the pre-endoscopic risk factors, Helicobacter serology (HP) and pepsinogen (PG), with demographic and epidemiologic factors in predicting IM and cancer. Method: A prospective cohort with 5,425 subjects who were referred for upper GI endoscopy for standard clinical indications. Blood was drawn HP and PG levels prior to gastroscopy. The correlation between the blood test results and findings from the clinical endoscopy were analyzed. Other factors examined include the following: gender, race, body mass index (BMI), family history of gastric cancer, smoking and alcohol use. Results: There were 5,425 participants recruited, of which 54 (1%) had gastric cancer and 791 (14.6%) had IM. For IM, univariate significant risk factors were: age >50 years, male gender, Chinese race, smoking, alcohol use, family history of cancer, PG and HP status. All factors apart from alcohol use and male gender remained significant on multivariate analysis. For gastric cancer, univariate significant risk factors were: age >50 years, male gender, and IM, HP status and PG. All factors remained significant on multivariate analysis. The modified 4 risk-factor score (Zhu F et al, DDW 2015) using age >50 years, smoking, HP and PG was assessed and gave an AUROC of 0.727 for gastric cancer and 0.658 for intestinal metaplasia. A score of 2 or more had a sensitivity of 83.3% and a specificity of 53.1% for gastric cancer. Conclusion: This study suggests risk stratification with non-invasive serum markers and demographic factors is useful in identifying a higher risk group for endoscopic screening for gastric cancer and IM, and validates the 4 risk-factor strategy in a real-world, endoscopic surveillance population. (Figure presented).

Kuipers, E. J., et al. (1996). "Atrophic gastritis and Helicobacter pylori infection in patients with reflux esophagitis treated with omeprazole or fundoplication." New England Journal of Medicine 334(16): 1018-1022.

Background. Helicobacter pylori infection plays an important part in the development of atrophic gastritis and intestinal metaplasia, conditions that predispose patients to gastric cancer. Profound suppression of gastric acid is associated with increased severity of gastritis caused by H. pylori, but it is not known whether acid suppression increases the risk of atrophic gastritis. Methods. We studied patients from two separate cohorts who were being treated for reflux esophagitis; 72 patients treated with fundoplication in Sweden and 105 treated with omeprazole (20 to 40 mg once daily) in the Netherlands. In both cohorts, the patients were followed for an average of five years (range, three to eight). After fundoplication, the patients did not receive acid-suppressive therapy. The presence of H. pylori was assessed at the first visit by histologic evaluation in the fundoplication group and by histologic and serologic evaluation in the omeprazole group. The patients were not treated for H. pylori infection. Before treatment and during follow-up, the patients underwent repeated gastroscopy, with biopsy sampling for histologic evaluation. Results. Among the patients treated with fundoplication, atrophic gastritis did not develop in any of the 31 who were infected with H. pylori at base line or the 41 who were not infected; 1 patient infected with H. pylori had atrophic gastritis before treatment that persisted after treatment. Among the patients treated with omeprazole, none of whom had atrophic gastritis at base line, atrophic gastritis developed in 18 of the 59 infected with H. pylori (P<0.001) and 2 of the 46 who were not infected (P=0.62). Conclusions: Patients with reflux esophagitis and H. pylori infection who are treated with omeprazole are at increased risk or atrophic gastritis.

Kuipers, E. J., et al. (2004). "Cure of Helicobacter pylori infection in patients with reflux oesophagitis treated with long term omeprazole reverses gastritis without exacerbation of reflux disease: results of a randomised controlled trial." Gut 53(1): 12‐20.

Kuipers, E. J., et al. (1995). "Helicobacter pylori and atrophic gastritis: Importance of the cagA status." Journal of the National Cancer Institute 87(23): 1777-1780.

Background: Infection with Helicobacter pylori is a major risk factor for the development of atrophic gastritis and gastric cancer. H. pylori strains can differ with respect to the presence of cagA (cytotoxin-associated gene A), a gene encoding a high-molecular-weight immunodominant antigen. H. pylori strains possessing cagA have been associated with enhanced induction of acute gastric inflammation. Purpose: We investigated the relationship between cagA status and the development of atrophic gastritis in a cohort of subjects infected with H. pylori. Methods: Gastrointestinal endoscopy with biopsy sampling was used to study the natural history of gastritis in 58 subjects infected with H. pylori. Biopsy specimens were obtained before and after a mean follow-up period of 11.5 years (range, 10-13 years). The cagA status of each individual was determined at the follow-up visit with the use of an enzyme-linked immunosorbent assay designed to detect the presence of serum immunoglobulin G directed against the CagA protein. Two-sided Fisher's exact tests, McNemar's tests, Student's t tests, and Wilcoxon sum rank tests were used to analyze the data. Results: Twenty-four (41%) of the 58 evaluated subjects had serum antibodies against CagA (i.e., they were cagA positive), and 34 subjects were cagA negative. At the initial visit, moderate to severe atrophic gastritis was observed in eight(33%) of the cagA-positive subjects and in six (18%) of the cagA-negative subjects. At that time, positive cagA status and gastric atrophy were not significantly related (P = .22; Fisher's exact test; odds ratio [OR] 2.33; 95% confidence interval [CI] = 0.58-9.65). During follow-up, 16 (36%) of the 44 initially atrophy-negative subjects developed atrophic gastritis (eight [50%] of 16 cagA-positive subjects versus eight [29%] of 28 cagA-negative subjects; P = .20, Fisher's exact test; relative risk [RR] = 1.75; 95% CI = 0.82-3.76). In six of these 16 subjects (five cagA positive versus one cagA negative), atrophic gastritis was accompanied by the development of intestinal metaplasia (i.e., a change in the type of specialized cells present) (P = .02; Fisher's exact test; RR = 9.06; 95% CI = 1.16-71.0). One of the initially atrophy-negative, cagA- positive subjects developed early gastric cancer. Four (29%) of the 14 subjects initially diagnosed with atrophic gastritis showed regression of atrophy during follow-up (one cagA positive and three cagA negative). Therefore, at the end of follow-up, 15 (62%) of the 24 cagA-positive subjects had atrophic gastritis compared with 11 (32%) of the 34 cagA-negative subjects (P = .02; Fisher's exact test; OR = 3.48; 95% CI = 1.02-12.18). Conclusion: Infection with cagA-positive H. pylori strains is associated with an increased risk for the eventual development of atrophic gastritis and intestinal metaplasia.

Kuipers, E. J., et al. (1995). "Long-term sequelae of Helicobacter pylori gastritis." Lancet 345(8964): 1525-1528.

Chronic Helicobacter pylori gastritis has been put forward as a risk factor for development of gastric mucosal atrophy and gastric cancer. The purpose of our study was to investigate the long-term effects of H pylori gastritis on the gastric mucosa. We prospectively studied 49 subjects negative for H pylori and 58 positive subjects for a mean follow-up of 11.5 years (range 10-13 years). Serum samples were obtained at the initial and follow-up visits for determination of H pylori IgG antibodies. Gastroscopies with biopsy sampling were done in all patients at both visits. Biopsy specimens were used for assessment of H pylori infection and histology. Development of atrophic gastritis and intestinal metaplasia occurred in 2 (4%) uninfected and 16 (28%) infected subjects. Regression of atrophy was noted in 4 (7%) infected subjects. Development of atrophic gastritis and intestinal metaplasia was significantly associated with H pylori infection (p = 0.0014; odds ratio 9.0, 95% CI 1.9-41.3). The proportion of atrophic gastritis in the study population showed an annual increase of 1.15% (0.5-1.8%). We conclude that H pylori infection is a significant risk factor for development of atrophic gastritis and intestinal metaplasia. Our findings support strongly the causative role of this infection in gastric carcinogenesis.

Kuvaev, R., et al. (2015). "Computer-aided diagnostic system for the realtime pathology prediction and clinical decision support during narrow band imaging magnification endoscopy in stomach." United European Gastroenterology Journal 3(5): A9.

Introduction: Narrow-band imaging endoscopy with magnification (NBI-M) is recommended to be utilized for clinical decision-making during screening or follow-up of individuals at high risk for gastric cancer [1]. Nevertheless, its application in clinical practice has some challenges due to the presence of various histological and endoscopic pattern changes of gastric mucosa. Nowadays computer- aided decision support systems in endoscopy are being designed to assist a medical expert in mastering advanced techniques that require a high level of expertise. Aims&Methods: The aim of this study was to design a computer-aided diagnosis hardware-software complex for real time clinical decision support during NBI-M in stomach. This complex was incorporated into endoscopic documentation system for real-time pathology prediction based on the automated assessment of mucosal patterns of saved images. Image processing techniques were applied for extracting of geometrical and topological features. For creating a multi-class classifier a naive Bayesian approach was used to combine results of several binary Adaboost classifiers. We selected and analyzed 91 endoscopy NBI-M images of gastric lesions from 52 patients (Olympus Exera GIF Q160Z, Lucera GIF Q260Z). All images were independently assessed by an expert and computeraided system according to validated simplified NBI-classification [2]: type A (circular), B (tubulo-villous), C (irregular). Histology was used as the ground truth information. Training and testing were performed for every image by a bootstrap method. Results: Among 91 images 25 had type A pattern (16 normal mucosa, 9 chronic gastritis), 31 had type B pattern (22 intestinal metaplasia, 9 pseudopyloric metaplasia), and irregular 35 has type C pattern (9 high-grade dysplasia, 26 adenocarcinoma). The average percentage of correctly recognized areas was 91.8±4.4% (92% in type A, 92% in B, 89% in C). The results of computeraided classification are summarized in the table. Conclusion: The newly designed endoscopic computer-aided diagnostic hardware- software system could provide effective recognition of three main types of gastric mucosal patterns and thus may lead to real-time pathology prediction and support for clinical decision-making.

Lage, J., et al. (2016). "Light-NBI to identify high-risk phenotypes for gastric adenocarcinoma: do we still need biopsies?" Scandinavian Journal of Gastroenterology 51(4): 501-506.

OBJECTIVE: Early diagnosis of gastric cancer may be achieved through surveillance of patients with extensive gastric intestinal metaplasia (eGIM). However, diagnosis of eGIM generally implies histology. We aimed at determining the accuracy of high-resolution endoscopy with light-narrow band imaging (NBI) to assess the presence of eGIM on a per-patient basis. MATERIAL AND METHODS: Prospective cohort of 60 patients divided into two groups: derivation cohort (n = 25) to evaluate the reliability and validity, and a real-time validation group (n = 35). In the derivation group, six endoscopists with two levels of expertise were asked to estimate the grade of GIM based in endoscopic images (white light endoscopy, light-NBI and amplification/near focus). In the real-time validation set, experienced endoscopists were asked to similarly record their real-time optical diagnosis. Histology was then considered as the gold standard. RESULTS: In the derivation group diagnosis accuracy was 60% with WLE (non-expert 59% vs. 61% experts), increasing to 73% after NBI magnification (non-expert 63% vs. 83% expert, p < 0.05). Moreover, proportion of agreement with histology was 83%, with a correct diagnosis of eGIM in 87% for experienced observers. In the real-time group experts obtained 89% global diagnostic accuracy correctly identifying 91% of the eGIM. The sensitivity, specificity, LR + and LR- of real-time endoscopic diagnosis of eGIM was 0.92 (CI95%:0.67-0.99), 0.96 (0.79-0.99), 21.1 (3.08-144) and 0.09 (0.013-0.57). CONCLUSION: For the first time the reliability of high-resolution endoscopy with light-NBI for extension of GIM is described. Our results suggest that more than 90% of individuals at risk could be identified without the need for biopsies, simplifying the current recommendations.

Lahner, E., et al. (2001). "First endoscopic-histologic follow-up in patients with body-predominant atrophic gastritis: when should it be done?" Gastrointestinal Endoscopy 53(4): 443-448.

BACKGROUND: Body-predominant atrophic gastritis is considered a risk factor for gastric cancer and carcinoid. Timing of follow-up for patients with this disorder has not been defined. This study was undertaken to determine the optimal time for the first endoscopic/histologic follow-up in patients with body-predominant atrophic gastritis. METHODS: Forty-two patients with body-predominant atrophic gastritis were randomly assigned to 1 of 2 follow-up intervals: group A (n = 22) at 24 months and group B (n = 20) at 48 months. At baseline and follow-up patients underwent gastroscopy at which biopsies were obtained from the antrum and body for histopathology and evaluation for enterochromaffin-like cells. RESULTS: In group A patients, 2 antral hyperplastic polyps (9.1%) were present at baseline and 4 antral hyperplastic polyps (18.2%) were found at follow-up. In group B patients, baseline gastroscopy revealed 2 antral hyperplastic polyps (10%) and follow-up 2 antral hyperplastic polyps (10%) and 1 carcinoid tumor (5%) in the body. Atrophy and intestinal metaplasia scores in gastric body and antral mucosa in both groups did not change significantly between baseline and follow-up, except an increase in antral mucosa atrophy in group B patients (p = 0.02) was revealed. CONCLUSIONS: The results of this study indicate that performing the first follow-up in patients with body-predominant atrophic gastritis need not be earlier than at 4 years after diagnosis. This interval is satisfactory for detection of potential neoplastic lesions.

Laine, L., et al. (2000). "Review article: potential gastrointestinal effects of long-term acid suppression with proton pump inhibitors." Alimentary Pharmacology and Therapeutics 14(6): 651-668.

This review examines the evidence for the development of adverse effects due to prolonged gastric acid suppression with proton pump inhibitors. Potential areas of concern regarding long-term proton pump inhibitor use have included: carcinoid formation; development of gastric adenocarcinoma (especially in patients with Helicobacter pylori infection); bacterial overgrowth; enteric infections; and malabsorption of fat, minerals, and vitamins. Prolonged proton pump inhibitor use may lead to enterochromaffin-like cell hyperplasia, but has not been demonstrated to increase the risk of carcinoid formation. Long-term proton pump inhibitor treatment has not been documented to hasten the development or the progression of atrophic gastritis to intestinal metaplasia and gastric cancer, although long-term studies are required to allow definitive conclusions. At present, we do not recommend that patients be tested routinely for H. pylori infection when using proton pump inhibitors for prolonged periods. Gastric bacterial overgrowth does increase with acid suppression, but important clinical sequelae, such a higher rate of gastric adenocarcinoma, have not been seen. The risk of enteric infection may increase with acid suppression, although this does not seem to be a common clinical problem with prolonged proton pump inhibitor use. The absorption of fats and minerals does not appear to be significantly impaired with chronic acid suppression. However, vitamin B12 concentration may be decreased when gastric acid is markedly suppressed for prolonged periods (e.g. Zolllinger-Ellison syndrome), and vitamin B12 levels should probably be assessed in patients taking high-dose proton pump inhibitors for many years. Thus, current evidence suggests that prolonged gastric acid suppression with proton pump inhibitors rarely, if ever, produces adverse events. Nevertheless, continued follow-up of patients taking proton pump inhibitors for extended periods will provide greater experience regarding the potential gastrointestinal adverse effects of long-term acid suppression.

Lakshmanan, S., et al. (2020). "Incidental finding of helicobacter heilmannii in two asymptomatic individuals." American Journal of Gastroenterology 115(SUPPL): S1567-S1568.

INTRODUCTION: Helicobacter heilmannii previously known as Gastrospirillum hominis is commonly seen in animals and may have zoonotic potential. It contributes to about 5% of human gastric infections, resulting in chronic gastritis, peptic ulceration, and rarely gastric carcinoma or mucosa-associated lymphoid tissue lymphoma. Most patients are symptomatic and present with dyspepsia, epigastric pain, or acid reflux. We report two cases in which incidental H.Heilmannii was found in the pathological report. CASE DESCRIPTION/METHODS: Both our patients had undergone esophagogastroduodenoscopy (EGD) in anticipation of bariatric surgery. One is a 22-year-old morbidly obese female without significant medical illness, who had mild patchy erythematous mucosa in the gastric antrum. Biopsy revealed moderate to severe chronic active gastritis. Both H.pylori and H.heilmannii organisms were identified on the Hematoxylin and eosin (H&E) stain. Next is a 25-year-old morbidly obese female with gastroesophageal reflux disease. Her EGD also revealed mild patchy erythematous mucosa in the gastric antrum and biopsy showed moderate inactive gastritis, reactive lymphoid follicles, and frequent long tightly coiled bacteria highlighted on H&E stain consistent with H.heilmannii. They were both treated with a 2-week course of amoxicillin, clarithromycin, and omeprazole. They remained asymptomatic during subsequent office visits and are scheduled for follow up EGD after their bariatric surgery. DISCUSSION: Gastric inflammation in humans infected with H.heilmannii is less severe and usually involves the gastric antrum like seen in our patients. Co-infection of H.heilmannii and H.pylori is often seen and is believed to have a higher prevalence of intestinal metaplasia than does infection with either strain alone. Studies have highlighted that H.heilmannii like H.pylori, is effectively eradicated with similar antimicrobial therapy. We are however unable to detect the presence or confirm eradication via ancillary tests such as urea breath test, serum antibody testing, or stool testing as with H.pylori. Whether in symptomatic patients or with incidental chronic gastritis findings, it is prudent to look for H.heilmannii in the absence of, or concomitant with H.pylori infection and treat them adequately to prevent further complications.

Langner, C. (2017). "[Precursors of gastric cancer : Dysplasia and adenoma]." Pathologe 38(2): 67-74.

Gastric cancer develops from preneoplastic and early neoplastic precursor lesions. In particular, the intestinal type according to the Lauren classification is driven by chronic inflammation and progresses via a chronic gastritis - atrophy/metaplasia - dysplasia - carcinoma sequence. Staging of the extent of atrophy (OLGA) or intestinal metaplasia (OLGIM) enables risk stratification and determines follow-up investigations according to the management of precancerous conditions and lesions in the stomach (MAPS) international guidelines. True adenomatous lesions are relatively rare in the stomach. Three major types need to be considered: the intestinal type (tubular, tubulovillous and villous), the foveolar type (with superficial gastric differentiation) and the pyloric gland adenoma (with deep gastric differentiation). The intestinal type is the most common and needs to be differentiated from nonneoplastic polypoid regenerative hyperplasia, but also from well-differentiated tubular adenocarcinoma.

Lastraioli, E., et al. (2019). "The hERG1 Potassium Channel Behaves As Prognostic Factor In Gastric Dysplasia Endoscopic Samples." OncoTargets and Therapy 12: 9377-9384.

PURPOSE: Gastric cancer (GC) is still a relevant health issue worldwide. The identification of prognostic factors for progression of gastric dysplasia (GD), the main pre-cancerous lesion of the intestinal-type GC, is hence mandatory. PATIENTS AND METHODS: A cohort of 83 GD endoscopic samples belonging to Italian subjects was collected. hERG1 expression was evaluated by immunohistochemistry and scored 0-3, depending on the percentage of stained cells. Expression data were analysed in conjunction with clinico-pathological and survival data. RESULTS: hERG1 turned out to be expressed in 67.47% (56 out of 83) of the GD samples. hERG1 expression was higher in high-grade GD compared to low-grade GD (29 out of 39, 74.36% vs 27 out of 44, 61.36%), although the statistical significance was not reached (P=0.246). No association emerged between hERG1 expression and clinical features of the patients (age, gender, localization, H. pylori infection, gastritis and intestinal metaplasia). In a subset of cases for which sequential samples of gastric lesions (from GD to Early Gastric Cancer and Advanced Gastric Cancer) were available, hERG1 expression was maintained in all the steps of gastric carcinogenesis from GD onwards. A general trend to increased expression in advanced lesions was observed. hERG1 score had a statistically significant impact on both Progression-Free Survival (P=0.018) and Overall Survival (P=0.031). In particular, patients displaying a high hERG1 score have a shorter survival. CONCLUSION: hERG1 is aberrantly expressed in human GD samples and has an impact on both PFS and OS, hence representing a novel prognostic marker for progression of GD towards GC of the intestinal histotype. Once properly validated, hERG1 detection could be included in the clinical practice, during endoscopic surveillance protocols, for the management of GD at higher risk of progression, as already proposed for Barrett's oesophagus.

Laszkowska, M., et al. (2020). "PREVALENCE OF EXTENSIVE AND LIMITED GASTRIC INTESTINAL METAPLASIA AND PROGRESSION TO DYSPLASIA AND GASTRIC CANCER." Gastroenterology 158(6): S-497.

Background: Gastric intestinal metaplasia (GIM) is a pre-cancerous lesion that increases risk of gastric adenocarcinoma (GA). Extensive GIM (involving the corpus and antrum) has been cited as having higher risk of GA than limited GIM (involving antrum alone). Recently proposed American Gastroenterological Association (AGA) guidelines and prior Management of Epithelial Precancerous Conditions in the Stomach (MAPS) II guidelines from Europe cite extensive GIM as an indication for endoscopic surveillance. Currently, there are no studies of the prevalence of extensive vs. limited GIM in the US, and only one study assessed progression of extensive GIM to GA. The aim of this study was to estimate the prevalence and progression rates of extensive and limited GIM in a US cohort. Methods: In this retrospective cohort study, we identified individuals with intestinal metaplasia diagnosed on biopsy between 1/1/1990 and 8/1/2019 at Columbia University Irving Medical Center. Samples with biopsy specimens available from both the distal stomach (antrum/pre-pylorus/pylorus) and proximal stomach (body/fundus) were included. Individuals with cancer or dysplasia at the time of initial biopsy were excluded. Specimens were characterized as limited (GIM found only in the distal stomach) or extensive (GIM in both the proximal and distal stomach, or proximal stomach alone). Helicobacter pylori infection was also noted. Data on age, gender, race, and ethnicity was obtained from the electronic medical record. Incidence of advanced lesions (low- and high-grade dysplasia and GA) on follow up was calculated as the number of new diagnoses divided by person-years of follow-up. Patients were censored at death or last documented visit. Results: Of 1,329 individuals with GIM, 396 (29.8%) had extensive GIM and 933 (70.2%) had limited GIM. Patients with extensive GIM were older than those with limited GIM (p=0.03) and more likely to be Hispanic (OR 1.5, 95% CI 1.12-2.01). On multivariable analysis, older age, Hispanic ethnicity (vs. non-Hispanic), and absence of H.pylori infection were predictive of extensive GIM (Table 1). The incidence rate of GA for extensive GIM was 151.3 cases per 100,000 person-years, compared to 93.3 cases for limited GIM, though this difference was not statistically significant (Incidence Rate Ratio 1.62, 95% CI 0.24-9.58; Table 2). There was also no significant difference in incidence of advanced lesions overall (Incidence Rate Ratio 1.00, 95% CI 0.31-2.81). Conclusion: 29.8% of individuals with intestinal metaplasia have the extensive subtype, and are more likely to be older and of Hispanic ethnicity than individuals with limited GIM. While the higher incidence of GA in the extensive subtype was not statistically significant in this study, additional large studies are needed to better understand the risk associated with extensive GIM in the US population.

Lau, J. W. L., et al. (2021). "Opportunistic upper endoscopy during colonoscopy as a screening strategy for countries with intermediate gastric cancer risk." Journal of Gastroenterology and Hepatology 36(4): 1081-1087.

BACKGROUND AND AIM: Screening upper endoscopy can detect esophagogastric (OG) cancers early with improved outcomes. Recent cost-utility studies suggest that opportunistic upper endoscopy at the same setting of colonoscopy might be a useful strategy for screening of OG cancers, and it may be more acceptable to the patients due to cost-saving and convenience. We aim to study the diagnostic performance of this screening strategy in a country with intermediate gastric cancer risk. METHODS: A retrospective cohort study using a prospective endoscopy database from 2015 to 2017 was performed. Patients included were individuals age > 40 who underwent opportunistic upper endoscopy at the same setting of colonoscopy without any OG symptoms. Neoplastic OG lesions are defined as cancer and high-grade dysplasia. Pre-neoplastic lesions include Barrett's esophagus (BE), intestinal metaplasia (IM), and atrophic gastritis (AG). RESULTS: The study population involved 1414 patients. Neoplastic OG lesions were detected in five patients (0.35%). Pre-neoplastic lesions were identified in 174 (12.3%) patients. IM was found in 146 (10.3%) patients with 21 (1.4%) having extensive IM. The number needed to scope to detect a neoplastic OG lesion is 282.8 with an estimated cost of USD$141 400 per lesion detected. On multivariate regression, age ≥ 60 (RR: 1.84, 95% CI: 1.29-2.63) and first-degree relatives with gastric cancer (RR: 1.64, 95% CI: 1.06-2.55) were independent risk factors for neoplastic or pre-neoplastic OG lesion. CONCLUSION: For countries with intermediate gastric cancer risk, opportunistic upper endoscopy may be an alternative screening strategy in a selected patient population. Prospective trials are warranted to validate its performance.

Lau, W. L. J., et al. (2019). "Opportunistic detection of oesophagogastric neoplastic and pre-neo plastic lesions during screening colonoscopy program-a worthwhile strategy?" United European Gastroenterology Journal 7(8): 247-248.

Introduction: Endoscopic screening for colon cancer is generally accepted for screening for colorectal cancer, whereas endoscopic screening for oesophagogastric (EG) cancer alone is not cost-effective in countries with low to intermediate incidence of gastric cancer. The utility of offering an opportunistic upper endoscopy during a screening colonoscopy was evaluated as a potential strategy for detection of early EG neoplastic and preneoplastic lesions. Aims & Methods: A retrospective review of a prospective database in a tertiary hospital was performed. Patients with age>40 who underwent opportunistic screening upper endoscopy and colonoscopy in the same session from January 2015 to December 2017 were included. Patients who underwent upper endoscopy for indications such as dyspepsia, weight loss and anaemia were excluded. EG neoplastic lesions were defined as EG carcinomas, and pre-neoplastic lesions were defined as Barret's oesophagus, intestinal metaplasia (IM), or atrophic gastritis. Results: Out of 9,566 patients who underwent simultaneous upper endoscopy and colonoscopy, we identified 1,414 patients who underwent screening upper endoscopy. On colonoscopy, 491 (34.7%) patients had adenomatous polyps detected, and colorectal malignancy was detected in 20 patients (1.4%). From our cohort, 179 (12.7%) patients undergoing opportunistic screening upper endoscopy had EG neoplastic and pre-neoplastic lesions. of these, IM was found in 146 (10.3%) patients with 112 (7.9%) focal IM while 21 (1.4%) had extensive IM. Atrophic gastritis was detected in 23 (1.6%) patients. Also, 19 (1.3%) patients were found to have Barrett's oesophagus with one high-grade dysplasia which was resected endoscopically. Early stage gastric cancers were diagnosed in three patients (0.2%) who underwent surgery. Two were T1bN0 and one was T2N0. Another patient was diagnosed with early MALT lymphoma. On multivariate regression, independent risk factors for upper GI neoplastic and pre-neoplastic lesions in this population include age > 50 (Risk Ratio (RR) 2.18, 95%CI 1.15-4.14), p = 0.018) and having a family history of first-degree relative with gastric cancer (RR 1.60, 95% CI 1.03-2.48, p = 0.035). Hence, using this strategy, the number needed to detect an incidental neoplastic or pre-neoplastic EG lesion is 7.90. At a cost of USD$500/upper endoscopy, it would cost $3950 per lesion detected. Conclusion: This observational cohort suggests the potential utility of incorporating upper endoscopy into an established screening colonoscopy program, for the purpose of detecting EG neoplastic and pre-neoplastic lesions in countries with intermediate risk. All pathologies detected are early lesions. In addition, this strategy may be more acceptable to patients as they are already planned for colonoscopy. Further studies are worthwhile to verify these observations.

Lee, A. A., et al. (2019). "FEASIBILITY OF GASTRIC INTESTINAL METAPLASIA SURVEILLANCE IN A HIGH RISK AMERICAN COHORT." Gastroenterology 156(6): S-519.

INTRODUCTION: Gastric intestinal metaplasia (GIM) surveillance is performed in many countries where gastric cancer is prevalent. Between 2009 and 2012 we identified gastric cancer in 4% of patients undergoing diagnostic upper endoscopy at our center. This prompted the initiation of an endoscopic surveillance program in February 2013. We aim to report on the surveillance and yield of GIM surveillance in a high-risk American population. METHODS: Patients with GIM on index upper endoscopy were identified during the mandatory biopsy follow-up clinic and counseled to undergo surveillance endoscopy in 3 years. This was also documented in the electronic record and the patients’ primary care providers were contacted to help ensure compliance. These patients were added to a prospectively maintained research database. At index and surveillance endoscopy, they underwent Sydney protocol biopsies (antrum, corpus, and incisura). The primary outcome was the proportion of patients identified who returned for follow-up endoscopy within the recommended 3 (+/- 0.5) year interval. Our secondary aims were to determine the proportion of patients who maintained stable lesions and those who had progression or regression based on gastric histology. Focal GIM involved one region of the stomach (antrum, incisura, body, fundus, or cardia) while multifocal GIM was defined by involvement of ≥2 discrete regions. RESULTS: Among 380 patients who underwent screening evaluation between February 2013 and September 2015 and were found to have GIM, 80 (21%) patients underwent surveillance endoscopy an average of 29.8 months following the index assessment (Table 1). Logistic regression analysis demonstrated that age, sex, and gender did not predict compliance with follow-up endoscopy. There was a trend toward greater compliance among those who underwent the index endoscopy for high versus low risk indications (OR 1.6 [95% CI 1.0-2.8])(Table 1). No patients developed dysplasia or cancer during this interval. Of the 23 patients who were initially found to have focal metaplasia, 4 progressed to multi-focal metaplasia, 4 maintained focal metaplasia, and 15 regressed to chronic gastritis. Of the 57 with multi-focal metaplasia, 24 continued to have multi-focal metaplasia, 10 regressed to focal, and 23 regressed to gastritis. Multinomial logistic regression analysis showed that patients with baseline multi-focal metaplasia were more likely to have multi-focal metaplasia on surveillance (OR 3.9 [95% CI 1.1-13.5])(Table 2) but did not identify other factors such as age or H. pylori status as predictors of histologic change. CONCLUSIONS: Surveillance of GIM in an American population is feasible and may be more important in those with multi-focal disease. The yield of surveillance, length of intervals, and methods to promote compliance require a larger and longer prospective assessment. [Table presented] [Table presented]

Lee, E., et al. (2018). "Risk factors of metachronous gastric neoplasm beyond 5 years after endoscopic resection for early gastric cancer." United European Gastroenterology Journal 6(8): A178.

Introduction: Endoscopic resection has been standard treatment for selected patients with early gastric cancer (EGC) and the risk factors of metachronous gastric cancer after endoscopic resection discovered throughout previous studies. However, the risk factors over a long period of time has not yet been well demonstrated. To develop an optimal endoscopic surveillance strategy, it is necessary to elucidate the risk factors associated with metachronous tumor development in long-term follow-up. Aims and Methods: This study aimed to clarify the risk factors of metachronous gastric neoplasm beyond 5 years after endoscopic resection for EGC. We performed a retrospective analysis of the patients who underwent endoscopic resection for EGC from Jan 2005 to May 2012 in Seoul National University Hospital. Results: Among 1280 patients with EGC, 663 patients were followed-up for over 5 years, in whom metachronous gastric neoplasm developed in 65 patients beyond 5 years after endoscopic resection for EGC. In multivariate analysis, male (odds ratio, OR 3.242; 95% confidence interval, CI 1.367-7.689; p=0.008), elevated gross type (OR 5.240; 95% CI 1.872-14.668; p=0.002), mixed Lauren classification (OR 5.240; 95% CI 2.535-92.054; p=0.003), intestinal metaplasia (OR 1.456; 95% CI 1.065-1.990; p=0.019), tumor-positive lateral margin (OR 3.322; 95% CI 1.092-10.104; p=0.034), synchronous adenoma (OR 2.832; 95% CI 1.261-6.364; p=0.012) were positive predictive factors for metachronous gastric neoplasm. Conclusion: Metachronous gastric neoplasm had developed in 9.8% of patients beyond 5 years after endoscopic resection for EGC. Male sex, elevated gross type, mixed Lauren classification, intestinal metaplasia, tumor-positive lateral margin, synchronous adenoma were significantly associated with metachronous tumor development in long-term follow-up.

Lee, J., et al. (2010). "Risk factors of synchronous or metachronous tumor development in early gastric cancer and precancerous lesion: A review of 1005 endoscopic resections of early gastric cancer and gastric adenoma." Gastrointestinal Endoscopy 71(5): AB260.

Background: Endoscopic submucosal dissection (ESD) has been an useful treatment option of early gastric cancer (EGC) and gastric adenoma (GA). Through complete pathologic mapping and serial endoscopic follow-up for years after ESD, multiple foci of malignant and precancerous lesions are frequently observed. This study aimed to evaluate associated factors of synchronous or metachronous tumor development after ESD for EGC or GA. Methods: From April 2005 to August 2008, 1005 cases (503 EGCs and 497 GAs) were enrolled prospectively after ESD in Seoul National University Hospital and followed-up for more than one year. Synchronous tumor was defined as an EGC or GA confirmed within one year from initial ESD, and metachronous tumor as an EGC or GA diagnosed after one year from initial ESD. Follow-up endoscopies were performed in 3, 6, 12, 18 months after ESD, and then annually. Complete resection rate, complications, final diagnosis and synchronous or metachronous tumor development were evaluated with associated factors during follow-up. Results: In 1005 cases, synchronous lesions were detected in 256 cases (25.4%), in which 160 cases (62.6%) were revealed from the pathologic mapping of initial resected specimens. Metachronous tumors were detected in 66 cases (6.6%) and the mean duration from initial diagnosis was 800 days (689-911 days, 95% C.I.) In GA cases, synchronous tumor was negatively associated with Helicobacter pylori (H.P) infection (p=0.001), and positively associated with the degree of intestinal metaplasia (p<0.001), whereas, metachronous tumor development was not associated with H.P infection, mucosal atrophy or the degree of intestinal metaplasia. In EGC cases, synchronous tumor was associated with the degree of intestinal metaplasia (p<0.001), whereas, metachronous tumor development was not associated with H.P infection, mucosal atrophy or the degree of intestinal metaplasia. Conclusion: Synchronous or metachronous tumor development was frequently observed in ESD-treated EGC or GA cases. The degree of intestinal metaplasia showed statistical correlation with synchronous lesions. Serial follow-up is warranted to elucidate synchronous or metachronous tumor development in ESD-treated EGC or GA cases.

Lee, J. W. J., et al. (2016). "Prospective cohort study of gastric intestinal metaplasia progression and risk factors." Gastroenterology 150(4): S867-S868.

Background: Intestinal metaplasia (IM) is recognized as a precancerous lesion for gastric carcinoma (GC), yet data to guide an appropriate surveillance strategy is lacking. Objectives: To investigate the progression of IM and risk factors thereof in the Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP) cohort. Method: The GCEP is a prospective multicentre study initiated in 2004 and presented at DDW 2013 (Lim et al, Gastroenterol 2013;144(5):S-95-S-96). Chinese subjects aged >50 years were recruited whereby endoscopy surveillance was offered for a minimum of 5 years. All subjects gave informed consent and IRB approvals obtained. IM was diagnosed by histology of gastric biopsies following the Updated Sydney Protocol. Severity of IM was graded using OLGIM scoring system. Predictive factors for IM progression were identified by univariate analysis and subsequent multivariate cox-regression analysis. Results: 2987 Chinese subjects (mean age 59.9±7.0, 51.3% male) were enrolled, of whom 1874 had IM on histology. 678 (36.2%) had at least one biopsy with marked IM, and had increased risk of high grade dysplasia (OR 19.7; 95%CI 2.5- 153.0, p=0.04), compared to those with only mild or moderate IM. 1657 had adequate longitudinal follow-up biopsies for analysis of progression of IM. At the end of 5 years, 432 (44.2%) had progressed in severity. The prevalence of marked IM increased from 11.5% at baseline to 25% at the end of 5 years. On multivariate analysis, positive family history for GC (HR 1.43; 95% CI 1.01-2.03, p=0.046), smoking (HR 1.52; 95% CI 1.02-2.59, p= 0.043) and atrophic gastritis (HR 1.56; 1.16-2.08, p=0.03) were significant predictors of a more rapid progression to marked IM. On OLGIM score, 11.6% had Stage III/IV IM and these subjects were at increased risk of developing high grade dysplasia (OR 11.0; 95%CI 3.47-35.2; p<0.001). Conclusions: One quarter of patients with IM had developed marked IM by the 5th year of surveillance, and marked IM carried an increased risk of dysplasia. Risk factors of a more rapid progression to marked IM include smoking and positive family history for GC, suggesting the need for further endoscopic surveillance for patients with the above risk factors even without extensive IM. The occurrence of progression despite the eradication of H pylori suggests that surveillance is necessary, and that the natural history of IM is not static.

Lee, J. W. J., et al. (2016). "Topographic distribution of multi-focal gastric intestinal metaplasia." Journal of Gastroenterology and Hepatology (Australia) 31: 108.

Background: Multi-focal intestinal metaplasia (IM) is a recognized risk factor for gastric carcinoma. We aim to describe the topographic distribution of multi-focal IM and its risk towards gastric carcinoma within the Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP) cohort. Method: The GCEP is a prospective multi-centre study in Singapore initiated in 2004 in which Chinese subjects aged >50 years were recruited and offered endoscopy surveillance for a minimum of 5 years. All patients underwent gastric biopsies, and IM severity was graded as per the Updated Sydney Protocol. Results: In total, 2987 Chinese subjects (mean age 59.9 ± 7.0, 51.3% male) were enrolled. A total of 2170 subjects who underwent a total of 7198 interval gastroscopies with minimum 5 biopsies were included for the following analysis. Approximately 49.3% were found to have IM. The diagnostic yield of IM was highest within the antrum and along the lesser curve of the stomach; antrum greater curve 52.9%, antrum lesser curve 73.2%, incisura angularis 53.1%, corpus greater curve 10.4% and corpus lesser curve 18.1%. Approximately 20.6% had focal IM and 28.7% had multi-focal IM. Majority of those with focal IM were low grade (70.3% mild, 17.4% moderate and 12.3% marked). Amongst those with multi-focal IM, 23.9% were antrum pre-dominant, 12.2% were magenstrasse and 3.3% were diffused. Both magenstrasse and diffuse gastric IM topography were significantly associated with subsequent high-grade dysplasia and carcinoma; Magenstrasse (OR 5.00 95% CI: 1.24-20.14, p = 0.02), Diffuse (OR 19.09 95% CI 4.67-78.06; p <0.01). Conclusions: Our findings are consistent with previous non-Asian studies, whereby multifocal IM, in particular the magenstrasse and the diffuse topographic distribution, are at higher risk of dysplasia and carcinoma. Surveillance biopsies for IM should include the gastric lesser curvature and adhere to the Updated Sydney Protocol.

Lee, K., et al. (2016). "Compare the characteristics of synchronous and metachronous gastric tumors aft er endoscopic resection with H. Pylori infection: Single center experience." Helicobacter 21: 136-137.

Background: Endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) have become a standard treatment for in a certain early gastric cancer (EGC). However, metachronous or synchronous tumor after endoscopic resec-tion become a main problem in follow up. We aimed to compare the characteristics of synchronous and metachronous tumor in patient with EGC or gastric adenoma after endoscopic resection. Methods: A total of 552 patients who underwent endoscopic resection between January 2002 and February 2016 in a single center were retrospectively reviewed. We analyzed the characteristic of synchronous or metachronous tumors with endoscopic findings, pathologic findings and Helicobacter pylori status. Results: In total, 33(5.9%) patients had synchronous tumors, and 30(5.4%) patients had metachronous tumors. The median period until discovery metachronous tumor after initial ESD was 28.75 months. Male and older (>65 years old) patients had more common in synchronous and metachronous group (69.8%, 73.0%). But there was no significant difference between two groups ( p = 0.595, p = 0.395). H. pylori infection rate was only 12.7% in both groups. But, severe mucosal atrophy (grade 2-3), known to related to H. pylori infection, had more frequent in metachronous group (90%, p = 0.010). Marginal involvement of primary tumor was more frequent in synchronous group (57.6% vs 26.7%, p = 0.013). Histological type, intestinal metaplasia and location of tumor was not showed difference between two groups ( p = 0.655, p = 0.126, p = 0.259). Conclusion: Syncronous and metachronous tumor after endoscopic resection is observed in 11.3%. We recommend careful follow- up in patients with severe mucosal atrophy regardless of H. pylori infection. Physicians should observe the stomach not only previous resection site but also whole stomach during follow- up EGD.

Lee, S., et al. (2014). "Does eradication of helicabacter pylori after endoscopic resection of early gastric cancer decrease recurrence of gastric cancer?" Helicobacter 19: 164.

Background: Eradication of Helicobacter pylori in patients' undergone endoscopic resection of early gastric cancer has been recommended by guidelines to decrease incidence of metachronous gastric cancer. The aim of our study was to evaluate effectiveness of Helicobacter pylori eradication after endoscopic resection of early gastric cancer in preventing recurrence of gastric cancer. Method: Patients with result of Helicobacter pylori study after endoscopic removal of early gastric cancer from Nov 2005 to Aug 2013 in Yeungnam university hospital were enrolled. Baseline characteristics, follow up period, presence of recurrent disease, status of Helicobacter pylori was reviewed retrospectively. Results: Mean age of the patients was 62.7 ± 9.8 years and 103 (72.5%) patients were male. Mean follow up time was 15.5 ± 18.2 months. Among total 353 patients, 226 (61.4%) had no Helicobacter pylori infection. Recurrence was seen in 11 (4.9%) patients with no Helicobacter pylori infection and 3 (2.1%) with Helicobacter pylori infection. Among patients with Helicobacter pylori infection, eradication of Helicobacter pylori was done in 69 (48.6%) patients. Recurrence of cancer was seen in 2 (2.9%) patients with Helicobacter pylori eradication and 1 (1.4%) with persistent Helicobacter pylori infection and recurrence rate was not statistically different between two groups. Conclusion: Presence and eradication of Helicobacter pylori infection in patients who underwent endoscopic removal of EGCA does not seem to affect recurrence of cancer. Further large scaled prospective studies defining relationship between status of Helicobacter pylori and cancer recurrence including status of intestinal metaplasia and chronic atrophic gastritis is needed.

Lee, S. E., et al. (2012). "Pyloric gland adenoma with mismatch repair protein loss and MSI-high is a precursor of gastric adenocarcinoma in lynch syndrome." Laboratory Investigation 92: 167A.

Background: Fundic gland polyposis is a gastric manifestation in patients with FAP. However, although gastric carcinoma is the second most common extra-colonic malignancy associated with Lynch syndrome, the detailed pathology or precursor lesions in the stomach are not described. In this study, we performed clinicopatholologic and molecular analyses using 13 gastric carcinomas from patients with Lynch syndrome. Design: After computer search, 392 patients were identified to have both gastric and colonic adenocarcinomas. Additionally, 311 patients enrolled in familial cancer clinic suspected as Lynch syndrome were also retrieved. All the medical records of 703 patients in a single comprehensive cancer center from 1995 to 2011 were reviewed. Twenty patients met the Amsterdam II criteria and had been treated for gastric and colonic adenocarcinomas. Immunohistochemistry for mismatch repair (MMR) proteins, MSI tests, MLPA for hMLH1 and hMSH2 were performed to confirm Lynch syndrome. Results: Thirteen patients were classified as Lynch syndrome and the average age of diagnosis of gastric carcinoma was 48 years. The location of tumor was antrum (n=8) followed by body (n=3) and cardia (n=2). Helicobacter pylori were demonstrated in 4 cases (30.8%) and background intestinal metaplasia and atrophy was identified in 11 cases (84.6%). The histology of gastric carcinoma included 10 tubular adenocarcinomas, 2 mucinous carcinomas, and a composite adenocarcinoma and endocrine carcinoma. In all cases, both gastric and colonic carcinomas were MSI-high and either hMLH1 or hMSH2 protein was lost in tumors. Unexpectedly, pyloric gland adenoma (PGA) was identified in 4 cases around the carcinomas. PGAs mimicked fundic gland polyp except for the absence of oxyntic cells. Most tumor glands in PGAs were strongly positive for MUC6 and superficial layer was positive for MUC5AC, while MUC2 and CD10 were totally negative. In a PGA with germline hMLH1 mutation, hMLH1 protein expression was lost. Three PGAs with hMSH2 protein loss showed abnormalities in MLPA. The carcinomas around PGA were tubular adenocarcinoma of gastric mucin phenotype. In three cases, there was a direct transition from PGA to carcinoma and one PGA transformed to carcinoma over the follow up of 2 years. Conclusions: We first identified that PGA may be a precursor lesion of gastric carcinoma in Lynch syndrome and accompanies MMR protein loss and MSI-high. Our findings suggest that MSI-phenotype is an early event and the MMR-deficient pathway also involves gastric carcinogenesis.

Lee, S. Y., et al. (2020). "Less than 10% of helicobacter pylori-seronegative subjects show true infection after seroconversion." Digestion 102(1): 105.

Introduction: Seroconversion and seroreversion of Helicobacter pylori occur during gastric cancer screening. This study aimed to determine the incidence and characteristics of seronegative subjects showing seroconversion in the follow-up tests. Methods: Consecutive H. pylori-seronegative Koreans who underwent biannual gastric cancer screening based on gastroscopy and serum assays were included. Past infection was defined as successful eradication history or endoscopic findings suggesting unintended eradication (gastric xanthoma, advanced atrophy, or intestinal metaplasia). Serum anti-H. pylori IgG (range: 5-200 AU/ mL) was followed up using the Chorus assay, which is acceptable in Koreans with a sensitivity of 100% and specificity of 75.0%. True H. pylori infection was confirmed based on endoscopic findings and Giemsa staining. Results: During the mean follow-up of 57.7±21.4 months, 61 (15.0%) of 407 seronegative subjects showed seroconversion. The seroconversion rate increased with a longer follow-up period (p <0.001) and higher initial serology titer (p <0.001). True infection was found in 6 (9.8%) of the 61 seroconverted subjects and in 2 seronegative subjects with positive Giemsa staining. All 8 infected subjects showed newly appeared spotty redness in the corpus. At the time of positive H. pylori test findings, the median serology titer was lower in 55 false- seropositive subjects (22.0 AU/mL, 12.1-99.3 AU/mL) than in 8 subjects with true infection (64.5 AU/mL, 6.2- 200 AU/mL, p <0.001). Most (80%) of false-seropositive subjects showed spontaneous seroreversion in the follow- up tests with a mean serology titer of 7.8 ± 2.0 AU/mL, whereas others (20 %) showed continuous false seropositivity with a mean serology titer of 29.4 ± 10.7 AU/mL. Conclusions: Seroconversion occurred in 3.3% of H. pyloriseronegative subjects per year; however, only 9.8% of the seroconverted subjects had true H. pylori infection. Most were false seropositivity with a relatively low serology titer. New appearance of spotty redness in the corpus indicates true infection..

Kang, S. J., et al. (2015). "Pepsinogen and incident chronic atrophic gastritis and intestinal metaplasia: A longitudinal study." United European Gastroenterology Journal 3(5): A14.

Introduction: Pepsinogen (PG) I and II are the two main precursors of pepsin, and are both produced by chief cells and mucous neck cells of the stomach.[1, 2] PG II is also produced by pyloric gland cells. When atrophic mucosal change develops, the chief cells are replaced by pyloric glands, leading to a decrease in PGI. However, PG II decreases in very small amount.[2] Thus, low serum PG I level and low PG I/II ratio are well known to be serological markers of gastric atrophy. Aims & Methods: This study was performed to investigate association between serum pepsinogen (PG) level and incidence of chronic atrophic gastritis (CAG) and intestinal metaplasia (IM). This is a retrospective cohort study. Our data were composed of 3,927 participants (over 30 years of age) who underwent upper endoscopy and serum PG test between March 2008 and December 2009 whose baseline endoscopy showed no evidence of CAG and IM. Of these, 2,166 participants underwent follow-up endoscopy after at least 1 year. Thus, the final study subjects consisted of 2,166 adults with follow-up data. Structured questionnaires were reviewed about purported risk factors for CAG and IM such as family history of gastric cancer, current smoking, and alcohol consumption. Serum PG I and PG II were measured by a latex-enhanced turbidimetric Immunoassay. Serum anti-Helicobacter pylori (H. pylori) IgG was detected by enzyme-linked immunosorbent assay. Follow-up endoscopy was performed either at 1-year or 2-year intervals by taking into account factors such as age, family history of gastric cancer, and patients' preference. CAG and IM were diagnosed endoscopically by experienced board-certified endoscopists. Results: Median follow-up in the 2,166 participants was 1490.5 days (interquartile range, 772.8-1898.0). There were a total of 783 patients with CAG and 166 patients with IM during the follow-up. Subjects with a PG I/II ratio of≤3.0 showed higher incidence of CAG and IM compared with those with a PG I/II ratio of>3.0 by using log-rank test (p<0.001, both for CAG and IM). The results of Cox's regression analysis confirmed that the PG I/II ratio was significantly inversely associated with incident CAG (HR, 0.86; 95% CI, 0.82- 0.90; p<0.001) after full adjustment for risk factors. The PG I/II ratio was also significantly inversely associated with incident IM (HR, 0.76; 95% CI, 0.68- 0.85; p<0.001). To test diagnostic performance of the PG I/II ratio for incident CAG, we performed a receiver-operating curve analysis. The cutoff value that is farthest from the line of equality was PG ratio of 4.6, with modest sensitivity (54.5%; 95% CI, 51.0%>58.1%) and specificity (66.1%; 95% CI, 63.5%>68.6%). Conclusion: The PG I/II ratio was found to be significantly inversely associated with development of CAG and IM in asymptomatic population without CAG and/or IM at baseline.

Karita, M., et al. (2004). "Atrophic progression induced by H. pylori infection is correlated with a changing pepsinogen I value and associated with the development of gastric cancer." Digestive Diseases and Sciences 49(10): 1615-1620.

It is well known that H. pylori infection induces gastric mucosal atrophy, and patients with gastric cancer, which is often complicated by H. pylori infection, possess gastric mucosal atrophy including intestinal metaplasia as a background. One hundred forty-seven patients with dyspeptic symptom and without gastric cancer diagnosed at first endoscopy have been prospectively studied to detect early gastric cancer every year by endoscopy for approximately 6 years. The status of H. pylori infection was detected by histology and ELISA, the value of pepsinogen I (PGI) determined by ELISA, and atrophic pattern determined by the histology of multiple specimens. After the follow-up period (mean, 6.1 years), 6 early gastric cancers had developed in the 49 H. pylori-positive patients with transformation of the atrophic pattern, and no cancer had developed in either the 48 H. pylori-positive patients without transformation of the atrophic pattern or the 50 H. pylori-negative patients. There is a significant relationship between the incidence of transformation of the atrophic pattern and that of the development of gastric cancer in the H. pylori-positive patients. PGI per year in the H. pylori-positive group with transformation of the atrophic pattern was significantly decreased compared with that in the other two groups. Gastric cancers have a background of progressive atrophy, and PGI per year can be a good marker to detect gastric cancer at early stages which is developing or has developed on the background of atrophic progression.

Kashiwagi, H. (2003). "Ulcers and gastritis." Endoscopy 35(1): 9-14.

This article reviews recently published literature regarding ulcers and gastritis. Although endoscopy is the most useful procedure for diagnosis in the upper gastrointestinal tract, complications do occur, and procedure-related costs are significant. The appropriate indication for endoscopy has recently been debated. Helicobacter pylori is known to be an important pathogen involved in gastric and duodenal inflammation. Peptic ulcer disease and severe gastric mucosal injury are caused by virulent strains, and many reports have focused on CagA. Follow-up studies on surveillance endoscopy in patients with peptic ulcer or gastritis report that patients with atrophic gastritis and intestinal metaplasia are at significantly higher risk for gastric cancer. H. pylori eradication sometimes causes gastroduodenal erosion and reflux esophagitis, and the mechanisms involved have been revealed. Proton-pump inhibitors are useful in the treatment of ulcers caused by nonsteroidal anti-inflammatory drugs (NSAIDs), reflux esophagitis, and for preventing rebleeding after endoscopic hemostasis, but the effect of long-term acid suppression on the gastric mucosa is still a matter of debate. H. pylori infection and NSAID intake are both risk factors for peptic ulcer disease, and are important aspects in this field.

Katelaris, P. H., et al. (2012). "A prospective evaluation of levofloxacxin based triple therapy for refractory H. pylori infection in a large Australian cohort." Journal of Gastroenterology and Hepatology 27: 16.

First line Helicobacter pylori eradication failure is a common and challenging problem. Salvage treatments may be hampered by antibiotic resistance (repeat clarithromycin therapies), difficult dosing schedules (quadruple therapy), adverse effects (rifabutin therapy), limited access to some antimicrobial agents and drug allergy. The aim of this study was to assess the efficacy of salvage levofloxacin triple therapy in unselected patients in clinical practice in Australia (where primary levofloxacin resistance is low). Methods: Prospective patients referred after prior treatment failure(s) were prescribed esomeprazole 40 mg, amoxicillin 1 g and levofloxacin 500 mg each twice daily for ten days. All patients received detailed written and verbal compliance support. Clinical and demographic data, including prior treatment number and type, compliance and adverse effects were recorded. Those with a history of penicillin allergy were tested immunologically and treated if amoxicillin was considered safe to use (20 patients). Outcome assessment was by 13C-urea breath test and/or histology and urease test. Results: In 150 evaluable patients (66% female, mean age 54 ± 14 years; 6 smokers), the main indications for treatment were peptic ulcer disease (17%), increased gastric cancer risk (family history or intestinal metaplasia, 20%), symptoms (35%) and other risk reduction (28%). The median number of previous treatments was 2 (range 1-7). Eradication of H. pylori was achieved in 90% of patients (ITT) and 90.6% (PP). The eradication rate did not differ according to the type or number of prior treatments: 92% when -2 (n = 106) compared with 83% when > 2 prior treatments, (n = 42; p = 0.13) or with age, ethnicity or indication for treatment but it was higher in females (94% vs 86%, p = 0.04). Compliance was excellent (95%). No serious adverse effects were observed; mild adverse effects were reported in 11% (nausea, thrush, sore throat, constipation, muscle aches). Conclusion: The efficacy and safety of this levofloxacin based triple therapy suggests it should be the first choice salvage regimen in clinical practice in Australia. Randomised comparative trials are unlikely to be done but these data compare favourably with local data for other salvage therapies.

Katicić, M., et al. (2014). "[Croatian guidelines for gastric cancer prevention by eradication of Helicobacter pylori infection]." Lijecnicki Vjesnik 136(3-4): 59-68.

Gastric cancer is the fourth most common type of cancer and the second leading cause of cancer-related death in the world. Although gastric cancer has a multifactorial etiology, infection with Helicobacter pylori is highly associated with gastric carcinogenesis. Carcinogenesis is also influenced by some environmental factors and host genetic diversity, which engenders differential host inflammatory responses that can influence clinical outcome. Chronic gastritis induced by H. pylori is the strongest known risk factor for adenocarcinoma of the distal stomach, but the effects of bacterial eradication on carcinogenesis have remained unclear up to now. Although eradication of H. pylori infection appears to reduce the risk of gastric cancer, several recent controlled interventional trials by H. pylori eradication to prevent gastric cancer have yielded disappointing results. To clarify this problem in a high-risk population, the investigators conducted a prospective, randomized, double-blind, placebo-controlled, population-based studies. The results of previous studies highlight the importance of longer and careful follow-up after eradication therapy. It seems that eradication treatment is effective in preventing gastric cancer if it is given before preneoplastic conditions/lesions, gastric atrophy, metaplasia, and dysplasia, have had time to develop. Furthermore, the significant efficacy of treatment observed in younger patients suggests the need to eradicate H. pylori as early as possible. This consensus aimed to propose guidelines for the diagnosis, management and control of individuals with chronic gastritis, atrophy, intestinal metaplasia, or dysplasia.

Khadija, B., et al. (2014). "Autoimmune gastritis: OLGA/OLGIM staging." Virchows Archiv 465(1): S144.

Objective: Few studies are available on staging auto-immune gastritis (AG) using Operative Link for Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia (OLGIM). In Helicobacter pylori gastritis, studies supported the association between OLGA/OLGIM stages III-IV and gastric cancer risk. The aim of our study was to compare the OLGA and OLGIM staging systems in the assessment of High-risk stages in AG. Method: A series (spanning the years 2008-2014) of 30 patients with serologically confirmedAGunderwent Sydney classification grading and OLGA/OLGIM staging. Results: High-risk stages (III-IV) gastritis was observed in 26.6 % of patients by both OLGA and OLGIM staging, but OLGIM down-staged 13.33 % of patients and down-staged to low risk stage 3.3 % of patients. No cases staged as high-risk by OLGIM were down-staged when OLGA criteria were applied. Conclusion: Because of its clinical impact, the stage of gastritis should be included as a conclusive message in gastritis histology report. Since it focuses on intestinal metaplasia alone and disregards those atrophy phenotypes occurring specifically in AG, OLGIMstaging is less sensitive than OLGA staging in identification high-risk gastritis and this may result in the down-staging of patients who should be offered follow-up.

Khor, C., et al. (2013). "Systematic endoscopic surveillance is feasible for the detection of early gastric neoplasia." Journal of Gastroenterology and Hepatology 28: 503.

Objective: Gastric cancer is a curable disease if detected early. Endoscopy surveillance is the only way to detect gastric cancer in the early stages. More targeted screening and surveillance is required in countries with intermediate incidence rate of gastric cancer. The Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP), initialized in 2004, is a prospective multicentre study with the ultimate goal of developing an optimal approach and cost-effective algorithm for targeted screening for gastric cancer in the Singapore Chinese population. We aim to determine whether systematic prospective endoscopic surveillance is feasible for the detection of early gastric cancer in Singapore Chinese cohort. Methods: Chinese subjects aged 50 years and above were recruited from gastroenterology clinics of four major public hospitals in Singapore from 2004-2010. Endoscopy surveillance was offered for a minimum of 5 years. Informed consent was obtained from all subjects and the study was approved by the institutional review boards. The main outcome measurement is the number of subjects who develop high grade dysplasia or gastric adenocarcinoma. Results: 3033 subjects with mean age 59 ± 7 years were recruited. 51% were male, 16% had family history of gastric cancer and 30% had H. pylori infection history based on their medical records. The prevalence of chronic gastritis, current H. pylori infection, atrophic gastritis and intestinal metaplasia at baseline were 81%, 20%, 19% and 44% respectively. The study is in progress, 1,300 have completed 5 years surveillance and the rest will complete by 2015.18 high grade dysplasia or early gastric cancers were detected so far after an average follow up period of 3 years. 12 of those cases were high grade dysplasia or intramucosal carcinoma and 6 were invasive cancers in stage 1A or 1B. The interval between the most recent endoscopy with no abnormal findings and the endoscopy where cancer was diagnosed is 4-25 months. Conclusion: Endoscopic surveillance is effective, and has already detected high grade dysplasia or early gastric cancer in a high risk Singaporean Chinese population.

Kim, G. H., et al. (2016). "Screening and surveillance for gastric cancer in the United States: Is it needed?" Gastrointestinal Endoscopy 84(1): 18-28.

BACKGROUND AND AIMS: Although the incidence of gastric cancer in the United States is relatively low, the incidence of gastric cancer is higher than for esophageal cancer, for which clear guidelines for screening and surveillance exist. With the increasing availability of endoscopic therapy, such as endoscopic submucosal dissection, for treating advanced dysplasia and early gastric cancer, establishing guidelines for screening and surveillance of patients who are at high risk of developing gastric cancer has the potential to diagnose and treat gastric cancer at an earlier stage and improve mortality from gastric cancer. The aims of this article were to review the data regarding the risk factors for developing gastric cancer, methods for gastric cancer screening, and results of national screening programs. METHODS: A review of the existing literature related to the aims was performed. RESULTS: Risk factors for gastric cancer that were identified include race/ethnicity (East Asian, Russian, or South American), first-degree relative diagnosed with gastric cancer, positive Helicobacter pylori status, and presence of atrophic gastritis or intestinal metaplasia. Endoscopy has the highest rate of detecting gastric cancer compared with other gastric cancer screening methods. The national screening program in Japan has demonstrated a mortality reduction from gastric cancer based on cohort data. CONCLUSIONS: Gastric cancer screening with endoscopy should be considered in individuals who are immigrants from regions associated with a high risk of gastric cancer (East Asia, Russia, or South America) or who have a family history of gastric cancer. Those with findings of atrophic gastritis or intestinal metaplasia on screening endoscopy should undergo surveillance endoscopy every 1 to 2 years. Large prospective multicenter studies are needed to further identify additional risk factors for developing gastric cancer and to assess whether gastric cancer screening programs for high-risk populations in the United States would result in improved mortality.

Kim, H., et al. (2017). "Risk factor of metachronous recurrence after endoscopic submucosal dissection for gastric epithelial neoplasm." Helicobacter 22: 70-71.

Background: Eradication of H. pylori after endoscopic submucosal dis-section of early gastric cancer is recommended to prevent metachro-nous recurrence of gastric neoplasm. However, the H. pylori infection does not seem to be significantly related to metachronous tumors in some other studies. Therefore, we conducted study to evaluate the association between H. pylori infection and recurrence of metachronous tumor after ESD. Method: A total of 176 patients with gastric neoplasm who had underwent ESD without Helicobacter eradication were included and the follow-up data were analyzed retrospectively. Result: 101 patients (57.4%) showed H. pylori infection (confirmed by CLO test). Metachronous gastric neoplasms developed in 26 (25.7%) in the CLO positive group and 16 (21.3%) in CLO negative group and there was no significant difference (P=.496). Pathologically confirmed mucosal atrophy (P=<.001) and intestinal metaplasia (IM) (P<.001) showed statistically significant association with metachronous recur-rence. In multivariate analysis, atrophy and IM were statistically associated with metachronous recurrence (P=.005 and 0.011, respectively). Among patients with H. pylori infection, metachronous recurrence was associated with atrophy (P=.052) or IM (P=.015). Similarly, in patients without H. pylori infection, there was significant relationship between metachronous recurrence and atrophy (P=.003) or IM (P<.001). In subgroup analysis of patients without significant IM (n=40), there was no significant association between H. pylori status and metachronous recurrence (P=.202). Conclusion: In context of metachronous recurrence after ESD of gastric neoplasm, mucosal atrophy and IM showed more significant rela-tionship than H. pylori infection status.

Kim, H. J., et al. (2008). "[The prevalence of atrophic gastritis and intestinal metaplasia according to gender, age and Helicobacter pylori infection in a rural population]." Journal of Preventive Medicine and Public Health. Yebang Uihakhoe Chi 41(6): 373-379.

OBJECTIVES: The objective of this study was to evaluate the prevalence of atrophic gastritis and intestinal metaplasia according to gender, age and Helicobacter pylori infection in a rural population in Korea. METHODS: Between April 2003 and January 2007, 713 subjects (298 men and 415 women, age range: 18-85) among the 2,161 adults who participated in a population-based survey received gastrointestinal endoscopy. All the subjects provided informed consent. Multiple biopsy specimens were evaluated for the presence of atrophic gastritis and intestinal metaplasia. The presence of Helicobacter pylori was determined using CLO and histology testing. RESULTS: The age-adjusted prevalence of atrophic gastritis was 42.7% for men and 38.1% for women and the prevalence of intestinal metaplasia was 42.5% for men and 32.7% for women. The prevalence of atrophic gastritis and intestinal metaplasia increased significantly with age for both men and women (p for trend<0.001). The age-adjusted prevalence of Helicobacter pylori was similar for men (59.0%) and women (56.7%). The subjects with Helicobacter pylori infection showed a significantly higher prevalence of intestinal metaplasia (44.3%) compared with that (26.8%) of the noninfected subjects (p<0.001). However, the prevalence of atrophic gastritis was not statistically different between the Helicobacter pylori-infected subjects and the noninfected individuals. CONCLUSIONS: Our findings suggest that the prevalence of atrophic gastritis and intestinal metaplasia is higher for a Korean rural population than that for a Western population; this may be related to the high incidence of gastric cancer in Koreans. Especially, the prevalence of intestinal metaplasia was high for the subjects with Helicobacter pylori infection. The multistep process of gastric carcinogenesis and the various factors contributing to each step of this process need to be determined by conducting future follow-up studies.

Kim, H. S., et al. (2012). "Heterotopic gastric mucosa with focal intestinal metaplasia and squamous epithelium in the rectum." Digestive Endoscopy 24(1): 46-48.

Heterotopic gastric mucosa has been described in all levels of the gastrointestinal tract. However, gastric heterotopia of the rectum is a rare finding. It is usually reported along with polyp located in the rectum between 5 and 8 cm from the anal verge. The most common symptom is painless rectal bleeding, and non-specific gastrointestinal symptoms may also be presented. We report an incidentally found case of a 46-year-old man without any gastrointestinal symptoms. The pathology showed gastric mucosa and squamous epithelium and focal intestinal metaplasia. This finding could be a clue as to the origins of the heterotopic gastric mucosa. Although there are no guidelines for treatment or the follow-up period, regular endoscopic surveillance is necessary for gastric cancer screening.

Kim, J. L., et al. (2020). "Long-term natural history after endoscopic resection for gastric dysplasia." Surgical Endoscopy.

BACKGROUND AND STUDY AIMS: Natural history after endoscopic resection (ER) for gastric dysplasia is still unclear. The aim of this study was to evaluate the long-term clinical outcomes and risk factors after ER for gastric dysplasia between control and cases with synchronous or metachronous gastric neoplasm. METHODS: A total of 1090 patients who had undergone ER for gastric dysplasia and been followed up for at least one year from December 2002 to December 2013 were finally analyzed. Risk factors affecting the development of synchronous or metachronous neoplasm (SMN) and long-term clinical outcomes after ER for gastric dysplasia were evaluated. RESULTS: Synchronous and metachronous neoplasms had developed in 126 (11.6%) and 133 patients (12.2%) during the mean follow-up duration of 63.6 months, respectively. Five-year and 10-year risk of metachronous neoplasm were 9.8% and 27.2%, respectively. Median duration to the development of metachronous neoplasm was 103.1 months. While age (P < 0.001) and mucosal atrophy (P = 0.09) of index cases were associated with the development of synchronous neoplasm, age (P = 0.017), incomplete resection (P = 0.025), and intestinal metaplasia (P = 0.017) of background mucosa of index cases were significantly related to the development of metachronous neoplasm in multivariate analysis. Cumulative incidence of SMN was not significantly different among H. pylori negative, eradicated, and persistent group. CONCLUSIONS: Age, incomplete ER, and background intestinal metaplasia of index gastric dysplasia were significantly associated with metachronous recurrence. Endoscopic surveillance for metachronous recurrence after ER for gastric dysplasia is mandatory for longer than 10 years.

Kim, J. W., et al. (2020). "METACHRONOUS CANCER AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER WITH UNDIFFERENTIATED HISTOLOGY: A RETROSPECTIVE ANALYSIS." Gastrointestinal Endoscopy 91(6): AB601-AB602.

Background: Endoscopic submucosal dissection (ESD) has become a widely accepted as a standard treatment for early gastric cancer (EGC) with differentiated histology. However, therapeutic outcome of ESD for undifferentiated cancer is still controversial. As ESD is a technique that leaves the at-risk native stomach, patients with EGC who have previously underwent ESD have the potential to develop metachronous gastric cancer (MGC). Given evidence has demonstrated that the cumulative incidence of MGC after endoscopic resection is not negligibly low. This study evaluated the incidence of MGC after complete endoscopic resection for EGC with undifferentiated histology. Methods: We retrospectively analyzed a prospectively collected registry (KHU-ESD registry) of clinical, endoscopic, and pathologic results of patients who underwent ESD for EGC. The study included 573 consecutive patients (465 differentiated and 108 undifferentiated carcinomas) who underwent complete endoscopic resection and followed more than 1 year. They were generally followed by annual esophagogastroduodenoscopy. Compared with differentiated carcinoma (DC group), we investigated the incidence of MGC in EGCs with undifferentiated histology (UDC group). Also, the risk factors for MGC were assessed over the follow-up period. Results: The median follow-up duration was 4.2 (2.1-7.0) years in DC group and 4.8 (2.5-6.0) years in UDC group (P = 0.683). Younger and female patients were more common in the UDC group compared to the DC group (all P < 0.001). Whereas, patients with both atrophy and intestinal metaplasia (IM) were more common in the DC group than in the UDC group. Cumulative incidence of MGC was significantly higher in the DC group than in the UDC group (2.5% vs. 0.7% per person year, P = 0.011) (Fig. 1). In logistic regression analysis, undifferentiated histology was not associated with the development of MGC (OR 0.428, 95% CI 0.149-1.229, P = 0.115) and presence of synchronous cancer was a significant risk factor (OR 2.335, 95% CI 1.345-4.052, P = 0.003). Meanwhile, atrophy, IM, and Helicobacter pylori infection were not associated. Conclusions: In analysis of large number of EGCs with undifferentiated histology, the incidence of MGC after complete resection by ESD was lower than that of differentiated cancer. Therefore, if complete resection is expected, ESD can be considered as initial therapeutic modality for undifferentiated type EGC in term of metachronous recurrence. [Formula presented]

Kim, K., et al. (2019). "Body Mass Index and Risk of Intestinal Metaplasia: A Cohort Study." Cancer Epidemiology, Biomarkers and Prevention 28(4): 789-797.

BACKGROUND: We examined the association between body mass index (BMI) and development of endoscopic intestinal metaplasia. METHODS: This retrospective cohort study included 142,832 Korean adults free of endoscopic intestinal metaplasia and atrophic gastritis who underwent upper endoscopy at baseline and subsequent visits and were followed for up to 5 years. A parametric proportional hazards model was used to estimate the adjusted HR with 95% confidence interval (CI) for incident intestinal metaplasia. RESULTS: In more than 444,719.1 person-years of follow-up, 2,281 participants developed endoscopic intestinal metaplasia (incidence rate, 5.1 per 1,000 person-years). Increased BMI categories were associated with increased risk of new-onset intestinal metaplasia in a dose-response manner. After adjustment for age, sex, center, year of screening exam, smoking status, alcohol intake, exercise, total calorie intake, history of diabetes and hypertension, and history of Helicobacter pylori infection, the multivariable adjusted HRs (95% CIs) for incident intestinal metaplasia comparing BMIs of <18.5, 23-24.9, 25.0-29.9, and >30 kg/m(2) with a BMI of 18.5-22.9 kg/m(2) were 0.84 (0.64-1.09), 1.03 (0.93-1.16), 1.07 (0.96-1.20), and 1.48 (1.20-1.83), respectively. These associations did not differ by clinically relevant subgroups. Risk of endoscopic atrophic gastritis also increased as the baseline BMI category increased. CONCLUSIONS: In a large cohort of Korean men and women, obesity was independently associated with increased incidence of endoscopic atrophic gastritis and intestinal metaplasia. IMPACT: Excessive adiposity appears to play a role in development of stomach precursor lesions of stomach cancer, requiring further studies to determine whether strategies to reduce obesity will also help reduce precancerous lesions and, in turn, gastric cancer.

Kim, K., et al. (2019). "Smoking and Urinary Cotinine Levels Are Predictors of Increased Risk for Gastric Intestinal Metaplasia." Cancer Research 79(3): 676-684.

Studies on a longitudinal relationship between smoking status and intestinal metaplasia (IM), a premalignant lesion of stomach cancer, are limited. Here we examined the association of smoking status and urinary cotinine levels, an objective measure of smoking, with the development of endoscopic IM. This cohort study included 199,235 Korean adults free of endoscopic IM who underwent upper endoscopy at baseline and subsequent visits and who were followed for up to 6.8 years (median, 3.7 years). Former and current smoking status and pack-years based on self-reports were associated with an increased risk of new-onset IM in men but not in women. However, urinary cotinine levels were positively associated with incident IM in a dose-response manner in both men and women. For men, the multivariable-adjusted HR [95% confidence interval (CI)] for incident IM comparing the urinary cotinine levels of 50 to 99 ng/mL, 100 to 499 ng/mL, and ≥500 ng/mL with <50 ng/mL were 1.20 (0.94-1.55), 1.26 (1.14-1.40), and 1.54 (1.44-1.64), respectively, whereas for women, corresponding HR (95% CI) were 0.75 (0.19-2.99), 1.86 (1.20-2.88), and 1.57 (1.07-2.30), respectively. These associations were observed when changes in smoking status and other confounders were updated during follow-up as time-varying covariates. In this large cohort of young and middle-aged men and women, urinary cotinine levels were independently associated with an increased incidence of endoscopic IM in a dose-response manner. Collectively, these data confirm smoking as an independent risk factor for the development of gastric IM, a precursor lesion of stomach cancer. SIGNIFICANCE: A large-scale cohort study of nearly 200,000 adults associates smoking with increased risk for gastric intestinal metaplasia, a precursor lesion of stomach cancer.

Kim, K., et al. (2020). "Low Levels of Alcohol Consumption and Risk of Intestinal Metaplasia: A Cohort Study." Cancer Epidemiology, Biomarkers and Prevention 29(12): 2633-2641.

BACKGROUND: The impact of alcohol drinking on gastric precancerous lesions remains unclear. We investigated the relationship of alcohol intake with risk of atrophic gastritis (AG) and intestinal metaplasia (IM). METHODS: This study included 202,675 Korean adults free from AG and IM on their initial endoscopy who were followed with repeated endoscopic examinations. A parametric proportional hazards model was used to estimate the adjusted HR (aHR) with 95% confidence interval (CI) for incident AG and IM based on endoscopic diagnosis. RESULTS: During a mean follow-up of 4.7 years, 64,853 incident AG cases and 4,536 IM cases were identified. Alcohol consumption including drinking frequency, quantity, and binge drinking were consistently associated with increased risk of both AG and IM in a dose-response manner. After adjustment for confounders, the multivariable aHRs (95% CIs) for incident IM comparing average alcohol intake of <10, 10-<20, 20-<40, and ≥40 g/day with lifetime abstainers were 1.27 (1.02-1.56), 1.34 (1.07-1.66), 1.50 (1.20-1.86), and 1.54 (1.23-1.93), respectively. Former drinkers were also at a higher risk for AG and IM compared with lifetime abstainers. These associations were consistently observed in never smokers and in time-dependent analyses. CONCLUSIONS: In a large cohort of Korean individuals, alcohol intake even at low levels was independently associated with increased risk of developing endoscopic AG and IM, supporting a role of alcohol consumption in the pathogenesis of AG and IM, the precursor lesions of stomach cancer. IMPACT: Alcohol consumption from low-level drinking may contribute to gastric carcinogenesis.

Kim, M. S., et al. (2013). "Long-term follow up Helicobacter Pylori reinfection rate after second-line treatment: bismuth-containing quadruple therapy versus moxifloxacin-based triple therapy." BMC Gastroenterology 13: 138.

Kim, N. (2019). "Chemoprevention of gastric cancer by Helicobacter pylori eradication and its underlying mechanism." Journal of Gastroenterology and Hepatology 34(8): 1287-1295.

The cascade of gastric cancer, a leading cause of cancer incidence and mortality, is multifactorial. Helicobacter pylori (HP) infection plays a major role in gastric cancer (GC), and there has been an accumulation of data regarding the chemopreventive effect of HP eradication. However, it remains unclear how HP infection causes GC and how HP eradication prevents GC. To clarify this issue, the following approaches were performed in this review article. First, how HP-induced atrophic gastritis (AG) and intestinal metaplasia (IM) provoke the development of GC is shown, followed by how long HP eradication takes to induce a reversible change in AG and IM. Second, epigenetic studies of PTPN6, MOS, DCC, CRK, and VAV1 were performed in noncancerous gastric specimens in terms of HP status. Among these genes, MOS was found to be a possible surrogate marker for GC development. HP eradication decreased aberrant DNA methylation in a gene-specific manner, and MOS played a role in metachronous gastric neoplasms. Third, transforming growth factor-β1 (TGF-β1) and TGF-β1-induced epithelial-mesenchymal transition (EMT) markers were investigated in gastric mucosa. HP infection triggered the TGF-β1-induced EMT pathway and caused the emergence of GC stem cells, such as CD44v8-10. When HP was eradicated, these two pathways were inhibited. Finally, a 2222 cohort study showed that HP eradication significantly decreased the risk of noncardiac GC. Taken together, HP eradication is effective as a primary GC prevention method, and its underlying mechanism includes reversibility of AG and IM, methylation, EMT, and stem cells.

Kim, N., et al. (2009). "[Diagnosis and treatment guidelines for Helicobacter pylori infection in Korea]." Korean Journal of Gastroenterology 54(5): 269-278.

Eleven years has passed since the guideline of the Korean College of Helicobacter and Upper Gastrointestinal Research group for H. pylori infection was produced in 1998. During this period the research for H. pylori has much progressed that H. pylori is now regarded as the major cause of gastric cancer. The seroprevalence of H. pylori in Korea was found to be decreased especially below the age of 40s and in the area of Seoul-Gyeonggi province, and annual reinfection rate of H. pylori has decreased up to 2.94%. In the aspect of diagnostic tests of H. pylori the biopsy is recommended in the body instead of antrum in the subjects with atrophic gastritis and/or intestinal metaplasia for the modified Giemsa staining or Warthin Starry silver staining. The urea breath test is the test of choice to confirm eradication when follow-up endoscopy is not necessary. Definite indication for H. pylori eradication is early gastric cancer in addition to the previous indications of peptic ulcer including scar and Marginal zone B cell lymphoma (MALT type). Treatment is also recommended for the relatives of gastric cancer patient, unexplained iron deficiency anemia, and chronic idiopathic thrombocytopenic purpura. One or two week treatment of proton pump inhibitor (PPI) based triple therapy consisting of one PPI and two antibiotics, clarithromycin and amoxicillin, is recommended as the first line treatment regimen. In the case of treatment failure, one or two weeks of quadruple therapy (PPI+metronidazole+tetracycline+bismuth) is recommended. Herein, Korean College of Helicobacter and Upper Gastrointestinal Research proposes a diagnostic and treatment guideline based on currently available evidence.

Kim, N., et al. (2008). "Helicobacter pylori infection and development of gastric cancer in Korea: long-term follow-up." Journal of Clinical Gastroenterology 42(5): 448-454.

BACKGROUND AND AIM: Infection of Helicobacter pylori is viewed as a major driver of progression to the precancerous state or to gastric cancer. This study was performed to investigate the effect of H. pylori infection on gastric cancer development and to determine to what extent H. pylori eradication is likely to reduce the prevalence of gastric cancer. METHODS: Gastric cancer development was investigated in 1790 Korean subjects who underwent gastroscopy and H. pylori testing between 1992 and 1998. The effects of H. pylori-positive and eradicated states on gastric cancer development were analyzed. RESULTS: Gastric cancer developed in 5 of the study cohort during a mean follow-up period of 9.4 years. All of these patients were positive for H. pylori infection, and 4 of the 5 had antral intestinal metaplasia (IM) at the time of study enrollment. One of these 5 patients was in an eradicated state when the gastric cancer was diagnosed, and had histologic IM before eradication therapy was performed. Gastric cancer was found to develop 10.9 times more frequently in the presence of IM than in its absence. CONCLUSIONS: The present study shows a close relationship between H. pylori infection and IM, and between IM and the development of gastric cancer. In addition, our finding suggests that chronic H. pylori infection looks like an important risk factor for the development of gastric cancer in Korea, where the prevalence of H. pylori remains high. This study indicates that to prevent gastric cancer H. pylori eradication is best performed before the development of IM.

Kim, N., et al. (2008). "Prevalence and risk factors of atrophic gastritis and intestinal metaplasia in a Korean population without significant gastroduodenal disease." Helicobacter 13(4): 245-255.

BACKGROUND AND AIM: The prevalence of gastric cancer and Helicobacter pylori infection is unacceptably high in Korea. This study was performed to evaluate the prevalence of atrophic gastritis (AG) and intestinal metaplasia (IM) and to identify their risk factors with respect to H. pylori virulence factors, and environmental and host factors, in Korean population without significant gastroduodenal disease. METHODS: The study cohort consisted of 389 subjects (> or = 16 years). AG and IM were scored histologically using the Sydney classification in the antrum and body, respectively. Prevalences and bacterial factors (i.e. cagA, vacA m1, and oipA), environmental factors (i.e. smoking and alcohol), and host factors (i.e. genetic polymorphisms of IL-1B-511, IL-1RN, TNF-A-308, IL-10-592, IL-10-819, IL-10-1082, IL-8-251, IL-6-572, GSTP1, p53 codon 72, and ALDH2) were evaluated. RESULTS: Prevalences of AG in the antrum and body were 42.5% and 20.1%, and those of IM were 28.6% and 21.2%, respectively. The presences of AG and IM were significantly higher in H. pylori-positive than in the H. pylori-negative subjects. Multivariate analysis showed that the risk factors for AG were H. pylori infection, age > or = 61 years, and cagA and vacA m1 positivity. For IM the risk factors were H. pylori infection, age > or = 61 years, a smoking history (rather than current smoking), strong spicy food, occupation (unemployed or nonprofessional vs. professional), and the presence of IL10-592 C/A as opposed to A/A. In addition, IL6-572 G carrier was found to have a protective effect against IM development as compared with C/C. CONCLUSION: H. pylori infection was most important risk factor of AG and IM. Bacterial factors were found to be important risk factor for AG but environmental and host factors were more important for IM.

Kim, S. B., et al. (2016). "Association between Helicobacter pylori status and metachronous gastric cancer after endoscopic resection." World Journal of Gastroenterology 22(44): 9794-9802.

AIM: To investigate the effect of Helicobacter pylori (H. pylori) status test and H. pylori eradication on the occurrence of metachronous gastric cancer (MGC) after endoscopic submucosal dissection (ESD) of early gastric cancer (EGC) and risk factors of MGC. METHODS: The authors retrospectively reviewed the medical records of 433 patients (441 lesions) who underwent ESD for EGC from January 2005 to January 2015 in Yeungnam University Hospital. Patients were categorized into two groups; the H. pylori tested group (n = 257) and the H. pylori non-tested group (n = 176) based on performance of H. pylori status test after ESD of EGC. The H. pylori tested group was further categorized into three subgroups based on H. pylori status; the H. pylori-eradicated subgroup (n = 120), the H. pylori-persistent subgroup (n = 42), and the H. pylori-negative subgroup (n = 95). Incidences of MGC and risk factors of MGC were identified. RESULTS: Median follow-up duration after ESD was 30.00 mo (range, 6-107 mo). Total 15 patients developed MGC during follow-up. MGC developed in 11 patients of the H. pylori tested group (7 in the H. pylori-negative subgroup, 3 in the H. pylori-eradicated subgroup, and 1 in the H. pylori-persistent subgroup) and 4 patients of the H. pylori non-tested group (P > 0.05). The risk factors of MGC were endoscopic mucosal atrophy in the H. pylori tested group and intestinal metaplasia in all patients. CONCLUSION: H. pylori eradication and H. pylori status test seems to have no preventive effect on the development of MGC after ESD for EGC. The risk factors of MGC development were endoscopic mucosal atrophy in the H. pylori tested group alone and intestinal metaplasia in all patients.

Kim, Y. M., et al. (2019). "Sarcopenia and Sarcopenic Obesity as Novel Risk Factors for Gastric Carcinogenesis: A Health Checkup Cohort Study." Frontiers in Oncology 9: 1249.

Background: Insulin resistance, the primary mechanism of metabolic syndrome, promotes gastric carcinogenesis. Metabolic syndrome is associated with sarcopenia. We aimed to investigate the association between sarcopenia and gastric carcinogenesis, including precancerous conditions such as atrophic gastritis (AG), intestinal metaplasia (IM), and dysplasia. Methods: The study included adult patients who underwent gastroduodenoscopy at a checkup center. AG and IM were evaluated using endoscopy. Based on muscle mass, sarcopenia was defined as a skeletal muscle index <1 standard deviation below the sex-specific mean for healthy adults aged 20-39 years (cutoff point: 29.3% for males and 26.7% for females). Obesity was defined as a body mass index (BMI) ≥25 kg/m(2) according to the Asia-Pacific criteria. Sarcopenic obesity was defined as a combination of sarcopenia and obesity. The association between gastric carcinogenesis and sarcopenia was evaluated. Results: Among 8,356 enrolled participants, 0.14 and 42.5% were diagnosed with gastric cancer and precancerous conditions, respectively. Approximately 41.7% of gastric cancer patients and 16.9% of patients with precancerous conditions were diagnosed with sarcopenia. Both sarcopenic obesity (odds ratio [OR] = 4.139, P = 0.016) and diabetes mellitus (DM) (OR = 5.152, P = 0.005) were significantly associated with gastric cancer. Sarcopenia, DM, hypertension, dyslipidemia, Helicobacter pylori infection, smoking, and alcohol consumption were significantly associated with precancerous conditions. Conclusions: Sarcopenia and sarcopenic obesity were associated with gastric carcinogenesis and may be novel risk factors for gastric carcinogenesis.

Kim, Y. M., et al. (2019). "Association between sarcopenia and gastric carcinogenesis: A health check-up cohort study." Journal of Clinical Oncology 37.

Background: Insulin resistance which is a mechanism of metabolic syndrome has been known to promote carcinogenesis of various malignancies. In addition, metabolic syndrome is associated with sarcopenia. Thus, the aim was to investigate the association between sarcopenia and gastric carcinogenesis including precancerous conditions: atrophic gastritis (AG), intestinal metaplasia (IM), and gastric adenoma. Methods: The study subjects were an adult population who underwent gastroduodenoscopy at Gangnam Severance Check-up Center. AG and IM were evaluated by endoscopic findings. Sarcopenia based on muscle mass was defined as appendicular skeletal muscle (ASM) as a percentage of body weight that was less than 1 standard deviation below the sex-specific mean for healthy adults aged 20 to 39 years (cutoff point: 29.3% in male and 26.7% in female). Obesity was defined as body mass index (BMI) ≥ 25 kg/m2 according to the Asia-Pacific criteria. Sarcopenic obesity was a condition of combined sarcopenia and obesity. The association between sarcopenia and gastric lesions was evaluated. Results: 8,356 patients were enrolled this study. Among them, 12 (0.14%) and 3,552 (42.5%) patients were diagnosed as gastric cancer and precancerous conditions, respectively. 5 (41.7%) of 12 gastric cancer patients and 594 (16.9%) of 3.552 patients with gastric precancerous conditions were diagnosed with sarcopenia. Both diabetes mellitus (DM) (OR = 5.152, P = 0.005) and sarcopenic obesity (OR = 4.139, P = 0.016) were independent predictive factors for gastric cancer. And smoking, alcohol, DM, hypertension, dyslipidemia, Helicobacter pylori, and sarcopenia were significantly associated with gastric precancerous conditions. Conclusions: Sarcopenia and sarcopenic obesity were significantly associated with gastric carcinogenesis. Thus, sarcopenia may be one of the risk factors for gastric carcinogenesis.

Kim, Y. M., et al. (2019). "ASSOCIATION BETWEEN SARCOPENIA AND GASTRIC CARCINOGENESIS: A HEALTH CHECK-UP COHORT STUDY." Gastroenterology 156(6): S-677-S-678.

Background/Aims Insulin resistance which is a mechanism of metabolic syndrome has been known to promote carcinogenesis of various malignancies. In addition, metabolic syndrome is associated with sarcopenia. Thus, the aim was to investigate the association between sarcopenia and gastric carcinogenesis including precancerous conditions: atrophic gastritis (AG), intestinal metaplasia (IM), and gastric adenoma. Methods: The study subjects were an adult population who underwent gastroduodenoscopy at Gangnam Severance Check-up Center. AG and IM were evaluated by endoscopic findings. Sarcopenia based on muscle mass was defined as appendicular skeletal muscle (ASM) as a percentage of body weight that was less than 1 standard deviation below the sex-specific mean for healthy adults aged 20 to 39 years (cutoff point: 29.3% in male and 26.7% in female). Obesity was defined as body mass index (BMI) ≥25 kg/m2 according to the Asia-Pacific criteria. Sarcopenic obesity was a condition of combined sarcopenia and obesity. The association between sarcopenia and gastric lesions was evaluated. Results: 8,356 patients were enrolled this study. Among them, 12 (0.14%) and 3,552 (42.5%) patients were diagnosed as gastric cancer and precancerous conditions, respectively. 5 (41.7%) of 12 gastric cancer patients and 594 (16.9%) of 3.552 patients with gastric precancerous conditions were diagnosed with sarcopenia. Both diabetes mellitus (DM) (OR = 5.152, P = 0.005) and sarcopenic obesity (OR = 4.139, P = 0.016) were independent predictive factors for gastric cancer. And smoking, alcohol, DM, hypertension, dyslipidemia, Helicobacter pylori, and sarcopenia were significantly associated with gastric precancerous conditions. Conclusion: Sarcopenia and sarcopenic obesity were significantly associated with gastric carcinogenesis. Thus, sarcopenia may be one of the risk factors for gastric carcinogenesis.

Kodama, M., et al. (2012). "Ten-year prospective follow-up of histological changes at five points on the gastric mucosa as recommended by the updated Sydney system after Helicobacter pylori eradication." Journal of Gastroenterology 47(4): 394-403.

BACKGROUND: Atrophic gastritis and intestinal metaplasia (IM) are well known as precancerous lesions of gastric cancer. The present study evaluated the gastric mucosa for 10 years after H. pylori eradication at five points of the stomach as recommended by the updated Sydney system to clarify the relationship between H. pylori eradication and gastric cancer prevention. METHODS: Among the comprised 373 patients, 323 were H. pylori-positive while 50 patients were H. pylori-negative. Patients with successful eradication underwent follow-up endoscopic examination every year. Biopsy specimens were taken from five points of the stomach, as recommended by the updated Sydney system, and were evaluated for the degree of gastritis prospectively. RESULTS: Two hundred ninety-four out of the 323 H. pylori-positive patients successfully achieved eradication. Of the 197 patients on whom five-point biopsy was performed, the courses of 30 patients were able to be observed every year for 10 years after successful eradication. Inflammation, activity, and atrophy score at all five points were significantly reduced half a year to 6 years after eradication. IM scores fluctuated intensely up and down during all observation periods; however, IM score of the lesser curvature of the corpus continued decreasing gradually and showed a significant decrease 6 years after (0.97 ± 0.09 to 0.42 ± 0.17, P < 0.05). CONCLUSION: In 10 years after H. pylori eradication, atrophy at all sites and IM in the lesser curvature of the corpus gradually and significantly decreased. These results suggest that the improvement of gastric atrophy and IM might have association with the reduction of gastric cancer occurrence.

Kodama, M., et al. (2012). "Long term prospective follow-up of histological alteration at 5 points on the gastric mucosa recommended by the updated sydney system after helicobacter pylori eradication." Gastroenterology 142(5): S477.

Background: Atrophic gastritis and intestinal metaplasia (IM) are recognized as premalignant lesions of gastric cancer. Many studies which described the histological change after eradication showed disagreement. We prospectively evaluated the change of gastric mucosa for 10 years period after H. pylori eradication at 5 points of the stomach to clarify the association between H. pylori eradication and gastric carcinogenesis. Materials and Methods: Of the 373 patients, H. pylori positive were 323, on the other hand 50 patients were H. pylori-negative. Successful eradicated group underwent follow-up endoscopic examination every year. Biopsy specimens were taken from 5 points of the stomach, which recommended by updated Sydney system, and were evaluated gastritis status, that of inflammation, activity, atrophy, and intestinal metaplasia. Results: 294 out of the 323 H. pylori-positive patients achieved successfull eradication. Of the 197 patients on whom 5-point biopsy was performed, 30 patients were able to be observed every year for 10 years after successful eradication. Inflammation, activity, and atrophy score at all 5 points were significantly reduced half a year to 6 years after eradication. IM scores fluctuated intensely up and down during all observation periods, however, IM score of the lesser curvature of the corpus continued decreasing gradually and showed a significant decrease 6 years after (0.97±0.09 to 0.42±0.17, P<0.05). Conclusion: Atrophy at all sites and IM in the lesser curvature of the corpus gradually and significantly decreased in 10 years follow after H. pylori eradication. It is considered that these findings suggested the improvement of gastric atrophy and IM may have association with the reduction of gastric cancer.

Kodama, M., et al. (2021). "Gastric mucosal changes, and sex differences therein, after Helicobacter pylori eradication: A long-term prospective follow-up study." Journal of Gastroenterology and Hepatology.

BACKGROUND AND AIM: Improvement of atrophic gastritis and intestinal metaplasia (IM) is considered to reduce the gastric cancer risk, but whether it can be achieved by H. pylori eradication (HPE) remains controversial. To evaluate the effect of HPE, we observed the gastric mucosa for up to17 years after HPE and sex differences in gastric mucosa. METHODS: In total, 172 patients (94 males, 78 females) with HPE were enrolled. Annual histological evaluations were performed for up to 17 years. The grades of mononuclear cells, neutrophils, atrophy, IM in the antrum and corpus were evaluated using the updated Sydney system. RESULTS: Relative to the pre-HPE period, atrophy had improved significantly 1 year after HPE in the antrum (1.50 ± 0.75 vs. 1.21 ± 1.25, P < 0.01) and corpus (0.59 ± 0.75 vs. 0.18 ± 0.52, P < 0.05). IM showed no significant change during 17 years after HPE at either biopsy site. Atrophy scores did not differ significantly between males and females. IM scores were significantly higher in males than in females before eradication (antrum, 0.67 ± 0.94 vs. 0.44 ± 0.77, P = 0.003, corpus, 0.20 ± 0.62 vs. 0.047 ± 0.21, P = 0.0027) and at most observation timepoints. CONCLUSIONS: During 17 years after HPE, atrophy, but not IM, improved significantly at the greater curvatures of the antrum and corpus. IM was significantly more severe in males than in females. Careful follow-up after HPE based on sex differences in gastric mucosal characteristics is important.

Koh, C. J., et al. (2016). "Predicting gastric intestinal metaplasia and cancer using pre-endoscopic risk factors." Journal of Gastroenterology and Hepatology (Australia) 31: 93.

Background: Gastric intestinal metaplasia (IM) is a pre-malignant condition and early identification of individuals with intestinal metaplasia facilitates further endoscopic screening for gastric cancer. Objective: To assess the pre-endoscopic risk factors, Helicobacter serology (HP) and pepsinogen (PG), with demographic and epidemiologic factors in predicting IM and cancer. Method: A prospective cohort with 5,425 subjects who were referred for upper GI endoscopy for standard clinical indications. Blood was drawn HP and PG levels prior to gastroscopy. The correlation between the blood test results and findings from the clinical endoscopy were analyzed. Other factors examined include the following: gender, race, body mass index (BMI), family history of gastric cancer, smoking and alcohol use. Results: There were 5,425 participants recruited, of which 54 (1%) had gastric cancer and 791 (14.6%) had IM. For IM, univariate significant risk factors were: age >50 years, male gender, Chinese race, smoking, alcohol use, family history of cancer, PG and HP status. All factors apart from alcohol use and male gender remained significant on multivariate analysis. For gastric cancer, univariate significant risk factors were: age >50 years, male gender, and IM, HP status and PG. All factors remained significant on multivariate analysis. The modified 4 risk-factor score (Zhu F et al, DDW 2015) using age >50 years, smoking, HP and PG was assessed and gave an AUROC of 0.727 for gastric cancer and 0.658 for intestinal metaplasia. A score of 2 or more had a sensitivity of 83.3% and a specificity of 53.1% for gastric cancer. Conclusion: This study suggests risk stratification with non-invasive serum markers and demographic factors is useful in identifying a higher risk group for endoscopic screening for gastric cancer and IM, and validates the 4 risk-factor strategy in a real-world, endoscopic surveillance population. (Figure presented).

Kuipers, E. J., et al. (1996). "Atrophic gastritis and Helicobacter pylori infection in patients with reflux esophagitis treated with omeprazole or fundoplication." New England Journal of Medicine 334(16): 1018-1022.

Background. Helicobacter pylori infection plays an important part in the development of atrophic gastritis and intestinal metaplasia, conditions that predispose patients to gastric cancer. Profound suppression of gastric acid is associated with increased severity of gastritis caused by H. pylori, but it is not known whether acid suppression increases the risk of atrophic gastritis. Methods. We studied patients from two separate cohorts who were being treated for reflux esophagitis; 72 patients treated with fundoplication in Sweden and 105 treated with omeprazole (20 to 40 mg once daily) in the Netherlands. In both cohorts, the patients were followed for an average of five years (range, three to eight). After fundoplication, the patients did not receive acid-suppressive therapy. The presence of H. pylori was assessed at the first visit by histologic evaluation in the fundoplication group and by histologic and serologic evaluation in the omeprazole group. The patients were not treated for H. pylori infection. Before treatment and during follow-up, the patients underwent repeated gastroscopy, with biopsy sampling for histologic evaluation. Results. Among the patients treated with fundoplication, atrophic gastritis did not develop in any of the 31 who were infected with H. pylori at base line or the 41 who were not infected; 1 patient infected with H. pylori had atrophic gastritis before treatment that persisted after treatment. Among the patients treated with omeprazole, none of whom had atrophic gastritis at base line, atrophic gastritis developed in 18 of the 59 infected with H. pylori (P<0.001) and 2 of the 46 who were not infected (P=0.62). Conclusions: Patients with reflux esophagitis and H. pylori infection who are treated with omeprazole are at increased risk or atrophic gastritis.

Kuipers, E. J., et al. (2004). "Cure of Helicobacter pylori infection in patients with reflux oesophagitis treated with long term omeprazole reverses gastritis without exacerbation of reflux disease: results of a randomised controlled trial." Gut 53(1): 12‐20.

Kuipers, E. J., et al. (1995). "Helicobacter pylori and atrophic gastritis: Importance of the cagA status." Journal of the National Cancer Institute 87(23): 1777-1780.

Background: Infection with Helicobacter pylori is a major risk factor for the development of atrophic gastritis and gastric cancer. H. pylori strains can differ with respect to the presence of cagA (cytotoxin-associated gene A), a gene encoding a high-molecular-weight immunodominant antigen. H. pylori strains possessing cagA have been associated with enhanced induction of acute gastric inflammation. Purpose: We investigated the relationship between cagA status and the development of atrophic gastritis in a cohort of subjects infected with H. pylori. Methods: Gastrointestinal endoscopy with biopsy sampling was used to study the natural history of gastritis in 58 subjects infected with H. pylori. Biopsy specimens were obtained before and after a mean follow-up period of 11.5 years (range, 10-13 years). The cagA status of each individual was determined at the follow-up visit with the use of an enzyme-linked immunosorbent assay designed to detect the presence of serum immunoglobulin G directed against the CagA protein. Two-sided Fisher's exact tests, McNemar's tests, Student's t tests, and Wilcoxon sum rank tests were used to analyze the data. Results: Twenty-four (41%) of the 58 evaluated subjects had serum antibodies against CagA (i.e., they were cagA positive), and 34 subjects were cagA negative. At the initial visit, moderate to severe atrophic gastritis was observed in eight(33%) of the cagA-positive subjects and in six (18%) of the cagA-negative subjects. At that time, positive cagA status and gastric atrophy were not significantly related (P = .22; Fisher's exact test; odds ratio [OR] 2.33; 95% confidence interval [CI] = 0.58-9.65). During follow-up, 16 (36%) of the 44 initially atrophy-negative subjects developed atrophic gastritis (eight [50%] of 16 cagA-positive subjects versus eight [29%] of 28 cagA-negative subjects; P = .20, Fisher's exact test; relative risk [RR] = 1.75; 95% CI = 0.82-3.76). In six of these 16 subjects (five cagA positive versus one cagA negative), atrophic gastritis was accompanied by the development of intestinal metaplasia (i.e., a change in the type of specialized cells present) (P = .02; Fisher's exact test; RR = 9.06; 95% CI = 1.16-71.0). One of the initially atrophy-negative, cagA- positive subjects developed early gastric cancer. Four (29%) of the 14 subjects initially diagnosed with atrophic gastritis showed regression of atrophy during follow-up (one cagA positive and three cagA negative). Therefore, at the end of follow-up, 15 (62%) of the 24 cagA-positive subjects had atrophic gastritis compared with 11 (32%) of the 34 cagA-negative subjects (P = .02; Fisher's exact test; OR = 3.48; 95% CI = 1.02-12.18). Conclusion: Infection with cagA-positive H. pylori strains is associated with an increased risk for the eventual development of atrophic gastritis and intestinal metaplasia.

Kuipers, E. J., et al. (1995). "Long-term sequelae of Helicobacter pylori gastritis." Lancet 345(8964): 1525-1528.

Chronic Helicobacter pylori gastritis has been put forward as a risk factor for development of gastric mucosal atrophy and gastric cancer. The purpose of our study was to investigate the long-term effects of H pylori gastritis on the gastric mucosa. We prospectively studied 49 subjects negative for H pylori and 58 positive subjects for a mean follow-up of 11.5 years (range 10-13 years). Serum samples were obtained at the initial and follow-up visits for determination of H pylori IgG antibodies. Gastroscopies with biopsy sampling were done in all patients at both visits. Biopsy specimens were used for assessment of H pylori infection and histology. Development of atrophic gastritis and intestinal metaplasia occurred in 2 (4%) uninfected and 16 (28%) infected subjects. Regression of atrophy was noted in 4 (7%) infected subjects. Development of atrophic gastritis and intestinal metaplasia was significantly associated with H pylori infection (p = 0.0014; odds ratio 9.0, 95% CI 1.9-41.3). The proportion of atrophic gastritis in the study population showed an annual increase of 1.15% (0.5-1.8%). We conclude that H pylori infection is a significant risk factor for development of atrophic gastritis and intestinal metaplasia. Our findings support strongly the causative role of this infection in gastric carcinogenesis.

Kuvaev, R., et al. (2015). "Computer-aided diagnostic system for the realtime pathology prediction and clinical decision support during narrow band imaging magnification endoscopy in stomach." United European Gastroenterology Journal 3(5): A9.

Introduction: Narrow-band imaging endoscopy with magnification (NBI-M) is recommended to be utilized for clinical decision-making during screening or follow-up of individuals at high risk for gastric cancer [1]. Nevertheless, its application in clinical practice has some challenges due to the presence of various histological and endoscopic pattern changes of gastric mucosa. Nowadays computer- aided decision support systems in endoscopy are being designed to assist a medical expert in mastering advanced techniques that require a high level of expertise. Aims&Methods: The aim of this study was to design a computer-aided diagnosis hardware-software complex for real time clinical decision support during NBI-M in stomach. This complex was incorporated into endoscopic documentation system for real-time pathology prediction based on the automated assessment of mucosal patterns of saved images. Image processing techniques were applied for extracting of geometrical and topological features. For creating a multi-class classifier a naive Bayesian approach was used to combine results of several binary Adaboost classifiers. We selected and analyzed 91 endoscopy NBI-M images of gastric lesions from 52 patients (Olympus Exera GIF Q160Z, Lucera GIF Q260Z). All images were independently assessed by an expert and computeraided system according to validated simplified NBI-classification [2]: type A (circular), B (tubulo-villous), C (irregular). Histology was used as the ground truth information. Training and testing were performed for every image by a bootstrap method. Results: Among 91 images 25 had type A pattern (16 normal mucosa, 9 chronic gastritis), 31 had type B pattern (22 intestinal metaplasia, 9 pseudopyloric metaplasia), and irregular 35 has type C pattern (9 high-grade dysplasia, 26 adenocarcinoma). The average percentage of correctly recognized areas was 91.8±4.4% (92% in type A, 92% in B, 89% in C). The results of computeraided classification are summarized in the table. Conclusion: The newly designed endoscopic computer-aided diagnostic hardware- software system could provide effective recognition of three main types of gastric mucosal patterns and thus may lead to real-time pathology prediction and support for clinical decision-making.

Lage, J., et al. (2016). "Light-NBI to identify high-risk phenotypes for gastric adenocarcinoma: do we still need biopsies?" Scandinavian Journal of Gastroenterology 51(4): 501-506.

OBJECTIVE: Early diagnosis of gastric cancer may be achieved through surveillance of patients with extensive gastric intestinal metaplasia (eGIM). However, diagnosis of eGIM generally implies histology. We aimed at determining the accuracy of high-resolution endoscopy with light-narrow band imaging (NBI) to assess the presence of eGIM on a per-patient basis. MATERIAL AND METHODS: Prospective cohort of 60 patients divided into two groups: derivation cohort (n = 25) to evaluate the reliability and validity, and a real-time validation group (n = 35). In the derivation group, six endoscopists with two levels of expertise were asked to estimate the grade of GIM based in endoscopic images (white light endoscopy, light-NBI and amplification/near focus). In the real-time validation set, experienced endoscopists were asked to similarly record their real-time optical diagnosis. Histology was then considered as the gold standard. RESULTS: In the derivation group diagnosis accuracy was 60% with WLE (non-expert 59% vs. 61% experts), increasing to 73% after NBI magnification (non-expert 63% vs. 83% expert, p < 0.05). Moreover, proportion of agreement with histology was 83%, with a correct diagnosis of eGIM in 87% for experienced observers. In the real-time group experts obtained 89% global diagnostic accuracy correctly identifying 91% of the eGIM. The sensitivity, specificity, LR + and LR- of real-time endoscopic diagnosis of eGIM was 0.92 (CI95%:0.67-0.99), 0.96 (0.79-0.99), 21.1 (3.08-144) and 0.09 (0.013-0.57). CONCLUSION: For the first time the reliability of high-resolution endoscopy with light-NBI for extension of GIM is described. Our results suggest that more than 90% of individuals at risk could be identified without the need for biopsies, simplifying the current recommendations.

Lahner, E., et al. (2001). "First endoscopic-histologic follow-up in patients with body-predominant atrophic gastritis: when should it be done?" Gastrointestinal Endoscopy 53(4): 443-448.

BACKGROUND: Body-predominant atrophic gastritis is considered a risk factor for gastric cancer and carcinoid. Timing of follow-up for patients with this disorder has not been defined. This study was undertaken to determine the optimal time for the first endoscopic/histologic follow-up in patients with body-predominant atrophic gastritis. METHODS: Forty-two patients with body-predominant atrophic gastritis were randomly assigned to 1 of 2 follow-up intervals: group A (n = 22) at 24 months and group B (n = 20) at 48 months. At baseline and follow-up patients underwent gastroscopy at which biopsies were obtained from the antrum and body for histopathology and evaluation for enterochromaffin-like cells. RESULTS: In group A patients, 2 antral hyperplastic polyps (9.1%) were present at baseline and 4 antral hyperplastic polyps (18.2%) were found at follow-up. In group B patients, baseline gastroscopy revealed 2 antral hyperplastic polyps (10%) and follow-up 2 antral hyperplastic polyps (10%) and 1 carcinoid tumor (5%) in the body. Atrophy and intestinal metaplasia scores in gastric body and antral mucosa in both groups did not change significantly between baseline and follow-up, except an increase in antral mucosa atrophy in group B patients (p = 0.02) was revealed. CONCLUSIONS: The results of this study indicate that performing the first follow-up in patients with body-predominant atrophic gastritis need not be earlier than at 4 years after diagnosis. This interval is satisfactory for detection of potential neoplastic lesions.

Laine, L., et al. (2000). "Review article: potential gastrointestinal effects of long-term acid suppression with proton pump inhibitors." Alimentary Pharmacology and Therapeutics 14(6): 651-668.

This review examines the evidence for the development of adverse effects due to prolonged gastric acid suppression with proton pump inhibitors. Potential areas of concern regarding long-term proton pump inhibitor use have included: carcinoid formation; development of gastric adenocarcinoma (especially in patients with Helicobacter pylori infection); bacterial overgrowth; enteric infections; and malabsorption of fat, minerals, and vitamins. Prolonged proton pump inhibitor use may lead to enterochromaffin-like cell hyperplasia, but has not been demonstrated to increase the risk of carcinoid formation. Long-term proton pump inhibitor treatment has not been documented to hasten the development or the progression of atrophic gastritis to intestinal metaplasia and gastric cancer, although long-term studies are required to allow definitive conclusions. At present, we do not recommend that patients be tested routinely for H. pylori infection when using proton pump inhibitors for prolonged periods. Gastric bacterial overgrowth does increase with acid suppression, but important clinical sequelae, such a higher rate of gastric adenocarcinoma, have not been seen. The risk of enteric infection may increase with acid suppression, although this does not seem to be a common clinical problem with prolonged proton pump inhibitor use. The absorption of fats and minerals does not appear to be significantly impaired with chronic acid suppression. However, vitamin B12 concentration may be decreased when gastric acid is markedly suppressed for prolonged periods (e.g. Zolllinger-Ellison syndrome), and vitamin B12 levels should probably be assessed in patients taking high-dose proton pump inhibitors for many years. Thus, current evidence suggests that prolonged gastric acid suppression with proton pump inhibitors rarely, if ever, produces adverse events. Nevertheless, continued follow-up of patients taking proton pump inhibitors for extended periods will provide greater experience regarding the potential gastrointestinal adverse effects of long-term acid suppression.

Lakshmanan, S., et al. (2020). "Incidental finding of helicobacter heilmannii in two asymptomatic individuals." American Journal of Gastroenterology 115(SUPPL): S1567-S1568.

INTRODUCTION: Helicobacter heilmannii previously known as Gastrospirillum hominis is commonly seen in animals and may have zoonotic potential. It contributes to about 5% of human gastric infections, resulting in chronic gastritis, peptic ulceration, and rarely gastric carcinoma or mucosa-associated lymphoid tissue lymphoma. Most patients are symptomatic and present with dyspepsia, epigastric pain, or acid reflux. We report two cases in which incidental H.Heilmannii was found in the pathological report. CASE DESCRIPTION/METHODS: Both our patients had undergone esophagogastroduodenoscopy (EGD) in anticipation of bariatric surgery. One is a 22-year-old morbidly obese female without significant medical illness, who had mild patchy erythematous mucosa in the gastric antrum. Biopsy revealed moderate to severe chronic active gastritis. Both H.pylori and H.heilmannii organisms were identified on the Hematoxylin and eosin (H&E) stain. Next is a 25-year-old morbidly obese female with gastroesophageal reflux disease. Her EGD also revealed mild patchy erythematous mucosa in the gastric antrum and biopsy showed moderate inactive gastritis, reactive lymphoid follicles, and frequent long tightly coiled bacteria highlighted on H&E stain consistent with H.heilmannii. They were both treated with a 2-week course of amoxicillin, clarithromycin, and omeprazole. They remained asymptomatic during subsequent office visits and are scheduled for follow up EGD after their bariatric surgery. DISCUSSION: Gastric inflammation in humans infected with H.heilmannii is less severe and usually involves the gastric antrum like seen in our patients. Co-infection of H.heilmannii and H.pylori is often seen and is believed to have a higher prevalence of intestinal metaplasia than does infection with either strain alone. Studies have highlighted that H.heilmannii like H.pylori, is effectively eradicated with similar antimicrobial therapy. We are however unable to detect the presence or confirm eradication via ancillary tests such as urea breath test, serum antibody testing, or stool testing as with H.pylori. Whether in symptomatic patients or with incidental chronic gastritis findings, it is prudent to look for H.heilmannii in the absence of, or concomitant with H.pylori infection and treat them adequately to prevent further complications.

Langner, C. (2017). "[Precursors of gastric cancer : Dysplasia and adenoma]." Pathologe 38(2): 67-74.

Gastric cancer develops from preneoplastic and early neoplastic precursor lesions. In particular, the intestinal type according to the Lauren classification is driven by chronic inflammation and progresses via a chronic gastritis - atrophy/metaplasia - dysplasia - carcinoma sequence. Staging of the extent of atrophy (OLGA) or intestinal metaplasia (OLGIM) enables risk stratification and determines follow-up investigations according to the management of precancerous conditions and lesions in the stomach (MAPS) international guidelines. True adenomatous lesions are relatively rare in the stomach. Three major types need to be considered: the intestinal type (tubular, tubulovillous and villous), the foveolar type (with superficial gastric differentiation) and the pyloric gland adenoma (with deep gastric differentiation). The intestinal type is the most common and needs to be differentiated from nonneoplastic polypoid regenerative hyperplasia, but also from well-differentiated tubular adenocarcinoma.

Lastraioli, E., et al. (2019). "The hERG1 Potassium Channel Behaves As Prognostic Factor In Gastric Dysplasia Endoscopic Samples." OncoTargets and Therapy 12: 9377-9384.

PURPOSE: Gastric cancer (GC) is still a relevant health issue worldwide. The identification of prognostic factors for progression of gastric dysplasia (GD), the main pre-cancerous lesion of the intestinal-type GC, is hence mandatory. PATIENTS AND METHODS: A cohort of 83 GD endoscopic samples belonging to Italian subjects was collected. hERG1 expression was evaluated by immunohistochemistry and scored 0-3, depending on the percentage of stained cells. Expression data were analysed in conjunction with clinico-pathological and survival data. RESULTS: hERG1 turned out to be expressed in 67.47% (56 out of 83) of the GD samples. hERG1 expression was higher in high-grade GD compared to low-grade GD (29 out of 39, 74.36% vs 27 out of 44, 61.36%), although the statistical significance was not reached (P=0.246). No association emerged between hERG1 expression and clinical features of the patients (age, gender, localization, H. pylori infection, gastritis and intestinal metaplasia). In a subset of cases for which sequential samples of gastric lesions (from GD to Early Gastric Cancer and Advanced Gastric Cancer) were available, hERG1 expression was maintained in all the steps of gastric carcinogenesis from GD onwards. A general trend to increased expression in advanced lesions was observed. hERG1 score had a statistically significant impact on both Progression-Free Survival (P=0.018) and Overall Survival (P=0.031). In particular, patients displaying a high hERG1 score have a shorter survival. CONCLUSION: hERG1 is aberrantly expressed in human GD samples and has an impact on both PFS and OS, hence representing a novel prognostic marker for progression of GD towards GC of the intestinal histotype. Once properly validated, hERG1 detection could be included in the clinical practice, during endoscopic surveillance protocols, for the management of GD at higher risk of progression, as already proposed for Barrett's oesophagus.

Laszkowska, M., et al. (2020). "PREVALENCE OF EXTENSIVE AND LIMITED GASTRIC INTESTINAL METAPLASIA AND PROGRESSION TO DYSPLASIA AND GASTRIC CANCER." Gastroenterology 158(6): S-497.

Background: Gastric intestinal metaplasia (GIM) is a pre-cancerous lesion that increases risk of gastric adenocarcinoma (GA). Extensive GIM (involving the corpus and antrum) has been cited as having higher risk of GA than limited GIM (involving antrum alone). Recently proposed American Gastroenterological Association (AGA) guidelines and prior Management of Epithelial Precancerous Conditions in the Stomach (MAPS) II guidelines from Europe cite extensive GIM as an indication for endoscopic surveillance. Currently, there are no studies of the prevalence of extensive vs. limited GIM in the US, and only one study assessed progression of extensive GIM to GA. The aim of this study was to estimate the prevalence and progression rates of extensive and limited GIM in a US cohort. Methods: In this retrospective cohort study, we identified individuals with intestinal metaplasia diagnosed on biopsy between 1/1/1990 and 8/1/2019 at Columbia University Irving Medical Center. Samples with biopsy specimens available from both the distal stomach (antrum/pre-pylorus/pylorus) and proximal stomach (body/fundus) were included. Individuals with cancer or dysplasia at the time of initial biopsy were excluded. Specimens were characterized as limited (GIM found only in the distal stomach) or extensive (GIM in both the proximal and distal stomach, or proximal stomach alone). Helicobacter pylori infection was also noted. Data on age, gender, race, and ethnicity was obtained from the electronic medical record. Incidence of advanced lesions (low- and high-grade dysplasia and GA) on follow up was calculated as the number of new diagnoses divided by person-years of follow-up. Patients were censored at death or last documented visit. Results: Of 1,329 individuals with GIM, 396 (29.8%) had extensive GIM and 933 (70.2%) had limited GIM. Patients with extensive GIM were older than those with limited GIM (p=0.03) and more likely to be Hispanic (OR 1.5, 95% CI 1.12-2.01). On multivariable analysis, older age, Hispanic ethnicity (vs. non-Hispanic), and absence of H.pylori infection were predictive of extensive GIM (Table 1). The incidence rate of GA for extensive GIM was 151.3 cases per 100,000 person-years, compared to 93.3 cases for limited GIM, though this difference was not statistically significant (Incidence Rate Ratio 1.62, 95% CI 0.24-9.58; Table 2). There was also no significant difference in incidence of advanced lesions overall (Incidence Rate Ratio 1.00, 95% CI 0.31-2.81). Conclusion: 29.8% of individuals with intestinal metaplasia have the extensive subtype, and are more likely to be older and of Hispanic ethnicity than individuals with limited GIM. While the higher incidence of GA in the extensive subtype was not statistically significant in this study, additional large studies are needed to better understand the risk associated with extensive GIM in the US population.

Lau, J. W. L., et al. (2021). "Opportunistic upper endoscopy during colonoscopy as a screening strategy for countries with intermediate gastric cancer risk." Journal of Gastroenterology and Hepatology 36(4): 1081-1087.

BACKGROUND AND AIM: Screening upper endoscopy can detect esophagogastric (OG) cancers early with improved outcomes. Recent cost-utility studies suggest that opportunistic upper endoscopy at the same setting of colonoscopy might be a useful strategy for screening of OG cancers, and it may be more acceptable to the patients due to cost-saving and convenience. We aim to study the diagnostic performance of this screening strategy in a country with intermediate gastric cancer risk. METHODS: A retrospective cohort study using a prospective endoscopy database from 2015 to 2017 was performed. Patients included were individuals age > 40 who underwent opportunistic upper endoscopy at the same setting of colonoscopy without any OG symptoms. Neoplastic OG lesions are defined as cancer and high-grade dysplasia. Pre-neoplastic lesions include Barrett's esophagus (BE), intestinal metaplasia (IM), and atrophic gastritis (AG). RESULTS: The study population involved 1414 patients. Neoplastic OG lesions were detected in five patients (0.35%). Pre-neoplastic lesions were identified in 174 (12.3%) patients. IM was found in 146 (10.3%) patients with 21 (1.4%) having extensive IM. The number needed to scope to detect a neoplastic OG lesion is 282.8 with an estimated cost of USD$141 400 per lesion detected. On multivariate regression, age ≥ 60 (RR: 1.84, 95% CI: 1.29-2.63) and first-degree relatives with gastric cancer (RR: 1.64, 95% CI: 1.06-2.55) were independent risk factors for neoplastic or pre-neoplastic OG lesion. CONCLUSION: For countries with intermediate gastric cancer risk, opportunistic upper endoscopy may be an alternative screening strategy in a selected patient population. Prospective trials are warranted to validate its performance.

Lau, W. L. J., et al. (2019). "Opportunistic detection of oesophagogastric neoplastic and pre-neo plastic lesions during screening colonoscopy program-a worthwhile strategy?" United European Gastroenterology Journal 7(8): 247-248.

Introduction: Endoscopic screening for colon cancer is generally accepted for screening for colorectal cancer, whereas endoscopic screening for oesophagogastric (EG) cancer alone is not cost-effective in countries with low to intermediate incidence of gastric cancer. The utility of offering an opportunistic upper endoscopy during a screening colonoscopy was evaluated as a potential strategy for detection of early EG neoplastic and preneoplastic lesions. Aims & Methods: A retrospective review of a prospective database in a tertiary hospital was performed. Patients with age>40 who underwent opportunistic screening upper endoscopy and colonoscopy in the same session from January 2015 to December 2017 were included. Patients who underwent upper endoscopy for indications such as dyspepsia, weight loss and anaemia were excluded. EG neoplastic lesions were defined as EG carcinomas, and pre-neoplastic lesions were defined as Barret's oesophagus, intestinal metaplasia (IM), or atrophic gastritis. Results: Out of 9,566 patients who underwent simultaneous upper endoscopy and colonoscopy, we identified 1,414 patients who underwent screening upper endoscopy. On colonoscopy, 491 (34.7%) patients had adenomatous polyps detected, and colorectal malignancy was detected in 20 patients (1.4%). From our cohort, 179 (12.7%) patients undergoing opportunistic screening upper endoscopy had EG neoplastic and pre-neoplastic lesions. of these, IM was found in 146 (10.3%) patients with 112 (7.9%) focal IM while 21 (1.4%) had extensive IM. Atrophic gastritis was detected in 23 (1.6%) patients. Also, 19 (1.3%) patients were found to have Barrett's oesophagus with one high-grade dysplasia which was resected endoscopically. Early stage gastric cancers were diagnosed in three patients (0.2%) who underwent surgery. Two were T1bN0 and one was T2N0. Another patient was diagnosed with early MALT lymphoma. On multivariate regression, independent risk factors for upper GI neoplastic and pre-neoplastic lesions in this population include age > 50 (Risk Ratio (RR) 2.18, 95%CI 1.15-4.14), p = 0.018) and having a family history of first-degree relative with gastric cancer (RR 1.60, 95% CI 1.03-2.48, p = 0.035). Hence, using this strategy, the number needed to detect an incidental neoplastic or pre-neoplastic EG lesion is 7.90. At a cost of USD$500/upper endoscopy, it would cost $3950 per lesion detected. Conclusion: This observational cohort suggests the potential utility of incorporating upper endoscopy into an established screening colonoscopy program, for the purpose of detecting EG neoplastic and pre-neoplastic lesions in countries with intermediate risk. All pathologies detected are early lesions. In addition, this strategy may be more acceptable to patients as they are already planned for colonoscopy. Further studies are worthwhile to verify these observations.

Lee, A. A., et al. (2019). "FEASIBILITY OF GASTRIC INTESTINAL METAPLASIA SURVEILLANCE IN A HIGH RISK AMERICAN COHORT." Gastroenterology 156(6): S-519.

INTRODUCTION: Gastric intestinal metaplasia (GIM) surveillance is performed in many countries where gastric cancer is prevalent. Between 2009 and 2012 we identified gastric cancer in 4% of patients undergoing diagnostic upper endoscopy at our center. This prompted the initiation of an endoscopic surveillance program in February 2013. We aim to report on the surveillance and yield of GIM surveillance in a high-risk American population. METHODS: Patients with GIM on index upper endoscopy were identified during the mandatory biopsy follow-up clinic and counseled to undergo surveillance endoscopy in 3 years. This was also documented in the electronic record and the patients’ primary care providers were contacted to help ensure compliance. These patients were added to a prospectively maintained research database. At index and surveillance endoscopy, they underwent Sydney protocol biopsies (antrum, corpus, and incisura). The primary outcome was the proportion of patients identified who returned for follow-up endoscopy within the recommended 3 (+/- 0.5) year interval. Our secondary aims were to determine the proportion of patients who maintained stable lesions and those who had progression or regression based on gastric histology. Focal GIM involved one region of the stomach (antrum, incisura, body, fundus, or cardia) while multifocal GIM was defined by involvement of ≥2 discrete regions. RESULTS: Among 380 patients who underwent screening evaluation between February 2013 and September 2015 and were found to have GIM, 80 (21%) patients underwent surveillance endoscopy an average of 29.8 months following the index assessment (Table 1). Logistic regression analysis demonstrated that age, sex, and gender did not predict compliance with follow-up endoscopy. There was a trend toward greater compliance among those who underwent the index endoscopy for high versus low risk indications (OR 1.6 [95% CI 1.0-2.8])(Table 1). No patients developed dysplasia or cancer during this interval. Of the 23 patients who were initially found to have focal metaplasia, 4 progressed to multi-focal metaplasia, 4 maintained focal metaplasia, and 15 regressed to chronic gastritis. Of the 57 with multi-focal metaplasia, 24 continued to have multi-focal metaplasia, 10 regressed to focal, and 23 regressed to gastritis. Multinomial logistic regression analysis showed that patients with baseline multi-focal metaplasia were more likely to have multi-focal metaplasia on surveillance (OR 3.9 [95% CI 1.1-13.5])(Table 2) but did not identify other factors such as age or H. pylori status as predictors of histologic change. CONCLUSIONS: Surveillance of GIM in an American population is feasible and may be more important in those with multi-focal disease. The yield of surveillance, length of intervals, and methods to promote compliance require a larger and longer prospective assessment. [Table presented] [Table presented]

Lee, E., et al. (2018). "Risk factors of metachronous gastric neoplasm beyond 5 years after endoscopic resection for early gastric cancer." United European Gastroenterology Journal 6(8): A178.

Introduction: Endoscopic resection has been standard treatment for selected patients with early gastric cancer (EGC) and the risk factors of metachronous gastric cancer after endoscopic resection discovered throughout previous studies. However, the risk factors over a long period of time has not yet been well demonstrated. To develop an optimal endoscopic surveillance strategy, it is necessary to elucidate the risk factors associated with metachronous tumor development in long-term follow-up. Aims and Methods: This study aimed to clarify the risk factors of metachronous gastric neoplasm beyond 5 years after endoscopic resection for EGC. We performed a retrospective analysis of the patients who underwent endoscopic resection for EGC from Jan 2005 to May 2012 in Seoul National University Hospital. Results: Among 1280 patients with EGC, 663 patients were followed-up for over 5 years, in whom metachronous gastric neoplasm developed in 65 patients beyond 5 years after endoscopic resection for EGC. In multivariate analysis, male (odds ratio, OR 3.242; 95% confidence interval, CI 1.367-7.689; p=0.008), elevated gross type (OR 5.240; 95% CI 1.872-14.668; p=0.002), mixed Lauren classification (OR 5.240; 95% CI 2.535-92.054; p=0.003), intestinal metaplasia (OR 1.456; 95% CI 1.065-1.990; p=0.019), tumor-positive lateral margin (OR 3.322; 95% CI 1.092-10.104; p=0.034), synchronous adenoma (OR 2.832; 95% CI 1.261-6.364; p=0.012) were positive predictive factors for metachronous gastric neoplasm. Conclusion: Metachronous gastric neoplasm had developed in 9.8% of patients beyond 5 years after endoscopic resection for EGC. Male sex, elevated gross type, mixed Lauren classification, intestinal metaplasia, tumor-positive lateral margin, synchronous adenoma were significantly associated with metachronous tumor development in long-term follow-up.

Lee, J., et al. (2010). "Risk factors of synchronous or metachronous tumor development in early gastric cancer and precancerous lesion: A review of 1005 endoscopic resections of early gastric cancer and gastric adenoma." Gastrointestinal Endoscopy 71(5): AB260.

Background: Endoscopic submucosal dissection (ESD) has been an useful treatment option of early gastric cancer (EGC) and gastric adenoma (GA). Through complete pathologic mapping and serial endoscopic follow-up for years after ESD, multiple foci of malignant and precancerous lesions are frequently observed. This study aimed to evaluate associated factors of synchronous or metachronous tumor development after ESD for EGC or GA. Methods: From April 2005 to August 2008, 1005 cases (503 EGCs and 497 GAs) were enrolled prospectively after ESD in Seoul National University Hospital and followed-up for more than one year. Synchronous tumor was defined as an EGC or GA confirmed within one year from initial ESD, and metachronous tumor as an EGC or GA diagnosed after one year from initial ESD. Follow-up endoscopies were performed in 3, 6, 12, 18 months after ESD, and then annually. Complete resection rate, complications, final diagnosis and synchronous or metachronous tumor development were evaluated with associated factors during follow-up. Results: In 1005 cases, synchronous lesions were detected in 256 cases (25.4%), in which 160 cases (62.6%) were revealed from the pathologic mapping of initial resected specimens. Metachronous tumors were detected in 66 cases (6.6%) and the mean duration from initial diagnosis was 800 days (689-911 days, 95% C.I.) In GA cases, synchronous tumor was negatively associated with Helicobacter pylori (H.P) infection (p=0.001), and positively associated with the degree of intestinal metaplasia (p<0.001), whereas, metachronous tumor development was not associated with H.P infection, mucosal atrophy or the degree of intestinal metaplasia. In EGC cases, synchronous tumor was associated with the degree of intestinal metaplasia (p<0.001), whereas, metachronous tumor development was not associated with H.P infection, mucosal atrophy or the degree of intestinal metaplasia. Conclusion: Synchronous or metachronous tumor development was frequently observed in ESD-treated EGC or GA cases. The degree of intestinal metaplasia showed statistical correlation with synchronous lesions. Serial follow-up is warranted to elucidate synchronous or metachronous tumor development in ESD-treated EGC or GA cases.

Lee, J. W. J., et al. (2016). "Prospective cohort study of gastric intestinal metaplasia progression and risk factors." Gastroenterology 150(4): S867-S868.

Background: Intestinal metaplasia (IM) is recognized as a precancerous lesion for gastric carcinoma (GC), yet data to guide an appropriate surveillance strategy is lacking. Objectives: To investigate the progression of IM and risk factors thereof in the Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP) cohort. Method: The GCEP is a prospective multicentre study initiated in 2004 and presented at DDW 2013 (Lim et al, Gastroenterol 2013;144(5):S-95-S-96). Chinese subjects aged >50 years were recruited whereby endoscopy surveillance was offered for a minimum of 5 years. All subjects gave informed consent and IRB approvals obtained. IM was diagnosed by histology of gastric biopsies following the Updated Sydney Protocol. Severity of IM was graded using OLGIM scoring system. Predictive factors for IM progression were identified by univariate analysis and subsequent multivariate cox-regression analysis. Results: 2987 Chinese subjects (mean age 59.9±7.0, 51.3% male) were enrolled, of whom 1874 had IM on histology. 678 (36.2%) had at least one biopsy with marked IM, and had increased risk of high grade dysplasia (OR 19.7; 95%CI 2.5- 153.0, p=0.04), compared to those with only mild or moderate IM. 1657 had adequate longitudinal follow-up biopsies for analysis of progression of IM. At the end of 5 years, 432 (44.2%) had progressed in severity. The prevalence of marked IM increased from 11.5% at baseline to 25% at the end of 5 years. On multivariate analysis, positive family history for GC (HR 1.43; 95% CI 1.01-2.03, p=0.046), smoking (HR 1.52; 95% CI 1.02-2.59, p= 0.043) and atrophic gastritis (HR 1.56; 1.16-2.08, p=0.03) were significant predictors of a more rapid progression to marked IM. On OLGIM score, 11.6% had Stage III/IV IM and these subjects were at increased risk of developing high grade dysplasia (OR 11.0; 95%CI 3.47-35.2; p<0.001). Conclusions: One quarter of patients with IM had developed marked IM by the 5th year of surveillance, and marked IM carried an increased risk of dysplasia. Risk factors of a more rapid progression to marked IM include smoking and positive family history for GC, suggesting the need for further endoscopic surveillance for patients with the above risk factors even without extensive IM. The occurrence of progression despite the eradication of H pylori suggests that surveillance is necessary, and that the natural history of IM is not static.

Lee, J. W. J., et al. (2016). "Topographic distribution of multi-focal gastric intestinal metaplasia." Journal of Gastroenterology and Hepatology (Australia) 31: 108.

Background: Multi-focal intestinal metaplasia (IM) is a recognized risk factor for gastric carcinoma. We aim to describe the topographic distribution of multi-focal IM and its risk towards gastric carcinoma within the Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP) cohort. Method: The GCEP is a prospective multi-centre study in Singapore initiated in 2004 in which Chinese subjects aged >50 years were recruited and offered endoscopy surveillance for a minimum of 5 years. All patients underwent gastric biopsies, and IM severity was graded as per the Updated Sydney Protocol. Results: In total, 2987 Chinese subjects (mean age 59.9 ± 7.0, 51.3% male) were enrolled. A total of 2170 subjects who underwent a total of 7198 interval gastroscopies with minimum 5 biopsies were included for the following analysis. Approximately 49.3% were found to have IM. The diagnostic yield of IM was highest within the antrum and along the lesser curve of the stomach; antrum greater curve 52.9%, antrum lesser curve 73.2%, incisura angularis 53.1%, corpus greater curve 10.4% and corpus lesser curve 18.1%. Approximately 20.6% had focal IM and 28.7% had multi-focal IM. Majority of those with focal IM were low grade (70.3% mild, 17.4% moderate and 12.3% marked). Amongst those with multi-focal IM, 23.9% were antrum pre-dominant, 12.2% were magenstrasse and 3.3% were diffused. Both magenstrasse and diffuse gastric IM topography were significantly associated with subsequent high-grade dysplasia and carcinoma; Magenstrasse (OR 5.00 95% CI: 1.24-20.14, p = 0.02), Diffuse (OR 19.09 95% CI 4.67-78.06; p <0.01). Conclusions: Our findings are consistent with previous non-Asian studies, whereby multifocal IM, in particular the magenstrasse and the diffuse topographic distribution, are at higher risk of dysplasia and carcinoma. Surveillance biopsies for IM should include the gastric lesser curvature and adhere to the Updated Sydney Protocol.

Lee, J. W. J., et al. (2021). "Severity of gastric intestinal metaplasia predicts the risk of gastric cancer: a prospective multicentre cohort study (GCEP)." Gut.

OBJECTIVE: To investigate the incidence of gastric cancer (GC) attributed to gastric intestinal metaplasia (IM), and validate the Operative Link on Gastric Intestinal Metaplasia (OLGIM) for targeted endoscopic surveillance in regions with low-intermediate incidence of GC. METHODS: A prospective, longitudinal and multicentre study was carried out in Singapore. The study participants comprised 2980 patients undergoing screening gastroscopy with standardised gastric mucosal sampling, from January 2004 and December 2010, with scheduled surveillance endoscopies at year 3 and 5. Participants were also matched against the National Registry of Diseases Office for missed diagnoses of early gastric neoplasia (EGN). RESULTS: There were 21 participants diagnosed with EGN. IM was a significant risk factor for EGN (adjusted-HR 5.36; 95% CI 1.51 to 19.0; p<0.01). The age-adjusted EGN incidence rates for patients with and without IM were 133.9 and 12.5 per 100 000 person-years. Participants with OLGIM stages III-IV were at greatest risk (adjusted-HR 20.7; 95% CI 5.04 to 85.6; p<0.01). More than half of the EGNs (n=4/7) attributed to baseline OLGIM III-IV developed within 2 years (range: 12.7-44.8 months). Serum trefoil factor 3 distinguishes (Area Under the Receiver Operating Characteristics 0.749) patients with OLGIM III-IV if they are negative for H. pylori. Participants with OLGIM II were also at significant risk of EGN (adjusted-HR 7.34; 95% CI 1.60 to 33.7; p=0.02). A significant smoking history further increases the risk of EGN among patients with OLGIM stages II-IV. CONCLUSIONS: We suggest a risk-stratified approach and recommend that high-risk patients (OLGIM III-IV) have endoscopic surveillance in 2 years, intermediate-risk patients (OLGIM II) in 5 years.

Lee, K., et al. (2016). "Compare the characteristics of synchronous and metachronous gastric tumors aft er endoscopic resection with H. Pylori infection: Single center experience." Helicobacter 21: 136-137.

Background: Endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR) have become a standard treatment for in a certain early gastric cancer (EGC). However, metachronous or synchronous tumor after endoscopic resec-tion become a main problem in follow up. We aimed to compare the characteristics of synchronous and metachronous tumor in patient with EGC or gastric adenoma after endoscopic resection. Methods: A total of 552 patients who underwent endoscopic resection between January 2002 and February 2016 in a single center were retrospectively reviewed. We analyzed the characteristic of synchronous or metachronous tumors with endoscopic findings, pathologic findings and Helicobacter pylori status. Results: In total, 33(5.9%) patients had synchronous tumors, and 30(5.4%) patients had metachronous tumors. The median period until discovery metachronous tumor after initial ESD was 28.75 months. Male and older (>65 years old) patients had more common in synchronous and metachronous group (69.8%, 73.0%). But there was no significant difference between two groups ( p = 0.595, p = 0.395). H. pylori infection rate was only 12.7% in both groups. But, severe mucosal atrophy (grade 2-3), known to related to H. pylori infection, had more frequent in metachronous group (90%, p = 0.010). Marginal involvement of primary tumor was more frequent in synchronous group (57.6% vs 26.7%, p = 0.013). Histological type, intestinal metaplasia and location of tumor was not showed difference between two groups ( p = 0.655, p = 0.126, p = 0.259). Conclusion: Syncronous and metachronous tumor after endoscopic resection is observed in 11.3%. We recommend careful follow- up in patients with severe mucosal atrophy regardless of H. pylori infection. Physicians should observe the stomach not only previous resection site but also whole stomach during follow- up EGD.

Lee, S., et al. (2014). "Does eradication of helicabacter pylori after endoscopic resection of early gastric cancer decrease recurrence of gastric cancer?" Helicobacter 19: 164.

Background: Eradication of Helicobacter pylori in patients' undergone endoscopic resection of early gastric cancer has been recommended by guidelines to decrease incidence of metachronous gastric cancer. The aim of our study was to evaluate effectiveness of Helicobacter pylori eradication after endoscopic resection of early gastric cancer in preventing recurrence of gastric cancer. Method: Patients with result of Helicobacter pylori study after endoscopic removal of early gastric cancer from Nov 2005 to Aug 2013 in Yeungnam university hospital were enrolled. Baseline characteristics, follow up period, presence of recurrent disease, status of Helicobacter pylori was reviewed retrospectively. Results: Mean age of the patients was 62.7 ± 9.8 years and 103 (72.5%) patients were male. Mean follow up time was 15.5 ± 18.2 months. Among total 353 patients, 226 (61.4%) had no Helicobacter pylori infection. Recurrence was seen in 11 (4.9%) patients with no Helicobacter pylori infection and 3 (2.1%) with Helicobacter pylori infection. Among patients with Helicobacter pylori infection, eradication of Helicobacter pylori was done in 69 (48.6%) patients. Recurrence of cancer was seen in 2 (2.9%) patients with Helicobacter pylori eradication and 1 (1.4%) with persistent Helicobacter pylori infection and recurrence rate was not statistically different between two groups. Conclusion: Presence and eradication of Helicobacter pylori infection in patients who underwent endoscopic removal of EGCA does not seem to affect recurrence of cancer. Further large scaled prospective studies defining relationship between status of Helicobacter pylori and cancer recurrence including status of intestinal metaplasia and chronic atrophic gastritis is needed.

Lee, S. E., et al. (2012). "Pyloric gland adenoma with mismatch repair protein loss and MSI-high is a precursor of gastric adenocarcinoma in lynch syndrome." Laboratory Investigation 92: 167A.

Background: Fundic gland polyposis is a gastric manifestation in patients with FAP. However, although gastric carcinoma is the second most common extra-colonic malignancy associated with Lynch syndrome, the detailed pathology or precursor lesions in the stomach are not described. In this study, we performed clinicopatholologic and molecular analyses using 13 gastric carcinomas from patients with Lynch syndrome. Design: After computer search, 392 patients were identified to have both gastric and colonic adenocarcinomas. Additionally, 311 patients enrolled in familial cancer clinic suspected as Lynch syndrome were also retrieved. All the medical records of 703 patients in a single comprehensive cancer center from 1995 to 2011 were reviewed. Twenty patients met the Amsterdam II criteria and had been treated for gastric and colonic adenocarcinomas. Immunohistochemistry for mismatch repair (MMR) proteins, MSI tests, MLPA for hMLH1 and hMSH2 were performed to confirm Lynch syndrome. Results: Thirteen patients were classified as Lynch syndrome and the average age of diagnosis of gastric carcinoma was 48 years. The location of tumor was antrum (n=8) followed by body (n=3) and cardia (n=2). Helicobacter pylori were demonstrated in 4 cases (30.8%) and background intestinal metaplasia and atrophy was identified in 11 cases (84.6%). The histology of gastric carcinoma included 10 tubular adenocarcinomas, 2 mucinous carcinomas, and a composite adenocarcinoma and endocrine carcinoma. In all cases, both gastric and colonic carcinomas were MSI-high and either hMLH1 or hMSH2 protein was lost in tumors. Unexpectedly, pyloric gland adenoma (PGA) was identified in 4 cases around the carcinomas. PGAs mimicked fundic gland polyp except for the absence of oxyntic cells. Most tumor glands in PGAs were strongly positive for MUC6 and superficial layer was positive for MUC5AC, while MUC2 and CD10 were totally negative. In a PGA with germline hMLH1 mutation, hMLH1 protein expression was lost. Three PGAs with hMSH2 protein loss showed abnormalities in MLPA. The carcinomas around PGA were tubular adenocarcinoma of gastric mucin phenotype. In three cases, there was a direct transition from PGA to carcinoma and one PGA transformed to carcinoma over the follow up of 2 years. Conclusions: We first identified that PGA may be a precursor lesion of gastric carcinoma in Lynch syndrome and accompanies MMR protein loss and MSI-high. Our findings suggest that MSI-phenotype is an early event and the MMR-deficient pathway also involves gastric carcinogenesis.

Lee, S. Y., et al. (2020). "Less than 10% of helicobacter pylori-seronegative subjects show true infection after seroconversion." Digestion 102(1): 105.

Introduction: Seroconversion and seroreversion of Helicobacter pylori occur during gastric cancer screening. This study aimed to determine the incidence and characteristics of seronegative subjects showing seroconversion in the follow-up tests. Methods: Consecutive H. pylori-seronegative Koreans who underwent biannual gastric cancer screening based on gastroscopy and serum assays were included. Past infection was defined as successful eradication history or endoscopic findings suggesting unintended eradication (gastric xanthoma, advanced atrophy, or intestinal metaplasia). Serum anti-H. pylori IgG (range: 5-200 AU/ mL) was followed up using the Chorus assay, which is acceptable in Koreans with a sensitivity of 100% and specificity of 75.0%. True H. pylori infection was confirmed based on endoscopic findings and Giemsa staining. Results: During the mean follow-up of 57.7±21.4 months, 61 (15.0%) of 407 seronegative subjects showed seroconversion. The seroconversion rate increased with a longer follow-up period (p <0.001) and higher initial serology titer (p <0.001). True infection was found in 6 (9.8%) of the 61 seroconverted subjects and in 2 seronegative subjects with positive Giemsa staining. All 8 infected subjects showed newly appeared spotty redness in the corpus. At the time of positive H. pylori test findings, the median serology titer was lower in 55 false- seropositive subjects (22.0 AU/mL, 12.1-99.3 AU/mL) than in 8 subjects with true infection (64.5 AU/mL, 6.2- 200 AU/mL, p <0.001). Most (80%) of false-seropositive subjects showed spontaneous seroreversion in the follow- up tests with a mean serology titer of 7.8 ± 2.0 AU/mL, whereas others (20 %) showed continuous false seropositivity with a mean serology titer of 29.4 ± 10.7 AU/mL. Conclusions: Seroconversion occurred in 3.3% of H. pyloriseronegative subjects per year; however, only 9.8% of the seroconverted subjects had true H. pylori infection. Most were false seropositivity with a relatively low serology titer. New appearance of spotty redness in the corpus indicates true infection..

Lee, T. Y., et al. (2016). "The Incidence of Gastric Adenocarcinoma Among Patients With Gastric Intestinal Metaplasia: A Long-term Cohort Study." Journal of Clinical Gastroenterology 50(7): 532-537.

BACKGROUND AND AIMS: Gastric intestinal metaplasia (IM) has been known as a premalignant condition, but estimates of its cancer risk vary widely. We aimed to analyze cancer risk of gastric IM by a long-term cohort study. METHODS: We conducted a hospital-based study that included all patients with gastric IM between 1992 and 2010, and the development of gastric adenocarcinoma was evaluated until July 2011. Patients developing gastric cancer ≤180 days after the index diagnosis of IM were excluded. The incidence rate, the cumulative incidence, and the standardized incidence ratio (SIR) of gastric cancer were determined, and hazard ratios (HRs) of risk factors were calculated. RESULTS: We identified 7059 patients with a median follow-up duration of 5.1 years, and 81 patients developed gastric adenocarcinoma during the study period. The 5-, 10-, and 15-year cumulative incidences of gastric cancer were 0.9% [95% confidence interval (CI), 0.6-1.1), 2.0% (95% CI, 1.5-2.6), and 3.0% (95% CI, 2.0-4.0), respectively. On multivariate analysis, older age (eg, 75 y and above; HR=7.4; 95% CI, 2.8-19.6), low-grade dysplasia (HR=4.0; 95% CI, 2.1-7.9), and high-grade dysplasia (HR=18.8; 95% CI, 9.0-39.5) were independent risk factors. As compared with the risk in the general population, the SIR of gastric cancer among patients with gastric IM was 2.5 (95% CI, 2.0-3.1). However, the SIR was only 2.0 (95% CI, 1.5-2.6) in the nondysplasia subgroup, but was up to 35.2 (95% CI, 15.2-69.4) in the high-grade dysplasia subgroup. CONCLUSIONS: Gastric IM is an important risk factor for gastric cancer, but surveillance should be arranged only for those at an especially high risk.

Lee, Y., et al. (2007). "[Histological changes of gastric atrophy and intestinal metaplasia after Helicobacter pylori eradication]." Korean Journal of Gastroenterology 50(5): 299-305.

BACKGROUND/AIMS: Long-term Helicobater pylori infection results in atrophic gastritis and intestinal metaplasia, and increases the risk of gastric cancer. However, it is still controversial that eradication of H. pylori improves atrophy or metaplasia. Therefore, we investigated histological changes after the H. pylori eradication in patients with atrophy or metaplasia. METHODS: One hundred seven patients who received successful eradication of H. pylori infection in Hanyang University, Guri Hospital from March 2001 to April 2006, were enrolled. Antral biopsy was taken before the eradication to confirm the H. pylori infection and grade of atrophy or metaplasia by updated Sydney System. After a certain period of time, antral biopsy was repeatedly taken to confirm the eradication and investigate histological changes of atrophy or metaplasia. RESULTS: Mean age of the patients was 55.3+/-11.3, and average follow-up period was 28.7+/-13.9 months. Endoscopic diagnosis included gastric ulcer, duodenal ulcer, non-ulcer antral gastritis. Atrophy was observed in 41 of 91 and their average score was 0.73+/-0.92. After the eradication of H. pylori, atrophy was improved (0.38+/-0.70, p=0.025). However, metaplasia which was observed in 49 of 107, did not significantly improve during the follow-up period. Newly developed atrophy (7 of 38) or metaplasia (18 of 49) was observed in patients who without atrophy or metaplasia initially. Their average scores were slightly lower than those of cases with pre-existing atrophy or metaplasia without statistical significance. CONCLUSIONS: After the eradication of H. pylori infection, atrophic gastritis may be improved, but change of intestinal metaplasia is milder and may take longer duration for improvement.

Lee, Y. C., et al. (2013). "The benefit of mass eradication of helicobacter pylori infection: A community-based study of gastric cancer prevention." Gut 62(5): 676-682.

Objective To evaluate the benefit of mass eradication of Helicobacter pylori infection in reducing premalignant gastric lesions. Design Mass eradication of H pylori infection was started from 2004 for a Taiwanese population with prevalent H pylori infection, who were >30 years of age. Participants positive for the 13C-urea breath test underwent endoscopic screening and 1-week clarithromycin-based triple therapy. For subjects whose initial treatment failed, 10-day levofloxacin-based triple therapy was administered. The main outcome measures were changes in the prevalence of H pylori infection and premalignant gastric lesions, and changes in the incidence of premalignant gastric lesions and gastric cancer before (1995-2003) and after (2004-2008) chemoprevention using various comparators. Results The reduction in H pylori infection was 78.7% (95% CI 76.8% to 80.7%), and the estimated incidence of re-infection/recrudescence was 1% (95% CI 0.6% to 1.4%) per person-year. The effectiveness of reducing the incidence of gastric atrophy resulting from chemoprevention was significant at 77.2% (95% CI 72.3% to 81.2%), while the reduction in intestinal metaplasia was not significant. Compared with the 5-year period before chemoprevention and in the absence of endoscopic screening, the effectiveness in reducing gastric cancer incidence during the chemoprevention period was 25% (rate ratio 0.753, 95% CI 0.372 to 1.524). The reduction in peptic ulcer disease was 67.4% (95% CI 52.2% to 77.8%), while the incidence of oesophagitis was 6% (95% CI 5.1% to 6.9%) after treatment. Conclusions Population-based eradication of H pylori infection has led to a significant reduction in gastric atrophy at the expense of increased oesophagitis. The ultimate benefit in reducing gastric cancer incidence and its mortality should be validated by a further long-term follow-up.

Lenoci, N., et al. (2018). "Olga-based staging and dysplasia relevance in 50-75 year old patients in open access endoscopy." Digestive and Liver Disease 50(2): e79.

Background and aim: Patients with gastric atrophy and intestinal metaplasia have an increased risk of gastric cancer than the general population. A recent European consensus statement suggested to perform biopsies of the proximal and distal stomach for adequate assessment of pre-malignant gastric conditions, and that systems for histopathological staging may be useful for identifying subgroups of patients with different risks of progression to gastric cancer. Operative link on gastritis assessment (OLGA) staging system was proposed to standardize the assessment of gastric atrophy. Aim: to evaluate the prevalence of pre-malignant lesions in an open primary access endoscopy Material and methods: From January 2016 to September 2017 unselected outpatients (age 50-75) referred for upper gastrointestinal endoscopy (UGIE) were considered eligible for the study. Two biopsies from antrum, one from angulus and one from corpus were obtained in patients with normal endoscopy according to Sydney protocol and additional biopsies on each discrete lesion were performed. Histological assessment according to OLGA staging system was performed by two experienced gastrointestinal pathol-ogists, who also evaluated Helicobacter pylori status. Patients with stage OLGA II-III-IV and those with dysplasia were indicated to surveillance. Results: During the study period 1806 UGIEs were performed (males 41.5%, mean age 60.2 years). The main indications for the UGIEs were gastroesophageal reflux disease or dyspepsia (74%). Biopsies were obtained from 968 (53.6%) patients who were enrolled in the study (males 38.2%, mean age 59.7 years); main reasons for exclusion were represented by comorbidity, previous gastric surgery, follow-up of other disease and ongoing anticoagu-lation. According to OLGA staging system 111 patients (11.4%) were OLGA II stage, 49 (5%) and 16 (1.6%) were OLGA III and OLGA IV, respectively. Overall dysplasia was diagnosed on normal appearing mucosa in 10 (1%) patients; in detail in 2 (0.2%) patients with OLGA I, in 1 (0.1%) OLGA II, in 3 (0.3%) OLGA III and in 3 (0.3%) OLGA IV a low grade dysplasia was diagnosed, respectively. Furthermore in 1 (0.1%) OLGA II patient a high grade dysplasia was diagnosed. Helicobacter pylori was detected in 38.6% of enrolled patients. In detail Hp was detected in 35.1%, 44.4%, 37.8%, 48.7% and 43.7% of OLGA 0 to IV respectively. Atrophic autoimmune gastritis was diagnosed in 55 pts (5.6%): 21/55 (38%), 17/55 (30%) and 6/55 (11%) were assigned to OLGA II, III and IV, respectively. Conclusions: About six percent of our enrolled patients with endoscopically normal mucosa has been classified as OLGA III-IV stages, which are considered as premalignant lesions eligible for surveillance. Another six percent of asymptomatic and endo-scopically normal patients were diagnosed as having autoimmune gastritis, which also represents an indication for surveillance. The cost-effectiveness of this strategy still remains under evaluation.

Lenoci, N., et al. (2016). "Olga-based staging and dysplasia relevance in 50-70 years old patients in a primary open access endoscopy: Preliminary results." Digestive and Liver Disease 48: e75.

Background and aim: Patients with gastric atrophy and intestinal metaplasia may have a greater than 10-fold increased risk of gastric cancer than the general population. A recent European consensus statement suggested that biopsies of the proximal and distal stomach are needed for adequate assessment of premalignant gastric conditions, and that systems for histopathological staging may be useful for identifying subgroups of patients with different risks of progression to gastric cancer (1). Operative link on gastritis assessment (OLGA) staging system was proposed for clinical purposes to simplify the assessment of gastric cancer. If low-grade dysplasia is detected a repeat surveillance gastroscopy with a topographic mapping biopsy strategy should be performed within 1 year. Material and methods: Patients (age 50-70 years) undergoing upper endoscopy from September 2013 to September 2015 in our open access Endoscopy Service were enrolled. Biopsies from antrum (2), angulus (1), and corpus (2) were obtained in patients with normal endoscopy. Histological assessment according to OLGA and OLGIM staging was performed by two experienced gastrointestinal pathologists, who also evaluated Helicobacter pylori status. OLGA III/IV and pts with dysplasia were considered eligible for surveillance of these lesions. Results: 2026 upper endoscopy were performed (female 61.3%). Biopsies were obtained from 1470 patients (F 1073 = 72,9% and M 397 = 27,1%). Eight patients presented with OLGA III stage (0,5%) and 5 with OLGA IV stage (0,34%). Furthermore, 2/8 pts with OLGA III stage and 1/5 with OLGA IV stage had low grade dysplasia without an endoscopic defined lesion; 1 patient with OLGA IV had low grade dysplasia with an endoscopic lesion represented by erosions and areas of scarring. Helicobacter pylori has been found in 5/13 pts with OLGA III/IV stage. One patient undergoing the endoscopic follow-up one year later presented the same OLGA IV stage without dysplasia. Conclusions: In our population with dyspepsia and epigastric pain without significant lesions at upper endoscopy 0,84% of patients presented with an OLGA III/IV stage. Four of these patients had low grade dysplasia, one with a visible lesion. Follow-up of these lesions and cost-effectiveness of this strategy are ongoing.

Leodolter, A., et al. (2006). "Prevalence of H pylori associated 'high risk gastritis' for development of gastric cancer in patients with normal endoscopic findings." World Journal of Gastroenterology 12(34): 5509-5512.

Aim: To investigate the prevalence of H pylori associated corpus-predominant gastritis (CPG) or pangastritis, severe atrophy, and intestinal metaplasia (IM) in patients without any significant abnormal findings during upper-GI endoscopy. Methods: Gastric biopsies from 3548 patients were obtained during upper GI-endoscopy in a 4-year period. Two biopsies from antrum and corpus were histologically assessed according to the updated Sydney-System. Eight hundred and forty-five patients (mean age 54.8 ± 2.8 years) with H pylori infection and no peptic ulcer or abnormal gross findings in the stomach were identified and analyzed according to gastritis phenotypes using different scoring systems. Results: The prevalence of severe H pylori associated changes like pangastritis, CPG, IM, and severe atrophy increased with age, reaching a level of 20% in patients of the age group over 45 years. No differences in frequencies between genders were observed. The prevalence of IM had the highest increase, being 4-fold higher at the age of 65 years versus in individuals less than 45 years. Conclusion: The prevalence of gastritis featuring at risk for cancer development increases with age. These findings reinforce the necessity for the histological assessment, even in subjects with normal endoscopic appearance. The age-dependent increase in prevalence of severe histopathological changes in gastric mucosa, however, does not allow estimating the individual risk for gastric cancer development-only a proper follow-up can provide this information. © 2006 The WJG Press. All rights reserved.

Leri, O., et al. (1998). "Improvement of intestinal metaplasia six month after misoprostol treatment." European Review for Medical and Pharmacological Sciences 2(1): 37-40.

PURPOSE: To establish whether misoprostol (a synthetic prostanoid) is effective in improving intestinal metaplasia of dyspeptic patients. PATIENTS: Of the 206 dyspeptic patients without Helicobacter pylori, 18 (7.1%) had histological evidence of intestinal metaplasia (2 presented mild metaplasia, 9 moderate and 7 severe). They were treated with misoprostol 200 mg twice daily for six months and, after stopping the treatment, they all underwent endoscopic control. RESULTS: There was a statistical significant improvement of intestinal metaplasia (p < 0.001) and of the activity of antral gastritis (p = 0.03). There were no significant changes in antral and body specimens during follow-up. DISCUSSION: Though the small number of the patients and the lack of control group, our results suggest that misoprostol allows regression and/or improvement of histological IM (p < 0.001). It has proved to be effective in prevention of both gastric and duodenal ulcers induced by NSAID therapy, probably related largely to replacement of endogenous prostaglandins inhibited by the use of NSAID and it may also exerts its protective effects through inhibition of gastric acid secretion. Moreover, misoprostol showed to increase the rate of gastric blood flow, inducing a mucosal protective effect against the factors damaging gastric mucosa. It has been also documented that misoprostol regulates inflammatory cytokines and prolonged the survival of transplants, reflecting both its immunosuppressive and anti-inflammatory effect. In conclusion, since intestinal metaplasia increases the risk of gastric cancer, the use of misoprostol, in this pathology, would be of some interest.

Leung, W. K., et al. (2021). "Applications of machine learning models in the prediction of gastric cancer risk in patients after Helicobacter pylori eradication." Alimentary Pharmacology and Therapeutics 53(8): 864-872.

BACKGROUND: The risk of gastric cancer after Helicobacter pylori (H. pylori) eradication remains unknown. AIM: To evaluate the performances of seven different machine learning models in predicting gastric cancer risk after H. pylori eradication. METHODS: We identified H. pylori-infected patients who had received clarithromycin-based triple therapy between 2003 and 2014 in Hong Kong. Patients were divided into training (n = 64 238) and validation sets (n = 25 330), according to period of eradication therapy. The data were used to construct seven machine learning models to predict risk of gastric cancer development within 5 years after H. pylori eradication. A total of 26 clinical variables were input into these models. The performances were measured by the area under receiver operating characteristic curve (AUC) analysis. RESULTS: During a mean follow-up of 4.7 years, 0.21% of H. pylori-eradicated patients developed gastric cancer. Of the seven machine learning models, extreme gradient boosting (XGBoost) had the best performance in predicting cancer development (AUC 0.97, 95%CI 0.96-0.98), and was superior to conventional logistic regression (AUC 0.90, 95% CI 0.84-0.92). With the XGBoost model, the number of patients considered at high risk of gastric cancer was 6.6%, with miss rate of 1.9%. Patient age, presence of intestinal metaplasia, and gastric ulcer were the heavily weighted factors used by the XGBoost. CONCLUSION: Based on simple baseline patient information, machine learning model can accurately predict the risk of post-eradication gastric cancer. This model could substantially reduce the number of patients who require endoscopic surveillance.

Leung, W. K., et al. (2006). "Effects of long-term rofecoxib on gastric intestinal metaplasia: results of a randomized controlled trial." Clinical Cancer Research 12(15): 4766‐4772.

Leung, W. K., et al. (2005). "Risk factors associated with the development of intestinal metaplasia in first-degree relatives of gastric cancer patients." Cancer Epidemiology Biomarkers and Prevention 14(12): 2982-2986.

Family relatives of gastric cancer patients have a higher risk of gastric cancer and premalignant gastric lesions. We sought to determine the risk factors associated with the presence of intestinal metaplasia in a large cohort of gastric cancer relatives. First-degree relatives of gastric cancer patients were invited for screening gastroscopy. Endoscopic gastric biopsies were obtained from the antrum and corpus. Gastric biopsies were analyzed for Helicobacter pylori infection, severity of inflammation, and presence of intestinal metaplasia. Stepwise logistic regressions were used to identify for risk factors associated with presence of intestinal metaplasia in cancer relatives. Two hundred seventy cancer relatives underwent screening endoscopy (median age, 42; 47% male and 48% siblings). Among them, 161 (59.6%) were H. pylori positive and 81 (30%) had confirmed intestinal metaplasia. The following factors were found to be associated with the presence of intestinal metaplasia: age, male sex, H. pylori infection, birth order, alcohol use, siblings with stomach cancer, childhood living conditions, and water supply. Individuals with intestinal metaplasia had more severe acute and chronic inflammation in the antrum and corpus (P < 0.003). With multiple logistic regression, H. pylori infection [odds ratio (OR), 3.23], male gender (OR, 2.09), age (OR, 1.07), and a history of gastric cancer in siblings (OR, 1.91) were independent factors associated with the development of intestinal metaplasia in cancer relatives. In conclusion, we have identified risk factors associated with gastric intestinal metaplasia in stomach cancer relatives, which may be useful in the understanding of gastric carcinogenesis in these high-risk individuals. Copyright © 2005 American Association for Cancer Research.

Leung, W. K. and J. J. Y. Sung (2002). "Review article: Intestinal metaplasia and gastric carcinogenesis." Alimentary Pharmacology and Therapeutics 16(7): 1209-1216.

Gastric intestinal metaplasia, an intermediate step in Correa's cascade of gastric carcinogenesis, is generally regarded as a pre-malignant lesion. Epidemiological studies suggest that patients with intestinal metaplasia have more than a 10-fold increased risk of developing gastric cancer. Within the subclassification of intestinal metaplasia, incomplete or type III intestinal metaplasia appears to be associated with even higher malignant potential. The topographical distribution of intestinal metaplasia may also have prognostic implications. Certain genetic and epigenetic alterations have been demonstrated in gastric intestinal metaplasia which straddle into gastric cancer. These findings suggest that genetic changes occur early in the multistep gastric carcinogenesis process. Unlike Barrett's oesophagus and colonic polyp, which have well-defined surveillance guidelines, there is no widely accepted surveillance programme for gastric intestinal metaplasia. An annual surveillance programme may allow early detection of gastric cancer, which theoretically may improve survival. It remains elusive whether the treatment of Helicobacter pylori infection may reverse gastric intestinal metaplasia or reduce the subsequent risk of cancer development. Further controlled studies with longer follow-up are needed to resolve this controversy. The role of chemo-prophylactic agents, e.g. cyclo-oxygenase-2 inhibitor, should be investigated.

Leung, W. K., et al. (2013). "Treatment of gastric dysplasia and metaplasia by endoscopic radiofrequency ablation: A pilot study." Journal of Gastroenterology and Hepatology 28: 68.

Objective: Patients with pre-neoplastic gastric lesions including intestinal metaplasia (IM) and dysplasia are at increased risk of developing gastric cancer. Endoscopic radiofrequency ablation (RFA) has been successfully used in the eradication of dysplasia and IM associated with Barrett's esophagus. We tested the feasibility of using RFA for the treatment of dysplasia and IM in the stomach. Methods: Patients who had histologically confirmed gastric dysplasia or IM were recruited. All patients had H. pylori eradicated prior to RFA. Gastroscopy was performed by high definition endoscope with narrow band imaging and chromoendoscopy. Gastric pre-neoplastic lesions were endoscopically visible, well defined, and flat. Lesion locations were documented and the boundaries were tattooed for future identification. Ablation was performed using a HALO90 catheter (Covidien, GI Solutions) attached to a gastroscope and conducted under direct visualization until the target gastric mucosal lesions were treated. All procedures were performed on an outpatient basis under intravenous sedation. Endoscopy and RFAwas repeated at 8 week intervals for a maximum of 3 sessions or when there were no further endoscopically visible lesions. All patients were followed up by endoscopy at 6 and 12 months post-RFA. During follow up examination, reference to previous tattoo marks and video-recordings were made to ensure accurate localization of previous RFA treated lesions. Areas suspicious for dysplasia and/or metaplasia were biopsied for histological examination. The primary outcome was the complete eradication of dysplasia and/or IM. The secondary outcome was improvement in grading of IM as stipulated in updated Sydney Classification. The histological assessment was made by two pathologists who were blinded to the timing of the biopsy samples. Results: A total of 12 patients were recruited (median age 73 years; 7 male). Four patients had low-grade dysplasia (LGD) and the remaining 8 patients had non-dysplastic IM at baseline. Up to the time of writing this abstract, a total of 29 treatment sessions were applied and 7 patients had completed 3 sessions of RFA. Six patients, including 2 patients with dysplasia, had completed their 12-month follow up endoscopy and3 patients had completed their 6-month follow up. Complete eradication of dysplasia was noted in both patients with LGD at baseline (100%). No patients with baseline metaplasia had complete eradication of IM but the severity of IM improved in 5 (62.5%) patients on follow up examination. The procedure was well tolerated with one patient demonstrating a minor mucosal laceration of the cricopharyngeus during insertion of the catheter. Conclusion: Radiofrequency ablation successfully eradicated low-grade dysplasia of the stomach. Although gastric IM persisted after RFA treatment, most patients had evidence of histological improvement on follow up examination.

Leung, W. K., et al. (2013). "Treatment of gastric dysplasia and metaplasia by endoscopic radiofrequency ablation: A feasibility study." Gastrointestinal Endoscopy 77(5): AB196.

Introduction: Patients with pre-neoplastic gastric lesions including intestinal metaplasia (IM) and dysplasia are at increased risk of developing gastric cancer. Endoscopic radiofrequency ablation (RFA) has been successfully used in the eradication of dysplasia and IM associated with Barrett's esophagus. We tested the feasibility of using RFA for the treatment of dysplasia and IM in the stomach. Methods: Patients who had histologically confirmed gastric dysplasia or IM were recruited. All patients had H. pylori eradicated prior to RFA. Gastroscopy was performed by high definition endoscope with narrow band imaging and chromoendoscopy. Gastric pre-neoplastic lesions should be endoscopically visible, well defined and not raised. Ablation was performed using a HALO90 catheter (Covidien GI Solutions) attached to gastroscope and conducted under direct visualization until the target gastric mucosal lesions were treated. All procedures were performed on an outpatient basis under intravenous sedation. Endoscopy and RFA was repeated at 8 week intervals for a maximum of 3 sessions or when there were no further endoscopically visible lesions. All patients were followed up by endoscopy at 6 and 12 months post-RFA. During follow up examination, reference to previous tattoo marks and video-recordings were made to ensure accurate localization of previous RFA treated lesions. Areas suspicious for dysplasia and/or metaplasia were biopsied for histological examination. The primary outcome was the complete eradication of dysplasia and/or IM. The secondary outcome was improvement in grading of IM as stipulated in updated Sydney Classification. The histological assessment was made by two pathologists who were blinded to the sequences of the biopsy samples. Results: A total of 12 patients were recruited (median age 73 years; 7 male). Four patients had low-grade dysplasia (LGD) and the remaining 8 patients had non-dysplastic IM at baseline. Up to the time of writing this abstract, a total of 25 treatment sessions were applied and 4 patients had completed 3 sessions of RFA. Nine patients, including 2 patients with LGD, had completed their 6- month follow up endoscopy and 5 patients had completed their 12-month follow up. Complete eradication of dysplasia was noted in both patients with LGD at baseline (100%). The severity of IM improved in 6 (67%) patients and the remaining 3 patients showed no interval changes on histology at 6-months. At 12-months, 3 (60%) patients had histological improvement in IM. Most patients tolerated the procedure well, except one patient who had a minor mucosal laceration of the cricopharyngeus during insertion of the catheter. Conclusion: Radiofrequency ablation successfully eradicated low-grade dysplasia of the stomach. Gastric IM persisted with RFA treatment, but most showed histological improvement on follow up.

Leung, W. K., et al. (2015). "Treatment of Gastric Metaplasia or Dysplasia by Endoscopic Radiofrequency Ablation: A Pilot Study." Hepato-Gastroenterology 62(139): 748-751.

BACKGROUND/AIMS: Patients with gastric intestinal metaplasia and dysplasia are at increased risk of gastric cancer development. We tested the feasibility of using endoscopic radiofrequency ablation for the treatment of dysplasia and metaplasia in the stomach. METHODOLOGY: Patients who had histologically confirmed low-grade gastric dysplasia or IM were recruited. Endoscopic RFA was performed at 8 week-intervals for a maximum of 3 sessions. All patients were followed up by endoscopy until 12 months post-RFA. The primary outcome was the complete eradication of dysplasia or IM on follow-up. Secondary outcome was adverse events related to RFA. RESULTS: A total of 12 patients were recruited. Four patients had low-grade dysplasia and the remaining 8 patients had non-dysplastic IM at baseline. At one year after RFA, complete eradication of dysplasia was noted in four patients with low-grade dysplasia (100%). Gastric IM persisted in all patients with baseline metaplasia but the severity of IM improved in 6 (75%) patients. Endoscopic RFA was safe with minimal complications encountered. CONCLUSIONS: RFA successfully eradicated low-grade dysplasia of the stomach. Gastric IM however persisted after RFA but most patients had evidence of histological improvement on follow up.

Li, H. Y., et al. (2012). "Current clinical applications of magnifying endoscopy with narrow band imaging in the stomach." Diagnostic and Therapeutic Endoscopy 2012: 271914.

Narrow band imaging (NBI), in conjunction with magnifying endoscopy (ME), has arisen more and more attention in the area of advanced endoscopy. By enhancing the mucosal microvascular architecture and surface pattern, it is feasible to use ME-NBI to identify subtle changes associated with gastric inflammation, atrophy, intestinal metaplasia, and early gastric cancer. The new technique thus plays a valuable role in therapeutic decision-making, endoscopic treatment process, postoperative evaluation, and follow-up examination. To date, many criteria or evaluation method of ME-NBI has been proposed. This paper aims to summarize the various diagnosing classifications and the current clinical applications of ME-NBI in the stomach. © 2012 Hai-Yan Li et al.

Li, W. Q., et al. (2009). "Association between genetic polymorphisms of DNA base excision repair genes and evolution of precancerous gastric lesions in a Chinese population." Carcinogenesis 30(3): 500-505.

Base excision repair pathway may play an important role in repairing DNA damage related to Helicobacter pylori-induced inflammatory process. To evaluate the association between genetic polymorphisms of X-ray repair cross-complementing group 1 (XRCC1, Arg194Trp and Arg399Gln), adenosine diphosphate ribosyl transferase (ADPRT, Val762Ala), 8-oxoguanine DNA glycosylase (OGG1, Ser326Cys) and apurinic/apyrimidinic endonuclease 1 (APE1, Asp148Glu) and evolution of H.pylori-associated precancerous gastric lesions, a population-based cohort study was conducted in Linqu County, a high-risk area of gastric cancer in China. Genotypes were determined by polymerase chain reaction (PCR)-based denaturing high-performance liquid chromatography and PCR-restriction fragment length polymorphism analysis in 1281 H.pylori-infected subjects. We found that subjects carrying the combined XRCC1-194Arg/Trp+Trp/Trp genotype had an elevated chance of regression of gastric lesions [adjusted odds ratio (OR) = 1.44; 95% confidence interval (CI) = 1.06-1.96], whereas subjects carrying the XRCC1-399Arg/Gln+Gln/Gln genotype had a decreased chance of regression (OR = 0.68; 95% CI = 0.49-0.92). Stratified analysis indicated that an increased risk of progression was observed in subjects carrying the XRCC1-399Arg/Gln+Gln/Gln genotype (OR = 1.60; 95% CI = 1.09-2.36) or OGG1-326Ser/Cys+Cys/Cys genotype (OR = 1.95; 95% CI = 1.03-3.71) with intestinal metaplasia or dysplasia at baseline or carrying the XRCC1-399Arg/Gln+Gln/Gln genotype and smoking (OR = 1.58; 95% CI = 1.02-2.45). Furthermore, a significantly increased risk of progression was observed in subjects carrying one or two hazard genotypes of XRCC1-399 or OGG1-326, the OR was 2.83 (95% CI = 1.32-6.08), 2.22 (95% CI = 1.24-3.98) or 2.27 (95% CI = 1.26-4.10), respectively. These findings suggest that genetic polymorphisms in XRCC1-Arg194Trp, XRCC1-Arg399Gln and OGG1-Ser326Cys may play important roles in the evolution of H.pylori-associated gastric lesions in this high-risk population.

Li, Z., et al. (2020). "The dynamic change of cancer genome and T-cell receptor repertoire of an early gastric cancer cohort." Journal of Clinical Oncology 38(15).

Background: The dynamics of the cancer genome and T-cell receptor (TCR) repertoire are largely unclear during the development of gastric cancer, especially in the early stage. In this study, we studied the characteristics of genome and tumor microenvironment changes chronologically in 15 early gastric cancer (EGC) patients and illustrated their influence on carcinogenesis. Methods: 75 gastric tissues including precancerous lesions, cancer lesions and paired reference gastric samples, and 29 peripheral blood samples were obtained chronologically from 15 patients. All the lesions were categorized into 3 groups according to its pathology type (group1: inflammation or intestinal metaplasia, group 2: low-grade dysplasia (LGD), group 3: EGC). Deep sequencing of whole-exome and CDR3 chain of TCR of each sample was performed. Tumor mutation burden (TMB), TCR repertoire diversity and clonality were evaluated based on the sequencing data. Results:Heterogeneity existed in cancer genome and TCR repertoire among different patients. During carcinogenesis, TMB increased at first and then decreased, reaching its peak at LGD, which was different from what we have known from other advanced cancer. A detailed analysis showed that only part of the driver gene mutations maintained in this process. Compared with T cells infiltrated in reference samples, tumor-infiltrating T cells shared more clones with peripheral blood T cells. Diversity and clonality of TCR repertoire didn't show significant change with the development of cancer (Shannon index: group 1 = 6.32, group 2 = 6.06, group 3 = 6.09, p = 0.836; Clonality: group 1 = 0.19, group 2 = 0.19, group 3 = 0.17, p = 0.374). Some CDR3 clones appeared in early-stage and maintained during the carcinogenesis process. Conclusions: Our research is the first to analyze the cancer genome and TCR repertoire changes from both the spatial and temporal perspectives during the development of early gastric cancer. Somatic mutations appeared in the very early stage of gastric cancer and may induce the immune microenvironment changes in gastric mucosa.

Li, Z. W., et al. (2010). "Inflammatory cytokine gene polymorphisms increase the risk of atrophic gastritis and intestinal metaplasia." World Journal of Gastroenterology 16(14): 1788-1794.

AIM: To investigate the effects of interleukin-8 (IL-8), macrophage migration inhibitory factor (MIF) gene polymorphisms, Helicobacter pylori (H. pylori) infection, on the risk of developing severe chronic atrophic gastritis (SCAG) and intestinal metaplasia (IM). METHODS: A total of 372 cases were selected from a cohort study in Linqu County, a high risk area for gastric cancer (GC) in northern China. To obtain a sufficient group size, patients with normal or superficial gastritis were included. Based on an average follow-up period of 56 mo, the 372 cases were divided into no progression group (no histological progression from normal or superficial gastritis, n = 137), group I (progressed from normal or superficial gastritis to SCAG, n = 134) and group II (progressed from normal or superficial gastritis to IM, n = 101). IL-8, MIF gene polymorphisms were detected by polymerase chain reaction-based denaturing high-performance liquid chromatography analysis and DNA sequencing. RESULTS: An increased risk of SCAG was found in subjects with IL-8-251 AA genotype [odds ratio (OR) = 2.62, 95% CI: 1.23-5.72] or IL-8-251 A allele carriers (AA + AT) (OR = 1.81, 95% CI: 1.06-3.09). An elevated risk of IM was found in subjects with IL-8-251 AT genotype (OR = 2.27, 95% CI: 1.25-4.14) or IL-8-251 A allele carriers (OR = 2.07, 95% CI: 1.16-3.69). An increased risk of SCAG was found in subjects with MIF-173 GC genotype (OR = 2.36, 95% CI: 1.38-4.02) or MIF-173 C allele carriers (GC + CC) (OR = 2.07, 95% CI: 1.21-3.55). An elevated risk of IM was found in subjects with MIF-173 CC genotype (OR = 2.27, 95% CI: 1.16-4.46) or MIF-173 C allele carriers (OR = 3.84, 95% CI: 1.58-9.34). The risk of SCAG and IM was more evident in subjects carrying IL-8-251 A allele (OR = 6.70, 95% CI: 1.29-9.78) or MIF-173 C allele (OR = 6.54, 95% CI: 2.97-14.20) and positive for H. pylori infection. CONCLUSION: IL-8-251 and MIF-173 gene polymorphisms are significantly associated with the risk of SCAG and IM in a population with a high risk of GC in Linqu County, Shandong Province, China.

Li, Z. X., et al. (2015). "NOD1 and NOD2 Genetic Variants in Association with Risk of Gastric Cancer and Its Precursors in a Chinese Population." PloS One 10(5): e0124949.

BACKGROUND: Genetic variants of nucleotide-binding oligomerization domain-containing protein (NOD) may influence the outcome of Helicobacter pylori (H. pylori) infection and gastric carcinogenesis. To explore genetic variants of NOD1 and NOD2 in association with gastric cancer (GC) and its precursors, a population-based study was conducted in Linqu County, China. METHODS: TagSNPs of NOD1 and NOD2 were genotyped by Sequenom MASS array in 132 GCs, and 1,198 subjects with precancerous gastric lesions, and were correlated with evolution of gastric lesions in 766 subjects with follow-up data. RESULTS: Among seven tagSNPs, NOD1 rs2709800 and NOD2 rs718226 were associated with gastric lesions. NOD1 rs2709800 TG genotype carriers had a decreased risk of intestinal metaplasia (IM, OR: 0.53; 95% CI: 0.31-0.92), while NOD2 rs718226 G allele (AG/GG) showed increased risks of dysplasia (DYS, OR: 2.96; 95% CI: 1.86-4.71) and GC (OR: 2.35; 95% CI: 1.24-4.46). Moreover, an additive interaction between rs718226 and H. pylori was found in DYS or GC with synergy index of 3.08 (95% CI: 1.38-6.87) or 3.99 (95% CI: 1.55-10.22), respectively. The follow-up data indicated that NOD2 rs2111235 C allele (OR: 0.52; 95% CI: 0.32-0.83) and rs7205423 G allele (OR: 0.56; 95% CI: 0.35-0.89) were associated with decreased risk of progression in H. pylori-infected subjects. CONCLUSIONS: NOD1 rs2709800, NOD2 rs718226, rs2111235, rs7205423 and interaction between rs718226 and H. pylori infection may be related to risk of gastric lesions.

Lim, J., et al. (2013). "Risk factors of multiple gastric neoplasms after endoscopic resection." Helicobacter 18: 151.

Background: To clarify risk factors for metachronous or synchronous gastric neoplasm. Methods: We reviewed medical records of patients who had endoscopic resection for gastric high-grade adenomas or early gastric cancers between April 2005 and February 2011. Metachronous neoplasm was defined as high-grade adenoma or carcinoma developing more than one year after endoscopic resection at another site in the stomach. Second neoplasm found within one year was defined as synchronous neoplasm. We reviewed following parameters: age, sex, H. pylori status, size and pathologic type of primary neoplasm, gastric atrophy and intestinal metaplasia. Results: Among 1044 subjects, 45 had metachronous neoplasms and 56 had synchronous neoplasms. In univariate analysis, male gender, age ≥65, antral location, absence of H. pylori,<4.5 cm of size, atrophy and intestinal metaplasia were related to multiple gastric neoplasms. In multivariate analysis, antral location (OR1.638, 95%CI: 1.028-2.609), absence of H. pylori (OR1.559, 95%CI: 1.010-2.406), intestinal metaplasia (OR6.765, 95%CI: 1.638-27.947) were revealed to be independent risk factors of multiple gastric neoplasm. For metachronous neoplasm, age of 65 or more (OR2.091.95% CI: 1.082-4.041) and absence of H. pylori (OR2.374, 95%CI: 1.216-4.636) were found to be independent risk factors. However, only intestinal metaplasia was an independent risk factor of synchronous neoplasm. H. pylori eradication did not affect the incidence of multiple gastric neoplasms. Conclusion: Among endoscopically resected gastric neoplasms, lesions located in the antrum and accompanied by intestinal metaplasia without H. pylori infection were likely to develop synchronous or metachronous neoplasms. For lesions with these characteristics, short term follow-up and meticulous endoscopic evaluation are recommended.

Lim, J. H., et al. (2013). "Risk factors of synchronous and metachronous gastric neoplasms." Gastroenterology 144(5): S521.

Background: Endoscopic resection is now widely used for early gastric cancer replacing surgical treatment. However, metachronous or synchronous neoplasm is one of the main concerns about endoscopic resection. Thus this study was designed to figure out independent risk factors for metachronous or synchronous gastric neoplasm. Methods: We reviewed medical records of patients who had endoscopic submucosal dissection or endoscopic mucosal resection for gastric high grade adenomas or early gastric cancers between April 2005 and February 2011 and checked their follow-up endoscopic findings. Metachronous neoplasm was defined as high grade adenoma or adenocarcinoma developing more than one year after endoscopic resection at another site in the stomach. Second neoplasm found within one year was defined as synchronous neoplasm. We reviewed following parameters: age, sex, H. pylori status, size and pathologic type of primary neoplasm, gastric atrophy and intestinal metaplasia. Results: Out of 1044 subjects, 45 had metachronous neoplasms and 56 had synchronous neoplasms. In univariate analysis, male gender, age of 65 or more, antral location, absence of H. pylori, less than 4.5cm of size, atrophy and intestinal metaplasia were related to multiple gastric neoplasms. In multivariate analysis, antral location(OR 1.638, 95% CI: 1.028-2.609), absence of H. pylori(OR 1.559, 95% CI: 1.010-2.406), intestinal metaplasia(OR 6.765, 95% CI: 1.638-27.947) were revealed to be independent risk factors of multiple gastric neoplasm. For metachronous neoplasm, age of 65 or more(OR 2.091, 95% CI: 1.082-4.041) and absence of H. pylori(OR 2.374, 95% CI: 1.216-4.636) were found to be independent risk factors. However, only intestinal metaplasia was an independent risk factor of synchronous neoplasm. H. pylori eradication did not affect the incidence of multiple gastric neoplasms. Conclusion: Among endoscopically resected gastric neoplasms, lesions located in the antrum and accompanied by intestinal metaplasia without H. pylori infection were likely to develop synchronous or metachronous neoplasms. For lesions with these characteristics, short term follow-up and meticulous endoscopic evaluation are recommended.

Lim, J. H., et al. (2015). "Risk factors for synchronous or metachronous tumor development after endoscopic resection of gastric neoplasms." Gastric Cancer 18(4): 817-823.

BACKGROUND: Despite many advantages, the development of synchronous or metachronous neoplasm is one of the main concerns with endoscopic resection. We aimed to clarify the independent risk factors for synchronous or metachronous gastric neoplasm. METHODS: We retrospectively reviewed the medical records of all patients who had undergone endoscopic resection for gastric high-grade dysplasia or early gastric cancer between April 2001 and February 2011. RESULTS: Among 971 subjects, 56 synchronous neoplasms and 42 metachronous neoplasms developed during 12-131 months of follow-up. In univariate analysis, age over 65 years, male gender, absence of Helicobacter pylori infection, lower third location, mucosal atrophy, and intestinal metaplasia were related to multiple gastric neoplasms. In multivariate analysis, absence of H. pylori infection [odds ratio (OR) 1.610, 95 % confidence interval (CI) 1.038-2.497)], lower third location (OR 1.704, 95 % CI 1.070-2.713), and intestinal metaplasia (OR 4.461, 95 % CI 1.382-14.401) were independent risk factors for multiple gastric neoplasms. For synchronous neoplasm, primary tumor size less than 1 cm was the only independent risk factor. For metachronous neoplasm, absence of H. pylori infection (OR 2.416, 95 % CI 1.214-4.810) was found to be the only independent risk factor. H. pylori eradication was found to be unrelated to the development of metachronous gastric neoplasms. CONCLUSIONS: For tumors located in the antrum and accompanied by intestinal metaplasia, meticulous endoscopic evaluation with close follow-up after endoscopic resection is recommended.

Lim, L. G., et al. (2013). "Systematic endoscopic surveillance in a high-risk cohort is feasible for the detection of early gastric neoplasia." Gastroenterology 144(5): S95-S96.

Background: Gastric cancer is a curable disease if detected early. Endoscopy surveillance is the only way to detect gastric cancer in the early stages. More targeted screening and surveillance is required in countries with intermediate incidence rate of gastric cancer. The Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP), initialized in 2004, is a prospective multicentre study with the ultimate goal of developing an optimal approach and cost-effective algorithm for targeted screening for gastric cancer in the Singapore Chinese population. Objective: To determine whether systematic prospective endoscopic surveillance is feasible for the detection of early gastric cancer in Singapore Chinese cohort. Method: Chinese subjects aged 50 years and above were recruited from gastroenterology clinics of four major public hospitals in Singapore from 2004-2010. Endoscopy surveillance was offered for a minimum of 5 years. Informed consent was obtained from all subjects and the study was approved by the institutional review boards. The main outcome measurement is the number of subjects who develop high grade dysplasia or gastric adenocarcinoma. Results: 3033 subjects with mean age 59±7 years were recruited. 51% were male, 16% had family history of gastric cancer and 30% had Helicobacter pylori infection history based on their medical records. The prevalence of chronic gastritis, current H.pylori infection, atrophic gastritis and intestinal metaplasia at baseline were 81%, 20%, 19% and 44% respectively. The study is in progress, 1300 subjects have completed 5 years of surveillance and the rest will complete by 2015. 18 high grade dysplasia or early gastric cancers were detected so far after an average follow up period of 3 years. 12 of those cases were high grade dysplasia or intramucosal carcinoma and 6 were invasive cancers in stage 1A or 1B. The interval between the most recent endoscopy with no abnormal findings and the endoscopy where cancer was diagnosed is 4-25 months. Conclusions: Endoscopic surveillance is feasible, and has already detected high grade dysplasia or early gastric cancer in a high risk Singaporean Chinese population.

Lin, J. T., et al. (2013). "The factors associated with development of intestinal metaplasia: A nested case-control study." United European Gastroenterology Journal 1(1): A572-A573.

INTRODUCTION: Gastric cancer remains one of the leading causes of cancer mortality worldwide. Intestinal metaplasia, the key precancerous lesion of stomach, increases 6-times risk of gastric cancer and usually has no specific symptoms to detect. AIMS&METHODS: We aim to investigate the factors associated the development of intestinal metaplasia in the general population and relatives of gastric cancer. We conducted a hospital-based nested case-control study based on gastric cancer family cohort and healthy control cohort. This is a hospital-based case control study with age- and gender-matching between 2007 and 2012 at Taichung Veterans General Hospital. Multivariate analyses were conducted to examine the independent factors associated with intestinal metaplasia. RESULTS: Between 2007 and 2012, we identified 199 subjects with IM and 597 age- and gender-matched controls. Multivariate analyses found family history of gastric cancer (OR: 2.16, 95%CI: 1.38-3.37), H. pylori infection (OR: 1.60, 95%CI: 1.14-2.24), and gastric ulcer (OR: 1.78, 95%CI: 1.18-2.68) were independent risk factors for intestinal metaplasia development. Daily consumption of fruit was found to be inversely related with intestinal metaplasia (OR: 0.51, 95%CI: 0.36-0.74). CONCLUSION: In conclusion, family history, H. pylori infection, and gastric ulcer were independent risk factors associated with intentional metaplasia. Daily fruit intake was a protective factor.

Lin, Y. S., et al. (2014). "Management of Helicobacter pylori infection after gastric surgery." World Journal of Gastroenterology 20(18): 5274-5282.

The Maastricht IV/Florence Consensus Report and the Second Asia-Pacific Consensus Guidelines strongly recommend eradication of Helicobacter pylori (H. pylori) in patients with previous gastric neoplasia who have undergone gastric surgery. However, the guidelines do not mention optimal timing, eradication regimens, diagnostic tools, and follow-up strategies for patients undergoing gastrectomy and do not indicate if eradication of H. pylori reduces the risk of marginal ulcer or stump cancer in the residual stomach after gastrectomy. The purpose of this review is to provide an update which may help physicians to properly manage H. pylori infection in patients who have undergone gastric surgery. This review focuses on (1) the microenvironment change in the stomach after gastrectomy; (2) the phenomenon of spontaneous clearance of H. pylori after gastrectomy; (3) the effects of H. pylori on gastric atrophy and intestinal metaplasia after gastrectomy; (4) incidence and clinical features of ulcers developing after gastrectomy; (5) does eradication of H. pylori reduce the risk of gastric stump cancer in the residual stomach? (6) does eradication of H. pylori reduce the risk of secondary metachronous gastric cancer in the residual stomach? and (7) optimal timing and regimens for H. pylori eradication, diagnostic tools and follow-up strategies for patients undergoing gastrectomy.

Liqun, G., et al. (1999). "Clinical implication of p53 gene expression in human gastric cancer." Chinese Journal of Clinical Oncology 26(8): 598-601.

Objective: To probe the relationship between the expression of p53 gene in gastric cancer and its clinical implication, pathogenesis and prognosis. Methods: The p53 gene in 98 gastric cancer tissue specimens were determined by immunohistochemical staining. Results: The p53 gene expression showed positive in 48 specimens (49%). p53 gene was not correlated with the gross type, histologic differentiation, growth pattern, depth of invasion and lymph node metastasis of gastric cancer. In 10 specimens of pericancerous tissue with atypical dysplasia, 2 of them showed positive expression, but in 4 specimens of pericancerous tissue with intestinal metaplasia and other normal tissues adjacent to the tumor, the p53 gene expressions were all negative. Follow - up study showed that there was no correlation between p53 expression and prognosis of gastric cancer (P > 0.05) . Conclusion: The results indicate that mutation of p53 gene may be an early event in the development of gastric cancer, and that it bears no relation with the process of invasion and metastasis of GC. Thus, assay of p53 gene expression in biopsy specimens might be useful in screening of high - risk populations.

Liu, H., et al. (2009). "Diet synergistically affects helicobacter pylori-induced gastric carcinogenesis in nonhuman primates." Gastroenterology 137(4): 1367-1379.e1361-1366.

BACKGROUND & AIMS: Gastric cancer results from a combination of Helicobacter pylori (H pylori) infection, exposure to dietary carcinogens, and predisposing genetic make-up. Because the role of these factors in gastric carcinogenesis cannot be determined readily in human beings, the present study examined the role of an oral carcinogen and H pylori infection in rhesus monkeys. METHODS: Gastroscopies were performed in 23 monkeys assigned to 4 groups: controls; nitrosating carcinogen ethyl-nitro-nitrosoguanidine administration alone; inoculation of a virulent H pylori strain alone (H); and ethyl-nitro-nitrosoguanidine in combination with H pylori (EH). Follow-up gastroscopies and biopsies were performed at 3-month intervals for 5 years for pathologic and molecular studies. RESULTS: Postinoculation, H and EH groups showed persistent infection and antral gastritis. Starting at 2 and 5 years, respectively, gastric intestinal metaplasia and intraepithelial neoplasia developed in 3 EH monkeys but in no other groups. Transcriptional analysis of biopsy specimens at 5 years revealed group-specific expression profiles, with striking changes in EH monkeys, plus a neoplasia-specific expression profile characterized by changes in multiple cancer-associated genes. Importantly, this neoplastic profile was evident in nonneoplastic mucosa, suggesting that the identified genes may represent markers preceding cancer. CONCLUSIONS: Gastric intraglandular neoplasia is induced in primates when H pylori infection is associated with consumption of a carcinogen similar to the nitrosamines found in pickled vegetables, suggesting that H pylori and the carcinogen synergistically induce gastric neoplasia in primates.

Liu, M. L., et al. (2016). "Application of endoscopic molecular imaging in diagnosis of gastric intestinal metaplasia." World Chinese Journal of Digestology 24(2): 203-208.

Gastric intestinal metaplasia (GIM) is a precancerous lesion of intestinal type gastric carcinoma. Early diagnosis and follow-up can improve the detection rate of early gastric cancer. In recent years, with the integration of molecular imaging into endoscopy, auto fluorescence endoscopy, Raman spectroscopy, two-photon fluorescence endomicroscopy and confocal laser endomicroscopy have emerged, which improves the detection rate of GIM. This paper reviews the progress of the application of endoscopic molecular imaging in the diagnosis of GIM.

Lu, B. and M. Li (2014). "Helicobacter pylori eradication for preventing gastric cancer." World Journal of Gastroenterology 20(19): 5660-5665.

Helicobacter pylori (H. pylori) infection is a major risk factor for gastric cancer (GC) development, which is one of the most challenging malignant diseases worldwide with limited treatments. In the multistep pathogenesis of GC, H. pylori infection slowly induces chronic active gastritis, which progresses through the premalignant stages of atrophic gastritis, intestinal metaplasia, and dysplasia, and then finally to GC. Although eradication of H. pylori is a reasonable approach for the prevention of GC, there have been some contradictory reports, with only some long-term follow-up data showing efficacy of this approach. The inconsistencies are likely due to the insufficient number of participants, relatively short follow-up periods, poor quality of study designs, and the degree and extent of preneoplastic changes at the time of H. pylori eradication. This review analyzes recent high-quality studies to resolve the discrepancies regarding the eradication of H. pylori for GC prevention. The relationship between H. pylori eradication and GC/precancerous lesions/metachronous GC is examined, and the cost-effectiveness of this strategy in the prevention of GC is assessed. Although it is assumed that eradication of H. pylori has the potential to prevent GC, the feasibility and appropriate timing of this strategy for cancer prevention remain to be determined. As a result, additional well-designed trials with longer follow-up periods are needed to clarify this issue.

Lu, C. Y., et al. (2005). "The best method of detecting prior Helicobacter pylori infection." World Journal of Gastroenterology 11(36): 5672‐5676.

Lu, H., et al. (2018). "The study of the correlative factors of the progressed low-grade gastric intraepithelial neoplasia." Journal of Gastroenterology and Hepatology 33: 178.

Background/Aims: This study aims to explore the outcome of patients with LGIN, and to analyze the correlative factors of the progression group. Methods: A total of 3308 patients were included, who were diagnosed as LGIN by endoscopic biopsy during 1980-2017, and have completed an endoscopic follow-up research for more than one year. The patient's basic information, endoscopic appearance, and biopsy diagnosis of each time were collected. Patients found HGIN or gastric cancer during follow-up were categorized as the Progression Group, while others, as Non-progression Group. We calculated the progression rate, and analyzed the distributions of the clinical factors between two groups. Results: (1) 114 of the 3308 patients progressed, and the progression rate is 3.4%. Among them, 68 patients were found gastric cancer, and the canceration rate is 2.0%. (2) Uni-variate analysis showed that there were significant differences in progression between genders, ages, stages of lesion, locations, and with or without gastric ulcer, while, the duration of follow-up, with or without H.pylori, atrophy, intestinal metaplasia, duodenal ulcer, reflux esophagitis, stump, polyp, or varices had no statistic differences. (3) Logistics regression analysis found that the stage of lesion, age, male gender, and gastric ulcer were the independent promotion factors of progression, female gender was the inhibition factor, and that LGIN in gastric angle, gastric stump, or in more than 2 locations were easier to progress. Conclusion: The progression of LGIN is related with many clinical factors, patients with heavier first-diagnosis, male gender, aged, gastric ulcer, may have a higher risk of progression. Lesions in gastric angle, gastric stump, or more than 2 locations, may also easier to progress.

Luigiano, C., et al. (2012). "Is Helicobacter pylori the infectious target to prevent gastric cancer? An interdisciplinary point of view." Infect Disord Drug Targets 12(5): 340-345.

Gastric carcinogenesis, which may well extend over decades, is characterized by a slow stepwise evolution from superficial gastritis to glandular atrophy, intestinal metaplasia, dysplasia, and finally, adenocarcinoma. This sequence provides an excellent opportunity for the prevention or early detection of the events preceding development of the neoplasm. In 1994, the International Agency for Research on Cancer defined Helicobacter pylori (H. pylori) as a group I carcinogen for gastric cancer (GC). Evidence supporting a causal association has been demonstrated by epidemiological data as well as by experimental animal models. A meta-analysis has shown an higher risk (odds ratio: 1.92) of progression to GC in infected compare to uninfected subjects, that increased to a value > 8 considering the surveys having a follow-up of more than 8 years. A crucial question remains whether and when precancerous lesions can reverse after H. pylori eradication. While several prospective studies have cast doubts about this reversibility others obtained opposing results. Currently, H. pylori is recognized as a necessary but insufficient cause of GC. The most accepted model of gastric carcinogenesis provides, like for other cancers, a multifactorial pathogenesis, linked with a number of initiators and other continuator agents. This review presents a multidisciplinary point of view to approaching the relationship between H. pylori infection and GC, focusing on the potential benefits of bacterial eradication in slowing down or in inducing regression of precancerous lesions.

Lv, B. (2011). "Gastric intraepithelial neoplasia: evolvement and reversal treatment." Chinese Journal of Gastroenterology 16(10): 577-579.

Gastric intraepithelial neoplasia is an important process in gastric carcinogenesis. Clinical follow-up studies showed that part of the low grade intraepithelial neoplasia is reversible and could regress after suitable treatment, and only a few will progress to cancer. Enhancing the reversal of intraepithelial neoplasia is of key importance for the prevention of gastric cancer. Eradication of Helicobacter pylori infection might reduce gastric mucosal atrophy, reverse intraepithelial neoplasia, and delay the progress of intestinal metaplasia. Antioxidant and micronutrients supplement might be helpful for preventing gastric cancer. However, the limited clinical trial evidence is not yet adequate for verifying the reversal effect. Inhibiting cyclooxygenase (COX)-2 expression might be a hopeful therapeutic target. Chinese traditional medicine has accumulated many experiences for the treatment of gastric intraepithelial neoplasia, however, high quality proofs of evidence-based medicine are needed for verification.

Ma, J. L., et al. (2005). "[Helicobacter pylori and the progression of gastric cancer: a 10-year cohort study]." Zhonghua Yi Xue Za Zhi 85(39): 2758-2761.

OBJECTIVE: To search the role of Helicobacter pylori (H. pylori) in the progression of gastric carcinogenesis. METHODS: A cohort study was conducted by cluster randomized sampling in Linqu County, a rural area in Shandong Province in northeast China, where the mortality of gastric cancer (GC) is among the highest in the world. In 1989-1990, a gastroscopic examination and serum test was launched among subjects aged 35-64 from 14 randomized villages. Histological diagnosis of gastric mucosa and enzyme-linked immunosorbent assay was used to detect gastric lesions and anti-H. pylori of all participants. A repeated gastroscopic screening was offered to all cohort members in 1994 and 1999 respectively, and all the GC cases, regardless of natural ones or ones by gastroscopy, were registered in the follow-up periods. RESULTS: Fifty-eight cases of GC were identified in 2469 subjects during the 10-year follow-up, 44 were observed in 1603 H. pylori-positive persons (2.74%) and 14 in 866 H. pylori-negative persons (1.62%). The incidence rate of GC in H. pylori-positive is significantly higher than in H. pylori-negative (OR = 1.871, 95% CI: 1.012 - 3.459). There was no significant difference in the progression of gastric carcinogenesis between H. pylori-positive and H. pylori-negative (P > 0.05) among subjects with normal or superficial gastritis (SG) at baseline. In contrast, the significant difference was found in baseline chronic gastritis (CAG) group (P < 0.01), and the GC incidence rate in H. pylori-positive (7/615) is higher than in H. pylori-negative (0/470, P = 0.019). The difference of gastric lesions between H. pylori-positive and H. pylori-negative in subjects with intestinal metaplasia (IM) and dysplasia (DYS) at baseline was statistically significant after a 10-year follow-up (P < 0.05, P < 0.01, respectively), but the GC incidence rate in H. pylori-positive is similar to the rate in H. pylori-negative at the two groups (17/573 and 7/224 in IM group, P = 0.907; 19/368 and 7/122 in DYS group, P = 0.806). CONCLUSIONS: H. pylori is a key risk factor that prompts the transition from chronic atrophic gastritis to advanced precancerous lesions and influences the whole progression of precancerous gastric lesions. H. pylori, perhaps can not cause GC directly, increases the risk of GC in company with other carcinogens. H. pylori seemingly has no important effect on the development of GC when gastric mucosa is normal or superficial gastritis, but this conclusion is required to be further confirmed.

Magalhaes, R., et al. (2019). "Narrow-band-imaging: A reliable indicator of gastric dysplasia." United European Gastroenterology Journal 7(8): 249.

Introduction: Gastric cancer is a major health concern worldwide, with significant morbidity and mortality rates. In western society, screening remains controversial regarding cost-efficiency issues. NBI (narrow-bandimaging) is a virtual chromoendoscopy tool that has been associated with higher detection of gastric premalignant conditions in comparison with white-light endoscopy (WLE). Endoscopic grading of gastric intestinal metaplasia (EGGIM) is a NBI grading score for metaplasia. Aims & Methods: Assess the correlation between NBI and histological diagnosis of gastric dysplasia. Retrospective, single center study, including consecutive patients that underwent upper endoscopy complemented with NBI for gastritis surveillance, from October 2016 to Jan 2019. Our cohort was analyzed by descriptive, parametric and non-parametric SPSS tools. Results: We included 71 upper endoscopies complemented with NBI evaluation, 40 men (56.3%) with a mean age of 62 years old. Gastric dysplasia was detected, histologically, in 23 cases (32.4%). The correlation between NBI targeted biopsies and histological findings was statistically significant (p< 0.001) with a Kappa coefficient of 0.81. EGGIM was associated with an increase of NBI diagnosis of dysplasia (odd 1.384; p=0.025). However, as EGGIM increases the odd of correlation between NBI and histological dysplasia decreases in 42% (odd 0.58; p = 0.041). We report 15 gastric non polypoid lesions (Paris classification 0-IIa, 0-IIb and 0-IIc). Applying NBI, we established a concordance with histological dysplasia diagnosis of 100%. Conclusion: NBI targeted biopsies presented a statistically significant correlation with histological findings, acknowledging an almost perfect agreement with a Kappa coefficient of 0.81. Applying NBI on non-polypoid lesions identified in WLE increases the rate of histological concordance, we report a 100% concordance. NBI is an accurate tool that, in the hands of experienced endoscopists, can lead to an easy identification of gastric dysplasia, with high concordance with histological findings.

Mai, M. and S. Takagi (1995). "[New concepts on precancerous lesions of the stomach]." Gan to Kagaku Ryoho 22(14): 2029-2037.

As for precancerous lesion of the stomach detail analysis of endoscopic follow-up cases and histopathological investigations brought some new informations on its carcinogenesis. In this paper recent several reports were introduced and discussed on new opinion of precancerous conditions such as adenoma, intestinal metaplasia, gastric ulcer, remnant stomach and H. pylori. Gastric adenoma was considered to be neoplastic because of high incidence of carcinoma in situ. The stomach coexisted with adenoma showed high percentage of new arising tumor in same stomach and therefore, we can say that these are thought to be high risk group for well differentiated adenocarcinoma. Concerning the relation between intestinal metaplasia and gastric cancer we have never obtained final conclusion. However, it is likely that incomplete type of intestinal metaplasia appeared to be coexistent with gastric cancer, especially intestinal type carcinoma, which was thought to be paracancerous lesions. Recent advance of molecular biology has indicated new knowledge on gastric carcinogenesis, suggestive of multistep pathways. According to their reports, genomic instanbility appeared frequently in gastric adenoma and intestinal metaplasia as well as gastric carcinoma. Gastric carcinogenesis for ulcer, remnant stomach and H. pylori was also discussed. In near future the mechanism of gastric carcinogenesis is expected to be solved from view point of genetic events.

Majima, A., et al. (2018). "Linked color imaging identifies novel risk factors of early gastric cancer detected after successful helicobacter pylori eradication: Role of map-like redness and patchy redness." Gastrointestinal Endoscopy 87(6): AB174.

Background: The effect of Helicobacter pylori (HP) eradication on a reduced incidence of gastric cancer has been shown by several clinical trials, while early gastric cancer (EGC) has been detected even after successful HP eradication. It has been reported that emergence of map-like redness and patchy redness are one of the endoscopic findings after HP eradication. In addition, linked color imaging (LCI), which is a novel image-enhanced endoscopy using a color tone similar to white-light imaging (WLI) by emphasizing minute differences in mucosal colors, is considered to identify map-like redness and patchy redness more clearly than WLI. However, the correlation between these endoscopic findings identified by LCI and EGC detected after HP eradication is still unknown. The aim of this study is to clarify whether map-like redness and patchy redness identified by LCI are correlated with EGC detected after successful HP eradication. Method: A single-center retrospective cohort study was conducted at Kyoto Prefectural University of Medicine from November 2015 to March 2017. Patients who underwent esophagogastroduodenoscopy (EGD) after successful HP eradication were enrolled in this study. The patients with a newly detected EGC were defined as cancer (CA) group. In contrast, the patients without EGC were defined as non-cancer (NC) group. The patients who underwent EGD within one year after HP eradication were excluded. We compared the frequency of endoscopic finding in each group according to Kyoto classification of gastritis as follows, mucosal atrophy (A), intestinal metaplasia (IM), enlarged fold (F), nodularity (N), diffuse redness (DR) and depressed redness (DepR, including map-like redness and patchy redness) using LCI. Result: A total of consecutive 223 patients (139 patients in CA group and 84 patients in NC group) were analyzed. There were no significant differences between the groups in terms of patient age and sex. Severe A and spreading DepR were observed more frequently in CA group than those in NC group (A, 83.5% vs 56.0%, P<0.01; DepR, 61.9% vs 41.7%, P<0.01). There were not significant differences in the frequency of IM, F, N and DR between two groups. Multivariate analysis indicated that severe A and spreading DepR were risk factors of EGC development after HP eradication (HR 3.11, 95% CI 1.53-6.32, P=0.002 for severe A; HR 2.64, 95% CI 1.40-4.96, P=0.003 for spreading DepR). Conclusion: Map-like redness and patchy redness identified by LCI are novel risk factors of EGC detected after successful HP eradication.

Malekzadeh, R., et al. (2013). "Hookah and opium: Two risk factors of gastric cancer and its precancerous lesions-a cohort study." Journal of Gastroenterology and Hepatology 28: 83.

Objective: A recent study showed an association between hookah/opium use and gastric cancer but no study has investigated the relationships with gastric precancerous lesions. We examined the association between hookah/opium and gastric precancerous lesions and subsequent gastric cancer. Methods: In a population-based cohort study, 928 randomly selected, healthy, Helicobacter pylori infected subjects in Ardabil Province, Iran, were followed for 10 years. The association between baseline precancerous lesions and lifestyle risk factors (including hookah/opium) was analyzed using logistic regression and presented as odds ratios (ORs) and 95% confidence intervals (CIs).We also calculated hazard ratio (HRs) and 95%CIs for the associations of lifestyle risk factors and endoscopic and histological parameters with incident gastric cancers using Cox regression models. Additionally, the proportion of cancers attributable to modifiable risk factors was calculated. Results: During 9,096 person-years of follow-up, 36 new cases of gastric cancer were observed (incidence rate: 3.96/1000 persons-years). Opium consumption was strongly associated with baseline antral (OR:3.2;95%CI:1.2-9.1) and body intestinal metaplasia (OR:7.3;95%CI:2.5-21.5). Opium (HR:3.2;95%CI:1.4-7.7), hookah (HR:3.4;95%CI:1.7-7.1) and cigarette use (HR:3.2;95%CI:1.4-7.5), as well as high salt intake, family history of gastric cancer, gastric ulcer and histological atrophic gastritis and intestinal metaplasia of body were associated with higher risk of gastric cancer. The fraction of cancers attributable jointly to high salt, low fruit intake, smoking (including hookah) and opium was 93% (95%CI:83-98). Conclusion: Hookah and opium use are risk factors for gastric cancer, as well as for precancerous lesions. Hookah, opium, cigarette and high salt intake are important modifiable risk factors in this high incidence gastric cancer area.

Malfertheiner, P. (2012). "H. pylori related strategies in the prevention of gastric cancer." Journal of Gastroenterology and Hepatology 27: 29.

Gastric cancer continues to remain an important cause of death with nearly 1 million casualties worldwide every year. As clinical manifestations are mostly absent in the early stage, gastric cancer is usually diagnosed in advanced stage when alarming symptoms, appetite loss, weight loss, anemia with or in the absence of concomitant abdominal complaints become apparent. Cure can only be offered to patients with gastric cancer in properly staged early disease by either endoscopic removal of the neoplasia or by surgical gastric resection. There has recently been some progress in survival time with new neoadjuvant strategies and complex palliative chemotherapies, but overall the expected 5 year survival rate for patients with gastric cancer does not go beyond 25%. Strategies for combating the dismal prognosis of gastric cancer need to adopt: a) screening strategies b) recognition and elimination on risk factors c) eradication of H. pylori a) Screening programs based on photofluorography and upper GI endoscopy have mainly been adopted in Japan with a significant reduction of gastric cancer mortality. However this option is far from representing a satisfactory solution and may be cost effective for application only in the general population of high risk areas. A progress in screening is the detection of preneoplastic conditions if extensive (i.e. atrophic gastritis) by a set of serological parameters that include pepsinogen-1, 2 and gastrin-17. b) The identification of risk factors in gastric cancer has long been a major target for intervention strategies. However neither dietary antioxidant supplements nor chemopreventive drugs have shown a sufficient effect in the attempt to reduce the gastric cancer incidence. With the recognition of H. pylori as the main risk factor with key trigger functions in the complex pathogenetic cascade of gastric cancer a target for gastric cancer prevention has been identified. c) The link between H. pylori infection and gastric cancer has been established through a series of epidemiological studies corroborated by further studies that all support a strong biological plausibility. The ultimate proof came from clinical observations and therapeutic trials which led to the formulation of the statement in the Maastricht 3 guidelines that: H. pylori eradication has the potential to prevent gastric cancer. A further and even more proactive position for the adoption of H. pylori eradication in the prevention of gastric cancer was professed in a recent Asian Pacific conference. Several prospective trials with the aim to prevent gastric cancer by H. pylori eradication have been conducted up to now and they provided a clear indication for a reduction in the incidence of gastric cancer in subjects following successful eradication. The number needed to treat was calculated to be 227 for prevention of one gastric cancer on the basis of these studies, and were recently presented in a metaanalysis. In one of these studies the remarkable observation was made that only patients with chronic gastritis and no preneoplastic changes would benefit and get protection from progression to gastric cancer. The issue of the 'point of no return' was consequently raised and is posing important concerns, as we do not have in hands a predictive marker available in clinical routine to identify patients at risk for progression to gastric cancer in spite of successful H. pylori eradication. Some patients with atrophic gastritis and intestinal metaplasia might progress while others do not. The challenge is to find a marker or a set of markers to complement the conventional histology for predictive assessment of progression. It remains undisputed that we need to keep patients with 'advanced' gastritis (atrophy, intestinal metaplasia) in a regular follow up even after H. pylori eradication. The available data indicate that H. pylori eradication is the most effective strategy in the prevention of gastric cancer at all stages of gastritis but patients with advanced forms of atrophic gastritis and intestinal metaplasia need to be losely followed up. Eradication of H. pylori in a global screen and treat strategy is currently not applicable and hazardous for some reasons, such as the wide use of antibiotics and the in duration of revisition therapies can not be neglected. At present we need to identify patients and populations at increased risk and embark in the development of novel treatments or even prophylactic concepts aiming at eradicating H. pylori from the population.

Malieckal, A., et al. (2014). "Prevalence of helicobacter pylori and intestinal metaplasia in a minority population registry of outcomes of upper endoscopy in minorities (ROUM): A hospital-based registry." Gastroenterology 146(5): S-401.

Introduction: The current national epidemiological data estimate the prevalence of Helicobacter Pylori (H.Pylori) in North America to be around 40%. Previous studies estimated that intestinal metaplasia (IM) is prevalent among 15% of the general US population. There has been a need for large population-based registries in the US focusing on outcomes of upper endoscopy in African Americans and Hispanics to explore the prevalence of these serious conditions as well as other gastroenterological problems in this population. This registry was created to fulfill this unmet need. Methods:Our cohort consisted of 2708 subjects who have undergone upper endoscopy at the Brooklyn Hospital center from January 2008 to January 2013. Information about demographics, endoscopic findings and histopathology reports were included.Diagnosis of H.Pylori was based on immunohistochemical testing. SPSS was used for statistical analysis. Patients with incomplete records were excluded from the registry. Results: Out of 2708 subjects, 1510 were African Americans and 785 were Hispanics. The cohort included 1013 males and 1695 females. The prevalence of H. pylori and IM were 22.1% and 9%, respectively. Peptic ulcer (PUD) was found in 12.9% of the study population. Gastric cancer was reported in 1.1% of the encounters. H.Pylori was found to be associated with IM and PUD with OR of 1.64 and 1.98 (P Value 0.001 and <0.001), respectively. Also, H.Pylori was reported in 20% of African Americans in comparison to 26% of Hispanics (P 0.003, OR 1.36). Conclusion(s):The prevalence of H.Pylori and IM in our minority population is significantly lower than what is reported by CDC and current literature. Gastric cancer prevalence is close to the national estimate (0.9%). H.Pylori is more prevalent among Hispanics in comparison to African Americans.Environmental and genetic factors might be responsible for these differences. These findings need to be validated by larger scale studies.

Malieckal, A., et al. (2014). "Prevalence of intestinal metaplasia and gastric cancer in a minority population registry of outcomes of upper endoscopy in minorities (roum): A hospital-based registry." Gastroenterology 146(5): S-569.

Introduction: The current national epidemiological data estimates the prevalence of intestinal metaplasia (IM) and gastric malignancy to be around 15% and 0.9%, respectively. However, very limited literature has been published about their prevalence in minorities. In this subgroup analysis, the prevalence and associations of these two conditions in a downtown Brooklyn population was investigated. Methods: Our cohort consisted of 2708 subjects who underwent upper endoscopy at the Brooklyn Hospital center from January 2008 to January2013. Information about demographics, endoscopic findings and histopathology reports were collected. Diagnosis of Helicobacter Pylori (H. Pylori) was based on immunohistochemical testing. SPSS was used for statistical analysis. Patients with incomplete records were excluded from the registry. Results: Out of 2708 subjects, 1510 were African Americans and 785 were Hispanics. The cohort included 1013 males and 1695 females. The prevalence of IM and gastric cancer were 9% and 1.1% respectively. In patients younger than 45 years old, 5% were found to have IM in comparison to 7.8% in patients 45-65 years old (P 0.02, OR 1.64) and 13% in elderly (P <0.001, OR 2.8). IM was also found to be associated with H. Pylori infection Thirteen percent of patients with H. Pylori had IM in comparison to eight percent of biopsy negative patients (P <0.001, OR 1.6). On multivariate logistic regression analysis, aging and H. Pylori retained significance. Gastric malignancy was found in 0.16 of patients younger than 45 years old in comparison to 1.7% in the elderly (P 0.05, OR 7.6). 3.8% of patients with metaplasia were found to have gastric cancer (P 0.001, OR 3.7). On a multivariate logistic regression analysis, aging and IM retained significance. There was no association observed between malignancy and H. Pylori in this cohort. There were no gender or ethnic differences noted in prevalence of IM or gastric cancer. Conclusion: Intestinal metaplasia prevalence was significantly lower in the studied population than the national estimate, while gastric cancer was close to the national estimate. Aging and H. Pylori infection were significantly associated with IM. Aging and IM were significantly associated with gastric cancer. Interestingly, a positive H.Pylori footprint was not readily detectable in most cases of gastric cancer, but was more detectable in 13% of cases with IM.

Malieckal, A., et al. (2013). "Racial and gender disparities in risk factors for intestinal metaplasia in the minority population." American Journal of Gastroenterology 108: S23.

Purpose: Intestinal metaplasia (IM) of the stomach is a significant risk factor in developing intestinal type gastric cancer. Few studies recently linked IM to H. pylori and aging. However, there have been no studies addressing the risk factors for developing IM in minorities. In this study, we aim to examine the impact of demographics and H. pylori infection on the development of IM in the urban minority population. Methods: Charts of all adult patients who underwent upper endoscopy with biopsy at our medical center in a two year period were reviewed. Data about demographics, endoscopic, and histological findings were collected and analyzed. The presence of H. pylori infection was based on the immunohistopathological analysis of the biopsy samples. SAS software was used for statistical analysis. Results: Our cohort included 970 subjects (37% males and 63% females). African Americans (AA) and Hispanics (HAS) represented 52.5% and 28.3%, respectively. Gastric IM was found in 13.8% of AA. AA were more likely to develop IM if they had H. pylori infection (17.3% vs. 10.5 in non infected patients, P 0.04) or if they were older (More than 65 years vs. <65 years, P 0.03). There was no gender difference in IM prevalence among AA (P 0.2). On multivariate logistic regression analysis, both H. pylori infection and aging retained significance OR 1.8 (1-3.2) and OR 1.9 (1.02-3.6), respectively). In Hispanics, 12.3% had IM. Hispanics with H. pylori infection were more likely to develop IM (18.4% vs. 8.5% in non infected patients, P 0.02). There was no age difference in IM prevalence among Hispanics (P 0.09). On multivariate regression analysis, H. pylori retained significance (odds ratio [OR] 2.7 [1.2-6.1]). Also, gender showed significance on this model (IM 15.8% in males while 5.8% in females and OR for female gender 0.3 [0.1-0.7]). Conclusion: The risk factors for intestinal metaplasia are different among different races. In AA, H. pylori infection and aging were significant risk factors for the development of IM. While in HAS H. pylori, but not aging was a significant risk factor for IM development. Female gender appeared to have less IM among the HAS cohort. The duration of infection may influence these differences with HAS males acquiring the infection at a younger age.

Malik, T. H., et al. (2017). "Gastric intestinal metaplasia: An intermediate precancerous lesion in the cascade of gastric carcinogenesis." Journal of the College of Physicians and Surgeons Pakistan 27(3): 166-172.

Gastric intestinal metaplasia, an intermediate lesion in the development of intestinal-type gastric cancer, is observed in the milieu of long standing non-atrophic gastritis and atrophic gastritis. Most patients with intestinal metaplasia remain asymptomatic unless cobalamin deficiency occurs secondary to loss of glands (that produce intrinsic factor and acid). Genetic events that predispose to development of gastric intestinal metaplasia remains an enigma. Mechanisms leading to the progression of atrophy to metaplasia still needs to be comprehensively explored. Many studies in the literature describe a positive effect of typing intestinal metaplasia and concluded that intestinal metaplasia type III carries the highest risk for developing gastric cancer while others refute it. It is well established that Helicobacter pylori infection is the most important factor for the development of chronic gastritis, gastric intestinal metaplasia as well as gastric cancer. Countries with a higher prevalence of Helicobacter pylori infection and gastric cancer also have a high tendency of being prevalent for intestinal metaplasia. However, it remains elusive whether eradication of Helicobacter pylori infection tends to regress gastric intestinal metaplasia or reduce the subsequent risk of cancer development. Putting together, more prospective cohort studies should be designed to identify factors (antioxidants; anti-inflammatory drugs; food therapy) that may contribute in the regression of intestinal metaplasia, when used simultaneously with eradication therapy. Furthermore, molecular markers for evaluation of intestinal metaplasia, and the potential point-of-no-return should be further investigated. Consensus is also required to advocate a timeframe for surveillance of patients with gastric intestinal metaplasia.

Malik, T. H., et al. (2017). "Gastric Intestinal Metaplasia: An Intermediate Precancerous Lesion in the Cascade of Gastric Carcinogenesis." Journal of the College of Physicians and Surgeons--Pakistan 27(3): 166-172.

Gastric intestinal metaplasia, an intermediate lesion in the development of intestinal-type gastric cancer, is observed in the milieu of long standing non-atrophic gastritis and atrophic gastritis. Most patients with intestinal metaplasia remain asymptomatic unless cobalamin deficiency occurs secondary to loss of glands (that produce intrinsic factor and acid). Genetic events that predispose to development of gastric intestinal metaplasia remains an enigma. Mechanisms leading to the progression of atrophy to metaplasia still needs to be comprehensively explored. Many studies in the literature describe a positive effect of typing intestinal metaplasia and concluded that intestinal metaplasia type III carries the highest risk for developing gastric cancer while others refute it. It is well established that Helicobacter pylori infection is the most important factor for the development of chronic gastritis, gastric intestinal metaplasia as well as gastric cancer. Countries with a higher prevalence of Helicobacter pylori infection and gastric cancer also have a high tendency of being prevalent for intestinal metaplasia. However, it remains elusive whether eradication of Helicobacter pylori infection tends to regress gastric intestinal metaplasia or reduce the subsequent risk of cancer development. Putting together, more prospective cohort studies should be designed to identify factors (antioxidants; anti-inflammatory drugs; food therapy) that may contribute in the regression of intestinal metaplasia, when used simultaneously with eradication therapy. Furthermore, molecular markers for evaluation of intestinal metaplasia, and the potential point-of-no-return should be further investigated. Consensus is also required to advocate a timeframe for surveillance of patients with gastric intestinal metaplasia.

Mansour-Ghanaei, F., et al. (2015). "Does treatment of Helicobacter pylori infection reduce gastric precancerous lesions?" Asian Pacific Journal of Cancer Prevention 16(4): 1571-1574.

BACKGROUND: Treatment of Helicobacter pylori (H. pylori) decreases the prevalence of gastric cancer, and may inhibit gastric precancerous lesions progression into gastric cancer. The aim of this study was to determine the effect of treatment on subsequent gastric precancerous lesion development. MATERIALS AND METHODS: We prospectively studied 27 patients who had low grade dysplasia at the time of enrollment, in addition to dysplasia atrophic gastritis and intestinal metaplasia observed in all patients. All were prescribed quadruple therapy to treat H. Pylori infection for 10 days. Patients underwent endoscopy with biopsy at enrollment and then at follow up two years later. Biopsy samples included five biopsies from the antrum of lesser curvature, antrum of greater curvature, angularis, body of stomach and fundus. RESULTS of these biopsies were compared before and after treatment. RESULTS: Overall, the successful eradication rate after two years was 15/27 (55.6%). After antibiotic therapy, the number of patients with low grade dysplasia decreased significantly (p=0.03), also with reduction of the atrophic lesions (p=0.01), but not metaplasia. CONCLUSIONS: Treatment of H. pylori likely is an effective therapy in preventing the development of subsequent gastric premalignant lesions.

Marcos-Pinto, R., et al. (2012). "First-degree relatives of patients with early-onset gastric carcinoma show even at young ages a high prevalence of advanced OLGA/OLGIM stages and dysplasia." Alimentary Pharmacology and Therapeutics 35(12): 1451-1459.

BACKGROUND: First-degree relatives (FDRs) of early-onset gastric carcinoma (EOGC) patients are at increased risk of cancer development. OLGA/OLGIM (Operative Link on Gastritis/Intestinal Metaplasia Assessment) classifications have been proposed for the identification of individuals at high risk of gastric cancer development. AIM: To estimate the prevalence and severity of premalignant conditions and lesions in FDRs of EOGC patients. METHODS: A case-control study was conducted encompassing 103 FDRs of EOGC patients (cases) and 101 age- and gender-matched controls, all submitted to upper GI endoscopy and OLGA and OLGIM used for staging as well as modified versions with exclusion of the biopsies from incisura angularis in the analysis. RESULTS: Helicobacter pylori infection was present in 82% of cases (P = 0.001). Atrophy was present in 70% of cases (OLGA stages I-IV). High-risk stages (III-IV) were identified only in cases (19%) (P < 0.001). Dysplasia was diagnosed only in cases (n = 7, P = 0.007). The application of OLGIM, modified OLGA and modified OLGIM classifications led to downgrade of stages in comparison with the original OLGA classification (27%, 15% and 30% respectively). In all classification systems, dysplastic lesions clustered (86%) in high-risk stages. CONCLUSIONS: FDRs of EOGC patients have, even at young ages, a high prevalence of H. pylori infection, high-risk OLGA and OLGIM stages and dysplasia. These patients should undergo accurate endoscopic observation with at least four biopsies in antrum and corpus to allow adequate staging and follow-up of premalignant conditions and lesions scored in high-risk stages, in accordance with international guidelines recently proposed.

Maric, L. V., et al. (2018). "Gastric Intestinal Metaplasia: Is it a Worrisome Finding Warranting Surveillance Endoscopy with Repeat Biopsies." Gastroenterology 154(6): S-514-S-515.

Aim: To determine the rate of histologic progression on follow-up gastric biopsies obtained on patients with initial findings of intestinal metaplasia (IM). Introduction: Gastric cancer is a third leading cause of cancer-related mortality worldwide. Incidence of gastric cancer within US is low, resulting in lack of screening and surveillance in clinical practice. The process of gastric carcinogenesis appears to be triggered by chronic gastritis (with H pylori playing a pivotal role) and subsequent development of intestinal metaplasia (IM). Factors associated with histological progression have included: advancing age, H pylori, ethnicity and first-degree relative with gastric cancer. While the risk of developing gastric cancer in an individual with gastric IM in the US has remained significantly low in comparison to Asia or Latin America, the actual progression to gastric adenocarcinoma in the presence of these risk factors is unclear in the US. Additional studies are needed to develop national consensus guidelines for the diagnosis and management of gastric IM. Methods and Results: Retrospective study of 2221 patients from a large referral center with confirmed diagnosis of IM on initial gastric biopsies from 1998 to 2015. Out of 2221 patients with IM on initial endoscopy, 677 (30.5%) underwent surveillance endoscopy with biopsies at our institution. The average time to interval follow-up surveillance endoscopy was 24 months. 26 patients were excluded from the study due to presence of high grade dysplasia (HGD), intramucosal carcinoma (IMC), or invasive carcinoma (IC) on initial biopsies. 312 (48%) patients had persistent IM on surveillance endoscopy. On follow-up surveillance biopsies over the years, 7.5% of patients had progression to more concerning findings (20 patients were found to have low grade dysplasia in addition to IM, 8 progressed to HGD, and 21 developed IC). Conclusion: Based on the patient population in our study, we found a significant trend in progression from IM to LGD, HGD and IC. Longitudinal studies are needed to develop guidelines for follow-up surveillance of patients with IM, and to better define not only the timeline but also who needs to be screened. This large progression of patients from IM to LGD, HGD or IC is concerning and justifies the need for surveillance. [Figure Presented]

Masanori, I., et al. (2006). "Causal role of Helicobacter pylori infection and eradication therapy in gastric carcinogenesis." World Journal of Gastroenterology 12(1): 10-16.

Many epidemiological reports indicate that Helicobacter pylori (H pylori) infection plays an important role in gastric carcinogenesis. Several genetic and epigenetic alterations contribute to the initiation, promotion, and progression of the cancer cells in a multi-step manner. H pylori is known to induce chronic inflammation in the gastric mucosa. Its products, including superoxides, participate in the DNA damage followed by initiation, and the inflammation-derived cytokines and growth factors contribute to the promotion of gastric carcinogenesis. By eradicating H pylori, gastric inflammation can be cured; the therapy diminishes the levels not only of inflammatory cell infiltration, but also atrophy/intestinal metaplasia in part. A randomized controlled trial revealed that the eradication therapy diminished the gastric cancer prevalence in cases without precancerous conditions. In addition, recent epidemiological studies from Japanese groups demonstrated that the development of gastric cancer, especially of the intestinal type, was decreased by successful eradication therapy, although these were designed in a nonrandomized manner. However, it should be mentioned that endoscopic detection is the only way to evaluate the degree of gastric carcinogenesis. We have reported that the endoscopic and histological morphologies could be modified by eradication therapy and it might contribute to the prevalence of gastric cancer development. Considering the biological nature of cancer cell proliferation, it is considered that a sufficiently long-term follow-up would be essential to discuss the anticancer effect of eradication therapy. © 2006 The WJG Press. All rights reserved.

Massarrat, S., et al. (2012). "Precancerous conditions after H. pylori eradication: a randomized double blind study in first degree relatives of gastric cancer patients." Archives of Iranian Medicine 15(11): 664-669.

BACKGROUND: Regression of precancerous lesions after H. pylori eradication remains controversial. This study evaluates the change and topography in first degree relatives (FDR) of gastric cancer (GC) patients following H. pylori eradication. METHODS: Participants underwent endoscopy with antrum and corpus histological examinations. Subjects with pangastritis were randomly allocated to placebo or eradication therapy and followed over 4½ years. RESULTS: Among 989 evaluated FDR, we excluded 468 patients as follows: 108 had macroscopic lesions, 243 had no evidence of any H. pylori infection, and 117 were excluded for other reasons. The remaining subjects (n = 521) were allocated to therapy (group A, n = 261) or placebo (group B, n = 260) groups. Interim analysis of 403 subjects (201 placebo, 202 therapy) showed regression of atrophy (60 out of 97 in the antrum and 37 out of 104 in the corpus) in H.pylori-eradicated versus regression of atrophy (57 out of 184 in the antrum and 23 out of 173 in the corpus) in non-H.pylori-eradicated cases over 2½ years (P < 0.0001). No regression of intestinal metaplasia (IM) occurred in the antrum and corpus of treated subjects over 4½ years. However, progression of IM occurred in the antrum in 17 out of 90 patients in the non-H. pylori-eradicated versus 4 out of 68 H. pylori-eradicated subjects after 4½ years (P < 0.05). CONCLUSION: Eradication of H. pylori is associated with regression of gastric atrophy but not IM, even in its early stages. Gastric atrophy and IM in the antrum have shown more rapid progression in cases not treated for H. pylori infection (over 4½ years follow-up) compared to H. pylori-eradicated cases.

Matko, I., et al. (1982). "Intestinal metaplasia: A high risk for gastric cancer? preliminary communication." Acta Endoscopica 12(2): 157-161.

A group of 279 subjects with gastric biopsies positive for intestinal metaplasia (IM) and a sex- and age-matched control group of 279 subjects with gastric biopsies negative for IM were identified by reviewing the gastric biopsies performed at the Gastroenterology Clinic of the University Clinical Center of Ljubljana, from 1962 to 1970. The two groups were similar in relation to certain demographic and clinical characteristics. The risk of developing gastric cancer was determined prospectively for both groups by direct follow-up of some subjects at the Gastroenterology Clinic and by an annual search at the Slovenian Cancer Registry. Follow-up was carried out up to December 1980. Twelve subjects developed gastric cancer in the IM group and one in the control group.

Matsukura, N., et al. (1995). "[Helicobacter pylori in peptic ulcer and gastric cancer]." Gan to Kagaku Ryoho 22(2): 169-178.

Recently many reports have shown a strong association between Helicobacter pylori infection in the stomach and recurrent peptic ulcer. Moreover, prospective cohort serological studies showed that H. pylori infected individuals have significantly increased rate of gastric cancer in the USA. H. pylori is a gram-negative spiral organism which has urease activity and produces ammonia and CO2 from urea, and nestles in the gastric pits and overlaying mucus gel layer. Many diagnostic methods of H. pylori infection are available; ie bacterial culture, 13C-urea breath test, histology, serum IgG antibody against H. pylori. We developed a new method, ie tissue IgA antibody against H. pylori and detection of H. pylori DNA in the gastric juice by PCR method. Triple therapies with metronidazole, bismuth compounds, and amoxicillin or tetracyclin are difficult to use in Japan because of their sever side effects. Thus, new methods with proton pump inhibitor (PPI) and amoxicillin have been introduced. We treated 14 patients of whom were H. pylori positive-active peptic ulcer with 30 mg/day of lansoprazole, a new PPI, plus 1,500 mg/day of amoxicillin for 2 weeks and 8 (57%) patients were eradicated. Gastric carcinogenesis are multi-steps and multifactorials process. Hypothetical sequence of intestinal type of gastric cancer is that superficial gastritis-->atrophic gastritis-->intestinal metaplasia-->dysplasia-->gastric cancer and H. pylori infection may play a role in the early stage of the sequence. We examined mucosal IgA antibody against H. pylori in chronic gastritis and intestinal metaplasia detected by the Tes-Tape method in 25 resected specimens after gastrectomy for gastric cancer. Positivity rates of tissue H. pylori IgA antibody were lower in the mucosa of intestinal metaplasia than in non-metaplastic gastric mucosa and were negative in carcinoma. Causal relationship between H. pylori infection and gastric cancer is not proven and factors other than H. pylori infection are also important in the gastric carcinogenesis. Finally we introduce 2 reports: (1) NIH Consensus Conference: Helicobacter pylori in peptic ulcer disease (JAMA. 1994; 272: 65-69). The consensus panel concluded that 1. ulcer patients with H. pylori infection require treatment with antimicrobial agents in addition to antisecretory drugs whether on first presentation with the illness or on recurrence; 2. the value of treating nonulcerative dyspepsia patients with H. pylori infection remains to be determined; and 3. the interesting relationship between H. pylori infection and gastric cancer requires further exploration. (2) World Health Organization: Working Group Meeting (Reported in World Congress of Gastroenterology, Los Angeles, 1994). H. pylori plays a causal role in the chain of events leading to cancer of the stomach. Group I: definite carcinogen.

Matsukura, N., et al. (1983). "[Recent advances in research on the intestinal metaplasia of the stomach]." Gan to Kagaku Ryoho 10(2 Pt 2): 471-481.

Intestinal metaplasia of the stomach is classified into two types, complete and incomplete, by enzymatical, mucin histochemical and histological differences. Complete type resembles the small intestine while incomplete type does not. But, even complete type differs from the small intestine from the point of cytological observations. Vascular structures of the metaplastic mucosa are different from those in the mucosae of stomach, small and large intestines. Focal intestinal metaplasia can be induced in rats by a gastric carcinogen, N-propyl-N'-nitro-N-nitrosoguanidine or regeneration after ulceration with 0.5 NaOH. There is no solid evidence that intestinal metaplasia is a precancerous change of the stomach. However, the patients with extensive intestinal metaplasia of the stomach belong to the high risk group for the gastric cancer. Therefore, careful follow-up studies are needed for these patients using endoscopy by dye-staining method.

Matysiak-Budnik, T., et al. (2020). "Recent Guidelines on the Management of Patients with Gastric Atrophy: Common Points and Controversies." Digestive Diseases and Sciences 65(7): 1899-1903.

Patients with gastric precancerous lesions (atrophic gastritis and intestinal metaplasia) have increased risk of developing gastric cancer, and adequate management and surveillance of these patients should allow to reduce gastric cancer-related mortality. The guidelines on the management of these patients have been recently published by the European Societies (MAPS II guidelines) and by the American Gastroenterological Association (AGA). The aim of this commentary is to compare these two guidelines by highlighting the common points and differences between them. Both guidelines recommend a systematic detection and eradication of Helicobacter pylori in all patients with gastric atrophy. However, there is a major difference in the recommendations for surveillance: while the MAPS II guidelines recommend systematic endoscopic surveillance in all patients with severe gastric atrophy (with or without intestinal metaplasia), the AGA guidelines focus only on intestinal metaplasia and plead against systematic surveillance, leaving the possibility of surveillance in individual patients based on shared decision between clinicians and patients. The difference between two guidelines comes essentially from the different arguments used by two authorities (randomized control studies by AGA and observational cohort studies by the European Societies), and may be, at least in part, related to the difference between the European and American health care systems and potential economic burden.

Mayer, B., et al. (1993). "De-novo expression of CD44 and survival in gastric cancer." Lancet 342(8878): 1019-1022.

We have examined the cell surface molecule CD44, which is attracting interest because of reports that isoforms are associated with metastasis. The prognostic value of CD44 expression has yet to be assessed for a solid tumour. Benign (59) and malignant (primary 61, metastatic 59) gastric tissues were examined with antibodies directed at epitopes common to known CD44 isoforms. Normal mucosa was CD44 negative. In atrophic gastritis and intestinal metaplasia expression was restricted to the epithelial cells of the basal glands and was positively correlated with an increased leucocyte infiltrate and with the expression of HLA DR by mucosal cells. These observations suggest a role for chronic inflammation in the induction of CD44 expression on benign mucosa. No such association was observed between inflammatory infiltrate and CD44 expression on gastric tumours. CD44 expression, observed in only 49% of primary tumours, was associated with distant metastases at time of diagnosis and, among 31 curatively resected patients, with tumour recurrence (p = 0.0014) and increased mortality (p = 0.001) during follow-up averaging 17 months. When we used an antibody directed against the CD44 variant exon 9v, we found a good correlation between the expression of total CD44 and of exon 9v containing isoforms, and 9v expression in primary tumours was significantly and positively associated with tumour recurrence and mortality.

Mc Nally, M., et al. (2017). "Gastric intestinal metaplasia outcomes: Results from a 17 year tertiary centre upper GI surveillance programme in ireland." United European Gastroenterology Journal 5(5): A809-A810.

Introduction: Adenocarcinoma of the stomach is the second leading cause of cancer related death in the world. Gastric intestinal metaplasia (GIM) is an important intermediate stage in the gastric cancer cascade through a series of well-defined precursor lesions including nonatrophic gastritis, multifocal atrophic gastritis, intestinal metaplasia, and dysplasia. The prevalence of GIM is unclear in many parts of the world and few studies have evaluated the rate of progression to gastric cancer in patients with GIM. There is a lack of clarity in published guidelines regarding appropriate surveillance of patients with GIM and there is wide disparity in the management of this premalignant condition. Aims & Methods: This study aimed to analyze surveillance practice and characterize the natural history of this premalignant condition by identifying all patients with GIM on an upper GI surveillance programme and reviewing follow up data. This is a retrospective study of patients with GIM who are currently enrolled in an upper GI surveillance programme. Patients with a history of GIM identified at any time during an 18 year surveillance period (from 1998 to 2016) were included in the study. Patient characteristics, endoscopy data including histology, rates of Helicobacter pylori infection, Barrett's oesophagus association and outcomes were reviewed. Results: 160 patients (including those with Barrett's oesophagus, GIM and family history of gastric cancer) were enrolled on the surveillance programme. 42 patients with GIM were identified-20 females (47.6%) and 22 males (52.3%). The mean age at which GIM was first diagnosed was 60.6 years (range from 17.9 to 71.5 years). 15/42 patients (35.7%) had co-existent Barrett's oesophagus and Helicobacter pylori was identified in 6/42 (14.3%). The follow-up period ranged from 0.5 to 17.3 years. 27 patients had repeat gastroscopies following initial diagnosis. 15 patients are still awaiting a repeat gastroscopy. A large degree of variability in the number and frequency of follow-up gastroscopies was observed. The average interval of follow-up gastroscopies was 3.3 years per person. 14/27 patients (51.8%) had no evidence of GIM on most recent gastroscopy, 7/27 patients (26%) had repeat findings of persistent focal GIM, 5/27 patients (18.5%) progressed to extensive GIM. No cases of dysplasia were recorded but 1 patient (3.7%) developed gastric cancer. Conclusion: This study suggests a low apparent risk of progression of gastric intestinal metaplasia in a small western cohort. Further studies may be necessary to address if the applicability of published surveillance guidelines can be generalised to regions with low gastric cancer prevalence.

Mc Nally, M., et al. (2017). "Gastric intestinal metaplasia outcomes: Results from a 17 year tertiary centre upper GI surveillance programme in Ireland." Gastrointestinal Endoscopy 85(5): AB452-AB453.

Background: Adenocarcinoma of the stomach is the second leading cause of cancer related death in the world. Gastric intestinal metaplasia (GIM) is an important intermediate stage in the gastric cancer cascade through a series of well-defined precursor lesions including nonatrophic gastritis, multifocal atrophic gastritis, intestinal metaplasia, and dysplasia. The prevalence of GIM is unclear in many parts of the world and few studies have evaluated the rate of progression to gastric cancer in patients with GIM. There is a lack of clarity in published guidelines regarding appropriate surveillance of patients with GIM and there is wide disparity in the management of this premalignant condition. Aim: This study aimed to analyze surveillance practice and characterize the natural history of this premalignant condition by identifying all patients with GIM on an upper GI surveillance programme and reviewing follow up data. Methods: Retrospective study on patients with GIM who are currently enrolled in an upper GI surveillance programme. Patients with a history of GIM identified at any time during an 18 year surveillance period (from 1998 to 2016) were included in the study. Patient characteristics, endoscopy data including histology, rates of Helicobacter pylori infection, Barrett's oesophagus association and outcomes were reviewed. Results: 160 patients (including those with Barrett's oesophagus, GIM and family history of gastric cancer) were enrolled on the surveillance programme. 42 patients with GIM were identified - 20 females (47.6%) and 22 males (52.3%). The mean age at which GIM was first diagnosed was 60.6 years (range from 17.9 to 71.5 years). 15/42 patients (35.7%) had co-existent Barrett's oesophagus and Helicobacter Pylori was identified in 6/42 (14.3%). The follow up period ranged from 0.5 to 17.3 years. See figure 1. 27 patients had repeat gastroscopies following initial diagnosis. 15 patients are still awaiting a repeat gastroscopy. A large degree of variability in the number and frequency of follow-up gastroscopies was observed. See figure 2. The average interval of follow-up gastroscopies was 3.3 years per person. 14/27 patients (51.8%) had no evidence of GIM on most recent gastroscopy, 7/27 patients (26%) had repeat findings of persistent focal GIM, 5/27 patients (18.5%) progressed to extensive GIM. No cases of dysplasia were recorded but 1 patient (3.7%) developed gastric cancer. Conclusion: This study suggests a low apparent risk of progression of gastric intestinal metaplasia in a small western cohort. Further studies may be necessary to address if the applicability of published surveillance guidelines can be generalised to regions with low gastric cancer prevalence. (Figure presented).

McFarlane, G. A., et al. (2000). "Trends over time in Helicobacter pylori gastritis in Kenya." European Journal of Gastroenterology and Hepatology 12(6): 617-621.

OBJECTIVE AND DESIGN: There is increasing evidence to link infection of the gastric mucosa by Helicobacter pylori with the subsequent development of gastric cancer. This study was undertaken to document the progression of H. pylori gastritis in a rural Kenyan population with a moderate gastric cancer risk. METHOD: Biopsy follow-up study of 51 H. pylori-positive patients over an average of 5.5 years. RESULTS: In the study group, the number of individuals with moderate to severe atrophy rose from 17 (33%) to 22 (43%), an annual increase of 1.8% [95% confidence interval (CI) -0.9% to 4.4%]. There was significant progression of atrophy (P< 0.05) in those with low overall scores for graded morphological variables at initial endoscopy. Intestinal metaplasia did not progress; indeed four out of 12 patients initially diagnosed with intestinal metaplasia showed no evidence of it in their follow-up biopsies. CONCLUSIONS: H. pylori gastritis with atrophy may provide a suitable environment within the gastric mucosa for the development of gastric cancer but it is likely that other factors in this population determine further progress towards dysplasia and cancer.

Meireles, S. I., et al. (2004). "Molecular Classifiers for Gastric Cancer and Nonmalignant Diseases of the Gastric Mucosa." Cancer Research 64(4): 1255-1265.

High incidence of gastric cancer-related death is mainly due to diagnosis at an advanced stage in addition to the lack of adequate neoadjuvant therapy. Hence, new tools aimed at early diagnosis would have a positive impact in the outcome of the disease. Using cDNA arrays having 376 genes either identified previously as altered in gastric tumors or known to be altered in human cancer, we determined expression signature of 99 tissue fragments representing normal gastric mucosa, gastritis, intestinal metaplasia, and adenocarcinomas. We first validated the array by identifying molecular markers that are associated with intestinal metaplasia, considered as a transition stage of gastric adenocarcinomas of the intestinal type as well as markers that are associated with diffuse type of gastric adenocarcinomas. Next, we applied Fisher's linear discriminant analysis in an exhaustive search of trios of genes that could be used to build classifiers for class distinction. Many classifiers could distinguish between normal and tumor samples, whereas, for the distinction of gastritis from tumor and for metaplasia from tumor, fewer classifiers were identified. Statistical validations showed that trios that discriminate between normal and tumor samples are powerful classifiers to distinguish between tumor and nontumor samples. More relevant, it was possible to identify samples of intestinal metaplasia that have expression signature resembling that of an adenocarcinoma and can now be used for follow-up of patients to determine their potential as a prognostic test for malignant transformation.

Mendoza, D., et al. (2008). "Variation in the prevalence of gastric cancer in Perú." International Journal of Cancer 123(2): 414-420.

Most cases of gastric cancers occur in non-industrialized countries but there is scarce information about the epidemiology of this illness in these countries. Our study examined whether there was a variation in the prevalence of gastric cancer in Lima, Perú over the last 2 decades. Subjects older than 29 years of age were included. They underwent an esophagogastroduedonoscopy at 3 socioeconomically different health facilities in Lima: a county hospital (7,168 subjects), a Peruvian-Japanese Clinic (14,794 individuals) and a private hospital (4,893 individuals). Birth cohort prevalence of gastric cancer was used. Regression models were calculated to predict the future prevalence of gastric cancer. It was found that the birth cohort prevalence of gastric cancer decreased in Perú from 22.7 to 2% (p < 0.001), from 12 to 0.5% (p < 0.001), and from 6.5 to 0.1% (p < 0.001) in the low, middle and high socioeconomic group, respectively. The prevalence of intestinal metaplasia decreased from 44.3 to 12.5% (p < 0.001), from 28.4 to 5% (p < 0.001), and from 19.4 to 2.2% (p < 0.001) in the low, middle and high socioeconomic status, respectively. These trends will likely persist over the future decades. Nevertheless, the prevalence of gastric cancer remains high in subjects older than 59 years of age in the low socioeconomic status. It is concluded that the prevalence of gastric cancer is decreasing in Perú, similar to the current trend undergoing in industrialized nations. However, there are still specific groups with high prevalence that might benefit from screening for early detection and treatment. © 2008 Wiley-Liss, Inc.

Mera, R. M., et al. (2017). "Dynamics of Helicobacter pylori infection as a determinant of progression of gastric precancerous lesions: 16-year follow-up of an eradication trial." Gut. (no pagination), 2017 Date of Publication: June 24.

Mera, R. M., et al. (2018). "Dynamics of Helicobacter pylori infection as a determinant of progression of gastric precancerous lesions: 16-year follow-up of an eradication trial." Gut 67(7): 1239‐1246.

Mewes, P. W., et al. (2011). "Chromoendoscopy with automatic lesion enhancement in magnetically guided capsule endoscopy: A feasibility study." Gastroenterology 140(5): S750.

Introduction: Gastric cancer is the 2nd most lethal digestive neoplasm in the world. Intestinal metaplasia and dysplasia are precancerous signs which can grow to gastric cancers. The identification of these lesions and follow-up of afflicted patients could lead to early diagnosis. Diagnosis via conventional endoscopy is characterized by low interobserver agreement and poor correlation with histopathologic findings. Chromoendoscopy has been proven to significantly enhance the visibility of mucosa irregularities, like metaplasia and dysplasia mucosa. In 2010 magnetically guided capsule endoscopy (MGCE) was introduced. In MGCE a patient swallows an endoscopic capsule, which is navigated by an external magnetic field in a waterfilled stomach. The procedure is virtually non-invasive, comfortable for the patient and requires no sedation (Clinical study: Rey et al., 2010). MGCE seems feasible and sufficiently accurate for gastric examination. Known difficulties in the diagnosis of metaplasia in conventional endoscopy transfer to MGCE. Therefore, MGCE may also require the use of stains, similar to chromoendoscopy. Aim: To prove the feasibility of a staining procedure in an MGCE examination of the stomach. Material & Methods: Commercially available endoscopy capsules and pig-stomachs with esophagus were used. The stomachs were stained through the esophagus to simulate the real-world procedure. 100 ml of methylene blue stain of 1.00g/L was introduced through the esophagus. After a time delay of 5 minutes, a 500mL lukewarm water was inserted via the esophagus three times and flushed out of the stomach. The stomach was then filled with 2L of water and the capsule was introduced. Images were manually captured from all anatomical sections. The images were post-processed (enhanced sharpness and broader color-spectrum) for better visualization of mucosal structure. Results: Similarly to the way that chromoendoscopy improves visibility over conventional endoscopy, MGCE with staining agents exhibits more prominent mucosa appearance. As in classic chromoendoscopy, we observed that stained mucosa appears more detailed than unstained mucosa. We also noted that the water is not dyed and hence does not impact the visibility. The applied staining procedure dyed the mucosa sufficiently. This observation holds for different camera poses, lighting conditions and scales. Conclusion: The results demonstrate that the proposed staining procedure can be applied to pig stomachs. Similar to the traditional chromoendoscopy the mucosa appears more detailed. Image processing algorithms can further improve the image quality. Though the visibility of metaplasia and dysplasia is enhanced, other pathologies may be masked. This, however, is acceptable for examinations focused on the detection of mucosa irregularities.

Michigami, Y., et al. (2018). "LONG-TERM EFFECTS OF H. PYLORI ERADICATION ON MOLECULAR ALTERATIONS IN PRECANCEROUS LESIONS, ATROPHIC MUCOSA AND INTESTINAL METAPLASIA." Gastroenterology 154(6): S-328.

Background: Meta-analyses showed that H. pylori eradication seems to reduce gastric cancer (GC). However, the risk of GC remains in precancerous conditions, e.g. atrophic mucosa (AM) and intestinal mucosa (IM), even after H. pylori treatment. GC develops through the accumulation of genetic and epigenetic alterations. Currently, it is considered that dysregulation of noncoding RNAs, such as miR-124a-3 and miR-34b/c, also plays important roles in the pathogenesis of GC. Aim: To clarify the molecular changes following H. pylori eradication, molecular alterations in the background mucosa with and without GC were evaluated in a long-term follow-up study. Materials and Methods: A total of 232 biopsy specimens from 78 consecutive patients, including chronic gastritis patients with follow-up ≥3 y after H. pylori eradication (AG group, n=30), patients who developed early GC after eradication (≥3 y) (GC group, n=27), and H. pylori-positive chronic gastritis patients (control group, n=21), were evaluated. The H. pylori status was analyzed in each patient by both Giemsa staining and serum H. pylori-IgG antibody measurement. Biopsy specimens were obtained from the stomach's antrum, angulus, and corpus. DNA was extracted separately from AM and IM by laser capture microdissection. Microsatellite instability (MSI) was evaluated at five loci based on the Bethesda panel. CpG island methylation at seven tumor-related genes, including CDH1, CDKN2A, MLH1, MINT1, MINT31, MGMT, and RUNX3, the phenotype (CIMP), and miR-124a-3 and miR-34c methylation status were assessed using methylation-sensitive high-resolution melting analysis. CIMP was defined as ≥3/7 methylated markers using the seven-marker CIMP panel. Results: H. pylori eradication was associated with significant reductions of CDH1 (OR: 0.12, 95% CI: 0.02-0.69, p=0.02) and MINT1 (OR: 0.03, 95% CI: 0.004-0.16, p<0.0001) methylation in AM, but not in IM. In contrast, the incidence of CIMP in IM did not show significant differences between the control and AG groups, however, the CIMP rate was significantly higher in the GC group than in the AG group (OR: 7.92, 95% CI: 1.92-31.60, p=0.005). The frequency of MSI was no significant difference in AM and IM. Methylation of miR-124a-3 and miR-34c were more frequently identified in IM, with very few in AM among the three groups. Conclusions: H. pylori eradication could reverse methylation only in AM but not in IM. CIMP in IM may be a surrogate marker of GC. Methylation of miR-124a-3 and miR-34c is a molecular event in IM and may not be associated with GC development, unlike in previous reports.

Miki, K. (2010). "Present status and future aspects of gastric cancer-risk gastritis screening (ABC screening)." Endoscopic Forum for Digestive Disease 26(1): 1-4.

Future aspects of gastric cancer screening will become to perform gastric cancer-risk gastritis screening using the following method: Subjects are classified into a 1 of 4 groups (A to D) based on the results of the 2 serologic tests, anti-Helicobacter pylori IgG antibody (Hp) titer and the pepsinogen (PG) I and II levels (the Pesinogen Test Method) ; Group A [Hp (-) PG (-)], infection free subjects; Group B [Hp (+) PG (-)], chronic atrophic gastritis free; Group C [Hp (+)PG (+)], chronic atrophic gastritis, and Group D [Hp (-)PG (+)], severe chronic atrophic gastritis with extensive intestinal metaplasia, respectively. Thereafter, continuous endoscopic follow-up examination should be performed to detect early stage of gastric cancer (the secondary prevention of gastric cancer). Asymptomatic Group A which is occupied 50-80 % of all subjects can be excluded from the secondary endoscopic examination for the efficiency of gastric cancer screening system. Hp infected subjects (H. pylori infectious disease); Group B and Group C should be eradicated aiming to prevent occurrence of gastric cancer (the primary prevention of gastric cancer), as well as the secondary prevention of gastric cancer.

Miki, K. (2011). "Gastric cancer screening by combined assay for serum anti-Helicobacter pylori IgG antibody and serum pepsinogen levels - "ABC method"." Proceedings of the Japan Academy. Series B: Physical and Biological Sciences 87(7): 405-414.

The current status of screening for gastric cancer-risk (gastritis A, B, C, D) method using combined assay for serum anti-Helicobacter pylori (Hp) IgG antibody and serum pepsinogen (PG) levels, "ABC method", was reviewed and the latest results of our ongoing trial are reported. It was performed using the following strategy: Subjects were classified into 1 of 4 risk groups based on the results of the two serologic tests, anti-Hp IgG antibody titers and the PG I and II levels: Group A [Hp(-)PG(-)], infection-free subjects; Group B [Hp(+)PG(-)], chronic atrophic gastritis (CAG) free or mild; Group C [Hp(+)PG(+)], CAG; Group D [Hp(-)PG(+)]), severe CAG with extensive intestinal metaplasia. Continuous endoscopic follow-up examinations are required to detect early stages of gastric cancer. Asymptomatic Group A, which accounts for 50-80% of all the subjects may be excluded from the secondary endoscopic examination, from the viewpoint of efficiency. Hp-infected subjects should be administered eradication treatment aimed at the prevention of gastric cancer.

Mitsunaga, A., et al. (2013). "A case of metachronous gastric cancer over a period of 13 years after eradication of H. pylori." Journal of Gastroenterology and Hepatology 28: 544.

Objective: The fact that stomach cancer under occurs the circumstances of chronic inflammation from Helicobacter Pylori (HP)infection is common knowledge. It is also becoming clear that stomach cancer occurrence is suppressed by eradication of HP. However, there is a limit to the results of suppressing stomach cancer by HP eradication, and it is a fact that even after HP eradication stomach cancer occurs at a fixed rate. As far as we could search in Ichushi (Japan Medical Abstracts Society), in cases of early gastric cancer treated with endoscopy, in metachronous cancer which occurred after successfully eradication via HP eradication treatment, 11.2 years after HP eradication was the longest observed period. On this occasion, in spite of HP eradication being carried out after treatment of early gastric cancer with endoscopy, we experienced a case of metachronous repeated cancer occurrences over a period of 13 years following and we therefore make this report. Methods: Case: 56 year old male. In March of 1998, Endoscopic Mucosal Resection (EMR)was performed on IIa type early gastric cancer (12 mm) in the posterior wall of the antrum. The level of gastric mucosal atrophy at the time of treatment was slight, Kimura-Takemoto classification was C-III, and no intestinal metaplasia was noticed with the naked eye. At that time, because he was positive for HP infection, HP eradication was conducted in October of the same year, and the success of HP eradication was confirmed via pathological findings and culture procedure. After that, through follow-up observation, a total of 4 (5 lesions) metachronous repeated cancer occurrences were observed by March 2011, as noted below. Results: It was proven by Fukase K. et al (Lancet 372:392-397, 2008) that HP eradication significantly suppresses stomach cancer occurrence after endoscopic treatment. For clinical cancer, the effectiveness of cancer suppression via HP eradication is not promising, but for dormant cancer and new cancer, the possibility is pointed out for suppression, stopping or withdrawal of cancer growth via HP eradication. The existence of dormant cancer in the stomach after endoscopic treatment of early gastric cancer cannot be denied. It is deemed to require 3.5 to 10 years for one cancer cell to grow large enough to be diagnosable by the naked eye, and with consideration for growth suppression through HP eradication as well, it is likely that quite a long period of surveillance will be required for the metachronous cancer occurrences after HP eradication. Conclusion: It is difficult to diagnose the existence of dormant cancer endoscopically, and as the possibility cannot be denied, it would seem to be essential to conduct long-term observation even if HP eradication was conducted after endoscopic treatment of early gastric cancer. (Figure Presented).

Miyasaka, K., et al. (1979). "A case of early gastric cancer (type IIa) disappeared during anti-cancer chemotherapy." Stomach and Intestine 14(12): 1663-1668.

A 72 year-old male patient was seen in our hospital with chronic bronchitis from April 14 to May 17, 1975. During admission, a barium meal study was done; he was found to have an irregular-shaped polypoid lesion on the posterior wall of the antrum, measuring 13x12 mm in diameter. The polypoid lesion was diagnosed as being Type IIa early gastric cancer, and the biopsy specimen was reported as Group IV (well differentiation found. It is concluded that 5-FU dry syrup, type IIa early gastric cancer had completely disappeared. tubular adenocarcinoma. He was advised to undergo surgery, but refused. Oral administration of 5-FU dry syrup 300 mg/day was begun on October 8, 1975. In November, 1975, follow-up X-ray and gastroscopy were performed and both showed slight flattening of the elevation. After feeling a sense of epigastric fullness, anorexia and belching, the patients discontinued anti-cancer chemotherapy, against medical advise on Noverber 31, 1975. The elevated lesion subsequently grew to pre-anti-cancer chemotherapy size as confirmed by gastroscopy. He was advised to have gastrectomy done, but again he refused. Anti-cancer chemotherapy with 5-FU dry syrup 300 mg/day was restarted again on April 24, 1976. A repeated barium meal study on July 23, 1976 failed to visualize the polypoid lesion, and no Type IIa early gastric cancer could be found at gastroscopy. Gastric biopsy was reported as showing Group II (intestinal metaplasia). Until April 24, 1978, the patient remained on 5-FU dry syrup with a total dose of 165.2 g. He also took P-SK between June 15, 1977 and April 23, 1978 with a total dose of 919 g. On September 1, 1979, gastroscopy was repeated, but no polypoid lesion could be found.

Mommersteeg, M., et al. (2019). "Evaluating the accuracy of discharging patients from surveillance for gastric premalignant lesions according to the MAPS guideline in a low risk population: A prospective cohort study." United European Gastroenterology Journal 7(8): 184.

Introduction: Intestinal type gastric cancer follows a cascade of premalignant lesions which makes gastric cancer suitable for screening and surveillance. The Management of epithelial precancerous conditions and lesions in the stomach (MAPS) guideline (first published in 2012 and revised in 2019) advises an histological-led diagnosis by performing random biopsies, in order to stage the extent and severity of premalignant gastric lesions, and determine if surveillance is recommended. No surveillance is deemed necessary for atrophic gastritis (AG) or intestinal metaplasia (IM) limited to either antrum or corpus. However, random biopsies may not properly reflect the extent of the lesions. The aim of this study was to assess the appropriateness of discharging patients from further surveillance according to the guideline in daily practice. Aims & Methods: Patients were included from the multicenter, prospectively followed PROREGAL cohort initiated in 2009 in which patients were identified with AG, IM and/or dysplasia of the gastric mucosa at index endoscopy (t0). In the PROREGAL protocol each patient underwent a first surveillance endoscopy with random biopsies one year after the index endoscopy (t1), and in case no high or low grade dysplasia was present, a second surveillance endoscopy was performed three years after the index endoscopy (t2). Further surveillance interval was in accordance with the MAPS guideline. For the current study, patients excluded from further surveillance according to MAPS-2012 were re-invited to undergo a followup endoscopy after three years (t3). Patients were included in the current study 1) if they met the MAPS-2012 or MAPS-2019 guideline recommendations to stop surveillance based on the outcome of the latest endoscopy (t1 or t2), and 2) underwent a subsequent follow-up endoscopy (t2 or t3) not included in the guideline recommendations. An inappropriate discharge from follow-up was defined if premalignant gastric lesions were present at t2 or t3 that gave reason to resume surveillance. Results: The PROREGAL cohort comprises 334 patients. Between 2009 and 2019,113 patients were supposed to be discharged according to MAPS-2012 but underwent follow up endoscopy according to the PROREGAL protocol. In 38/113 (33.6%; 95%CI 25.2-43.2) patients (progressions of) gastric lesions for which surveillance is recommended were found at t2 or t3. If MAPS-2019 was followed, inclusion increased to 173 patients who were supposed to be discharged from surveillance. In 62/173(35.8%; 95%CI 28.8-43.5) of these patients, gastric lesions for which surveillance is recommended were present at t2 or t3. In two cases high grade dysplasia (both corpus) and in one case gastric adenocarcinoma of the angulus was diagnosed. Conclusion: 1/3rd of patients who are discharged from gastric cancer surveillance according to MAPS recommendations appeared to be misclassified as low risk according to results found at follow-up endoscopy. Three of them had developed high grade dysplasia or gastric cancer. Therefore improvement of endoscopic and histological staging of premalignant gastric lesions is warranted.

Mommersteeg, M., et al. (2018). "Enteroendocrin cell compartment size decreases during H. pylori infection in patients with intestinal metaplasia but is restored after eradication." United European Gastroenterology Journal 6(8): A321.

Introduction: Gastric cancer, the fifth leading cause of cancer, develops following Correa's cascade: well defined steps involving several premalignant lesions, the most common of which is intestinal metaplasia (IM). The mechanism by which these premalignant lesions develop and progression is driven is still largely unknown. The largest risk factor for development of both IM and gastric cancer is infection with the pathogen Helicobacter Pylori (HP). One of the theories is that HP-associated inflammation causes a disbalance of gastric hormone levels by causing destruction of the somastatin-producing D-cell compartment. This in turn would cause a relative increase of gastrin which has several proliferative and pro-oncogenic effects. In this study we determine the effect of both HP and eradication on the enteroendocrine cell compartments of the antral stomach in patients with intestinal metaplasia. Aims and Methods: Antral gastric biopsies were taken systematically in a surveillance cohort of patients with IM or gastric atrophy (PROREGAL Cohort). HP positivity was determined by serology and histology. Patients were scored as having active infection when histology was positive, and negative when both histology and serology were negative. Presence or absence of IM was scored by trained pathologist. We included 24 HP-naïve patients and 23 biopsies from patients infected with HP. Of the HP infected patients, also biopsies were obtained 1 year after successful eradication of HP. Immunohistochemical staining of G-cells and D- cells was performed using anti-gastrin and anti-somatostatin antibodies respectively. The number of positive cells per high power field were counted and intensity of staining was scored. Means of 4 biopsies were represented using the Allred score. Significance was determined using students T-test. Results: As expected, antral biopsies from IM patients show patches of IM as well as normal crypts. In IM both the G-cell (p<0.0001) and D-cell (p=0.0002) compartments are reduced as compared to non-IM crypts. In patients infected with HP, total D-cell numbers were significantly reduced as compared to patients without HP (p=0.0001), in line with findings described in literature. Unexpectedly however, we also observed a significant reduction of G-cells in in patients with active HP infection (p=0.0008). Interestingly, 1 year after HP eradication, this reduction in enteroendocrine cell compartment size was no longer apparent and both D-cell and G-cell levels were normalized to the levels seen in patients that have never been infected. Enteroendocrine cell compartment size is not associated with either progression or regression of gastric premalignant lesions in this cohort. Conclusion: These results confirm previous studies showing that HP infection causes a reduction in the antral D-cell compartment in IM crypts. However, we further demonstrate that this reduction is not restricted to D-cells, but also affects antral G-cells. After eradication of HP, enteroendocrine cell compartments return to sizes comparable to non-infected patients even though the gastric premalignant lesions persist. These results suggest that antral G-cell compartment size is likely of minor importance in early gastric carcinogenesis.

Mommersteeg, M., et al. (2018). "Helicobacter pylori, gastric carcinogenesis and the association with er-stress and autophagy." United European Gastroenterology Journal 6(8): A29.

Introduction: Helicobacter Pylori (HP) is one of the most successful pathogens in the world, infecting nearly half of the world's population. Importantly, HP is the biggest risk factor in the development of gastric pathology including gastric atrophy, intestinal metaplasia (IM) and dysplasia, all of which are considered precursor lesions to gastric cancer. Autophagy is a cellular degradation mechanism, the physiological role of which is to recycle cytoplasmic components. A specialized form of autophagy, xenophagy, contributes to clearance of intracellular pathogens. Recently it has been shown that HP may modulate autophagy through activation of the endoplasmic reticulum stress (ER stress) pathway. Our previous studies have shown that a single nucleotide polymorphism (SNP) in the autophagy gene ATG16L1 (rs2241880) modulates intestinal ER stress. The aim of this study was to investigate the role of this SNP in HP-mediated autophagy, ER stress and intestinal metaplasia. Aims and Methods: DNA (n=262) was isolated from EDTA blood of a cohort of IM patients (PROREGAL Cohort), and the ATG16L1 SNP (rs2241880) status was determined by PCR-RFLP. ER stress and autophagy experiments were performed with gastric cancer cell line SK-GT-2 and immortalized gastric cell line GES-1. ER stress was induced by tunicamycin. ER stress (GRP78) and autophagy (LC3B) were detected by western blot analysis. HP (ATCC 43504) was cultured on Columbia sheep blood agar and heat-killed before cell stimulation. Antral biopsies were taken from 47 patients with IM of which 23 were actively infected with HP (determined by histology), these same patients were biopsied 1 year after eradication. The other 24 biopsies were from patients with IM who have never been infected with HP (determined by serology). Immunohistochemistry was performed on these biopsies using GRP78 as a marker for ER stress. Positivity was scored using the Allredscore taking the average of 4 high powered fields. Statistical significance was determined by Students T-test. Results: The minor allele frequency (MAF) of rs2241880 (i.e. the A allele, associated with lower intestinal ER stress levels) was calculated as 0.53 in the IM cohort, which was significantly higher than the reference population (Rotterdam study, MAF 0.45, p=0.0003). After stimulation with HP, ER stress levels in gastric cell lines were reduced, whereas autophagy was induced, as determined by LC3BI to LC3BII conversion. These differences were not observed when cells were stimulated with non-pathogenic E. coli bacteria. Biopsies from patients actively infected with HP showed a reduced amount of GRP78 positivity as compared to uninfected patients (p=0.0171) and the same patients one year after eradication (p=0.0006). Conclusion: These results show that HP upregulates the autophagy pathway and thereby reduces ER-stress in vitro and in vivo. Furthermore we show that a genetic variant of the ATG16L1 gene which causes reduced levels of ER stress is more prevalent in patients who have developed precancerous gastric lesions, suggesting that promotion of autophagy and thereby reduction of ER stress contributes to HP-induced changes of the gastric epithelium.

Mommersteeg, M. C., et al. (2021). "Accuracy of upper endoscopies with random biopsies to identify patients with gastric premalignant lesions who can safely be exempt from surveillance." Gastric Cancer 24(3): 680-690.

INTRODUCTION: Guidelines recommend endoscopy with biopsies to stratify patients with gastric premalignant lesions (GPL) to high and low progression risk. High-risk patients are recommended to undergo surveillance. We aimed to assess the accuracy of guideline recommendations to identify low-risk patients, who can safely be discharged from surveillance. METHODS: This study includes patients with GPL. Patients underwent at least two endoscopies with an interval of 1-6 years. Patients were defined 'low risk' if they fulfilled requirements for discharge, and 'high risk' if they fulfilled requirements for surveillance, according to European guidelines (MAPS-2012, updated MAPS-2019, BSG). Patients defined 'low risk' with progression of disease during follow-up (FU) were considered 'misclassified' as low risk. RESULTS: 334 patients (median age 60 years IQR11; 48.7% male) were included and followed for a median of 48 months. At baseline, 181/334 (54%) patients were defined low risk. Of these, 32.6% were 'misclassified', showing progression of disease during FU. If MAPS-2019 were followed, 169/334 (51%) patients were defined low risk, of which 32.5% were 'misclassified'. If BSG were followed, 174/334 (51%) patients were defined low risk, of which 32.2% were 'misclassified'. Seven patients developed gastric cancer (GC) or dysplasia, four patients were 'misclassified' based on MAPS-2012 and three on MAPS-2019 and BSG. By performing one additional endoscopy 72.9% (95% CI 62.4-83.3) of high-risk patients and all patients who developed GC or dysplasia were identified. CONCLUSION: One-third of patients that would have been discharged from GC surveillance, appeared to be 'misclassified' as low risk. One additional endoscopy will reduce this risk by 70%.

Moon, C. M., et al. (2014). "Chronic tamoxifen use is associated with a decreased risk of intestinal metaplasia in human gastric epithelium." Digestive Diseases and Sciences 59(6): 1244-1254.

BACKGROUND: Intestinal metaplasia (IM), a premalignant lesion, is associated with an increased risk of gastric cancer. Although estrogen exposure, including tamoxifen, has been studied in correlation with gastric cancer, little has been investigated about its effects on IM. AIMS: Therefore, we investigated whether chronic tamoxifen use was associated with the risk of IM in human stomach. METHODS: We evaluated 512 gastric biopsies from 433 female breast cancer patients that underwent endoscopic gastroduodenoscopy (EGD) ≥6 months after breast surgery. Histopathological findings were scored according to the updated Sydney classification. Demographic and clinical characteristics were also included to identify predictive factors for IM. RESULTS: In a multivariate logistic regression analysis, age at EGD (odds ratio [OR], 1.04; P = 0.002), biopsies from antrum (OR 2.08; P < 0.001), and Helicobacter pylori positivity (OR 1.68; P = 0.016) were significantly associated with an increased risk of IM, whereas chronic tamoxifen use (≥3 months) was associated with a decreased risk of IM (OR 0.59; P = 0.025). After stratifying by biopsy site, association between tamoxifen use and IM persisted for corpus (OR 0.42; P = 0.026) but not for antrum (OR 0.74; P = 0.327). In analysis limited to patients with follow-up EGD, chronic tamoxifen use also correlated with improved IM score compared to no tamoxifen use (improved, 77.8 vs. 22.2%; no change, 65.4 vs. 34.6%; worsened, 30.0 vs. 70.0%; P = 0.019). CONCLUSIONS: This study suggests that chronic tamoxifen use can decrease the risk of IM in human stomach. The effect of tamoxifen is predominantly observed in the corpus.

Moon, H. S., et al. (2016). "Risk factors for metachronous gastric carcinoma development after endoscopic resection of gastric dysplasia." Annals of Oncology 27: ii108.

Introduction: Gastric dysplasia is known for precursor lesion of invasive adenocarcinoma. Therefore, endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is being routinely performed for removal of this premalignant lesion. After removal of dysplasia, gastric adenocarcinoma (GAC) can be detected during follow-up period but there are few study about the related factors of gastric cancer occurrence to know the occurrence rate of GAC and related factors, we evaluated the follow-up results of patients who had been conformed to gastric dysplasia after endoscopic resection. Methods:We analyzed retrospectively the medical records, endoscopic examination records, endoscopic procedure records and histological records in 667 cases of 641 patients being followed up over 1 year, among the 1,273 patients who had been conformed to gastric dysplasia after EMR or ESD for gastric mucosal lesion between January 2007 and august 2013 at the Chungnam National University Hospital. Results: The mean follow-up period was 33.8 months and median follow-up period was 29months (range, 12 ~ 87). During the follow-up period, occurrence of metachronous GAC was 4.0% (27/667). The mean and median interval period between occurrence of metachronous GAC and endoscopic treatment of GA were 36.3 months and 34 months, respectively (range, 16 ∼ 71). The factors related to metachronous GAC occurrence after endoscopic resection for gastric dysplasia were male sex (5.3% vs 1.0%), open type of atrophic gastritis (9.5% vs 3.4%), intestinal metaplasia (6.8% vs 2.4%) and high grade dysplasia (8.4% vs 3.2%). Among them, male sex [OR: 5.05 (1.18-21.68) p = 0.029], intestinal metaplasia [OR: 2.78 (1.24-6.23) p = 0.013] and high grade dysplasia [OR: 2.70, (1.16-6.26) p= 0.021] were independent related factors in multivariate analysis. The 24 cases among the 27 GAC occurred cases (88.9%) were occurred at the other sites of previous resection sites and the 3 cases (11.1%) were occurred in the same site of previous resection site. Conclusion: Male sex, intestinal metaplasia and high grade dysplasia were significantly related to occurrence of metachronous GAC after EMR/ESD for gastric dysplasia and most of them were occurred at the other sites of previous resection sites.

Moon, H. S., et al. (2017). "Risk factors for metachronous gastric adenocarcinoma development after endoscopic resection of gastric dysplasia." Gastrointestinal Endoscopy 85(5): AB434.

Background/Aims: Gastric dysplasia is a precursor lesion of an invasive adenocarcinoma. Endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is routinely performed for removal of this premalignant lesion. After the removal of the lesion, a gastric adenocarcinoma (GAC) is sometimes detected during the follow-up period. The literature on factors associated with gastric cancer occurrence is scarce. To shed light on the occurrence rate of GAC and related factors, the follow-up results of patients who had been confirmed with gastric dysplasia after endoscopic resection were evaluated. Methods: This was a retrospective analysis of the medical records, endoscopic examination records, endoscopic procedure records, and histological records of 1,273 patients diagnosed with gastric dysplasia after undergoing EMR or ESD for gastric mucosal lesions between January 2007 and August 2013 at the Chungnam National University Hospital. The study consisted of data on 667 lesions in 641 patients. Results: The mean follow-up period was 33.8 months, and the median follow-up period was 29 months (range, 12-87). During the follow-up period, the incidence of metachronous GAC was 4.0% (27/667). The mean and median interval between the occurrence of metachronous GAC and endoscopic treatment of GA was 36.3 months and 34 months, respectively (range, 16-71). The factors related to the occurrence of metachronous GAC after endoscopic resection for gastric dysplasia were male sex (5.3% vs. 1.0%), open type of atrophic gastritis (9.5% vs. 3.4%), intestinal metaplasia (6.8% vs. 2.4%), and high-grade dysplasia (8.4% vs. 3.2%). Among these factors, male sex (odds ratio [OR]: 5.05(1.18-21.68),p=0.029), intestinal metaplasia (OR: 2.78(1.24-6.23),p=0.013), and high-grade dysplasia (OR: 2.70(1.16-6.26),p=0.021]were independent risk factors in a multivariate analysis. Of the 27 cases of GAC, 24 (88.9%) occurred at locations other than the original resection sites, and 3 (11.1%) occurred at the same location as the previous resection site. Conclusions: Male sex, intestinal metaplasia, and high-grade dysplasia were significantly related to the occurrence of metachronous GAC after EMR/ESD for gastric dysplasia, and most dysplasic lesions occurred at sites other than the original resection sites.

Moon, H. S., et al. (2016). "Risk factors for metachronous gastric carcinoma development after endoscopic resection of gastric dysplasia; retrospective, single center study." Journal of Gastroenterology and Hepatology (Australia) 31: 104.

Background/Aims: Gastric dysplasia is a known precursor lesion of invasive adenocarcinoma, so endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is routinely performed to remove this premalignant lesion. We determined the occurrence rate of GAC and related factors by evaluating the follow-up results of patients who had been confirmed with gastric dysplasia after endoscopic resection. Methods: We retrospectively analyzed the medical records, endoscopic examination records, endoscopic procedure records, and histological records for 667 cases in 641 patients being followed up over 1 year among the 1,273 patients who had been confirmed with gastric dysplasia after EMR or ESD for gastric mucosal lesions between January 2007 and August 2013 at the Chungnam National University Hospital. Results: During the follow-up period, the occurrence of metachronous GAC was 4.0% (27/667). The mean and median interval periods between occurrence of metachronous GAC and endoscopic treatment of GA were 36.3 months and 34 months, respectively (range, 16-71). The factors related to metachronous GAC occurrence after endoscopic resection for gastric dysplasia were male sex (5.3% vs. 1.0%), open type of atrophic gastritis (9.5% vs. 3.4%), intestinal metaplasia (6.8% vs. 2.4%), and high grade dysplasia (8.4% vs. 3.2%). Among these, male sex [OR: 5.05 (1.18-21.68) p = 0.029], intestinal metaplasia [OR: 2.78 (1.24-6.23) p = 0.013], and high grade dysplasia [OR: 2.70, (1.16-6.26) p = 0.021] were independent related factors in a multivariate analysis. Among the 27 GAC cases, 24 cases (88.9%) occurred at locations other than the previous resection sites and 3 cases (11.1%) occurred at the same locations as the previous resection sites. Conclusions: Male sex, intestinal metaplasia, and high grade dysplasia were significantly related to the occurrence of metachronous GAC after EMR/ESD for gastric dysplasia, and most cases occurred at locations other than the previous resection sites.

Moon, H. S., et al. (2016). "Risk factors for metachronous gastric carcinoma development after endoscopic resection of gastric dysplasia; retrospective, single center study." United European Gastroenterology Journal 4(5): A384.

Introduction: Gastric dysplasia is a known precursor lesion of invasive adenocarcinoma, so endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is routinely performed to remove this premalignant lesion. Upon removal of the dysplasia, gastric adenocarcinoma (GAC) can be detected during the follow-up period, but few studies have addressed the factors related to gastric cancer occurrence. Aims & Methods: We determined the occurrence rate of GAC and related factors by evaluating the follow-up results of patients who had been confirmed with gastric dysplasia after endoscopic resection. We retrospectively analyzed the medical records, endoscopic examination records, endoscopic procedure records, and histological records for 667 cases in 641 patients being followed up over 1 year, among the 1,273 patients who had been confirmed with gastric dysplasia after EMR or ESD for gastric mucosal lesions between January 2007 and August 2013at the Chungnam National University Hospital. Results: The mean follow-up period was 33.8 months and the median follow-up period was 29 months (range, 12-87). During the follow-up period, the occurrence of metachronous GAC was 4.0% (27/667). The mean and median interval periods between occurrence of metachronous GAC and endoscopic treatment of GA were 36.3 months and 34 months, respectively (range, 16-71). The factors related to metachronous GAC occurrence after endoscopic resection for gastric dysplasia were male sex (5.3% vs. 1.0%), open type of atrophic gastritis (9.5% vs. 3.4%), intestinal metaplasia (6.8% vs. 2.4%), and high grade dysplasia (8.4% vs. 3.2%). Among these, male sex [OR: 5.05 (1.18- 21.68) p=0.029], intestinal metaplasia [OR: 2.78 (1.24-6.23) p=0.013], and high grade dysplasia [OR: 2.70, (1.16-6.26) p= 0.021] were independent related factors in a multivariate analysis. Among the 27 GAC cases, 24 cases (88.9%) occurred at locations other than the previous resection sites and 3 cases (11.1%) occurred at the same locations as the previous resection sites. Conclusion: Male sex, intestinal metaplasia, and high grade dysplasia were significantly related to the occurrence of metachronous GAC after EMR/ESD for gastric dysplasia, and most cases occurred at locations other than the previous resection sites.

Moon, H. S., et al. (2017). "Risk factors for metachronous gastric carcinoma development after endoscopic resection of gastric dysplasia: Retrospective, single-center study." World Journal of Gastroenterology 23(24): 4407-4415.

AIM: To determine the gastric adenocarcinoma (GAC) occurrence rate and related factors, we evaluated the follow-up results of patients confirmed to have gastric dysplasia after endoscopic resection (ER). METHODS: We retrospectively analyzed the medical records, endoscopic examination records, endoscopic procedure records, and histological records of 667 cases from 641 patients who were followed-up for at least 12 mo, from among 1273 patients who were conformed to have gastric dysplasia after Endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) of gastric mucosal lesions between January 2007 and August 2013 at the Chungnam National University Hospital. RESULTS: The mean follow-up period was 33.8 mo, and the median follow-up period was 29 mo (range: 12-87). During the follow-up period, the occurrence of metachronous GAC was 4.0% (27/667). The mean and median interval periods between the occurrence of metachronous GAC and endoscopic treatment of gastric dysplasia were 36.3 and 34 mo, respectively (range: 16-71). The factors related to metachronous GAC occurrence after ER for gastric dysplasia were male sex (5.3% vs 1.0%), open-type atrophic gastritis (9.5% vs 3.4%), intestinal metaplasia (6.8% vs 2.4%), and high-grade dysplasia (HGD; 8.4% vs 3.2%). Among them, male sex [OR: 5.05 (1.18-21.68), P = 0.029], intestinal metaplasia [OR: 2.78 (1.24-6.23), P = 0.013], and HGD [OR: 2.70 (1.16-6.26), P = 0.021] were independent related factors in multivariate analysis. Furthermore, 24 of 27 GAC cases (88.9%) occurred at sites other than the previous resection sites, and 3 (11.1%) occurred at the same site as the previous resection site. CONCLUSION: Male sex, intestinal metaplasia, and HGD were significantly related to the occurrence of metachronous GAC after ER of gastric dysplasia, and most GACs occurred at sites other than the previous resection sites.

Moore, A. R., et al. (2015). "A combination of fasting serum gastrin concentration, pepsinogen 1/2 ratio and helicobacter pylori igg antibody serotype accurately predicts gastric mucosal preneoplasia in a large european cohort." Gastroenterology 148(4): S54.

Introduction H. pylori infected subjects who develop corpus-predominant gastritis have an increased risk of developing gastric cancer. Gastric adenocarcinoma develops via a welldefined series of pathological changes namely multi-focal atrophy, intestinal metaplasia, dysplasia and finally cancer. In high-risk populations, serological biomarkers for screening and surveillance have been well validated. In European populations with a lower prevalence of gastric cancer however, circulating biomarkers have only been evaluated in small series and contradictory results have been described. Methods We recruited 1400 symptomatic adults (57.5% female, mean age 58 years, 98.4% Caucasian) after referral to our hospital in North-West England for diagnostic upper gastrointestinal endoscopy. Blood and gastric biopsy specimens were obtained. H. pylori status was determined by histology and serum IgG antibody ELISA. Fasting serum gastrin concentrations were measured by radioimmunoassay using a C-terminal specific antibody and serum pepsinogen (PG) 1 and 2 concentrations by ELISA. A single, expert gastrointestinal histopathologist examined antral and corpus biopsy specimens and produced standardized reports. Results H. pylori serology was positive in 577 (41.2%) patients. Of these 294 (51.3%) also had histological evidence of current H. pylori infection. Preneoplastic mucosal lesions were reported in 338 (24.1%). The prevalence of H. pylori antibodies in subjects with preneoplasia (68.3%) was significantly greater than in those without (36.6%) (p<0.0001). Subjects with preneoplasia also exhibited significantly higher fasting serum gastrin concentrations (mean=148.4pM) than normal controls who were H. pylori negative and did not take proton pump inhibitors (mean=39.7pM) (p< 0.0001). There was no significant difference between serum PG1 concentration in normal controls (98.9μg/l) and patients with preneoplasia (115.0μg/l). Serum PG2 concentration however differed significantly in preneoplasia patients (17.2μg/l) compared with controls (9.23μg/l), as did PG1/2 ratio (7.20 versus 11.54) (p<0.0001). PG1/2 ratio performed better as a diagnostic test for preneoplasia than either PG1 or PG2 concentration. With a cutoff of 8.8, we observed a sensitivity of 70.0% and a specificity of 79.1% with an area under the receiver-operating curve of 0.80. Combining PG1/2 ratio, fasting serum gastrin concentration and H. pylori serology improved the diagnostic accuracy. The combined test yielded a sensitivity of 90.0% and a specificity of 74.4% with positive and negative predictive values of 52.1% and 96.0% respectively. Conclusion The combined test is an accurate predictor of the presence of gastric mucosal preneoplasia in a European cohort. Clinical applications including screening of symptomatic patients or surveillance of at-risk groups and merit further investigation.

Morales, T. G., et al. (2001). "Inability to noninvasively diagnose gastric intestinal metaplasia in Hispanics or reverse the lesion with Helicobacter pylori eradication." Journal of Clinical Gastroenterology 32(5): 400-404.

BACKGROUND: Helicobacter pylori infection has been linked with the development of gastric adenocarcinoma and its precursor lesion, intestinal metaplasia (IM). The presence of gastric IM is not associated with symptoms, which makes identification of individuals with this lesion difficult. It is not clear whether eradication of H. pylori infection leads to reversal of gastric IM or the potential decrease in the risk of cancer in these patients. GOALS: The purpose of this pilot study was to define the prevalence of gastric IM in a population at high risk for gastric cancer (Southwestern Hispanics), examine the ability of noninvasive testing to identify individuals with the lesion, and determine whether eradication of H. pylori infection reverses gastric IM in this population. STUDY: Subjects from the Tucson metropolitan area were recruited, and baseline data, including the presence of upper gastrointestinal (UGI) symptoms, urinary sodium, and serum pepsinogen levels, were obtained. Upper endoscopy was performed and six gastric biopsies from specific anatomic sites were obtained, followed by methylene blue staining with targeted biopsies from blue-stained mucosa. Biopsies were evaluated for the presence of H. pylori infection and gastric IM. A subset of patients with gastric IM were treated to eradicate H. pylori infection. Follow-up exams with methylene blue staining, including biopsies for histology and rapid urease testing, were performed for up to 48 months. RESULTS: There were 84 subjects with a mean age of 53.0 years; 24 (29%) had gastric IM and 65 (77%) had H. pylori. There was no significant association between gastric IM and age, gender, UGI symptoms, H. pylori, or urine sodium. There was an association identified between gastric IM and a decreased pepsinogen I:II ratio (p = 0.03). Of the 11 individuals with gastric IM treated for H. pylori infection, 9 had successful therapy and underwent at least 2 follow-up examinations. The mean length of follow-up was 3.3 years. Eight of the nine (89%) had gastric IM identified histologically at the final endoscopic exam. CONCLUSIONS: H. pylori infection and gastric IM are frequent findings in Southwestern Hispanics, a high-risk population for gastric cancer. Noninvasive testing is not clinically useful in distinguishing individuals within this group who harbor gastric IM. Although eradication of H. pylori infection may lead to a decrease in the amount of gastric IM in some individuals, the lesion may be detected in the majority of individuals after more than 3 years of follow-up. These data suggest that therapy for H. pylori may not eliminate the risk of gastric cancer once IM has developed.

Moretó, M. (2003). "Diagnosis of esophagogastric tumors." Endoscopy 35(1): 36-42.

It has been suggested that certain histological criteria may serve to indicate a good prognosis in patients with esophageal carcinoma. These include absence of subepithelial extension of the carcinoma cells, stage no higher than m2, and no neoplastic involvement near the resection margin. As endoscopic mucosal resection is becoming an accepted treatment option in this type of tumor, prognostic parameters of this type are of particular interest. By contrast, when metastases are detected in the celiac lymph nodes, it implies that the tumor is unresectable and that palliative treatment is required. Endoscopic ultrasound (EUS)-guided fine-needle aspiration has been found to be the most cost-effective option in this setting. Although autofluorescence endoscopy is being tested as a new technique for endoscopic diagnosis, its value is at present unclear. However, such developments may lead to improved diagnosis in the future, particularly in relation to the initial stages of carcinoma. For the moment, EUS is still the most widely accepted method for early diagnosis and staging. Esophageal squamous-cell carcinoma appears to be commonly associated with head and neck cancer, but the cost-effectiveness of surveillance is a matter of controversy. With regard to Barrett's esophagus and adenocarcinoma, p53 staining in areas of low-grade dysplasia appears to be helpful for predicting progression to high-grade dysplasia. The prevalence of short-segment Barrett's esophagus increases with age, but the length of the segment does not increase with time; the length probably depends on individual conditions, not merely on elapsed time. Helicobacter pylori infection appears to be associated with intestinal metaplasia at the esophagogastric junction. However, the most recent data appear to suggest that this scenario (usually termed "carditis") may be different from intestinal metaplasia in the lower esophagus, related to acid reflux. A follow-up program might be able to detect Barrett's esophagus adenocarcinoma at earlier stages, but only a minority of Barrett's esophagus patients are likely to be detected before neoplasia has developed. Gastric cancer appears to develop in individuals with H. pylori infection, but not in uninfected persons. In addition, those with severe gastric atrophy, corpus-predominant gastritis, and intestinal metaplasia may be at greater risk for gastric cancer. This again raises the question of H. pylori eradication in asymptomatic individuals with infection, and surveillance of patients with severe intestinal metaplasia. The most recent data appear to support the notion that healing of MALT lymphoma depends not only on H. pylori eradication and on the stage of the tumor, but also on individual factors (possibly immunology-related).

Moretó, M. (2005). "Diagnosis of esophagogastric tumors." Endoscopy 37(1): 26-32.

With regard to esophageal tumors, important reports on several topics have been published recently. 1) The place of endoscopic ultrasonography (EUS) as the best locoregional staging technique for cancer of the esophagus has been further consolidated. The addition of fine-needle aspiration makes EUS more sensitive than computed tomography (CT) and more accurate than CT or EUS alone for nodal staging. 2) High-resolution endoscopy with chromoendoscopy has been found to be very effective for mucosal lesions, but not for submucosal lesions. In combination with EUS, the sensitivity for submucosal tumors increases up to 60 %. 3) Autofluorescence-guided biopsy has been reported to be a good tool for detecting high-grade dysplasia. A narrow-band imaging system improved the overall accuracy for depth of invasion. 4) The incidence of hypopharyngeal cancer increases after resection for esophageal carcinoma. Patients with a scattered staining pattern after application of Lugol's solution are more prone to develop upper lesions. 5) Fluorescence imaging makes it possible to detect low-grade intraepithelial neoplasia in Barrett's mucosa, with fewer biopsies. 6) Patients with Barrett's esophagus with a length of over 3 cm had a significantly greater prevalence of dysplasia in comparison with those in the whom the Barrett's segment was shorter than 3 cm (23 % vs. 9 %, P = 0.0001). With regard to gastric tumors, 1) Helicobacter pylori eradication can significantly reduce the development of gastric cancer, but only in patients without precancerous lesions. 2) Intestinal metaplasia types II and III have been shown to have a higher rate of progression to low-grade dysplasia than type I. 3) With regard to screening in asymptomatic individuals, serum pepsinogen may represent an alternative to conventional fluoroscopy methods. 4) In patients who have undergone esophagectomy for esophageal cancer, annual follow-up endoscopies are vital for detecting early secondary gastric cancer and ulcerations in which curative treatment is possible. 5) High-resolution endoscopy allows more precise diagnosis of early gastric cancer. The presence of irregular minute vessels and variations in vessel caliber were found to be specific of early gastric cancer. The small regular pattern of sulci and ridges was observed significantly more frequently in differentiated carcinoma than in undifferentiated carcinoma. 6) Infrared-ray electronic endoscopy combined with indocyanine green injection appears to be effective in detecting sentinel nodes that contain metastases in patients with gastric cancer. 7) Gastric adenocarcinoma was found to show specific changes in the fluorescence spectra emitted, in comparison with normal gastric mucosa. However, there was wide variation in the emitted autofluorescence spectra in gastric cancer with signet-ring cells in comparison with normal mucosa.

Murakami, K. (2017). "Gastric cancer risk assessment by Kyoto classification of gastritis." Gastroenterological Endoscopy 59: 2106.

Over the past few years, the profile of Helicobacter pylori infection has changed in Japan. In particular, the relationship between H. pylori and gastric cancer has been demonstrated more clearly. In 2016, the committee of the Japanese Society for Helicobacter Research has revised the guidelines for diagnosis and treatment of H. pylori infection in Japan. In 2013, Treatments for H. pylori-associated gastritis was covered by health insurance. In fact, all H. pylori- infected patients in Japan can receive these insurance-covered combination therapies for the eradication. Before diagnosing and treating H. pylori infection, an endoscopic examination is required to obtain a definitive diagnosis of H. pylori gastritis. Successful eradication of H. pylori improves histological gastritis and may prevent various diseases associated with H. pylori infection, such as gastric/duodenal ulcer and gastric cancer. Recently, we have a newly developed potassium-competitive acid blocker( PCAB), Vonoprazan, and triple therapy containing PCAB has better efficacy than PPI-containing eradication therapy. It is necessary to evaluate the risk of gastric cancer by endoscopic findings, and also necessary to make a long follow-up after the eradication. Especially for atrophic gastritis, intestinal metaplasia, enlarged fold, and nodular gastritis, which are considered as being in a high-risk group of gastric cancer, and endoscopic diagnosis of them is undeniably required. Improvements of them after the eradication may be regarded as one reason for prevention of gastric cancer. We attempt to score for these findings according to the grades of the lesions.

Murakami, K. (2020). "Gastric cancer risk assessment by Kyoto classification of gastritis and features of gastric cancer after eradication." Digestion 102(1): 95.

Over the past few years, the profile of Helicobacter pylori infection has changed in Japan. In particular, the relationship between H. pylori and gastric cancer has been demonstrated more clearly. In 2016, the committee of the Japanese Society for Helicobacter Research has revised the guidelines for diagnosis and treatment of H. pylori infection in Japan. In 2013, Treatments for H. pylori-associated gastritis was covered by health insurance. In fact, all H. pylori-infected patients in Japan can receive these insurance-covered combination therapies for the eradication. Before diagnosing and treating H. pylori infection, an endoscopic examination is required to obtain a definitive diagnosis of H. pylori gastritis. In 2014, first version of Kyoto classification of gastritis was published, and in 2018, it was revised. Successful eradication of H. pylori improves histological gastritis and may prevent various diseases associated with H. pylori infection, such as gastric cancer. It is necessary to evaluate the risk of gastric cancer by endoscopic findings, and also necessary to make a long follow-up after the eradication. Especially for atrophic gastritis, intestinal metaplasia, enlarged fold, and nodular gastritis, which are considered as being in a high-risk group of gastric cancer, and endoscopic diagnosis of them is undeniably required. Improvements of them after the eradication may be regarded as one reason for prevention of gastric cancer. We also attempt to score for these findings according to the grades of the lesions..

Murakami, K., et al. (2012). "Long-term monitoring of gastric atrophy and intestinal metaplasia after Helicobacter pylori eradication." Clinical Journal of Gastroenterology 5(4): 247-250.

Improvements of atrophy and intestinal metaplasia which is seen after H. pylori eradication may be regarded as an important factor of gastric cancer prevention. Although many studies reported the alteration of gastric mucosa after H. pylori eradication, most of the results do not agree. Recently, two meta-analyses showed significant improvement of atrophy (one study showed improvement in both corpus and antrum, and the other showed improvement in corpus but not in antrum), whereas improvement of intestinal metaplasia was not shown in either corpus or antrum. However, one reason why conclusions are different is considered to be that the observation period after eradication was short, and another reason is considered to be that almost studies examined only two points in gastric mucosa for histological analysis. Further examination with a greater number of subjects and with longer follow up period should be required to clarify the mechanism of gastric injury and improvement of gastric mucosa, especially atrophy and intestinal metaplasia after H. pylori eradication.

Murakami, K., et al. (2013). "Histological characteristics of gastric mucosa prior to helicobacter pylori eradication may predict gastric cancer." United European Gastroenterology Journal 1(1): A54.

INTRODUCTION: Although Helicobacter pylori eradication has been shown to inhibit gastric cancer, it does not completely suppress it. In our previous study, significant improvement of atrophy was observed during a ten-year follow-up period following eradication. However, intestinal metaplasia(IM) did not show a similar improvement, except for IM at the lesser curvature of the corpus (1). Therefore risk factors associated with gastric cancer development following H. pylori eradication were examined. AIMS&METHODS: A total of 2355 patients (1501 males, 824 females) underwent successful eradication of H. pylori. Endoscopical atrophy, serum pepsinogen, and histological gastritis were evaluated after eradication. RESULTS: Following H. pylori eradication, 33/2355 patients (25 males, 8 females) developed gastric cancer. When a non-gastric cancer group was matched according to gender and age of the gastric cancer group, the incidence of endoscopic atrophy (3.52 ± 1.45 vs. 4.71 ± 1.31, P < 0.001), histological atrophy (1.42 ± 0.80 vs. 2.00 ± 0.87, P = 0.0028) at the greater curvature of the antrum, inflammation (2.05 ± 0.59 vs. 2.32 ± 0.65, P = 0.036), and intestinal metaplasia (IM) (0.06 ± 0.30 vs. 0.23 ± 0.53, P = 0.034) at the greater curvature of the corpus for the gastric cancer group was significantly higher than for the non-gastric cancer group. Multivariate analysis also showed that the odds ratio and 95%confidence interval (CI) for these categories were 2.20 (1.36-3.55) (P = 0.001), 3.26 (1.45-7.34) (P = 0.004), 2.69 (1.01-7.26) (P = 0.05), and 5.98 (1.27-28.10) (P = 0.023), respectively. CONCLUSION: Severe endoscopical atrophy, histological atrophy at the antrum, inflammation, and particularly IM at the corpus, were identified as risk factors for gastric cancer development following H. pylori eradication. Therefore, eradication should be performed before these predictors develop.

Murayama, H., et al. (1990). "Changes in gastric mucosa that antedate gastric carcinoma." Cancer 66(9): 2017-2026.

Endoscopic biopsy specimens of the gastric mucosa from 13 patients who were found at follow-up examination to have gastric carcinoma were compared for abnormal histologic features, type of intestinal metaplasia, and presence of immunoreactive carcinoembryonic antigen (CEA), with specimens from 40 tumor-free controls. Villus-like changes and angular infolding, cytologic nuclear pleomorphism, distinct nuclear border, irregular thickness of the nuclear membrane, irregular chromatin clumping, prominent nucleoli, and distinct nucleoli were manifestations of the carcinoma group. Angular infolding, distinct nuclear border, irregular thickness of the nuclear membrane, and distinct nucleoli were also observed in the latent stage before detection of carcinoma. The individual features, however, lacked specificity. Histochemically, a IIB subtype of intestinal metaplasia, and immunoreactive CEA in the cytoplasm of foveolar epithelium appeared exclusively in the patients with carcinoma. These findings indicate that the gastric epithelium of patients with gastric carcinoma tends to be morphologically and histochemically abnormal even before the recognition of classical dysplasia. This can be described as abnormal epithelium and is believed to provide the soil on which gastric carcinoma develops.

Nagubandi, S., et al. (2019). "Standardized upper gastrointestinal screening questions in a bowel cancer screening clinic have a high clinical yield." Journal of Gastroenterology and Hepatology 34: 187-188.

Background and Aim: Colorectal cancer (CRC) is the second most common cause of cancer-related death in Australia. The National Bowel Cancer Screening Program (NBCSP) has been shown to reduce CRC morbidity and mortality. Participation in the NBCSP has been improved by the institution of streamlined direct access clinics. Patients attending these clinics are typically asymptomatic, but positive fecal occult blood test results are associated with higher rates of upper gastrointestinal pathology,1 and some patients may have high-risk upper gastrointestinal symptoms requiring investigation. It is not known what the yield of upper gastrointestinal endoscopy is in bowel cancer screening patients. We aimed to determine the rate of significant pathology and/or clinically significant management change in patients with upper gastrointestinal symptoms or risk factors using a standardized set of upper gastrointestinal screening questions in a nurse-led rapid access bowel cancer screening clinic. Methods: Patients referred to a nurse-led direct access clinic for fecal immunochemical test-positive bowel cancer screening were included. A clinic referral form included questions on iron deficiency anemia and weight loss. Patients were reviewed by a clinical nurse specialist (CNS) and scheduled for colonoscopy. Screening questions were asked according to a standardized pro forma. Questions covered reflux symptoms, dysphagia, weight loss, iron deficiency anemia, and family history of esophageal or gastric cancer. Patients with risk factors were scheduled for concurrent gastroscopy. The CNS delivered structured education on bowel preparation. A medical doctor reviewed and consented each patient. After endoscopy, rates of significant pathology were examined. Significant pathology was defined as esophagitis, Barrett's esophagus, esophageal cancer, intestinal metaplasia or dysplasia, gastric cancer, esophageal, gastric or duodenal ulceration, celiac disease, or other. Clinically significant management change was defined as the gastroscopy results affecting clinical advice for follow-up or resulting in a new diagnosis. Adverse events related to gastroscopy and colonoscopy (clinically significant bleeding, perforation, clinically significant sedation, or anesthesia adverse event) were assessed. Ethics approval for the studywasobtainedfrom the local health district human research ethics committee. Results: Atotal of679patients(median age, 63.1 years;mean, 62.4;SD,10.0; 51.1% male) were referred to the direct access clinic between June 1, 2016, and January 31, 2019. Eighty patients did not undergo endoscopy (39 arranged endoscopy elsewhere or declined, 20 had comorbidities, seven had recent colonoscopy, and 14 did not attend or were lost to follow-up). A total of 599 proceeded to endoscopy; 318 (51.9%) were asymptomatic or had rectal bleeding only. Overall, 27.5% had one or more predefined risk factors for upper gastrointestinal pathology (6.5% weight loss, 11.5% iron deficiency or iron deficiency anemia, 12.2% reflux symptoms, 4.5% dysphagia, and 5.0% family history of esophageal or gastric cancer). In total, 201 patients (33.6%) received simultaneous gastroscopy and colonoscopy. At least one clinically significant pathology was found in 47.8% of gastroscope procedures (esophagitis, 16.9%; Barrett's esophagus, 4.5%; esophageal cancer, 0; gastric intestinal metaplasia, 18.9%; gastric low-grade dysplasia, 0.5%; gastric cancer, 0; gastric submucosal lesions, 2.0%; esophageal, gastric or duodenal ulceration, 5.0%; and celiac disease, 1.0%). Clinically significant management change occurred in 27.3% (40.3% if including Helicobacter pylori treatment). Adverse events occurred in two patients undergoing colonoscopy alone and one patient undergoing gastroscopy and colonoscopy. Conclusion: Clinically relevant upper gastrointestinal pathology is common in patients with risk factors or high-risk symptoms who are referred to a bowel cancer screening direct access clinic. Nurse-administered screening questions for high-risk upper gastrointestinal symptoms resulted in a clinical management change in a significant proportion of patients.

Naidu, H., et al. (2016). "Retrospective analysis of gastric intestinal metaplasia and dysplasia in an ethnically diverse urban safety-net population." Gastroenterology 150(4): S864.

Introduction: Gastric intestinal metaplasia (GIM) has been established as a pre-cancerous lesion, which can develop into dysplasia and gastric cancer. Despite high global incidence of gastric cancer, there are no consensus guidelines for surveillance of GIM in the U.S. due to relatively low national prevalence. Given the increasing immigrant population from endemic areas in certain parts of the U.S., a standardized surveillance plan for cases of GIM may be useful especially in high risk populations. The aim of this study was to evaluate the prevalence of dysplasia among GIM in an ethnically diverse population and analyze surveillance strategies used in clinical practice. Methods: We performed an IRB-approved retrospective analysis of GIM cases from an ethnically diverse patient population at a single urban safety net hospital between 2004 and 2014. Using the pathology database, we identified all cases of GIM and those that progressed to gastric dysplasia. Cases of dysplasia were confirmed by two pathologists. Information on demographics, recommendations for follow-up, and subsequent EGDs were obtained from the medical record. Our primary outcome was to identify patients with development of gastric dysplasia in the follow-up surveillance of known GIM. We used descriptive statistics in our analysis. Results: 680 GIM cases and 24 dysplasia cases (3.5%; 11 men and 13 women) were identified over a 10 year period between 2004- 2014. Of the 24 dysplasia cases, 14 (54%) were categorized as resulting from GIM and 9 (62%) occurred in non-US born citizens (Haiti, Colombia, Dominican Republic, Puerto Rico, Albania, Congo, El Salvador). The most common ethnicities in the GIM-dysplasia group were Hispanic (42%), Caucasian (28%), Haitian (21%), and Black (14.2%). Mean age was 64, and only 1 patient was H. pylori positive in the dysplasia group. Repeat surveillance EGD was recommended in 8 of the 14 (57%) GIM-dysplasia cases, with intervals ranging from 1 to 12 months (median 3 months). Surveillance was performed at the planned interval in all cases when recommended. Of the 14 GIM-dysplasia cases, 3 (21%) progressed to invasive carcinoma. 2 of these cases were detected during diagnostic EGD and 1 occurred despite treatment with EMR and surveillance. Conclusion: Gastric intestinal metaplasia and resulting dysplasia may be more common in the U.S. than previously estimated, especially in areas with higher immigrant populations. Surprisingly, surveillance EGD for dysplasia seen in GIM was only recommended 57% of the time and recommendations ranged widely in terms of timing of next surveillance. This raises concern regarding inadequate surveillance of dysplasia in GIM, especially given the high rate (21%) of progression from dysplasia to gastric cancer. This also demonstrates the need for standardized GIM surveillance guidelines among high risk populations in the U.S.

Nakazawa, S., et al. (1977). "Gastric lesions in the aged on the clinical aspect. Gastric cancer (including gastric polyp)." Stomach and Intestine 12(5): 605-613.

80 cases of gastric cancer (50 patients in their sixties and 30 patients in their seventies) were selected by random sampling. A comparative study was made with 50 patients in their forties and 20 patients under the age of 30. Approximately half the gastric cancers in the aged involved the antrum showing marked intestinal metaplasia. The rate of gastric resection in the aged was rather low. The average follow-up period in non-resected cases was 26 months in the aged, but 2.5 months in the others. The follow-up period in different age groups in early gastric cancer, which could be resected after follow-up observation, was 50.3 months in patients over the age of 70, 32.2 in those in their sixties, 25.8 in those in their forties and 6 in those in their twenties. This suggests that in older patients the progress of gastric cancer is more gradual.

Navarro-Rodriguez, T., et al. (2015). "Diabetes and dislipidemia increase significantly the risk of gastric intestinal metaplasia: A prospective study." Gastroenterology 148(4): S566-S567.

Introduction: Chronic gastric inflammation and intestinal metaplasia (IM) are known risks for gastric cancer. Other risk factors have been recently linked to this type of neoplasia, one of these is diabetes. In order to better understand the relation between diabetes and gastric cancer, we have performed a cohort of dyspeptic patients. Patients and methods: Between 2010 and 2012, 399 patients with dyspeptic symptoms were submitted to an upper digestive endoscopy. Patients with chronic gastritis and/or IM, were enrolled in a repeated endoscopy protocol. Clinical commorbidities were registered. Results: Expressed in tables 1 and 2. Conclusions: Diabetes increases the risk of gastric intestinal metaplasia with an OR = 3.2 (table 1). When diabetes is associated with dislipidemia the risk is even higher OR = 7.2 (table 2). Our results identified a possible high risk population for gastric cancer. Patients with these clinical conditions should be carefully followed. (Table presented).

Nct (2006). "A Randomized Multi-Intervention Trial to Inhibit Precancerous Gastric Lesions in Lingu, Shandong Province." https://clinicaltrials.gov/show/NCT00339768.

Nct (2008). "Clarithromycin, Amoxicillin, and Metronidazole Based Regimens to Treat Helicobacter Pylori Infections in Colombia." https://clinicaltrials.gov/show/NCT00719420.

Nct (2012). "Confocal Laser Endomicroscopy for the Diagnosis of Gastric Intestinal Metaplasia, Intraepithelial Neoplasia, and Carcinoma." https://clinicaltrials.gov/show/NCT01642797.

Nct (2016). "Curcumin in Preventing Gastric Cancer in Patients With Chronic Atrophic Gastritis or Gastric Intestinal Metaplasia." https://clinicaltrials.gov/show/NCT02782949.

Nct (2020). "SUrveillance of PREMalignant Stomach - Individualized Endoscopic Follow-up." https://clinicaltrials.gov/show/NCT04613570.

Nebiki, H., et al. (2013). "Clinicopathological features of gastric cancer that developed 3 years or more after helicobacter pylori eradication." Gastroenterology 144(5): S326.

Background: A prospective, randomized trial showed that Helicobacter pylori (H. pylori ) eradication significantly reduced the incidence of metachronous gastric cancer in a 3-year follow-up (Fukase K, et.al. Lancet. 372(9636):392-7. 2008). However, gastric cancer can still develop 3 years or more after H. pylori eradication. Purpose: This study characterized the clinicopathological features of gastric cancer that developed 3 years or more after H. pylori eradication. Patients and methods: We investigated 20 patients in whom gastric cancer developed 3 years or more after H. pylori eradication at Osaka City General Hospital and Osaka City University Graduate School of Medicine. The histological change of the background gastric mucosa was investigated before H. pylori eradication and at the time of diagnosis of gastric cancer using the updated Sidney system. Results: Gastric cancer developed at a median of 5.6 years after H. pylori eradication. Indications for H. pylori eradication were gastric ulcer in 13 patients, gastric cancer in four patients, duodenal ulcer in two patients, and malignant lymphoma in one patient. The gastric cancer lesions were identified in the antrum (n = 11), corpus (n = 7) and fundus (n = 2) of the stomach. The histological types of gastric cancer were well-differentiated adenocarcinoma (n = 10), moderately differentiated adenocarcinoma (n = 8), and signet-ring cell carcinoma (n = 2). Fourteen patients were treated by endoscopic resection, and six patients were treated by gastrectomy. The activity score and inflammation score were significantly reduced when comparing values at the time of H. pylori eradication and values at the time of diagnosis of gastric cancer. The atrophy score when the gastric cancer developed was significantly reduced both at the antrum (1.75 ± 0.72 to 1.00 ± 0.89; p <0.05) and body (1.45 ± 0.99 to 0.60 ± 1.02; p <0.05) compared with that at the time of H. pylori eradication. The intestinal metaplasia score was not significantly reduced at the antrum (1.58 ± 1.11 to 1.00 ± 0.89; p = NS) and the body (1.18 ± 1.11 to 0.93 ± 1.06; p = NS ) . Conclusion: Gastric cancer can develop long after H. pylori eradication, despite reduction of gastric atrophy.

Nejad, P. A., et al. (2017). "Efficacy of PPI + ASA regimen versus PPI alone on the course of advanced gastritis: Preliminary results of a prospective randomized 5 years follow up study." Gastroenterology 152(5): S471.

Aim: to evaluate the efficacy of ASA + PPI regimen in comparison with PPI single therapy on the course of advanced gastritis and its progression toward early gastric cancer. Method: during a 5y period, every case of advanced gastritis based on pathology report including intestinal metaplasia, mucosal atrophy and or low grade dysplasia in a referral center included. All of the positive H Pylori cases obtained a course of eradication which confirmed by UBT. Then the participants randomly allocated to each groups of ASA 80mg + Pantoprazole 40mg (group A) or Pantoprazole 40mg alone (group B). The participants followed by every 6months to 1 year endoscopy and gastric mapping. The histologic changes among two groups and any potential progression toward more advanced stages determined and compared. Results: overall during a five years period, 61 cases of advanced gastritis included for preliminary analysis. The median age of participants was 47y (24-81) and 46% of them were male. The average duration of follow up was 19.2 months (8 To 60). Based on their first endoscopy and pathologic report 26 cases reported as incomplete intestinal metaplasia, 23 cases as complete intestinal metaplasia, 9 cases as mild atrophy beside intestinal metaplasia, 2 cases as moderate atrophy and one case reported as mild dysplasia. 54% of patients were H Pylori positive which received a course of H Pylori eradication at the beginning of study. 22 cases allocated to group A (ASA + PPI) and rest of participants treated with PPI alone (group B). During their follow up, overall 19 cases got improve based on pathology report which defined as complete resolution of intestinal metaplasia or changing from sever to mild. 15 cases belonged to group B (PPI alone) and 4 cases in group A (PPI + ASA) (P= 0.09). During this period, 3 cases encountered deterioration of intestinal metaplasia as changing from mild to sever or recurrence of intestinal metaplasia after previous resolution (2 in group A and 1 in group B). None of the cases evolved to gastric cancer or sever dysplasia during follow up. Conclusion: it seems that long term acid suppression with proton pomp inhibitor could be effective on the course of advanced gastritis and prevention of intestinal metaplasia aggravation but adding ASA to PPI have not any statistically significant positive effect.

Nguyen, T. H., et al. (2020). "Prevalence of Helicobacter pylori Positive Non-cardia Gastric Adenocarcinoma Is Low and Decreasing in a US Population." Digestive Diseases and Sciences 65(8): 2403-2411.

BACKGROUND: Helicobacter pylori infection is an established causal factor for non-cardia gastric cancer. H. pylori negative gastric cancer prevalence among US patients is unclear. METHODS: This retrospective cohort study examined H. pylori prevalence among consecutive patients with incident non-cardia gastric adenocarcinoma at the Houston VA Hospital (11/2007-10/2018). H. pylori positivity was defined by H. pylori on histopathology, positive antibody serology, stool antigen, or urea breath testing. We examined for trends in H. pylori negative gastric cancer based on year of diagnosis. Associations between histopathologic and cancer-related outcomes with H. pylori positivity were determined using regression models. RESULTS: Of 91 patients with gastric adenocarcinoma, most were men (N = 87, 95.6%), black (N = 47, 51.6%), with mean age at diagnosis of 68.0 years (SD 10.8). In addition to gastric cancer biopsy histopathology, 74 patients (81.3%) had ≥ 1 testing for H. pylori, including antibody serology (n = 34), non-cancer gastric biopsy histopathology (n = 63), or stool antigen (n = 1). The overall prevalence of H. pylori infection was 38.5% and 45.9% among patients with ≥ 2 H. pylori tests. The proportions of H. pylori positive gastric cancer decreased from 50.0% (2007-2010) to 43.4% (2011-2014) and 29.3% (2015-2018) (p = 0.096). Active/acute gastritis (adjOR 3.74), atrophic gastritis (adjOR 15.30), and gastric intestinal metaplasia (adjOR 3.65) were associated with H. pylori positive gastric cancer. DISCUSSION: The prevalence of H. pylori infection among patients with non-cardia gastric adenocarcinoma is relatively low (38.5-45.9%) and decreasing over time. This finding suggests there may be other important causal factors apart from H. pylori for gastric adenocarcinoma.

Nguyen, T. H., et al. (2020). "RISK PREDICTION MODEL FOR DETECTING GASTRIC INTESTINAL METAPLASIA IN U.S. VETERANS." Gastroenterology 158(6): S-785-S-786.

Background: Screening and surveillance of individuals at high risk for gastric intestinal metaplasia (GIM) may lead to the early detection of gastric cancer. However, identification of individuals at high risk of GIM in Western populations is difficult. We aimed to develop a risk prediction model based on demographic, clinical and lifestyle factors to aid in deciding which individuals to refer for endoscopic screening for GIM. Methods: We analyzed data from a cross-sectional study of patients attending primary care and endoscopy clinics at the Michael E. DeBakey VA Medical Center in Houston, Texas between 2/2008 and 8/2013. All patients completed standardized questionnaires and underwent endoscopy with gastric mapping biopsies (7 gastric sites). We defined cases as those with GIM on any non-cardia gastric biopsy. Controls were patients without GIM on all non-cardia gastric biopsies. We used multivariable logistic regression to estimate adjusted odds ratios (OR) and 95% confidence intervals (CI) for associations with risk of GIM. For the final model, we assessed its predictive accuracy in terms of discrimination using the area under the receiver operating characteristic curve (AUROC). We performed cross-validation using the Hosmer-Lemeshow test for goodness of fit and calibration plots. Finally, we compared the predictive ability of our comprehensive risk model with that of Helicobacter pylori infection alone. Results: We identified 423 cases with GIM and 1796 controls without GIM. The following variables were included in the risk prediction model: age (ref <60; 60-69.9: OR, 1.64; 95% CI, 1.27-2.12; ≥70: OR, 2.22; 95% CI, 1.54-3.21), male sex (OR, 2.58; 95% CI, 1.39-4.79), race/ethnicity (ref White; Hispanic: OR, 2.18; 95% CI, 1.53-3.11; African-American: OR, 1.79; 95% CI, 1.39-2.31), smoking status (former smoker: OR, 1.36; 95% CI, 1.00-1.84; current smoker: OR, 1.94; 95% CI, 1.41-2.68), and H. pylori infection (OR, 3.44; 95% CI, 2.72-4.35). The AUROC was 0.73 (95% CI, 0.70-0.75). There was little evidence for over-fitting as the AUROC was not dissimilar to the derivation cohort (cross-validation AUROC, 0.71; 95% CI, 0.68-0.74; p<0.001). Risk prediction with H. pylori infection, age, sex, race/ethnicity, and smoking status was better than that achieved by using only H. pylori infection (AUROC, 0.65; 95% CI, 0.63-0.68; p<0.001; Figure 1). Conclusion: Based on data from a large cross-sectional study among U.S. Veterans, a risk prediction model containing age, sex, race/ethnicity, smoking status, and H. pylori infection may be an effective method to identify individuals at high risk of GIM who would benefit from surveillance for gastric cancer and performs better than H. pylori infection alone as a predictor. External validation of this model is required.

Nieminen, A., et al. (2015). "Long-term gastric cancer risk in smoking men with atrophic gastritis." United European Gastroenterology Journal 3(5): A296.

Introduction: The incidence of gastric cancer has declined dramatically during last decades in western countries. In Finland, the age-standardized incidence being 6.3 / 100 000 for men and 3.6 / 100 000 for women 1. Because of the low incidence, screening programs are not considered effective in the West. Early gastric cancer rarely causes symptoms, and, thus majority of gastric cancers are diagnosed in advanced, symptomatic stage. Atrophic gastritis in the best known premalignant condition of gastric cancer, and it has been suggested that persons who have extensive atrophic changes in stomach should undergo surveillance. Aims & Methods: Our aim was to evaluate the long-term gastric cancer risk in smoking men with atrophic gastritis. Serum pepsinogens (SPGs) were measured from 22,436 smoking men (age 50-69 years) who participated The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study in Finland 2-3. Low serum pepsinogen I (SPGI) was measured in 2132 men, and they were invited to gastroscopy 4. Endoscopy was performed to 1344 men, and after excluding the men with gastric cancer in a beginning of study, 1326 men were enrolled in this study. The first gastroscopies were performed between years 1989-1993, and the surveillance continued until the end of year 2012, the gastric cancer diagnosis, or the death. The median follow-up time was 13.6 years (range 16 days - 23.3 years). Thirty three gastric cancers were diagnosed during the follow-up period. Results: Most of the men (80.2%) had atrophic gastritis of some degree in the histological samples of the corpus (mild 11.4%, moderate 41.7%, marked 27.1%). Atrophic gastritis of the antrum was found only in 34.0% of the subjects. Mild to marked intestinal metaplasia appeared in 66.5% patients in corpus and 40.1% in antrum. The gastric cancer incidence was 1.89 / 1000 patient-years. The incidence of gastric cancer increased as the grade of the atrophy of the corpus mucosa increased: 1.54/1000, 1.77/1000, and 2.05/1000 in mild, moderate, and severe mucosal corpus atrophy, respectively. In the antrum mucosa, the effect of the degree of the atrophy had similar effect on the gastric cancer incidence: 2.16/ 1000, 2.21/1000, and 3.44/1000 in mild, moderate, and severe atrophy. The gastric cancer incidence was 1.35/1000, 2.27/1000, and 2.84/1000 in mild, moderate, and severe corpus intestinal metaplasia (IM), respectively. In the antrum, the incidence of gastric cancer was 1.87/1000, 2.23/1000, and 3.99/ 1000, in mild, moderate, and severe IM, respectively. Conclusion: The risk of gastric cancer increased as the grade of the mucosal atrophy and intestinal metaplasia increased. The risk of gastric cancer seems to be within limits of previous publications (0.1-0.2% person years).

Nieminen, A., et al. (2015). "OLGA and OLGIM staging systems in men with atrophic gastritis." United European Gastroenterology Journal 3(5): A296-A297.

Introduction: Intestinal type of gastric cancer develops through precancerous changes, but minority of these changes progress to cancer. Endoscopical surveillance is allocated for patients with extensive gastric atrophy or intestinal metaplasia. To target endoscopy for high-risk patients, two staging systems (Operative Link for Gastritis Assessment [OLGA]1 and Operative Link on Gastric Intestinal Metaplasia Assessment [OLGIM]2) have been created. The focus is on severity and topography of atrophy and intestinal metaplasia. Aims & Methods: In our scope was to investigate the predictive value of OLGA and OLGIM staging systems in smoking males with atrophic gastritis. Serum pepsinogens (SPGs) were measured from 22,436 smoking men, aged 50-69 years, who participated The Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study 3 in Finland. Low serum pepsinogen I (SPGI) was measured in 2132 men, and they were invited to gastroscopy 4. Endoscopy was performed to 1344 men, and after excluding the men with gastric cancer in a beginning of study and 180 men with history of gastric surgery by benign cause, 1146 men were enrolled in this study. The first gastroscopies were performed between years 1989-1993, and the surveillance continued until the end of year 2012, the gastric cancer diagnosis, or the death. The median follow-up time was 13.7 years (range 16 days - 23.3 years). Twenty seven gastric cancers were diagnosed during the follow-up period. Results: Gastric cancers (n=27) distributed by OLGA stages following: 1, 3, 17, 1, and 5 (stages 0-IV, respectively), and OLGIM stages: 2, 7, 10, 4, and 4 (stages 0-IV, respectively). By OLGIM staging system, gastric cancer risk elevated with stages (p=0.02). The trend was not as distinct with OLGA staging (p=0.10). Three gastric cancers developed to patients with OLGA / OLGIM stage 0, and histological type was known in only one of these patients, who had diffuse type of cancer. Conclusion: Interobserver agreement is excellent with intestinal metaplasia, but weaker with atrophy and dysplasia 2,5. Also in our study, OLGIM was more sensitive to predict gastric cancer risk over OLGA. Histological type can confound the interpretation, as cancerous cascade with atrophy and intestinal metaplasia are illustrated with intestinal, not diffuse, type of gastric cancer.

Nieminen, A. A., et al. (2019). "Long-term gastric cancer risk in male smokers with atrophic corpus gastritis." Scandinavian Journal of Gastroenterology 54(2): 145-151.

OBJECTIVES: The aim of this study was to evaluate long-term gastric cancer risk in male smokers with and without atrophic gastritis. MATERIALS AND METHODS: A total of 22,346 elderly male smokers participated in the Helsinki Gastritis Study between the years 1989 and 1993. Serum pepsinogen I (PGI) was measured for the men, and 2,132 men with low PGI (<25 µg/L; a marker of atrophic corpus gastritis) were invited to undergo gastroscopy because of increased gastric cancer risk. Endoscopy was performed to 1,327 men, who were followed up for a median of 13.6 years and a maximum of 25.3 years thereafter. In addition, the gastric cancer risk of men with low PGI was compared to that of the men with normal PGI and to the general Finnish male population of the same age. RESULTS: Thirty-five cases of gastric cancer were diagnosed in men with gastroscopy during the follow-up. The incidence rate was 1.94 per 1000 patient years. The men with a history of gastric surgery (n = 180) due to a benign cause had even higher gastric cancer incidence (3.2 per 1000 patient-years). Gastric cancer risk was highest in men with marked intestinal metaplasia in primary biopsies. Compared to the general Finnish male population of the same age, the cancer risk was 1.13 times higher in male smokers with normal serum PGI, and 2.43 times higher in men with low serum PGI. CONCLUSION: In male smokers, atrophic gastritis and intestinal metaplasia increase the risk of gastric cancer.

Nieminen, A. A., et al. (2020). "Comparison of operative link for gastritis assessment, operative link on gastric intestinal metaplasia assessment, and TAIM stagings among men with atrophic gastritis." World Journal of Gastroenterology 26(24): 3447-3457.

BACKGROUND: Gastric cancer is the world's third most lethal malignancy. Most gastric cancers develop through precancerous states of atrophic gastritis and intestinal metaplasia. Two staging systems, operative link for gastritis assessment (OLGA) and operative link on gastric intestinal metaplasia assessment (OLGIM), have been developed to detect high gastric cancer risk. European guidelines recommend surveillance for high-risk OLGA/OLGIM patients (stages III-IV), and for those with advanced stage of atrophic gastritis in the whole stomach mucosa. We hypothesize, that by combining atrophy and intestinal metaplasia into one staging named TAIM, more patients with increased gastric cancer risk could be detected. AIM: To evaluate the clinical value of the OLGA, OLGIM, and novel TAIM stagings as prognostic indicators for gastric cancer. METHODS: In the Helsinki Gastritis Study, 22346 elderly male smokers from southwestern Finland were screened for serum pepsinogen I (PGI). Between the years 1989 and 1993, men with low PGI values (PGI < 25 μg/L), were invited to undergo an oesophagogastroduodenoscopy. In this retrospective cohort study, 1147 men that underwent gastroscopy were followed for gastric cancer for a median of 13.7 years, and a maximum of 27.3 years. We developed a new staging system, TAIM, by combining the topography with the severity of atrophy or intestinal metaplasia in gastric biopsies. In TAIM staging, the gastric cancer risk is classified as low or high. RESULTS: Twenty-eight gastric cancers were diagnosed during the follow-up, and the incidence rate was 1.72 per 1000 patient-years. The cancer risk associated positively with TAIM [Hazard ratio (HR) 2.70, 95%CI: 1.09-6.69, P = 0.03]. The risk increased through OLGIM stages 0-IV (0 vs IV: HR 5.72, 95%CI: 1.03-31.77, P for trend = 0.004), but not through OLGA stages 0-IV (0 vs IV: HR 5.77, 95%CI: 0.67-49.77, P for trend = 0.10). The sensitivities of OLGA and OLGIM stages III-IV were low, 21% and 32%, respectively, whereas that of TAIM high-risk was good, 79%. On the contrary, OLGA and OLGIM had high specificity, 85% and 81%, respectively, but TAIM showed low specificity, 42%. In all three staging systems, the high-risk men had three- to four-times higher gastric cancer risk compared to the general male population of the same age. CONCLUSION: OLGIM and TAIM stagings show prognostic value in assessing gastric cancer risk in elderly male smokers with atrophic gastritis.

Nieuwenburg, S. A., et al. (2019). "FACTORS ASSOCIATED WITH THE PROGRESSION OF GASTRIC INTESTINAL METAPLASIA IN A LOW RISK POPULATION - A MULTICENTER, PROSPECTIVE COHORT STUDY." Gastroenterology 156(6): S-21-S-22.

Background Gastric cancer (GC) is the third cause of cancer-related death worldwide. GC is preceded by gastric precursor lesions (GPL) often initiated by Helicobacter pylori (Hp) infection. These GPL make GC suitable for surveillance. Especially in low risk GC areas the method and frequency of endoscopic surveillance is still under debate. Identifying patients at risk for progression of GPL could help to prevent patients to undergo unnecessary endoscopies. Serology markers such as pepsinogens (PG) and gastrin-17 were previously described as a discriminative factor for severity of lesions. This study aims to investigate if patient characteristics and serology at baseline could be used to predict progression of GPL in low risk areas. Methods The PROREGAL study (PROgression and REgression of precancerous GAstric Lesions) started in 2009 and is one of the largest ongoing prospective cohorts in the Western world. It is performed in 7 hospital: in the Netherlands and Norway. Inclusion criteria are: 1) >18 years of age, 2) previous diagnosis of atrophic gastritis, intestinal metaplasia (IM) and/or dysplasia of the gastric mucosa. All patients completed a questionnaire on lifestyle factors and underwent at least one surveillance endoscopy after the index endoscopy. Biopsies were obtained from visible lesions and from 12 standardised sites in corpus and antrum. All were assessed according to the operative link on gastric intestinal metaplasia (OLGIM) system. At baseline, PG and gastrin-17 samples were drawn. Progression of IM was defined as progression of the OLGIM classification between any follow-up (FU) endoscopy. Potential risk factors (RF) for progression were analysed by cox-regression with a significance level of 0.05. Analyses were performed in IBM SPSS v.24. Results 308 patients (median age 61 years, IQR17; male 48.4%) were included. Median FU time was 48 months (IQR 24). During FU 116 patients showed progression of OLGIM stage (37.7%) providing an incidence rate of 9 events/100 personyears (95%CI 8.8-9.2). Six patients (1.9%) developed gastric carcinoma (0.4 events/100 personyears (95%CI 0.002-0.01)). History of Hp-infection, smoking, alcohol use and increased BMI were not significantly associated with IM progression. Also serum levels of PG I/II, and gastrin-17 at baseline were not significantly correlated with progression of IM (Fig. 1). Conclusion This is the first study to assess potential risk factors for progression of IM in a low risk area. Over 1/3 of the study cohort showed progression of IM, indicating surveillance remains of importance. Lifestyle factors were not correlated with progression of IM. Moreover, baseline serum markers are not predictive for future progression of IM. Further study should focus on the longitudinal assessment of serology markers during FU. This research was funded by the UEG Research Prize awarded to EJK. [Figure Presented]

Nieuwenburg, S. A. V., et al. (2019). "Risk factors for the progression of gastric intestinal metaplasia in a low risk population: A multicenter, prospective, cohort study." United European Gastroenterology Journal 7(8): 25-26.

Introduction: Gastric cancer (GC) is mostly preceded by gastric precursor lesions (GPL). The recently updated MAPS guideline for surveillance of GPL now includes the recommendation for surveillance in case of a positive family history for GC. However, the evidence for this recommendation and our tools to identify patients at risk for progression are still scarce. This study therefore aimed to investigate if risk factors such as family history, lifestyle, genetic polymorphisms, and serology at baseline are possible predictors for progression of GPL in low risk areas. Aims & Methods: Patients with GPL were included in the PROREGAL study; a multicenter, prospective cohort study. At upper endoscopy biopsies were obtained from 12 standardised sites in the stomach and from visible lesions. These were histologically assessed according to the operative link on gastric intestinal metaplasia (OLGIM) system. At baseline, patients completed a questionnaire on family history and lifestyle factors, and fastening blood samples were taken for pepsinogen and gastrin-17. All patients underwent at least two upper endoscopies. Progression of intestinal metaplasia (IM) was defined as progression of OLGIM classification between follow-up (FU) endoscopies. Previously associated single nucleotide polymorphisms (SNPs) with H. pylori infection or GC were determined using polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP): NCF4 (rs4821544), TLR1 (rs28393318), TLR4 (rs11536889) and ATG16L1 (rs2241880). Cox-regression was performed for analysis on risk factors. Differences in proportions for the presence of SNPs were calculated using z-test. For all tests a significance level of 0.05 was used. Results: 308 patients (median age 61 years, IQR 17;male 48.4%) were included. Median FU was 48 months (IQR 24). During FU 116 (37.7%) patients showed progression of their OLGIM status and six patients (1.9%) developed high grade dysplasia or GC. Family history (HR 1.4; p=0.154), smoking (HR 1.3; p=0.260), and history of Hp-infection (HR 1.1; p=0.684) were associated with non-significant risks for progression. Alcohol use (HR 0.8; p=0.428), serum levels of PG I/II (HR1.0; p=0.446) and gastrin-17 (HR 1.0; p=0.908) were not associated with an increased progression risk. The minor allele (C) on the TLR4 (rs11536889) was negatively associated with progression (OR 0.4; p< 0.001), while the minor allele (G) in the ATG16L1 (rs2241880) was positively associated with progression (OR 1.5; p=0.001). Conclusion: This is the first study to assess potential risk factors for the progression of IM in a low risk area. Over one third of patients showed progression of IM during surveillance. We did not find any significant risk factors for progression. However, SNPs in TLR4 and ATG16L1 showed significant associations with progression of IM, suggesting that genetic risk stratification may contribute to the identification of patients eligible for surveillance.

Nieuwenburg, S. A. V., et al. (2021). "Factors associated with the progression of gastric intestinal metaplasia: a multicenter, prospective cohort study." Endosc Int Open 9(3): E297-e305.

Background and study aims  Gastric cancer (GC) is usually preceded by premalignant gastric lesions (GPLs) such as gastric intestinal metaplasia (GIM). Information on risk factors associated with neoplastic progression of GIM are scarce. This study aimed to identify predictors for progression of GIM in areas with low GC incidence. Patients and methods  The Progression and Regression of Precancerous Gastric Lesions (PROREGAL) study includes patients with GPL. Patients underwent at least two upper endoscopies with random biopsy sampling. Progression of GIM means an increase in severity according to OLGIM (operative link on gastric intestinal metaplasia) during follow-up (FU). Family history and lifestyle factors were determined through questionnaires. Serum Helicobacter pylori infection, pepsinogens (PG), gastrin-17 and GC-associated single nucleotide polymorphisms (SNPs) were determined. Cox regression was performed for risk analysis and a chi-squared test for analysis of single nucleotide polymorphisms. Results  Three hundred and eight patients (median age at inclusion 61 years, interquartile range (IQR: 17; male 48.4 %; median FU 48 months, IQR: 24) were included. During FU, 116 patients (37.7 %) showed progression of IM and six patients (1.9 %) developed high-grade dysplasia or GC. The minor allele (C) on TLR4 (rs11536889) was inversely associated with progression of GIM (OR 0.6; 95 %CI 0.4-1.0). Family history (HR 1.5; 95 %CI 0.9-2.4) and smoking (HR 1.6; 95 %CI 0.9-2.7) showed trends towards progression of GIM. Alcohol use, body mass index, history of H. pylori infection, and serological markers were not associated with progression. Conclusions  Family history and smoking appear to be related to an increased risk of GIM progression in low GC incidence countries. TLR4 (rs11536889) showed a significant inverse association, suggesting that genetic information may play a role in GIM progression.

Nieuwenburg, S. A. V., et al. (2019). "Factors associated with the progression of gastric intestinal metaplasia in a low risk population-a multicenter, prospective cohort study." Endoscopy 51(4): S21.

Aims: Gastric cancer (GC) is preceded by several gastric precursor lesions (GPL) which makes it suitable for surveillance. For low risk areas method and frequency of endoscopic surveillance is still under debate. This study aims to identify high and low risk subjects for progression of GPL to prevent unnecessary performed endoscopies. Patient characteristics and previously described discriminative serum markers at baseline (pepsinogens (PG) and gastrin-17) are assessed to predict progression of PGL. Methods: The PROREGAL study started in 2009 and is one of the largest prospective cohorts in the Netherlands and Norway. Inclusion: 1) > 18 years of age, 2) previous diagnosis of GPL. Patients completed a questionnaire on lifestyle factors and underwent at least two endoscopies. Biopsies were obtained from visible lesions and 12 standardised stomach sites and assessed according to the operative link on gastric intestinal metaplasia (OLGIM) system. At baseline, PG and gastrin-17 samples were drawn. Progression of IM was defined as progression of OLGIM classification between follow-up (FU) endoscopy. Cox-regression was performed with a significance level of 0.05. Results: 308 patients (median age 61 years, IQR17;male 48.4%) were included. Median FU time was 48 months (IQR 24). During FU 116 patients showed progression of OLGIM stage (37.7%) providing an incidence rate of 9 events/100 personyears (95% CI 8.8 - 9.2). Six patients (1.9%) developed GC (0.4 events/100 personyears (95% CI 0.002 - 0.01)). History of Hp-infection, smoking, alcohol use and increased BMI did not show significant associations. Also serum levels of PG I/II, and gastrin-17 were not significantly correlated with progression of IM. Conclusions: This is the first study to assess RF for the progression of IM in low risk areas. Lifestyle factors were not correlated with progression of IM. Moreover, baseline serum markers are not predictive for future progression of IM during FU. Future studies should focus on the longitudinal assessment of these markers.

Noh, G., et al. (2019). "The long-term follow-up of serum pepsinogens in patient with gastric cancer and dysplasia after Helicobacter pylori eradication." United European Gastroenterology Journal 7(8): 734-735.

Introduction: Recently we have shown reversibility of atrophic gastritis and intestinal metaplasia after Helicobacter pylori eradication up to 10-year follow-up study. Only a few studies have evaluated pepsinogen (PG) change after eradication of H. pylori but there was no study regarding this issue in patients with gastric cancer (GC) and dysplasia. Aims & Methods: The aim of this study is to evaluate the effect of H. pylori eradication on PG in GC and dysplasia patients in comparison to control group with a long-term follow-up. From March 2003 to February 2019, we prospectively enrolled 368 subjects with GC and dysplasia and 610 subjects with non-GC and non-dysplasia as control group. All of GC and dysplasia patients were treated by enodoscopic mucosal resection or submucosal dissection. H. pylori tests (Giemsa stain, CLOtest and culture) were performed to evaluate HP status. Serum PG levels were measured using a Latex-enhanced Turbidimetric Immunoassay (Shima Laboratories, Tokyo, Japan) before and after eradication, compared by using linear mixed model and student's t-test. The follow-up points were classified as 1-11 months, 12-23 months, 24-35 months and more than 36 months. Results: Among 368 GC/dysplasia patients, 102 (27.7%) were H. pylori-negative, 179 (48.6%) were H. pylori-eradicated, and 87 (23.7%) were H. pylori non-eradicated/eradication failure. Among 610 control group patients, 373 (61.1%) were H. pylori-negative, 168 (27.6%) were H. pylori-eradicated, and 69 (11.3%) were H. pylori non-eradicated/eradication failure. In GC/dysplasia there were not significantly different in PG values in H. pylori-negative and H. pylori non-eradicated/eradication failure group at all follow-up points compared to those at baseline (Table). In contrast H. pylori-eradicated group of GC/dysplasia mean serum PG I (55.7 vs. 41.0, p< 0.001) became significantly lower and mean PG I/II ratio (2.80 vs. 4.04, p< 0.001) became higher at 1-11 months after eradication compared to those at baseline (Table). This improvement of PG values after eradication maintained during all follow-up points with no significant differences between H. pylori-eradicated and H. pylori-negative group. However, mean serum PG II did not show any change in both of control or GC/dysplasia group. Control group showed similar tendency to the GC/ dysplasia (Table). Between the control and GC/dysplasia groups significant difference in mean serum PG I and mean PG I/II ratio were observed at 1-11 months (PG I: 41.0 vs. 64.0, p<0.001, PG I/II ratio: 4.04 vs. 5.99, p<0.001) and 12-23 months (PG I: 40.3 vs. 55.2, p = 0.01, PG I/II ratio: 4.38 vs. 5.38, p = 0.001) after eradication. These differences disappeared from ≥ 24 months of follow-up Conclusion: Considering the PG I and PG I/II ratio of GC/dysplasia group become similar to those of control group at the long-term follow-up after eradication, H. pylori eradication plays an important role in the prevention of metachronous cancer/dysplasia development.(Table Presented).

Noh, G., et al. (2020). "Long-term follow up of serum pepsinogens in patients with gastric cancer or dysplasia after Helicobacter pylori eradication." Journal of Gastroenterology and Hepatology 35(9): 1540-1548.

BACKGROUND AND AIM: Few studies have evaluated the change in serum pepsinogen (sPG) levels after the eradication of Helicobacter pylori. The aim of this study was to evaluate the effect of H. pylori eradication on sPG levels in patients with gastric cancer/dysplasia in comparison to a control group. METHODS: We prospectively enrolled 368 patients with gastric cancer/dysplasia and 610 control subjects. H. pylori status and sPG levels were measured before and after eradication. The follow-up time points were classified as < 12, 12-23, 24-35, and ≥ 36 months. RESULTS: In 179 H. pylori-eradicated patients with gastric cancer/dysplasia and 168 control group subjects, sPG I significantly decreased, and the sPG I/II ratio significantly increased after eradication compared to baseline, and this improvement in sPG values was maintained during all follow-up time points. Significant differences in sPG I and the sPG I/II ratio were observed between the gastric cancer/dysplasia group and the control group < 24 months after eradication. However, these differences in sPG values disappeared after ≥ 24 months of follow up. Moreover, significant differences in the intestinal metaplasia grade were observed between these two groups before eradication until < 24 months after eradication. However, these differences in the intestinal metaplasia grade disappeared after ≥ 24 months of follow up in the corpus. CONCLUSION: The sPG values and intestinal metaplasia grade (corpus) in the gastric cancer/dysplasia group became similar to those in the control group at long-term follow up after H. pylori eradication. It might be related with the reduction of metachronous gastric neoplasm.

Novis, B. H. and D. G. Burns (1982). "Adenocarcinoma at the site of a healed gastric ulcer after 10 years of endoscopic observations." American Journal of Gastroenterology 77(2): 99-100.

An adenocarcinoma developed in a 52-yr-old man during the course of a 10-yr gastroscopic and biopsy follow-up of a benign gastric ulcer that had remained healed for over 7 yr after a recurrence of the initially healed lesion. Histologically the lesion was an early gastric carcinoma of the intestinal type, with the rest of the mucosa showing an element of intestinal metaplasia and chronic gastritis. Development of a carcinoma in the healed scar of a benign gastric ulcer is rare; however, patients with healed gastric ulcers should be followed up endoscopically.

O’Connor, A., et al. (2020). "Risk of Progression of Gastric Intestinal Metaplasia Is Significantly Greater When Detected in Both Antrum and Body." Digestive Diseases and Sciences.

Background: Gastric cancer (GC) is the fifth leading cause of cancer-related death worldwide. GC is usually preceded by a cascade of well-defined precursor lesions, set in place by an environmental trigger (H. pylori) including intestinal metaplasia (GIM) and dysplasia. Aims: To investigate the rates of progression of GIM to dysplasia and GC in a region of low gastric cancer incidence. Methods: We identified all patients diagnosed with GIM between January 1, 2008, and June 30, 2012. Any repeat upper endoscopy more than 1 year after index diagnosis and before December 31, 2018, was considered follow-up. Carcinomas the bulk of which were macroscopically located below the OGJ were considered primary gastric cancer. Results: Progression to more advanced lesions was observed in six patients (0.6%). Four patients (three male) developed GC at median age 74 years (SD 6). Two patients progressed to dysplasia (one male) at median age 71 years (SD 4). Patients with GIM in both gastric antrum and body were significantly more likely to progress than those with GIM in only one location (3.1% vs. 0.4%) (p value 0.017). Fifty-eight patients who had H. pylori eradicated were followed up. No progression to dysplasia or GC was noted in this group, with 28 patients having persistent GIM at follow-up. Conclusion: Patients with GIM in both antrum and body had a significantly increased risk of progression and warrant close attention. This is comparable to routinely followed premalignant conditions such as Barrett’s esophagus and Colonic Polyps, and appropriate surveillance protocols should be followed in this group.

O'Connor, A., et al. (2011). "Departmental attitudes for the awareness and prevention of gastric cancer prevent missed diagnoses." Helicobacter 16: 92-93.

Introduction: Missed and new gastric cancers occurring after oesophago-gastroduodenoscopies (OGD) are reportedly frequent. Our endoscopy department employs a “triple-lock” strategy for the prevention of gastric cancer with three principles. 1 Biopsies are taken at every OGD for rapid urease testing and at least two for histology. 2 H. pylori is treated when found and eradication confirmed. 3 Premalignant lesions such as intestinal metaplasia are followed up with repeat OGD. Aims and Methods: We aimed to identify if instituting policies aimed at the detection and prevention of gastric cancers was efficacious. We examined all cases of gastric cancer identified in the region in a 5 year period and cross-checked to see how many of these patients had passed through the endoscopy unit in the 7 years before their cancer diagnosis and examined their diagnoses and management from first point of contact. Results: Thirty-three thousand five hundred and fifty-nine OGDs were done between 1998 and 2009. Between 2005 and 2009 193,24 OGD were performed and 46 cases of gastric cancer were detected. Of these, five (10.87%) had had a previous OGD. In four cases the diagnoses were found in asymptomatic patients undergoing surveillance for premalignant lesions. In the other case the patient had been diagnosed with H. pylori infection and intestinal metaplasia but defaulted follow-up and was re-referred with symptoms. All five patients remain alive with a mean time since diagnosis of 3.16 years. Conclusion: Endoscopy units offer excellent opportunities for gastric cancer prevention. Institutional policies fpr gastric cancer prevention reduced missed cancers and can lead to early diagnosis and favourable outcomes in those developing neoplasia.

O'Connor, A., et al. (2011). "Surveillance of gastric intestinal metaplasia leads to earlier stage diagnosis of gastric adenocarcinoma." Helicobacter 16: 92.

Introduction: Gastric cancer is the end result of a series of mutations begun in early life. During the precancerous phase, histological changes takes place from chronic gastritis to intestinal metaplasia (IM), dysplasia and cancer. It is unknown whether endoscopic surveillance of intestinal metaplasia is worthwhile in low prevalence populations. Adelaide and Meath Hospital serves a population of 350,000 which performs approximately 4000 Oesophago-gastro-duodenoscopies (OGD) per year. All patients with IM are offered follow-up. Aims and Methods: We examined all cases of gastric cancer diagnosed between 2005 and 2009 and identified how many were diagnosed having undergone surveillance for IM. Results: There were 46 diagnoses of cancer during the timeframe. 8.7% (n = 4, 95% CI 3.43% > 20.32%) of these occurred in patients with previous diagnosis of IM, three of whom were having endoscopic surveillance. 69.56% (n = 32, 95% CI 55.19% > 80.92%) of all cancers were gastric adenocarcinoma. In two cases of adenocarcinoma patients were asymptomatic and had their tumours found by scheduled surveillance endoscopy. Both of these patients had T1N0M0 lesions. This is compared to 14.28% of the gastric adenocarcinomata that were not in patients with identified previous premalignant lesions were T1N0M0 (p-value = .0302). The patient with a history of IM not under surveillance (focal IM) was symptomatic and had been re-referred after defaulting to follow-up. This patient had a T2N1M0 adenocarcinoma. A fourth patient with IM under surveillance was found to have a non-MALT gastric lymphoma (focal IM). Conclusion: This study shows an encouraging trend towards earlier diagnosis of malignancy in patients with gastric intestinal metaplasia who undergo surveillance OGD.

O'Connor, A., et al. (2012). "Age, smoking, male gender and regular aspirin use predict premalignant conditions of the stomach in a low gastric cancer prevalence cohort." Gastroenterology 142(5): S633.

INTRODUCTION: Adenocarcinoma of the stomach is the second leading cause of cancer related death in the world. It causes approximately 750,000 deaths on an annual basis worldwide. Prevalence of gastric cancer is lower in western European countries but still carries a significant disease burden. Gastric Intestinal metaplasia (GIM) is a recognised premalignant condition of the stomach which results from gastric stem cells that are diverted from proliferation into cells specific to the stomach towards those of the small intestine. It is usually caused by chronic inflammation of the stomach, often induced by H. pylori. AIMS & METHODS: We aimed to assess the prevalence of premalignant lesions of the stomach in our western european population at a university teaching hospital and identify factors which may be associated with the conditions. Biopsies were taken from the cardia, fundus, corpus, incisura and antrum of 160 consecutive patients presenting for gastroscopy. Clinical information was obtained at clinical examination and direct interview. P-values were calculated using fisher's exact test. RESULTS: 52.5% of patients undergoing biopsy were female (N=84). GIM was found in 22.5% (N=36) of patients. The median age of patients with GIM was 68.5 years compared to 53 years in those without IM. 31.6% (N=24) of males had GIM compared to 14.3% (N=13) of females (p=0.01). There was no difference in BMI between the two groups. 11.1% (N=6) of those who never smoked had GIM compared to 29.2% (N=31) of past or current habitual smokers (p=0.01). Regarding drug use, 13.9% (N=5) of patients with IM were NSAID users compared to 21% (N=26) of those without (p=0.4735). 44.4% (N=16) of patients with IM were Aspirin users compared to 14.5% (N=18) of those without (p=0.0003). 44.4% (N=16) of patients with IM were PPI users compared to 58.8% (N=73) of those without (p=0.1328). Rates of GIM in Aspirin users under the age of 65 were not statistically different from those over 65% (42.9% vs 47.4%)(p=1.000). H. pylori was observed in 27% (N=10) of patients with GIM compared to 17.7% (N=22) of patients without (p=0.2357). 61.5% (N=8) of male smokers taking aspirin were observed to have GIM. CONCLUSION: Premalignant lesions of the stomach are common and may be clinically significant. Older males are at greatest risk. Smoking is an important modifiable risk factor. The association with Aspirin use may be confounded by age. Awareness of risk factors such as age, gender, smoking history and medication history may identify patients at greatest risk who may benefit from more extensive biopsy sampling and surveillance if necessary.

Offerhaus, G. J. A., et al. (1989). "The mucosa of the gastric remnant harboring malignancy. Histologic findings in the biopsy specimens of 504 asymptomatic patients 15 to 46 years after partial gastrectomy with emphasis on nonmalignant lesions." Cancer 64(3): 698-703.

Endoscopic bioptic screening of 504 asymptomatic postgastrectomy patients, 15 to 46 years after initial surgery, revealed ten gastric stump cancers of which six turned out to be early cancers; three of the early carcinomas were found during follow-up after prior severe dysplasia. At first endoscopy mild dysplasia was found in 58, moderate dysplasia in 11, and severe dysplasia in none of the patients. Follow-up biopsies in 177 patients showed mild dysplasia in 30, moderate dysplasia in six, and severe dysplasia in six patients. Regression of severe dysplasia was not observed. Both progression and regression of mild and moderate dysplasia occurred. At the first endoscopy the frequency of atrophy, intestinal metaplasia, cystic dilatation of glands, and foveolar hyperplasia in the stomal biopsy specimens was 45%, 35%, 54%, and 47%, respectively; during follow-up, 47%, 48%, 56%, and 56% respectively. These four lesions were significantly more frequent in the biopsy specimens of patients with gastric carcinoma or dysplasia than in the other patients and they were present in the environment of the tumor in all the surgical specimens of the six early cancers detected by the screening. Preoperatively a combination of these four lesions could be demonstrated in only those early gastric cancer patients, in whom more than eight stomal biopsy specimens were taken. Of 34 patients with severe atrophy in three or more stomal biopsy specimens taken at the same time, two manifested early stump cancer during follow-up. Severe dysplasia is a marker of malignancy and demands close follow-up; the value of mild and moderate dysplasia is less clear. The combination of atrophy, especially severe atrophy, intestinal metaplasia, cystic dilatation, and foveolar hyperplasia in the biopsy specimens of a single patient may also point to increased cancer risk. It is advisable to obtain multiple biopsy specimens of the anastomosis, also because early gastric cancer may occur without a suspect macroscopic appearance.

Oh, S., et al. (2013). "Risk factors of atrophic gastritis and intestinal metaplasia in first-degree relatives of gastric cancer patients compared with age-sex matched controls." J Cancer Prev 18(2): 149-160.

BACKGROUND: To identify whether first-degree relatives (FDRs) of gastric cancer (GC) patients have increased risk for atrophic gastritis (AG) and intestinal metaplasia (IM) in relation to other risk factors of GC. METHODS: The study cohort consisted of 224 pairs of age-sex matched controls and FDRs. AG and IM in the gastric mucosa were scored histologically using the updated Sydney classification. Risk of having AG and IM was studied by comparing FDRs to controls. Impacts of age, H. pylori infection, smoking, dietary and socioeconomic factors on the presence of AG and IM were studied. RESULTS: In multivariate regression analysis, FDRs had adjusted OR of 2.69 (95% CI 1.06-6.80, P=0.037) for antral IM in male population. Adjusted OR for antral AG and IM were 9.28 (95% CI 4.73-18.18, P<0.001) and 7.81 (95% CI 3.72-16.40, P<0.001) for the H. pylori infected subjects in total population. Getting old by 5 years increased the ORs of having AG and IM by approximately 1.25 fold (P<0.001). Spicy food increased the OR of antral IM by 2.28 fold (95% CI 1.36-3.84, P=0.002). CONCLUSIONS: Family history of GC was an independent risk factor for antral IM in male in our study, which could be one reason for the increase of gastric cancer in the family member of gastric cancer. It could be an evidence for the necessity of frequent endoscopy in the presence of family history of GC compared to general population in male.

O'Hara, A., et al. (2015). "Polymorphisms in the relb gene identify a haplotype associated with reduced risk of pangastric atrophy." Gastroenterology 148(4): S566.

Gastric adenocarcinoma develops via a series of stereotypical preneoplastic stages. Members of the NF-κB family of transcription factors regulate inflammation and other cellular pathways involved in gastric carcinogenesis. Single nucleotide polymorphisms (SNPs) at loci encoding genes involved in the canonical NF-κB activation pathway including NFKBIA and NFKB1 are associated with altered gastric cancer risk. We previously demonstrated that germline Nfkb2 deletion protects mice from developing H. felis induced gastric preneoplasia. However, associations between SNPs affecting alternative pathway NF-κB signaling and gastric cancer have not previously been reported. To assess this, a cohort of 1400 adult patients attending for symptom directed diagnostic upper gastrointestinal endoscopy were genotyped for SNPs at loci thought to influence signaling in this pathway. Genomic DNA was extracted from whole blood. Gene selection in alternative pathway NF-κB signaling was based on biological plausibility. SNPs were identified from dbSNP using HapMap minor allele frequency data. Haploview was used to identify tag SNPs mapping 6 genes involved in alternative pathway NF-κB signaling. 50 SNPs were selected for analysis, each with a MAF of >5%, patients were genotyped using MALDI-TOF mass spectrometry (Sequenom® MassARRAY®). SNPs and patients with <90% call rates were excluded from further analysis. Association analyses for individual markers and haplotypes were carried out using Haploview with correction for multiple comparisons by permutation analysis and Benjamini-Hochberg false discovery rate (FDR). 1134 patients and 42 SNPs fulfilled our inclusion criteria. All 42 SNPS passed the Hardy-Weinberg threshold (p>0.001), and case control comparisons were carried out. In patients with gastric preneoplastic pathology (atrophic gastritis and/or intestinal metaplasia and/or dysplasia, n=207 vs control, n=274), a SNP in the NIK gene conferred an increased risk of pathology (OR 1.4, 95%CI = 1.02-1.88). After FDR and permutation analysis, this SNP did not retain statistical significance. In patients with pangastric atrophy (n=13) vs control (n=282), seven SNPs were observed to confer an altered risk (p<0.05 on individual testing), however these SNPs did not reach significance following permutation or FDR analyses. A RELB haplotype block was associated with an OR of 0.26 (95% CI = 0.107- 0.627, p=0.0014, corrected p=0.03) for developing pangastric atrophy. Identification of a RELB haplotype that may be associated with a reduced risk of developing pangastric atrophy provides further evidence of a role for the alternative NF-κB activation pathway in gastric carcinogenesis. These findings require validation in other cohorts of patients with preneoplastic gastric pathology, and identify the need to investigate how the identified RELB haplotype influences NF-κB signaling.

Ohata, H., et al. (2004). "Progression of chronic atrophic gastritis associated with Helicobacter pylori infection increases risk of gastric cancer." International Journal of Cancer 109(1): 138-143.

We conducted a longitudinal cohort study to determine the association of Helicobacter pylori infection and the progression of chronic atrophic gastritis (CAG) with gastric cancer. A cohort of 4655 healthy asymptomatic subjects was followed for a mean period of 7.7 years. H. pylori infection was established by serum specific antibodies and the presence of CAG was confirmed by serum pepsinogen. During the follow-up period, 45 gastric cancer cases were detected (incidence rate, 126/100000 person-years). A univariate analysis after adjustment for age showed that both H. pylori and CAG were significantly associated with gastric cancer. To clarify the interaction between H. pylori and CAG, an analysis stratified by H. pylori- and CAG-status was performed. No cancer developed in the H. pylori(-)/CAG(-) group during the study period. This supports the theory that it is quite rare for any type of gastric cancer to develop in an H. pylori-free healthy stomach. With the progression of H. pylori-induced gastritis, the risk of gastric cancer increased in a stepwise fashion from CAG-free gastritis [H. pylori(+)/CAG(-) group] (HR=7.13, 95%CI=0.95-53.33) to CAG [H. pylori(+)/CAG(+) group] (HR=14.85, 95%CI=1.96-107.7) and finally to severe CAG with extensive intestinal metaplasia [H. pylori(-)/CAG(+) group] (HR=61.85, 95%CI=5.6-682.64) in which loss of H. pylori from the stomach is observed. Therefore, it is probable that H. pylori alone is not directly associated with stomach carcinogenesis. Instead, H. pylori appears to influence stomach carcinogenesis through the development of CAG. The observed positive correlation between the extent of H. pylori-induced gastritis and the development of cancer was strong, especially for the intestinal type. These results are compelling evidence that severe gastritis with extensive intestinal metaplasia is a major risk factor for gastric cancer, and they confirm the previously described model of stomach carcinogenesis: the gastritis-metaplasia-carcinoma sequence.

Ojetti, V., et al. (2007). "A case-control study comparing methylene blue directed biopsies and random biopsies for detecting pre-cancerous lesions in the follow-up of gastric cancer patients." European Review for Medical and Pharmacological Sciences 11(5): 291-296.

Objectives: To compare the, accuracy of Methylene Blue (MB) targeted biopsies with random biopsies in detecting intestinal metaplasia and dysplasia in the follow-up of patients after gastrectomy for gastric cancer. Methods: Thirty patients (21 Billroth II, 9 Billroth I) for cancer, referred to the Gastroenterology Unit for an elective esophagogastroduodenoscopy (EGD), were enrolled. All endoscopies were performed with a high-resolution videoendoscope with an adjustable image magnification: EG-485ZH (Fujinon, Omlya, Japan). During EGD three random biopsies were taken in the stomach and, after staining with MB, three targeted biopsies were taken from every stained area. Results: In 28 patients traditional endoscopy showed hyperemia of the anastomosis, in 2 patients a lesion. After MB in 6/30 there were stained area (2 lesions seen with traditional endoscopy and 4 blue areas in other patients). As regards hystology: 24 patients showed inflammation, while 2 patients with alterations in traditional endoscopy and with MB showed metaplasia and high grade dysplasia. In 4/30 (13.30/6) patients MB guided biopsies showed significant lesions (3 intestinal metaplasia, 1 low grade dysplasia) while random biopsies showed only inflammation. Conclusions: After partial gastrectomy, the mucosa of the residual stomach usually undergoes severe changes, and these lesions are known to be pre-cancerous. The diagnostic accuracy of the MB technique seems to be superior to random biopsies for identification of intestinal metaplasia, dysplasia, and may be helpful in targeting biopsies and early endoscopic treatment.

Okada, T. and G. Adkins (2017). "Okadaella gastrococcusike bacteria positive reactive gastropathy (OGLBP-RG): Endoscopic, histochemical, immunohistochemical and electron microscopic studies." Gastroenterology 152(5): S814.

Backgrounds: Reactive gastropathy, known as chemical or reflux gastritis, is the second most common diagnosis made on gastric biopsies in North America. Bile, pancreatic secretions, alcohol, NSAIDs and many drugs have been suggested as the cause. Okadaella gastrococcus, which co-exists with H. pylori, is an intracellular acid tolerant Gram-variable bacterium. It produces various enzymes, chemicals and cytotoxins, and is associated with various gastropathies including gastric malignancy and RG. The aim was to investigate the characteristics of OGLBP-RG by endoscopy, histochemistry, immunohistochemistry (IHC) and transmission electron microscopy (TEM). Methods: The data of 22 patients (M:F 7:15, age: 21-80 years) who were found to suffer from OGLBP-RG by histology (H&E, WSS, AYTB, Diff Quick stains) were used. They were free from NSAIDs, alcohol, smoking and renal dysfunction. The formalin-fixed, paraffin-embedded specimens from 5 patients were examined with O. gastrococcus and H. pylori IHC. An avidin biotin peroxidase complex method with rabbit polyclonal antibodies against H. pylori (Dako) and O. gastrococcus was used. The specimens from 9 patients were examined under TEM. Culture of gastric biopsy specimens was attempted from 11 patients. Statistical analysis was performed by Fisher's Exact test. Results: Gastric erosion, petechial hemorrhage/hematin (PH/H), duodenitis, and inflammation of squamo-columnar junction were found in 20 (90.91%, n=22), 14 (82.35%, n=17), 14 (82.35%, n= 17), 11 (100%, n= 11), respectively. Statistical analysis revealed the positive association of PH/H with duodenitis (p=0.001), and of chronic gastritis with post-H. pylori eradication (p=0.02) in OGLBP-RG. Two Japanese patients (9.09%) had past history of gastric cancer. OGLB were found in the interstitial space involving leukocytes, macrophages, and vascular endothelial cells and elongated smooth muscle fibers, and additionally in areas of intestinal metaplasia. An unidentified OGLB was cultured and isolated successfully from a middle aged Japanese male. Three types of OGLBP-RG classification are proposed from the present results. Type I (4.55%): RG without gastric erosion, petechial hemorrhage or hematin. Type II (59.09%): RG with or without gastric erosion in the presence of small hemorrhage or PH/H. Type III (36.36%): RG with gastric atrophy and intestinal metaplasia in Type II background. Conclusion: OGLBP-RG supports a possible involvement of bacteria in the development of the pathology. Pre-neoplastic mucosal changes in Type III RG warrant careful follow-up in the population who has a higher incidence of gastric cancer in addition to further investigation of OGLBP-RG.

Okamura, T., et al. (2013). "Clinicopathological study of three generations of nodular gastritis-when should nodular gastritis be eradicated?" United European Gastroenterology Journal 1(1): A269-A270.

INTRODUCTION: Nodular gastritis (NG) is typically and frequently found in children who are infected with Helicobacter pylori (HP). NG has been recognized in adults infected with HP as well, and although it is considered to be a pangastritis, NG has been strongly associated with diffuse-type gastric cancer of the corpus as well. The natural history of NG remains elusive. Thus, we aimed to evaluate the clinicopathological hallmarks of NG over three generations of patients. AIMS&METHODS: We recruited 103 patients (average age: 29 years, range: 4- 79 years) who were diagnosed as having NG by upper gastrointestinal endoscopy at our hospital. The subjects were divided into three groups: 13 patients aged younger than 15 years (9 female; average age: 10.5 years) were assigned to the pediatric group, 50 patients aged between 16 and 30 (25 female; average age: 19.1 years) were classified into the young group, and 40 patients older than 31 years of age (29 female; average age: 47.7 years) comprised the elder group. We evaluated the clinical, endoscopic, and pathological features of NG among these three generations. Pathological features were evaluated using the updated Sydney System (USS). RESULTS: NG was more frequently found in women in the pediatric and elder groups. Although the endoscopic finding of atrophic gastritis tended to increase with age, it was generally mild in our cohort. There was no significant difference among the three groups regarding scores for mononuclear cell infiltration in the greater curvature of the antrum. However, scores for mononuclear cell infiltration in the greater curvature of the gastric body was significantly higher in the elder group than in the pediatric and young groups (1.31 vs. 1.36 and 1.98, both P<0.001). Scores for neutrophil infiltration in the greater curvature of the gastric body were also significantly higher in the elder group than in the other two groups (0.92 vs. 1.08 and 1.65, both P<0.001), but those for neutrophil infiltration in the greater curvature of the antrum were comparable among the groups. The scores for atrophy, intestinal metaplasia, and HP infection did not differ significantly in our study. CONCLUSION: In pediatric and young patients, inflammatory cell infiltration in the gastric body is milder than in elder patients. As pangastritis is considered to be a risk factor for diffuse-type gastric cancer, HP eradication therapy in younger people, especially before 30 years of age, may prevent this type of cancer of the corpus.

Olaywi, M., et al. (2013). "Predictors of intestinal metaplasia in minorities: Not always helicobacter pylori." American Journal of Gastroenterology 108: S26.

Purpose: Intestinal metaplasia (IM) of the stomach is a significant risk factor in developing intestinal type gastric cancer. IM has been linked to H. pylori infection and there has been emerging evidence that IM may be reversible with eradication of H. pylori. In this study, we investigated if the IM- H. pylori association exists in minority patients. One focus was looking for other predictors of IM in this population Methods: Charts of all adult patients who underwent upper endoscopy with biopsy at our medical center in a two year period were reviewed. Data about demographics, endoscopic, and histological findings were collected and analyzed. The presence of H. pylori infection was based on the immunohistopathological analysis of the biopsy samples. SAS software was used for statistical analysis. Results: Our cohort included 970 patients (37% males and 63% females). African American, Hispanics, and Asian Americans represented 52.5%, 28.3%, and 3.8% of the study population, respectively. The mean age was 59.1 (SD 17.1). The prevalence of H. pylori and gastric intestinal metaplasia were 24.64% and 11.6%, respectively. On a univariate analysis, gastric IM in patients with H. pylori infection was 18% in comparison to 7% in non-infected patients (P 0.0002). IM was also significantly associated with aging (6% in >65years, 3% in 50-65 years, 2% in <50 years, P <0.0001). There was no association found between IM and race or gender. On a multivariate logistic regression analysis, H. pylori infection and age more than 65 years retained significance in association with IM (OR 2.2 (1.4-3.3) and OR 2.3 (1.3-3.9), respectively). Conclusion: Gastric IM is relatively common among minority patients. H. pylori infection and aging are independent predictors of developing IM in this population. Further studies are warranted to elucidate the mechanism behind these findings.

O'Riordan, F., et al. (2019). "Monitoring gastric intestinal metaplasia." Irish Journal of Medical Science 188: S107-S108.

Background: Gastric cancer is the second leading cause of cancer-related death in the world. Gastric intestinal metaplasia [IM] is a precancerous change inmucosa known to increase the risk of gastric cancer. Modifiable risk factors include H-pylori infection, smoking and alcohol. At present, there are no consensus guidelines on surveillance once IM diagnosis is made. Aims: Our aims were to review the demographics, rate of H-pylori infection, smoking history and alcohol use for patients diagnosed with IM together with the current practice for endoscopic biopsy and surveillance at Naas General Hospital [NGH]. Method: A retrospective analysis of prospective data collected on all patients diagnosed with IM by Oesophago-Gastro-Duodenoscopy [OGD] from June 2017 - June 2018. Results: A total of 37 patients were included. Mean age was 65.8years [age range 26-92years]. Twenty-three females (62%) and 14 males (38%). Sixteen patients (43%) had a weekly alcohol intake of 8 units or more and 12 patients (32%) were current/ex-smokers of 5 pack-years or more. The antrum was the most common biopsy location; 25/37(67.6%) followed by the body 11/37 (29.7%), pylorus 5/37(13.5%) and fundus 5/37(13.5%). Twenty-eight patients (76%) were diagnosed with H-pylori infection. Follow-up included out-patient clinic for 22/37 patients (59.5%) and virtual clinic for 3/37 (8.1%). Repeat OGD was arranged for 11/37 patients (29.7%) at time of diagnosis or at follow-up clinic. Conclusions: In our study, females weremore likely to be diagnosed with IM. A high proportion of patients had concurrent H-pylori infection. The location and number of biopsies varied and there was no clear protocol for ongoing surveillance with less than one-third scheduled for follow-up OGD. Given the low survival rate of gastric cancer, our patients with IM would greatly benefit from surveillance guidelines similar to other premalignant conditions to detect neoplasia at an earlier, potentially curative stage.

Pan, K. F., et al. (2014). "Helicobacter pylori antibody responses and evolution of precancerous gastric lesions in a Chinese population." International Journal of Cancer 134(9): 2118-2125.

Helicobacter pylori-specific proteins are involved in gastric carcinogenesis. To investigate the seroprevalence of six H. pylori-specific antibodies in patients with different gastric histology, and the impact of seropositivities on the evolution of precancerous gastric lesions, a follow-up study was conducted in Linqu County, China. The seropositivities for CagA, VacA, GroEL, UreA, HcpC and gGT were assessed by recomLine analysis in 573 H. pylori-positive subjects and correlated with evolution of precancerous gastric lesions. We found that the score of H. pylori recomLine test was significantly increased in subjects with chronic atrophic gastritis (CAG, p < 0.0001) or intestinal metaplasia (IM, p = 0.0125), and CagA was an independent predictor of advanced gastric lesions, adjusted odds ratios (ORs) were 2.54 (95% CI = 1.42-4.55) for IM and 2.38 (95% CI = 1.05-5.37) for dysplasia (DYS). Moreover, seropositivities for CagA and GroEL were identified as independent predictors for progression of gastric lesions in a longitudinal study, and ORs were 2.89 (95% CI = 1.27-6.59) and 2.20 (95% CI = 1.33-3.64), respectively. Furthermore, the risk of progression was more pronounced in subjects with more than three positive antigens (p(for) trend = 0.0003). This population-based study revealed that seropositivities for CagA and GroEL might be potential markers to identify patients infected with high-risk H. pylori strains, which are related to the development of GC in a Chinese high-risk population, and recomLine test might serve as a tool for risk stratification.

Panarese, A., et al. (2018). "Detection of lesions in helicobacter pylori gastritis before and after eradication by expert endoscopists." United European Gastroenterology Journal 6(8): A734.

Introduction: Helicobacter pylori (HP) infection is commonly responsible of multifocal atrophic gastritis without intestinal metaplasia, intestinal metaplasia and dysplasia, which is the most relevant premalignant gastric condition (PGC). HPeradication is mandatory to stop the chronic gastric inflammation, but the longterm risk of gastric premalignant/malignant lesions progresses even after HPeradication. Several studies showed that high-resolution endoscopy with narrow-band imaging (HRE-NBI) could be more accurate than white-light endoscopy (WLE) alone in diagnosing PGC. Nevertheless, no study focused on the diagnostic performance of endoscopy in detecting PGC after HP eradication on an interim follow-up. Aims and Methods: In the present study, we aimed to assess the efficacy of HRENBI in the diagnosis of PGC, before and after HP eradication. A prospective study was performed in our institution involving the regular use of high-resolution gastroscopes with and without NBI. From June 2016 to June 2017, all patients that received an endoscopic diagnosis of HP-related gastritis by an expert endoscopist, were reassessed by WLE and HRE-NBI, including biopsy samples according to the Sydney system, within six months after the proved HP eradication. Kimura-Takemoto modified classification and endoscopic grading of gastric intestinal metaplasia (EGGIM), proposed by Pimentel-Nunes et al. were used to evaluate the degree of atrophy and IM. Histologic result was considered the diagnostic gold standard. Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia (OLGIM) were assessed by an expert gastrointestinal pathologist. Results: Of 83 screened patients, 36 were enrolled and a total of 72 HRE-NBI were performed before and after the proved HP eradication. The major indications for endoscopy were gastroesophageal reflux (60%), abdominal pain (30%), dyspepsia (5%), or anemia (5%). The median age of the all patients was 58 years (range 32-72), and they were prevalently female (86.1%). Among them, 17 patients (47.2%) were current drinkers, 4 (11.1%) were active smokers and 2 (5.5%) had a familiar history for gastric cancer. The proportion of patients with degree 3-4 of EGGIM scale, significantly decreased after HP eradication (33.3% vs. 11.1%, p=0.04), whereas the proportion of patients with more advanced degree of EGGIM scale (5-6) showed a trend of increase (16.7% vs. 36.1%, p=0.06). In the latter group, the majority of patients (69.2%) had a lower degree of EGGIM scale (3-4) before anti-HP therapy, whereas the minority (15.4%) had the same degree (p<0.05). Moreover, the proportion of OLGA and OLGIM stages did not change after HP-eradication. Interestingly, the proportion of patients with histological diagnosis of dysplasia on random biopsies did not change significantly after HP eradication (36.1% vs. 16.7%; p=0.06), whereas the proportion of patients with histological dysplasia on “de novoappeared” superficial lesions, significantly increased after HP disappearance (0% vs. 38.9%; p<0.001). Conclusion: HRE-NBI could be more precise in diagnosing dysplasia after HPeradication, presumably as the gastric mucosal aspect is less corroborated by the inflammatory changes induced by the HP chronic infection, which could lead to an underestimation of the premalignant lesions. These findings suggest that a non-invasive test for HP identification should be performed in at risk patients as a first step, and only after achieving HP eradication they should undergo a gastroesophageal endoscopy to identify more correctly PGC.

Pandey, R. and A. Millar (2011). "Management of gastric intestinal metaplasia in the UK: A preliminary survey." Gut 60: A105.

Introduction Gastric intestinal metaplasia (GIM) is considered a risk factor for gastric cancer1. Management and follow-up of these lesions is uncertain, as there are no standard UK guidelines. Current evidence suggests that patients with GIM should be considered for H pylori eradication and undergo endoscopic surveillance, depending on histological subtype and risk factors1. The aim of this study was to identify current practices within the UK, assess awareness of evidence-based GIM guidelines, and gauge opinion on the usefulness of such guidelines. Methods An online survey composed of 10 questions was distributed via email to 984 recipients across the UK, including Gastroenterologists, Gastrointestinal surgeons and GPs with a specialist interest in Gastroenterology (GPwSI). Questions related to the clinical and endoscopic management of GIM, and the knowledge and value of GIM guidelines. Response data was analysed descriptively. Results 75 responses were obtained with the majority from Consultant Gastroenterologists. In an example case of an incidental finding of GIM in a 50 year old male with mild gastritis, a negative CLO test and no risk factors or alarm features suggestive of cancer: 51% would take no further action. 15% would test or empirically treat H pylori. 34% would offer a repeat endoscopy, of which nearly half would offer at 1 year. In clinical practice, 40% of respondents do not offer routine endoscopic surveillance for GIM. However, factors infl uencing the decision to offer surveillance include family history of gastric cancer (51%); persistence of GIM at subsequent endoscopy (19%) or patient request (17%). In the endoscopic surveillance for GIM: 45% take 3-5 biopsies and 42% take 6-10 biopsies. The majority (53%) do not use additional imaging techniques for example, narrow band imaging/chromoendoscopy. 62% do not routinely re-review GIM biopsies with a histopathologist. If GIM is found, 29% inform patients of an increased gastric cancer risk, while 16% tell them there is no convincing evidence of increased risk. 31% do not mention the diagnosis at all. 96% are not aware of any guidelines on the management of GIM. 65% think guidelines would be useful, 30% do not feel strongly and only 5% would not find them useful. Conclusion The management of GIM varies widely among clinicians in the UK. A large proportion do not offer endoscopic surveillance routinely, although consider alternative management strategies and take individual factors into account. In those that offer surveillance, the timing of repeat endoscopy varies, and there are differences in the endoscopic techniques employed. Although there are no existing universal UK guidelines, the majority of clinicians would welcome guidelines on the management of GIM.

Pandey, R. and A. Millar (2013). "Management of gastric intestinal metaplasia in the UK: A preliminary survey." Gastroenterology 144(5): S483.

Introduction: Gastric intestinal metaplasia (GIM) is considered a risk factor for gastric cancer. Management and follow-up of these lesions is uncertain, as there are no standard UK guidelines. Current evidence suggests that patients with GIM should be considered for H pylori eradication and undergo endoscopic surveillance, depending on histological subtype and risk factors. The aim of this study was to identify current practices within the UK, assess awareness of evidence-based GIM guidelines, and gauge opinion on the usefulness of such guidelines. Methods: An online survey composed of 10 questions was distributed via email to 984 recipients across the UK, including Gastroenterologists, Gastrointestinal surgeons and GPs with a specialist interest in Gastroenterology (GPwSI). Questions related to the clinical and endoscopic management of GIM, and the knowledge and value of GIM guidelines. Response data was analysed descriptively. Results: 75 responses were obtained with the majority from Consultant Gastroenterologists. In an example case of an incidental finding of GIM in a 50 year old male with mild gastritis, a negative CLO test and no risk factors or alarm features suggestive of cancer: 51% would take no further action. 15% would test or empirically treat H pylori. 34% would offer a repeat endoscopy, of which nearly half would offer at 1 year. In clinical practice, 40% of respondents do not offer routine endoscopic surveillance for GIM. However, factors influencing the decision to offer surveillance include family history of gastric cancer (51%); persistence of GIM at subsequent endoscopy (19%) or patient request (17%). In the endoscopic surveillance for GIM: 45% take 3-5 biopsies and 42% take 6-10 biopsies. The majority (53%) do not use additional imaging techniques for example, narrow band imaging/chromoendoscopy. 62% do not routinely re-review GIM biopsies with a histopathologist. If GIM is found, 29% inform patients of an increased gastric cancer risk, while 16% tell them there is no convincing evidence of increased risk. 31% do not mention the diagnosis at all. 96% are not aware of any guidelines on the management of GIM. 65% think guidelines would be useful, 30% do not feel strongly and only 5% would not find them useful. Conclusion: The management of GIM varies widely among clinicians in the UK. A large proportion do not offer endoscopic surveillance routinely, although consider alternative management strategies and take individual factors into account. In those that offer surveillance, the timing of repeat endoscopy varies, and there are differences in the endoscopic techniques employed. Although there are no existing universal UK guidelines, the majority of clinicians would welcome guidelines on the management of GIM.

Parasa, S. (2019). "The incidence of gastric cancer in patients with gastric intestinal metaplasia: A systematic review and meta-analysis." Turkish Journal of Gastroenterology 30: S523.

Background/Aims: The risk of Gastric cancer in patients with Gastric Intestinal Metaplasia (GIM) is unclear. The objective was to estimate the incidence of Gastric cancer (GC) in patients with GIM. Materials and Methods: An electronic database search was conducted in Pubmed/ Medline, EMBASE and Google Scholar from 1966 to 2018 including a bibliographic review of previous publications excluding abstracts and those not published in English, for prospective or retrospective studies of the incidence of GC in patients with GIM. Studies were independently reviewed by two individuals. Data on the number of patients with GIM, duration of follow-up, incident cases of GC, prospective or retrospective study were obtained. Data on the incidence of gastric cancer in 2017 was obtained from global burden of disease (reference: http://ihmeuw.org/4npo) to determine the rates of gastric cancer incidence. Data was sub classified based on the incidence of GC - <7, 7-14, >14 per 100,000 years. Study quality was assessed using Ottawa Newcastle Criteria. The primary outcome was the annual incidence of GC in patients with GIM per 100 person-years and the secondary outcome was pooled annual incidence rates stratified based on the incidence of GC in countries. The pooled rates were reported with 95% CI and I2 for heterogeneity with p-value < 0.05 considered significant. Results: A total of 15 studies were included for final analysis which comprised of 81,552 patients and 457, 089 person years of follow-up. The mean age was 61.1 years and the mean follow-up duration was 5.2 years. The pooled annual incidence of GC among patients with GIM was 0.31 (95% CI: 0.21-0.45, I2 - 92%) per 100 person years. When stratified by incidence of GC based on the study country of origin, the pooled annual incidence for <7, 7-14, > 14 gastric cases per person years was 0.12 (95% CI: 0.09-0.15), 0.31(95% CI: 0.25-0.38) and 0.81 (95% CI: 0.58-1.2) per 100 person years respectively with a statistically significant increase in the trend (p < 0.001). Conclusion: The incidence of GC in GIM patients is around 0.3 per 100 patients per year. The rate of progression of GIM to GC varies strikingly among countries based on the baseline incidence of GC with higher annual progression rate of GIM to GC in countries with higher baseline incidence of GC. Other additional risk factors could also be associated with increase in the risk of progression to GC apart from GIM which were not investigated in this study.

Parasa, S., et al. (2019). "THE INCIDENCE OF GASTRIC CANCER IN PATIENTS WITH GASTRIC INTESTINAL METAPLASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS." Gastroenterology 156(6): S-522.

Introduction: The risk of Gastric cancer in patients with Gastric Intestinal Metaplasia (GIM) is unclear. The objective was to estimate the incidence of Gastric cancer (GC) in patients with GIM. Methods: An electronic database search was conducted in Pubmed/ Medline, EMBASE and Google Scholar from 1966 to 2018 including a bibliographic review of previous publications excluding abstracts and those not published in English, for prospective or retrospective studies of the incidence of GC in patients with GIM. Studies were independently reviewed by two individuals. Data on the number of patients with GIM, duration of followup, incident cases of GC, prospective or retrospective study were obtained. Data on the incidence of gastric cancer in 2017 was obtained from global burden of disease (reference: http://ihmeuw.org/4npo) to determine the rates of gastric cancer incidence. Data was sub classified based on the incidence of GC – <7, 7-14, >14 per 100,000 years. Study quality was assessed using Ottawa Newcastle Criteria. The primary outcome was the annual incidence of GC in patients with GIM per 100 person-years and the secondary outcome was pooled annual incidence rates stratified based on the incidence of GC in countries. The pooled rates were reported with 95% CI and I2 for heterogeneity with p-value < 0.05 considered significant. Results: A total of 15 studies were included for final analysis which comprised of 81,552 patients and 457, 089 person years of follow-up. The mean age was 61.1 years and the mean follow-up duration was 5.2 years. The pooled annual incidence of GC among patients with GIM was 0.31 (95% CI: 0.21-0.45, I2 – 92%) per 100 person years (figure 1). When stratified by incidence of GC based on the study country of origin, the pooled annual incidence for <7, 7-14, > 14 gastric cases per person years was 0.12 (95% CI: 0.09-0.15), 0.31(95% CI: 0.25-0.38) and 0.81 (95% CI: 0.58-1.2) per 100 person years respectively with a statistically significant increase in the trend (p < 0.001) (figure 2). Conclusions: The incidence of GC in GIM patients is around 0.3 per 100 patients per year. The rate of progression of GIM to GC varies strikingly among countries based on the baseline incidence of GC with higher annual progression rate of GIM to GC in countries with higher baseline incidence of GC. Other additional risk factors could also be associated with increase in the risk of progression to GC apart from GIM which were not investigated in this study.

Parbhu, S. K., et al. (2019). "INCIDENT DIAGNOSES OF GASTRIC INTESTINAL METAPLASIA IN THE US: PATIENT CHARACTERISTICS, EGD FINDINGS, AND CLINICAL PRACTICE PATTERNS AT A LARGE US TERTIARY CARE CENTER." Gastroenterology 156(6): S-520.

Background: Gastric intestinal metaplasia (GIM) is a premalignant lesion with risk of progression to gastric cancer. In the US, GIM is often incidentally detected during esophagogastroduodenoscopy (EGD) with biopsy. US incidence, prevalence, and outcomes data are limited, and practice patterns are suspected to be highly variable based on a single prior survey of GI providers. No studies have assessed actual US practice patterns after incidentally detected GIM in a large cohort of patients. Objectives: 1) To accurately identify incident GIM cases detected after EGD using natural language processing (NLP); 2) Determine patient characteristics, endoscopy findings, biopsy practice patterns, histology, H. Pylori detection and treatment outcomes, and surveillance and follow-up recommendations after incidental GIM diagnosis. Methods: A retrospective review of all EGD procedure and pathology notes from 9/2011 – 11/2016 in the University of Utah data warehouse was performed. A rule-based NLP tool (PyConText) was developed and validated to determine EGD biopsy location and GIM pathology. GIM cases were manually confirmed and reviewed for relevant demographics and clinical, endoscopic and histologic characteristics. Results: The NLP tool was 98.8% accurate at identifying GIM. NLP identified 516 patients (out of 16,505 total patients) with a likely diagnosis of GIM; after patients with a prior history of GIM were excluded, 434 patients with an index diagnosis of GIM were confirmed (prevalence = 2.6%). Patient characteristics and endoscopy indications are described in Table 1. GIM location was not determined in 181 patients (41.7%) due to lack of documentation. The most common documented biopsy locations were: 1) antrum alone (N=146, 33.6%), antrum and body (N=52, 12%), 3) body alone (N=39, 9%). GIM histology was extensive in 36 patients (8.3%), focal in 165 patients (38%), and unspecified in 233 patients (53.7%). H. Pylori testing was documented in 375 (86.4%) patients and positive in 98 patients (26.1%). Treatment and eradication outcomes are highlighted in Table 2. Follow-up recommendations were variable, and a majority of patients (N=230, 53%) were not given specific follow-up or were told to see their primary care provider (Table 2). Of the 113 patients with repeat EGD recommended in <1 year, only 62 patients (55%) had an EGD performed. Conclusion: Using NLP, we identified the largest US GIM cohort described to date, with a prevalence of 2.6% over 5 years. There was wide variability in clinical practice patterns including biopsy practice, H. Pylori treatment and eradication confirmation, surveillance recommendations, and adherence to follow up. This work will drive quality improvement efforts to standardize care for patients with GIM and inform prospective studies on cancer risk after GIM diagnosis in a US population. [Table presented] [Table presented]

Park, C. H., et al. (2019). "Network construction of gastric microbiome and organization of microbial modules associated with gastric carcinogenesis." Scientific Reports 9(1): 12444.

In addition to Helicobacter pylori infection, nitrosating/nitrate-reducing bacteria and type IV secretion system (T4SS) protein gene-contributing bacteria have been proposed as potential causes of gastric cancer development. However, bacterial modules related with gastric carcinogenesis have not been clarified. In this study, we analyzed gastric microbiome using the gastric mucosal samples obtained from the Hanyang University Gastric Microbiome Cohort by 16S rRNA gene sequencing. Weighted correlation network analysis was performed to construct a microbiome network and to identify microbial modules associated with gastric carcinogenesis. At the family level, 420 bacterial taxa were identified in the gastric microbiome of 83 participants. Through network analysis, 18 microbial modules were organized. Among them, two modules-pink and brown-were positively correlated with a higher-risk of gastric cancer development such as intestinal metaplasia with no current H. pylori infection (correlation coefficient [γ]: pink module, 0.31 [P = 0.004], brown module, 0.26 [P = 0.02]). At the family level, twenty-two and thirty-two bacterial taxa belonged to the pink and brown modules, respectively. They included nitrosating/nitrate-reducing bacteria, T4SS protein gene-contributing bacteria, and various other bacteria, including Gordoniaceae, Tsukamurellaceae, Prevotellaceae, Cellulomonadaceae, Methylococcaceae, and Procabacteriaceae. The blue module, which included H. pylori, was correlated negatively with intestinal metaplasia (γ = -0.49 [P < 0.001]). In conclusion, intragastric bacterial taxa associated with gastric carcinogenesis can be classified by network analysis. Microbial modules may provide an integrative view of the microbial ecology relevant to precancerous lesions in the stomach.

Park, D. R., et al. (2011). "Clinical study for synchronous and metachronous occurrence in EGC patients after ESD." Journal of Gastroenterology and Hepatology 26: 273.

Background or introduction Recent advances in endoscopy have made it possible to detect early gastric cancer, endoscopic submucosal dissection (ESD) have become common treatment modality for early gastric cancer. although ESD contributes to preserving most of the stomach, the risk of metachronous cancers developing at other sites in the stomach is a major problem. We aims to evaluate risk factors and clinicopathologic features of metachronous and synchronous gastric cancer. Materials and methods A total of 64 patients with early gastric cancers were retrospectively evaluated. The patients were initially treated with ESD from October 2004 to September 2009. After ESD, a regular endoscopic follow up (6 or 12 months) was performed. Histologic classification, macroscopic types, and the location of the tumors were categorized. Results The incidence of synchronous and metachronous gastric neoplasm was as high as 8% and 11%. The average time to detect the metachronous gastric cancer was 23.4 months. Secondary lesions of metachronous cancer are most commonly located in cardia and body lesser curvature. The incidence of multiple lesions is increased when intestinal type and intestinal metaplasia of primary lesion. Conclusions With EGC combined with intestinal metaplasia and intestinal histology type, we need to display caution and circumspection. we should focus on the metachronous and synchronous multiplicity of gastric cancer, be careful not to miss the blind spots located in cardia and lesser curvature of body. For the present, there is no definite guideline for appropriate the intervals between follow-up examinations, annual endoscopic examinations are considered to be acceptable.

Park, J., et al. (2019). "CLINICOPATHOLOGIC AND ENDOSCOPIC FEATURES OF HELICOBACTER PYLORI NEGATIVE EARLY GASTRIC CANCER TREATED BY ENDOSCOPIC SUBMUCOSAL DISSECTION." Gastrointestinal Endoscopy 89(6): AB505.

Background: Helicobacter pylori negative gastric cancer (HpNGC)is a rare disease of less than 5%, and its clinical features are not well known. Early gastric cancer usually develops according to the Correa’s hypothesis, therefore, Helicobacter pylori negative early gastric cancer is less common. The aim of this study was to evaluate the endoscopic and pathologic features of Helicobacter pylori negative early gastric cancer treated by endoscopic resection. Methods: At the single tertiary center, patients who had been diagnosed with early gastric cancer through endoscopic biopsy from January 2010 to June 2018 and who had received all three tests of Helicobacter pylori were included. The definition of HpNGC was limited to negative cases in which there was no previous history of eradication and all negative results of serologic test, rapid urease test and polymerase chain reaction of gastric specimen. Clinical, endoscopic, and pathologic findings of patients with Helicobacter pylori gastric cancer were analyzed retrospectively. Results: A total of 89 patients (61.8%)had endoscopic treatment in 144 patients diagnosed early gastric cancer in this study. In early gastric cancer patients who underwent endoscopic resection, 21 patients were negative for all three tests related to Helicobacter. Median age was 67 and 9 patients (42.9%)were male. The most common location and morphologic type were antrum (80.9%)and IIc type (52.4%), respectively. Pathologically, only 3 cases showed undifferentiated type including signet-ring cell carcinoma or poorly differentiated and the other 18 cases were differentiated type. Moreover, endoscopic findings showed atrophy in all patients, intestinal metaplasia in 66.7% and red-color change in 81%. During median follow-up of 13. 8 months, four patients recurred and all patients treated by endoscopic resection. Conclusion: In this study, differentiated adenocarcinoma is more prevalent in patients with Helicobacter pylori negative early gastric cancer, unlike previous reports. Considering the background of the endoscopic mucosa, atrophic change and intestinal metaplasia may be more closely related to carcinogenesis than the positivity of Helicobacter pylori.

Pellicano, R., et al. (2005). "[Intestinal metaplasia, dysplasia, gastric cancer and Helicobacter pylori: epidemiological observations]." Minerva Medica 96(1): 1-10.

Gastric cancer (GC) is the world's second leading cause of cancer-related mortality, and carries a bad prognosis. In 1994, Helicobacter pylori (H. pylori) has been classified by the International Agency for Research on Cancer as a group I carcinogen. There are increasing indications that this infection is associated with both the initiation and progress of gastric carcinoma and lymphoma. Evidence supporting a causal association has been demonstrated by epidemiological data and in experimental animal models. Despite this, there is still lack of final conclusion regarding the association between the infection and the malignancy due both to marked geographic variations and heterogeneity in study designs. Given the high rate of morbidity and mortality associated with GC, any means of reducing the occurrence of the disease or increase its early detection is most desirable. In this paper, the epidemiological aspects on the evidence of a causal relationship between H. pylori and GC are discussed. Prospective cohort studies and interventional trials focused on the effects of H. pylori eradication on lesions predisposing to GC should be performed in order to provide further data.

Pepper, M., et al. (2020). "Interobserver agreement among gastrointestinal pathologists using the updated sydney system for gastric biopsy interpretation." Modern Pathology 33(3): 749-750.

Background: The updated Sydney system for the classification of gastritis is widely used in clinical practice and in research settings for stratification of gastric cancer risk. Accurate grading of morphologic variables is important for informing the clinical decision to offer endoscopic follow-up and surveillance. This study was conducted to investigate the interobserver agreement for graded morphologic variables in the updated Sydney system. Design: Gastric biopsy specimens from patients in a gastric intestinal metaplasia (GIM) endoscopic surveillance program were independently evaluated by five gastrointestinal pathologists according to the updated Sydney classification system. Morphologic grading was performed for GIM, mucosal atrophy, chronic inflammation (CI), acute inflammation (AI), and dysplasia. Biopsies with GIM were subclassified as complete, incomplete, or mixed types on the basis of morphology. Inter-rater reliability was determined using Fleiss' kappa (κ) and Krippendorff's alpha (α) coefficients for categorical and weighted ordinal (graded) variables, respectively. Results: H&E sections of 104 gastric biopsies from 27 endoscopy procedures (24 patients) were evaluated. Mucosa from the gastric antrum and body was sampled from each patient, and GIM was present in at least one biopsy per case. Interobserver agreement was highest for the detection of Helicobacter (κ=1), GIM (κ=0.95), and AI (κ =0.88); whereas, there was moderate agreement on the presence of CI (κ=0.59). Agreement was lower for the detection of atrophy (κ=0.43) and for subtyping GIM (κ=0.37). Among the variables graded by study pathologists, GIM and CI were assessed more consistently than atrophy, which exhibited poor inter-rater reliability (α=0.54, 0.52, 0.13, respectively). One adenocarcinoma with associated high-grade dysplasia was detected by all study participants. Conclusions: While there is high interobserver agreement for the detection of Helicobacter, GIM, and gastric inflammation, inter-rater reliability is lower for the detection and grading of mucosal atrophy and for subclassification of GIM, even among subspecialized gastrointestinal pathologists. This study highlights the need for continued investigation into objective and reproducible strategies, such as a two-tiered grading system, well-defined histologic criteria, and/or judicious use of biomarkers (e.g. mucin stains), for evaluating and reporting prognostic variables in stomach biopsies from patients at risk for gastric cancer.

Pereira, A. C., et al. (2010). "Gastric adenocarcinoma development in patients with atrophy or/and intestinal metaplasia: The role of COX-2 polymorphisms in a Northern Portuguese population." European Journal of Cancer, Supplement 8(5): 28-29.

Background: COX-2 overexpression observed in 69% of gastric cancers (GC) and precancerous tissues is closely intertwined with key mechanisms of gastric carcinogenesis, namely inhibition of apoptosis, tumour growth, angiogenesis, invasion and metastasis. Genetic variations that modify6 the levels of COX-2 protein would be anticipated to have a substantial influence on disease phenotype. Hence, with this study we aimed at understanding the contribution of two functionally expected COX-2 polymorphisms (-1195A>G and 8473T>C) in the development and progression of gastric lesions. Material and Methods: A hospital-based case-control study was developed that gathered 134 patients diagnosed with gastric lesions (94 with GC and 40 with atrophy and/or intestinal metaplasia (AIM)) and 255 healthy individuals all from the Northern region of Portugal and recruited at Portuguese Institute of Oncology, Porto. The -1195A>G and 8473T>C COX-2 polymorphisms genotypes were characterized through PCR-RFLP and allelic discrimination techniques, respectively. Results: The -1195A>G COX-2 polymorphism did not appear to modulate the susceptibility for the development of gastric lesions in normal individuals (OR = 0.764; 95%CI:0.448-1.303 and OR = 1.823; 95% CI: 0.926-3.588 in -1195AG+GG genotypes carriers for GC and AIM onset, respectively). However, once the precancerous lesions were installed the -1195G allele was associated with a decreased risk for GC onset in AIM patients (OR = 0.419; 95% CI: 0.193-0.911). This protective effect in G allele carriers increased when we included the age and gender as covariates in a multivariate analysis (OR = 0.194; 95% CI: 0.075-0.499). Antagonically, for the 8473T>C genetic variation a 2.4-fold increased predisposition for AIM progression was reported in C allele carriers in the adjusted analysis. Conclusion: The -1195A>G and 8473T>C COX-2 polymorphisms emerged as susceptibility markers for AIM progression into cancer. The incorporation of genetic biomarkers in gastric cancer risk models might be of relevant importance as at this point there are no guidelines for the follow-up of individuals diagnosed with gastric precancerous lesions that ultimately may contribute to an early diagnosis of GC.

Perri, F., et al. (2007). "Aberrant DNA methylation in non-neoplastic gastric mucosa of H. Pylori infected patients and effect of eradication." American Journal of Gastroenterology 102(7): 1361-1371.

BACKGROUND: Gene promoter methylation is an epigenetic event leading to gene silencing. This mechanism is particularly relevant in cancer since it can interfere with the activity of specific "suppressor" genes. AIM: To evaluate promoter methylation of CDH1, p16, APC, MLH1, and COX2 in patients with H. pylori (Hp) infection before and after eradication. METHODS: Fifty-seven dyspeptic outpatients who had never performed previous endoscopy or Hp testing and treatment underwent clinical interview, endoscopy with three paired gastric biopsy specimens from the antrum, angulus, and corpus, and (13)C-urea breath test (UBT). Biopsies were scored for the presence of Hp and intestinal metaplasia (IM). DNA methylation of five tumor-related genes (CDH1, p16, MLH1, APC, and COX2) was evaluated by methylation-specific PCR in each biopsy. Infected patients were given a standard eradicating treatment and, after 1 yr, underwent endoscopy with biopsies and UBT. RESULTS: Hp infection was found in 45 patients. IM was detected in 17 out of 45 (38%) infected patients. Mean number of methylated genes was 0, 1.1 +/- 0.9, and 1.6 +/- 0.9 among the 12 Hp-/IM-, the 28 Hp+/IM-, and the 17 Hp+/IM+ patients, respectively (P < 0.0001). Specifically, promoter hypermethylation of CDH1, p16, APC, MLH1, and COX2 was found in 68%, 25%, 7%, 0%, and 14% of Hp+/IM- patients and in 71%, 29%, 35%, 12%, and 12% of Hp+/IM+ patients. No significant difference was found among the three groups of patients as far as age, smoking, alcohol, meat and vegetable consumption, and family history of gastric cancer were considered. Twenty-three out of 45 (51%) infected patients underwent the 1-yr follow-up endoscopy: 17 out of 23 (74%) were successfully eradicated. After Hp eradication, CDH1, p16, and APC methylation significantly decreased while COX2 methylation completely disappeared. Conversely, MLH1 methylation did not change significantly in patients with IM. CONCLUSION: Hp infection is associated with promoter methylation of genes which are relevant in the initiation and progression of gastric carcinogenesis. While CDH1 methylation seems to be an early event in Hp gastritis, MLH1 methylation occurs late along with IM. Hp eradication is able to significantly reduce gene methylation thus delaying or reversing Hp-induced gastric carcinogenesis.

Piazuelo, M. B., et al. (2019). "ASSESSMENT OF GASTRIC PREMALIGNANT LESIONS BY ANATOMIC SUBSITE IN INDIVIDUALS WHO SUBSEQUENTLY DEVELOPED HELICOBACTER PYLORI-ASSOCIATED GASTRIC CANCER IN A HIGH-RISK COLOMBIAN COHORT." Gastroenterology 156(6): S-523.

Background: Helicobacter pylori infection induces a series of gastric epithelial transformations known as the Correa cascade which include non-atrophic gastritis, multifocal atrophic gastritis without intestinal metaplasia (MAG), intestinal metaplasia (IM), and dysplasia, and which ultimately may lead to gastric cancer (GC). Antibiotics targeting H. pylori should be offered to infected individuals, but this may not prevent the subsequent development of GC, especially in those with advanced premalignant lesions. Endoscopic surveillance of individuals with IM is used in many areas of the world as a strategy to reduce GC mortality. However, European guidelines recommend endoscopic surveillance only in individuals with IM in antrum and corpus. In the United States, clinical guidelines do not recommend endoscopic surveillance of IM. Aim: To define precancerous lesions in individuals who participated in an H. pylori eradication trial in Colombia and developed GC during 16 years of follow-up (median time to GC, 8 years). Methods: Endoscopies were performed at enrollment, and 795 individuals with precancerous lesions (MAG, IM and dysplasia) at the initial endoscopy were randomized to anti-H. pylori treatment or placebo. Individuals were then followed up with endoscopy at 3, 6, 12, and 16 years. Four gastric biopsies were obtained at each endoscopy: incisura angularis, lesser and greater curvature of the antrum, and anterior wall of the corpus. Additional targeted biopsies were obtained from suspicious lesions. Results: A total of 27 sets of biopsies obtained at different time points were available from 10 individuals who subsequently developed GC. Such biopsies were available from the following number of subjects: 10 at baseline, and 8, 5, 3, and 1 at years 3, 6, 12 and 16, respectively. Of the individuals who progressed to GC (n=10), all had IM in antral biopsies at enrollment, while only 5 had IM in the corpus (Table 1). IM was observed in 85% (68/80) of all antral biopsies and in 67% (18/27) of corpus biopsies. Lesions indefinite for dysplasia (ID), low-grade (LGD), or high-grade dysplasia (HGD)/GC were observed in 5 (19%), 5 (19%), and 2 (7%) biopsy sets in non-targeted antral biopsies, and in 2 (7%), 2 (7%), and 0 (0%) of non-targeted corpus biopsies, respectively. Targeted biopsies (n=6), all corresponding to antral or transitional mucosa, were obtained from 4 individuals. Four biopsies (one biopsy of each individual) showed HGD/GC and 2 additional biopsies of one individual showed LGD. Conclusion: In our population, premalignant lesions were more frequent and more advanced in the gastric antrum. These findings suggest that endoscopic surveillance of individuals with IM should be individualized, and not only considered in individuals with extension of IM to the corpus. [Table presented]

Piazuelo, M. B., et al. (2020). "ASSOCIATIONS OF OLGA AND OLGIM STAGING SYSTEMS WITH HISTOLOGICAL PROGRESSION IN A COHORT OF INDIVIDUALS WITH GASTRIC INTESTINAL METAPLASIA DURING TWENTY YEARS OF FOLLOW-UP." Gastroenterology 158(6): S-566-S-567.

Background: Gastric cancer (GC) is preceded by a series of precancerous lesions triggered by Helicobacter pylori infection: nonatrophic gastritis, atrophic gastritis without intestinal metaplasia (MAG), intestinal metaplasia (IM), and dysplasia. OLGA and OLGIM staging systems are used for atrophy assessment, with stages III and IV associated with higher GC risk than stages 0-II. We aimed to evaluate the associations of OLGA and OLGIM with progression of precancerous lesions over 20 years of follow-up in a cohort of individuals with IM who participated in a H. pylori eradication trial. Methods: 795 Colombian adults with precancerous lesions (MAG, IM, or dysplasia) were randomized at baseline to anti-H. pylori treatment or placebo. Gastric biopsies were collected at 3, 6, 12, 16, and 20 years from the incisura angularis, antrum and corpus. Histopathology was scored according to our published Correa score (ranged 1-6, with increasing values along the precancerous cascade, from normal to cancer), as well as by OLGA and OLGIM systems. This analysis included 188 individuals with IM at baseline who had 20-year biopsies. Multivariable logistic regression models including sex, age, anti-H. pylori treatment at baseline, and H. pylori infection status at 16 years were performed to assess associations of OLGA and OLGIM with progression. Progression was defined as: 1) diagnosis of dysplasia (including indefinite, low grade and high grade) in 20-year biopsies, or 2) an increase of at least 0.1 units in the Correa score between baseline and 20 years. Results: OLGA at baseline was significantly associated with progression to dysplasia. As compared to stage I, the adjusted odds ratios (ORs) of progression were 2.05 (p=0.14), 3.88 (p=0.009), and 4.24 (p=0.006) for stages II, III and IV, respectively. Similarly, the ORs of progression in the Correa score for OLGA stages II, III and IV at baseline (vs. OLGA I) were 1.86 (p=0.10), 3.86 (p=0.007), and 2.12 (p=0.10), respectively. OLGIM was not associated with progression to dysplasia or the Correa score (p-values?>0.05). Associations with OLGA remained statistically significant after adjustment for OLGIM. Conclusion: In individuals with IM, OLGA staging system, but not OLGIM, was associated with histological progression. Considering that OLGA includes extension of both IM (OLGIM) and non-IM atrophy, our findings highlight the importance of including the entire spectrum of atrophy in the surveillance of high-risk individuals.

Piazuelo, M. B., et al. (2020). "The Colombian chemoprevention trial. Twenty-year follow-up of a cohort of patients with gastric precancerous lesions." Gastroenterology.

Piazuelo, M. B., et al. (2016). "Biopsy sampling of the incisura angularis for the diagnosis of gastric precancerous lesions." Gastroenterology 150(4): S863.

BACKGROUND: Gastric cancer is a major public health problem worldwide. The intestinal type of gastric cancer is preceded by a sequence of well-orchestrated lesions that comprise the Correa cascade: non-atrophic gastritis, multifocal atrophic gastritis without intestinal metaplasia (MAG), intestinal metaplasia (IM), and dysplasia. The latter three stages are considered to represent precancerous lesions. Surveillance of subjects with precancerous lesions may lead to the diagnosis of gastric cancer at an earlier stage and, ultimately, improvement in survival rates. There is a lack of consensus in the current guidelines for surveillance regarding the inclusion of incisura angularis biopsy samples as part of the mapping protocol. The aim of our study was to assess the importance of incisura angularis biopsy sampling in the evaluation of the severity of precancerous lesions. METHODS: 322 adult subjects from a Colombian cohort study who underwent upper gastrointestinal tract endoscopy were included in this analysis. Four gastric mucosal biopsies were obtained for histology: two from antrum: lesser curvature (ALC) and greater curvature (AGC), both within 3 cm from the pylorus; one from the incisura angularis (IA); and one from the corpus, anterior wall (C). Two expert gastrointestinal pathologists independently graded biopsies for MAG, IM and dysplasia according to established international guidelines. Discrepancies were resolved by review of the slides by a third senior gastrointestinal pathologist. The global diagnosis was defined as the most advanced lesion detected in any of the biopsies. There were 19 cases of MAG, 239 cases of IM and 64 cases of dysplasia. To assess the diagnostic value of incisura histologic results based on the same number of specimens, 3- biopsy sets were assembled and overall diagnoses were determined: ALC+AGC+C; ALC+IA+C; and IA+AGC+C. Variation in diagnosis distributions was evaluated by chi2 test. RESULTS: IM and dysplasia were observed significantly more frequently in the mucosa of the IA and ALC than in the mucosa of the AGC or C (p-values <0.001; Table 1). As compared to the biopsy set excluding the incisura, the sets that included the incisura upgraded the overall diagnosis of 19% of the patients (Table 2). In particular, 62% of the cases were upgraded to IM and 31% to dysplasia. CONCLUSIONS: Our findings highlight the importance of including an IA biopsy in the sampling protocol for surveillance of subjects with precancerous lesions. The IA is an area that appears to be more susceptible to metaplastic and dysplastic changes than the antrum or the corpus. (Table Presented).

Pickford, I. R., et al. (1984). "Endoscopic examination of the gastric remnant 31-39 years after subtotal gastrectomy for peptic ulcer." Gut 25(4): 393-397.

In York between 1941 and 1949, 632 patients underwent Polya partial gastrectomy for peptic ulcer. Of 307 patients who were followed up in the York Gastric Clinic from 1971 to 1980, nine died of gastric cancer, three times the expected number. If gastrectomy was performed for gastric ulcer the risk of later development of carcinoma (7%) was significantly greater than that following operation for duodenal ulcer (1.6%) (p less than 0.001). No cancers were diagnosed in the 54 patients endoscoped. Atrophic gastritis was found in 98% of patients and intestinal metaplasia in 44%. Dysplasia was present in 35% but in no case was it severe. Although we have found that there is an increased risk of cancer developing in the gastric remnant we do not consider routine endoscopic follow up of all postgastrectomy patients to be a practical proposition.

Pinto, R. J. M., et al. (2009). "Long term follow up of the low grade gastric dysplasia." Helicobacter 14(4): 377-378.

Despite the recognized importance of dysplasia as being the penultimate stage of gastric carcinogenesis, its natural history remains to be defined. In this study, we aimed to explore the longterm evolution of low-grade dysplasia which was not suitable for primary endoscopic treatment. We have analyzed 32 cases of low grade dysplasia, with a minimum follow-up of 12 months (mean 40.2 months). A statistical correlation (x2 test) was performed between the following variables: the progression of low-grade dysplasia(regression, maintenance, or progression of histologic grade); type of endoscopic appearance (flat, nodular, or depressed mucosa), and anatomical distribution.We found that 9.4% of patients were younger than 55 years and with family history of gastric cancer; 97% had/extensive atrophy and intestinal metaplasia and 78% showed only antrum dysplasia. Concerning the endoscopic appearance, 50% showed dysplasia in flat mucosa, 41% nodular mucosa, and 9% revealed depressed mucosa. The histologic grade has regressed in 66% of cases (mean time of 9.1 months), unchanged in 28% and progressed in 6% (median time of 48 months). Regarding the lesions that have regressed, 15 of 21 (71.4%) were initially detected in flat mucosa (p <.008). The two cases (6%) which had progression of histologic grade were initially multifocal low-grade dysplasia, while the others showed no multifocal distribution (p <.001). Altogether our results demonstrated that almost all patients with low grade dysplasia had extensive atrophy/intestinal metaplasia. Furthermore, the majority of the patients showed regression of lesions in clinical follow up and 6% of the cases have progressed in the histological grade. Moreover we found that the initial detection of changes in flat mucosa significantly correlates with their regression. In addition the multifocallity of the lesions was significantly correlated with its progression.

Pittayanon, R., et al. (2016). "The difference in dynamicity during the 5-year follow up of the immature and mature gastric intestinal metaplasia (GIM) of the patients from the area with low prevalence of gastric cancer." Gastroenterology 150(4): S246.

Background: Gastric intestinal metaplasia (GIM) is a premalignant condition of an intestinaltype gastric cancer. There are two types of GIM, immature and mature GIMs and the risk of progression to more advanced level of neoplasia or regress back between the two have never been demonstrated. The objective of this study was to determine the dynamicity of the two types of GIM during a 5-year follow up by surveillance upper endoscopy with targeted biopsy in patients from a low prevalence area of gastric cancer (5-7/100,000) such as Thailand. Materials and Methods: Ninety-one patients with previously diagnosed GIM between 2004 and 2014 were recruited and underwent a surveillance EGD with targeted biopsy at 6 to 12 months interval until the completion of 5-year follow-up or gastric cancer was detected. The changes in the level of neoplasm from each area that contained GIM either immature or mature type were mapped and recorded during each EGD. Results: The mean of follow-up period was 4.05±2.5 years. 81 from 91 patients (89%) started with mature GIM (mGIM) whereas 11% was firstly diagnosed as immature GIM (iGIM). Only 2 (2.5%) and 1 (1.2%) of mGIM progressed to iGIM and high grade dysplasia (HGD), respectively, and no cancer developed in this group at the end of follow-up. In contrast, 5 from 10 cases of iGIM (50%) progressed to HGD (n=2) and cancer (n=3) whereas the other 5 cases regressed to mGIM (n=2) or chronic atrophic gastritis.(n=3) All 6 cases of HGD from both groups and cancer cases in iGIM group underwent either endoscopic submucosal dissection (n=5) or laparoscopic resection (n=1). No recurrence occurred at 1-4 year-follow up. During 3-year follow up, one case expired from colon cancer and another expired from unrelated cause to GIM. (Table) Conclusion: Patients with iGIM have much more higher risk to develop high grade dysplasia or early gastric cancer than those with mGIM. A 6-12 months interval of surveillance EGD in patient with iGIM is justified to detect the progression so a curative treatment can be offered. (Table Presented).

Prskalo, M., et al. (2002). "[Helicobacter pylori and malignant diseases of the stomach]." Lijecnicki Vjesnik 124 Suppl 1: 57-60.

The association between Helicobacter pylori infection and gastric malignancies, cancer and MALT lymphoma, has been suggested through several lines of evidence during the last decade. Although unresolved issues still cast doubts on the real weight of these association, in the sequence of events that leads to gastric cancer or lymphoma, Helicobacter pylori appears to play a prominent role in the very initial steps as causative agent of chronic gastritis. The subsequent events in the sequence--atrophy, intestinal metaplasia, dysplasia and cancer are multifactorial involving environmental agents, host response and characteristics of the bacterial strain itself. Recognition of the causal role of Helicobacter pylori infection in the cancer induction theoretically presents tools for its prevention. The ongoing studies will show in the future whether eradication or prevention of infection are followed by a reduction in risk of cancer. Lymphomas arising from gastric mucosa-associated lymphoid tissue (MALT) may be a clonal evolution starting from the infection. In low-grade gastric MALT lymphoma cure of the infection induces complete remission in the majority of patients. Longer follow-up investigations are necessary to determine if remissions indicate a cure of the disease.

Qin, Y., et al. (2021). "Cancer-associated fibroblasts in gastric cancer affect malignant progression via the CXCL12-CXCR4 axis." Journal of Cancer 12(10): 3011-3023.

Background: Cancer-associated fibroblasts (CAFs) are principal constituents of the tumor microenvironment (TME) and play a critical role in tumor progression. The CXCL12/CXCR4 axis regulates multiple facets of the TME. The aim of this study was to determine the relationship between CXCL12 expression in CAFs and the malignant progression of gastric cancer (GC). Methods: In the GEO (Gene Expression Omnibus) database, we performed transcriptome analysis on paired gastric cancer RNA sequencing samples, and scRNA analysis was performed on advanced malignant GC samples from the scRNA sequencing data set. Fibroblast cells were co-cultured with GC cells, and invasion, migration, epithelial-mesenchymal transformation (EMT) were determined. After blocking the expression of fibroblast CXCL12, cells were co-cultured with a GC cell line. Detection of GC cell line invasion, migration, EMT and CXCR4, Wnt5a and β-Catenin expression levels was performed. Primary CAFs and gastric normal fibroblasts were isolated and CXCL12 mRNA and protein expression were determined. In addition, a cohort of 285 GC cases was established, protein expression was evaluated immunohistochemically, and prognostic results were analyzed. Results: GC transcriptome analysis suggested that cytokine-cytokine receptor interaction and the Wnt signaling pathway in GC tissues were significantly up-regulated. scRNA analysis of advanced malignant GC samples showed that severe intestinal metaplasia (SIM) in GC specimens of different malignant grades had obvious fibroblast clusters compared to non-atrophic gastritis (NAG) and early gastric cancer (EGC). In the SIM group, fibroblast cluster, CXCL12, CXCR4, and Wnt5a were overexpressed. Co-culturing with fibroblast cells significantly increased the invasion, migration, and EMT of GC cells, and blocking CXCL12 in CAFs disturbed the expression of Wnt5a and β-catenin. In our cohort of GC patients, high CXCL12 expression in CAFs significantly correlated with histological grade (P = 0.012) and TNM stage (P = 0.014), as well as with poor overall survival (p = 0.0107). Conclusion: High expression of CXCL12 in CAFs in a GC microenvironment can affect the migration, invasion, and EMT of GC cells. Furthermore, it can cause poor prognosis in patients with GC.

Qu, M., et al. (2017). "Reduced miR-490-3p expression is associated with poor prognosis of Helicobacter pylori induced gastric cancer." European Review for Medical and Pharmacological Sciences 21(15): 3384-3388.

OBJECTIVE: Helicobacter pylori (HP) infection has been demonstrated to be a risk factor accounting for the initiation and development of gastric cancer (GC). The aim of the present study was to investigate the clinical significance of miR-490-3p in HP associated GC. PATIENTS AND METHODS: We measured the expression level of miR-490-3p in human GC tissues by quantitative Real-time PCR (qPCR). Then the association between miR-490-3p and clinical features of GC was further investigated. RESULTS: Our results showed that miR-490-3p levels exhibited a progressive downregulation in gastritis, intestinal metaplasia, HP negative GC and HP positive GC. In addition, miR-490-3p expression was significantly correlated with various clinicopathological parameters such as lymph node metastasis and clinical stage in HP-positive GC. Moreover, GC patients with lower miR-490-3p had a shorter 5 years overall/disease free survival time in the HP positive cohort. Finally, multivariate analysis showed that low miR-490-3p was an independent risk factor for HP associated GC. CONCLUSIONS: miR-490-3p is downregulated in HP-positive GC and associated with poor clinical outcome, indicating that miR-490-3p is a promising prognostic biomarker for HP positive GC.

Raderer, M., et al. (2003). "Early cancer of the stomach arising after successful treatment of gastric MALT lymphoma in patients with autoimmune disease." Scandinavian Journal of Gastroenterology 38(3): 294-297.

BACKGROUND: Extranodal marginal zone B-cell lymphoma of the mucosa associated lymphoid tissue (MALT lymphoma) arises in lymphoid tissue acquired through chronic antigenic stimulation as exemplified by Helicobacter pylori. Secondary development of gastric cancer, however, is thought to be a rare event. The detection of a signet ring cell carcinoma during follow-up endoscopy after successful therapy of MALT lymphoma in a patient with Sjögren's syndrome prompted us to analyse the frequency of subsequent gastric cancer in patients with underlying autoimmune disease (AD). METHODS: Patients with early stage MALT lymphoma and an underlying AD were evaluated for the occurrence of a secondary gastric cancer during the course of follow-up. Data analysed included the type of AD, stage of MALT lymphoma, H. pylori status, treatment for MALT lymphoma and response, follow-up, the presence of a secondary cancer, and time to development of cancer. In all patients, histologic samples were reassessed for the extent of gastritis, presence of intestinal metaplasia or focal atrophy at the time of lymphoma diagnosis. RESULTS: A total of eight patients with overt AD at the time of diagnosis of MALT lymphoma were identified. All patients were women aged between 56 and 77 years; 5 had Sjögren's syndrome, 2 had autoimmune thyroiditis (1 along with psoriasis) and 1 suffered from polymyalgia rheumatica. All patients had early stage MALT lymphoma restricted to the mucosa and submucosa at the time of diagnosis, and the presence of H. pylori was found in all cases. Two of these patients achieved complete remission (CR) of the lymphoma following H. pylori eradication, while six were judged unresponsive and underwent chemotherapy, resulting in CR in all cases. One patient died from stroke while being in CR for 2 months following chemotherapy. Two patients (25%) developed early cancer limited to the gastric mucosa while being in CR from lymphoma for 9 and 27 months, respectively, and underwent partial gastrectomy. Final staging of gastric cancer revealed pT1pN0M0 in both cases. Of the remaining 5 cases, 1 patient had a local lymphoma relapse 18 months after CR and was salvaged with radiotherapy. In the remaining 4 patients, no evidence of lymphoma recurrence or a second malignancy has been found so far by regular follow-up every 3 months for a time-span between 52 and 63 months after initial diagnosis. CONCLUSION: Patients with concurrent MALT lymphoma and an underlying autoimmune condition show not only an impaired response to H. pylori eradication but might also be at increased risk for the development of gastric cancer. In view of this, such patients should be followed closely by regular endoscopies after remission of MALT lymphoma.

Rajnakova, A., et al. (2009). "Detection of pre-neoplastic gastric lesions in a high risk chinese cohort using endoscopic autofluorescence imaging followed by narrow band imaging versus standard white light endoscopy - Prospective randomized double blind crossover study." Gastrointestinal Endoscopy 69(5): AB107.

Background: Autofluorescence Imaging (AFI) and Narrow Band Imaging (NBI) are new endoscopic techniques that may improve the detection of pre-neoplastic gastric mucosal changes and early gastric cancer. Objective: Prospective Randomized Double Blind Cross-Over Study using combined AFI and NBI modalities vs standard white light endoscopy (WLE) to improve the detection of pre-neoplastic gastric lesions, such as intestinal metaplasia and mucosal atrophy and in high risk cohort. Patients: Informed consent was obtained from all subjects enrolled prospectively in study. Sixty-five Chinese patients age > 50 years with dyspepsia were examined by both standard WLE and combined AFI/NBI techniques consecutively in a randomized sequence at the same setting by two independent endoscopists blinded for the results of different endoscopic modality used. In the combined technique, the stomach was first examined by AFI followed by NBI. All identified lesions were documented in systematic order and biopsied. Lesional and two random biopsies from antrum, body, incisura and cardia were examined by two expert pathologists in a blinded fashion. Results: Of 65 patients recruited, one patient was excluded for advanced gastric cancer diagnosed by both methods. In remaing 64 patients, 228 lesions were identified and confirmed by histopathology, of which 146 (64%) lesions were identified by AFI/NBI technique and 82 (36%) by WLE. For the AFI/NBI technique 43/95 (45.3%) false positives and 20/51 (39.2%) were false negatives whereas for WLE it was 13/34 (38.2%) and 13/48 (27.1%) respectively. In total 30/63 (47.6%) subjects had intestinal metaplasia, of which 26 (86.7%) were correctly identified by AFI/NBI technique (sen = 83.9%, spec = 31.9%) and only 12 (40%) by WLE (sen = 54.5, spec = 71.0), p = 0.004. For mucosal atrophy, it was 10/12 (83.3%, sen = 58.8%, spec = 65.1%) for AFI/NBI and 4/12 (33.3%, sen = 50.0%, spec = 80.0%) for WLE, p = 0.109. The overall sensitivity and PPV to identify any abnormal mucosal changes for AFI/NBI was 72.2% and 41.9% respectively compared to WLE 61.8% and 72.9% respectively. Random biopsies analysis showed that from 11 subjects, 15/82 (18.3%) sites were missed by WLE compared to only 7/146 (4.8%) for AFI/NBI, p = 0.001. For intestinal metaplasia, from 8 subjects, 10 (12.2%) sites were missed by WLE compared to 3 (2.1%) by AFI/NBI, p = 0.002. There were no differences in the sites missed mucosal atrophy, from 6 subjects, by WLE (6.1%) and AFI/NBI (2.7%), p = 0.211. Conclusion: This study confirms that AFI/NBI technique is increases the detection of intestinal metaplasia which is a pre-malignant gastric lesion of clinical significance.

Ramirez-Lazaro, M., et al. (2015). "Spanish follow-up multicentric study on H. pylori virulence factors associated with the progression of gastric cancer precursor lesions. results at baseline biopsies." Helicobacter 20: 111-112.

Gastric cancer (GC) develops via a sequence of precursor lesions (PL): chronic atrophic gastritis (CAG), intestinal metaplasia (IM), and dysplasia. Progression depends on host background, virulence factors (VF) and environmental factors. Among the VF, cagA and vacA are by now the most relevant. The Spanish follow-up multicentric study of the progression of PL includes patients diagnosed with PL between 1995 and 2004. Patients who accepted to participate in the follow-up underwent a second endoscopy during the period 2011-2013. We show the results for the H. pylori genotyping at the baseline biopsy and report the risk of developing IM in the presence of VF. The study included 582 patients (53.6% men, age 51.8 years). DNA from FFPE blocks was used for analysis of VF vacA and cagA by LNA-PCR. Patients were classified into CAG, complete-IM (CIM), incomplete-IM (IIM) or dysplasia. Totally 390(67%) patients with PL were H. pylori-positive. Among these, 30.0% had CAG, 33.4% CIM, 32.8%IIM, and 3.8% dysplasia. cagA was present in 65.6% of H. pylori-positive patients. VacA alleles s1, m1 and the presence of cagA were more frequent in CIM-IIM (P < 0.0001). The calculated OR are in Table 1. In conclusion, patients with CAG infected with cagA+ and vacA s1/m1 are at higher risk of developing CMM-IMM. Table. Risk for CIM, IIM and dysplasia associated to the presence of CagA and VacA genotypes (Table Presented).

Ramírez-Mendoza, P., et al. (2011). "[Staging gastritis with the OLGA system: prevalence of advanced stages of gastric atrophy in Mexican patients]." Revista de Gastroenterología de México 76(4): 302-308.

INTRODUCTION: Gastric adenocarcinoma of intestinal type is preceded by inflammation, which produces mucosal atrophy and intestinal metaplasia, progressing eventually to dysplasia and invasive cancer. Recently an international group, the Operative Link on Gastritis Assessment (OLGA) proponed a staging system for gastric biopsies. OBJECTIVE: To recognize the distribution of advanced stages of gastric mucosal atrophy in Mexican patients with dyspepsia according to the OLGA system. METHODS: We apply the OLGA system for cancer risk (Stages 0 to IV) to 322 gastric biopsies from consecutive patients with dyspepsia. Using the Sydney protocol, we recorded the presence of atrophy, dysplasia and the relationship with ulcer disease. We report the stage of atrophy for each region and the Helicobacter pylori infection status. RESULTS: We documented 72 (22.4%) cases with atrophy, 50 of them (69.4%) were metaplastic-type. Overall, nine biopsies (2.78%) were stage III (all of them with metaplastic-type atrophy) and there was not stage IV cases. We did not find high-grade dysplasia or intramucosal carcinoma. In 8 of subjects with stage III, we observed low-grade dysplasia. We documented gastric ulcer in 5 patients with stage II, 60% of them with associated low-grade dysplasia. Five patients with duodenal ulcer were found in stages 0 and I. CONCLUSIONS: We found low prevalence of advanced stages of mucosal gastric atrophy among patients with dyspepsia. However we recognized 9 patients with stage III according to OLGA system worthy of follow-up because the high risk for developing gastric cancer.

Ray-Offor, E. and C. C. Obiorah (2018). "Helicobacter pylori and precancerous lesions of the stomach in a Nigerian Metropolis: A Cohort Study." Nigerian Journal of Clinical Practice 21(3): 375-379.

INTRODUCTION: Helicobacter pylori (H. pylori)-related atrophic gastritis transits through a sequential pathway of intestinal metaplasia, dysplasia to gastric cancer. Gastroscopy offers early detection, treatment and surveillance of gastric cancer. AIMS: This study aims to study the prevalence of H. pylori infection and evaluate precancerous lesions (PCLs) of the stomach. PATIENTS AND METHODS: This is a case controlled study of patients with dyspepsia undergoing gastroscopy at a referral endoscopy facility in Port Harcourt metropolis of Nigeria. The variables studied included demographics, clinical, endoscopic, and histopathologic findings. Statistical analysis of data was done using IBM SPSS Statistics for Windows, Version 20.0. (Armonk, NY, USA). RESULTS: A total of 104 patients were included in the study. Age ranged from 20 to 80 years (mean 47.1 ± 14.4 years); 56 were males and 48 were females. H. pylori were detected in 40 (38.5%) mucosal biopsies. The prevalence of PCLs was: chronic atrophic gastritis 6.7% (7 cases); intestinal metaplasia 2.9% (3 cases); and dysplasia 5.8% (6 cases). There was no statistical significance in sex distribution of PCLs (P = 0.245). CONCLUSION: There is a low prevalence of H. pylori in this metropolitan population. Mandatory multiple topographically targeted biopsies, even with normal mucosal appearance, at gastroscopy in addition to surveillance of PCL are recommended for early detection of gastric cancer.

Raza, M. and H. Bhatt (2021). Atrophic Gastritis. StatPearls. Treasure Island (FL), StatPearls Publishing

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Gastric atrophy (GA) and intestinal metaplasia of the gastric mucosa (GIM) are collectively known as chronic atrophic gastritis (CAG). These early conditions can lead to the development of gastric adenocarcinoma (GC). This review focuses on the current evidence and guidelines in diagnosis, management, and surveillance of chronic atrophic gastritis to identify those at risk of progression to gastric adenocarcinoma. Chronic atrophic gastritis is considered a precursor lesion for gastric cancer, which is the fifth most common cancer globally and carries third-highest cancer-related mortality in the world. This aggressive cancer presents late in most countries with no screening program and leads to numerous deaths due to late diagnosis. The common etiologies of this premalignant lesion are Helicobacter pylori (H. pylori) and autoimmune gastritis. Chronic inflammation leads to the loss of gastric mucosa leading to an acid depleted environment hypothesized as an early precursor to distal gastric cancer. H. pylori is a microaerophilic gram-negative bacterial pathogen. Its role has been implicated in not only atrophic gastritis but also peptic ulcers, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (MALT). Identification and eradication of the pathogen have a significant role in reducing the risk of CAG. It is of utmost importance to identify the precancerous lesions by identifying those at risk. It is also crucial to follow-up with surveillance endoscopy and, if needed, endoscopically intervening to avoid major resection surgery in advanced stage gastric cancer. The popular Correa Cascade suggested the linear progression from chronic atrophic gastritis (CAG) with metaplastic intestinal epithelium to low-grade dysplasia (LGD), high-grade dysplasia (HGD), and eventually gastric adenocarcinoma.

Reddy, K., et al. (2014). "Gastric intestinal metaplasia and risk of gastric cancer in a diverse integrated healthcare setting." Gastroenterology 146(5): S-513.

Background: Gastric intestinal metaplasia (GIM) is a common finding on routine endoscopy. Although GIM is an established early step in gastric carcinogenesis, controversy exists regarding whether routine surveillance should be performed in individuals with GIM in low prevalence regions such as the United States. Objective: Our study aims were to 1) determine frequency of gastric cancer among patients with GIM in a large diverse integrated healthcare setting and 2) evaluate risk factors for gastric cancer in this patient population. Methods: We conducted a retrospective cohort study using data from an integrated health system in Southern California between 2000 and 2011. Patients with GIM identified on endoscopic biopsy were identified by key word search of pathology reports. Individual pathology reports were manually reviewed to confirm the diagnosis of GIM. Cases of gastric cancer were identified by cross-reference with a prospectively collected internal gastric cancer registry. Patients with history of gastric cancer diagnosed prior to detection of GIM were excluded. Patients with gastric cancer diagnosed within 30 days of GIM were considered to have gastric cancer present at the time of initial diagnosis. Risk factors for gastric cancer examined in the study included race/ethnicity, smoking status, H. pylori status, family history of gastric cancer, and body mass index. Results: We identified a total of 935 patients with GIM on routine endoscopy during the study period. Eleven patients were excluded based on prior history of gastric cancer. Among the remaining 924 patients, median age at diagnosis was 68.1 years (interquartile range IQR 58.3, 76.3). Median duration of follow-up was 4.6 years (IQR 3.0, 6.7). There were a total of 26 cancers detected during the study period. Seventeen [65%] of cancers were diagnosed at the time of GIM and 9 [35%] cancers were diagnosed after GIM. For those cancers diagnosed after GIM, the median time until diagnosis of cancer was 55 months (IQR 24, 68). Mortality among patients with gastric cancer was 50%. Among the risk factors we evaluated, only family history was associated with increased risk of gastric cancer in this cohort (odds-ratio 3.8 [95% CL 1.5, 9.7]), χ2 p=0.012). Conclusions: Among patients with gastric intestinal metaplasia, 2.8% had gastric cancer diagnosed during the study period. The majority of cancers were present at the time of GIM diagnosis. Of the risk factors evaluated, family history was the only risk factor associated with a statistically significant increase in gastric cancer. Given the high mortality among patients with gastric cancer, surveillance of patients with both GIM and a family history of gastric cancer could potentially lead to improvement in survival based on earlier detection. (Table presented) .

Reddy, K. M., et al. (2016). "Risk of Gastric Cancer Among Patients With Intestinal Metaplasia of the Stomach in a US Integrated Health Care System." Clinical Gastroenterology and Hepatology 14(10): 1420-1425.

BACKGROUND & AIMS: Gastric intestinal metaplasia (GIM) is a common finding from routine endoscopies. Although GIM is an early step in gastric carcinogenesis, there is controversy regarding routine surveillance of patients with GIM in regions with a low prevalence of gastric cancer. We aimed to determine the incidence of gastric cancer among patients with GIM and risk factors for gastric cancer. METHODS: We performed a retrospective cohort study of patients from the Kaiser Permanente Southern California region diagnosed with GIM from 2000 through 2011. GIM was identified by a keyword search of pathology reports; gastric cancer cases were identified by cross-reference with an internal cancer registry. The incidence of gastric cancer in patients with GIM (n = 923; median age at diagnosis, 68 y) was compared with that of an age- and sex-matched reference population (controls). Risk factors such as ethnicity, smoking status, history of Helicobacter pylori infection, and family history of gastric cancer were evaluated by individual Cox proportional hazards regression. We then performed a second case-cohort study to evaluate the risk of gastric cancer based on the location and extent of GIM. The median duration of follow-up evaluation was 4.6 years (interquartile range, 3.0-6.7 y). RESULTS: We identified 25 patients with GIM who developed gastric cancers. Seventeen cases of cancer were diagnosed at the same time as the diagnosis of GIM. Eight cases of cancer were identified within a median time period of 4.6 years after a diagnosis of GIM (interquartile range, 2-5.7 y). The overall incidence rate for the cohort was 1.72 (95% confidence interval, 0.74-3.39). Among the risk factors evaluated, only family history (hazard ratio, 3.8; 95% confidence interval, 1.5-9.7; P = .012) and extent of GIM (odds ratio, 9.4; 95% confidence interval, 1.8-50.4) increased the risk for gastric cancer. The incidence rate for gastric cancer in patients with a positive family history was 8.12 (95% confidence interval, 1.67-23.73). CONCLUSIONS: In an analysis of patients with GIM listed in the Kaiser Permanente Southern California database, 2.7% were diagnosed with gastric cancer; almost 70% of cases of gastric cancer were detected at the time of GIM diagnosis. Family history and extensive metaplasia were associated with an increased risk of subsequent gastric cancer. Targeted surveillance of patients with these criteria could increase early detection of gastric cancer.

Reddy, S. B., et al. (2017). "Gastric intestinal metaplasia-survey of current perceptions and practices among gastroenterologists." Gastrointestinal Endoscopy 85(5): AB194.

Purpose: Gastric cancer is a leading cancer worldwide. While the prevalence of gastric cancer in United States is low, its incidence is high in certain subgroups of patients. Patients with gastric intestinal metaplasia (GIM) may have a 10-fold increased risk of gastric cancer than general population. There are no optimal surveillance guidelines although the ASGE recommends endoscopy for GIM in patients who are at increased risk of gastric cancer such as family history or ethnicity. We aimed to survey the practices of gastroenterologists who encounter this endoscopic pathology in daily practice. Methods: An online web based survey was sent to 2,123 Board-certified and Board-eligible gastroenterologists across the Southeastern United States. Information from the survey included years spent in practice, setting of practice, protocol for performing gastric biopsies for Helicobacter pylori, and protocol for management and follow up of GIM. Result: Of the 46 respondents, the majority (69.6%) had been in in practice for over 10 years. 42 (91.3%) respondents would send an antral biopsy for Helicobacter pylori for histology testing as opposed to a rapid urease test. Of these 42 respondents, if the histology revealed chronic gastritis without H. pylori, 12.5% would further order a urea breath test and 80.0% would consider this clinically insignificant and not do any further workup. If gastric biopsies showed intestinal metaplasia, 35.1% consider this clinically insignificant and would not pursue any further follow-up endoscopy workup while 64.9% of respondents would perform a surveillance endoscopy at a later date. Of those who would perform a surveillance endoscopy, 7.1% would repeat the endoscopy in 6 months, 28.6% in 1 year, 32.1% in 2 years, and 32.1% in 3 years. Conclusion: Higher proportion of gastroenterologists prefers sending antral biopsies for histology while remaining opting for a rapid urease test. There is no clear consensus on the follow-up of GIM while majority pursue surveillance endoscopy irrespective of risk factors. Larger multicenter prospective studies are needed to study the follow-up and risk stratification of patients with GIM.

Reed, P. I. and B. J. Johnston (1995). "Primary prevention of gastric cancer - The ECP-IM intervention study." Acta Endoscopica 25(1): 45‐54.

Rico, F. P. and J. Cruz-Cruz (2017). "Gastric intestinal metaplasia: Epidemiological and demographic characterization in hispanics." American Journal of Gastroenterology 112: S1508.

Introduction: Gastric intestinal metaplasia (GIM), a key event in gastric carcinogenesis, is the replacement of gastric mucosa by an epithelium that histologically resembles intestinal mucosa. Helicobacter pylori (H. pylori), the most common chronic bacterial infection in humans, is known to be associated with gastric carcinogenesis. Classification of GIM by histological subtype and pattern sets an important goal for proper surveillance measures. Incomplete GIM confers 4- to 11-fold increased risk for gastric cancer. Despite this, there is no previous data available of GIM prevalence and characterization in Puerto Rico (PR). The aim of this study is to determine the prevalence of GIM within the cohort of patients in PR who underwent diagnostic endoscopy for the period of 2012-2014, and to characterize the demographical and clinicopathological profile of individuals with GIM. Methods: A cross sectional study design using pathology reports of 4,707 endoscopic biopsies with confirmed diagnosis of GIM between 2012-2014 was performed. These reports were reviewed, and the demographic, geographic, and histopathological data provided were analyzed for characterization of this condition. Study characteristics were described using frequency distributions for categorical variables. SPSS version 17 was used for statistical analysis. Results: Between 2012-2014, the prevalence of GIM was 10.7%, of which 26.9% of cases were positive for H. pylori. GIM was frequently found at incisura angularis and antrum biopsies. Approximately 99.6% and 71.2% of the reviewed pathology reports lack information about GIM histological subtype and pattern respectively. Conclusion: The prevalence of GIM is difficult to establish due to asymptomatic nature of the lesion, insufficient number of biopsies or inappropriate localization of biopsies. Despite this, the prevalence of GIM in PR appears to be higher than in United States. We observed that pathology reports lack the proper characterization of GIM necessary to provide adequate surveillance.

Riquelme, A., et al. (2017). "Trefoil-family-factor-3 as a non-invasive biomarker of gastric intestinal metaplasia and gastric cancer in a country with high prevalence of gastric cancer." Gastroenterology 152(5): S1031.

Introduction: Gastric cancer (GC) is preceded by a histological cascade of premalignant lesions starting with atrophic gastritis (AG) and followed by gastric intestinal metaplasia (IM). Several non-invasive biomarkers have been proposed to detect GC and its premalignant lesions. Trefoil Family Factor 3 (TFF3) is a peptide secreted by goblet cells, which increase during intestinal metaplasia. While TFF3's potential as a GC biomarker has been studied in Asian countries, these results have not been validated in other high prevalence areas, such as Latin America. In this cross-sectional study, we aim to assess the sensitivity and specificity of TFF3 in the diagnosis of AG, IM and GC in a high-risk population in Chile. Methods: We performed esophagogastroduodenoscopy (EGD) in 289 symptomatic patients >40 years old, in a region of Chile with a high prevalence of GC. Gastric biopsies were obtained following the Sydney protocol. Biopsy tissue was assessed using the Operative Link Gastric Atrophy Assessment (OLGA) and the Operative Link Gastric Intestinal Metaplasia (OLGIM) staging systems. Additionally, 14 cases with GC were included in this study for comparison. Blood samples were obtained in all patients and serum TFF3 levels were assessed using ELISA. Results: Two-hundred and six (71.3%) of study participants were female. Mean age was 57.3 years old (Range: 40-84). One hundred and ninety-eight (68.5%) patients had GA and 114 (39.4%) had IM. Mean serum levels of TFF3 in the group with normal histology (OLGA/OLGIM stage 0) was 13.8 ng/mL. The group with GA had 19.5 ng/mL (p=0.804), IM group had 15.9 ng/mL (p=0.007) and finally, the group of patients with GC has 28.7 ng/mL (p=0.001). Based on the previous results, ROC curves were constructed for TFF3 and GA with an area under the curve (AUC) of 0.488 (CI95%; 0.407-0.570; p=0,804). The AUC for serum TFF3 and IM was 0.594 (CI95%; 0.527-0.662; p=0.007). AUC for serum TFF3 and GC was 0.767 (CI95%; 0.632-0.903; p=0.001) including all ages but a similar model assessment was performed including patients between 40 to 60 years-old showing AUC of 0.824 (CI95%; 0.689-0.959; p<0.001). In this group of patients, a cut-off value of 13 ng/mL was established (sensitivity 80% and specificity 70%) and a higher cutoff (19 ng/mL) increased the specificity (sensitivity 60% and specificity 94%) Conclusion: TFF3 is a useful non-invasive serum marker of IM and GC. However, it is not associated with GA. Combination of other serum markers of GA like pepsinogen I/II with TFF3 can be used as a screening strategy to detect premalignant lesions (GA and IM) in order to select patients to prioritize their access to EGD and establish follow-up strategies in patients in countries with high prevalence of GC like Chile.

Robinson, K., et al. (2016). "Bacterial DNA integrations in the genomes of gastric tumor and adjacent samples." Cancer Research 76(14).

There are 10 times more bacterial cells in the human body than human cells, and various bacteria are known to influence carcinogenesis. While viral DNA integrations in the human genome have been shown to promote carcinogenesis, bacterial DNA integrations (BDI) into the human genome are rarely investigated. Our previous analysis of publicly available sequencing data from the Cancer Genome Atlas showed BDIs from Pseudomonas spp. rRNA into the 5'-UTR of four proto-oncogenes as well as in Ig (the immunoglobulin gene) of gastric cancer samples. However, we were left with many unanswered questions when we were unable to obtain the materials required to validate our findings. Therefore, we sought to sequence a different cohort of gastric cancer patients in order to identify BDIs. Whole exome sequencing was completed on seven tumor samples and six adjacent gastric samples, as well as one intestinal metaplasia sample and one non-atrophic gastritis sample. Four of those samples were also investigated with transcriptomics and whole genome sequencing. Using our previously published BWA-based pipeline, we identified putative BDIs from Helicobacter pylori rRNA into numerous genes in one tumor sample as well as in its adjacent matched sample, including BDIs in the Ig locus. Helicobacter pylori is considered a carcinogen by the World Health Organization due to its ability to promote carcinogenesis in gastric tissue, causing us to speculate that these integrations could be carcinogenic. Similarly to our analysis of the Cancer Genome Atlas data, we also identified a few samples with BDIs from Pseudomonas spp. and about half of the samples possessed BDIs from other bacteria. We identified at least one BDI in each sample regardless of the sequencing data type. Validation of these results is ongoing and will be presented. Given these results, more consideration should be given to BDIs into the human genome when bacterial associations with diseases are suspected.

Rocco, A., et al. (2002). "Gastric atrophy and intestinal metaplasia changes 8 years after Helicobacter pylori eradication. A blind, randomised study." Minerva Gastroenterologica e Dietologica 48(2): 175-178.

BACKGROUND: Chronic atrophic gastritis and intestinal metaplasia are regarded as predisposing factors for gastric cancer associated with Helicobacter pylori infection, and their severity appears to influence gastric cancer risk. Our purpose was to determine the outcome of chronic gastritis after H. pylori eradication in a long-term follow-up. METHODS: Fifty-four consecutive patients with duodenal ulcer and H. pylori infection were enrolled in the study. Endoscopic examination with antral and corporal biopsy was done at baseline and yearly after conventional eradication therapy (omeprazole 40 mg b.i.d., amoxocyllin 1 g b.i.d and clarithromycin 500 mg b.i.d.). Gastritis, atrophy, and metaplasia were graded according to the updated Sydney System. RESULTS: Twenty-four patients were successfully treated; infection persisted in 14 and 16 dropped out (during the first 5 years of follow-up). Inflammation and mean neutrophil activity significantly decreased in patients in whom H. pylori was eradicated. Glandular atrophy improved in 2 and disappeared in 5/17 patients, whereas intestinal metaplasia improved in 3 and disappeared in 2/12. In the patients in whom H. pylori persisted, inflammatory infiltrate, atrophy and intestinal metaplasia had not significantly decreased during follow-up. In contrast, glandular atrophy worsened in 2 and developed in 5/7 patients. Similarly, intestinal metaplasia did not improve when present and developed in 5/13 cases. CONCLUSIONS: In a long-term follow-up, H. pylori eradication does not affect glandular atrophy, but it seems to prevent the development of precancerous lesions such as intestinal metaplasia.

Rodríguez De Santiago, E., et al. (2018). "Characteristics, risk factors and survival of missed gastric cancer: A multicentric cohort study." United European Gastroenterology Journal 6(8): A520-A521.

Introduction: Missed gastric cancer (MGC) at upper gastrointestinal endoscopy (UGE) is a poorly documented entity in Western populations. Aims and Methods: 1. To assess the rate, predictors and survival of MGC. 2. To compare MGC and non-MGC and detect factors associated with negative UGE. Retrospective-cohort study conducted at 4 tertiary Spanish hospitals. Gastric adenocarcinomas diagnosed between 2008-2015 were included. Patients referred for treatment from other centers (n=64) or without follow-up (n=21) were excluded. MGC was defined as a cancer detected within 36 months after a negative UGE for malignancy. Demographic, clinical, endoscopic, histological and survival data were recorded. Statistics: Unconditional binomial logistic regression and Kaplan-Meier with the log-rank test. Results: 123,395 UGE were performed during the study period, and 1374 GC were diagnosed (1.11%). 1289 patients with GC were finally included in the analysis. Mean age was 74.1 years (SD: 11.2) and 62% were males. Global MGC rate was 4.73% (61/1289, CI 95%: 3.7-6 %), without significant differences across centers (p=0.23). Median time between negative UGE and MGC diagnosis was 13.1 months (range: 3.1-35.2). The median number of negative UGEs in MGC group was 1 (range:1-3). Gastritis (51%), intestinal metaplasia (41%), gastric atrophy (31%) and gastric ulcers (29.5%) were the most common findings at negative UGE. These ulcers were benign at histology and were not endoscopically monitored. Compared to confirmed malignant ulcers in Non-MGC group (n=610), ulcers at negative UGE were smaller (median: 10 vs 30 mm, p=0.02) and less frequently biopsied (median: 1 vs 3.5, p<0.001). At multivariate analysis, negative UGE was independently associated with younger age (OR: 0.96, p=0.001), PPI therapy (OR: 5.72, p<0.001), previous Billroth II surgery (OR: 5.2, p=0.002) and absence of alarm symptoms (OR 0.21, 47.5% vs 78.5%, p<0.001) (Table 1). The gastric body (52.4%) and intestinal-type (55.6%) were the most common location and histological subtype of MGC, respectively, without differences with Non-MGC. Compared to Non-MGC, MGC were smaller (31 vs 41 mm, p=0.04), more frequently flat-depressed (49.2% vs 29%, p=0.003) and diagnosed at an earlier stage (Stage I-II: 47.4% vs 28.3%, p=0.023). Overall 2-year survival rate was similar for MGC (34%) and Non-MGC (35.3%) (log-rank p=0.59). Conclusion: MGC is frequent and associated with poor 2-year survival. Our study found independent factors associated with MGC and negative UGE that may be helpful for clinical practice. High-quality UGE may help to reduce MGC incidence. (Table Presented).

Rokkas, T., et al. (2017). "A systematic review and meta-analysis of the role of Helicobacter pylori eradication in preventing gastric cancer." Ann Gastroenterol 30(4): 414-423.

BACKGROUND: Increasing evidence has suggested that Helicobacter pylori (H. pylori) eradication might prevent the development of gastric cancer (GC). This systematic review and meta-analysis aimed to better explore the role of H. pylori eradication in preventing GC, with particular reference to patients with precancerous lesions at baseline histology. METHODS: Searches for human studies were performed through October 2016 and risk ratios (RRs), were obtained. Heterogeneity between studies was estimated using the Cochran Q test and I(2) values, whereas the possibility of publication bias was estimated with funnel plots. Additionally, we performed subgroup and sensitivity analyses. RESULTS: In 26 studies suitable for meta-analysis (10 randomized controlled trials and 16 cohort studies) 52,363 subjects were included. The risk of GC among patients in whom H. pylori was successfully eradicated was significantly lower than that among controls: pooled RRs [95% CI] 0.56 [0.48-0.66], Z= -7.27, P=0.00001. This finding applied separately for randomized controlled trials (0.65 [0.51-0.84], Z= -3.33, P=0.0009) and for cohort studies (0.51 [0.42-0.62], Z= -6.63, P=0.00001). Concerning H. pylori eradication in patients with precancerous lesions, subgroup analyses showed that patients with non-atrophic or atrophic gastritis benefited from H. pylori eradication for the risk of GC development, whereas those with intestinal metaplasia or dysplasia did not. CONCLUSION: H. pylori eradication is associated with a significantly lower risk of GC; this finding has significant implications for the prevention of this cancer. The benefit is maximized when H. pylori eradication is applied at early stages of the infection.

Rokkas, T., et al. (2010). "Helicobacter pylori infection and gastric histology in first-degree relatives of gastric cancer patients: a meta-analysis." European Journal of Gastroenterology and Hepatology 22(9): 1128-1133.

OBJECTIVES: Helicobacter pylori (H. pylori) is believed to predispose to gastric cancer by inducing the precancerous changes, that is, atrophy and intestinal metaplasia (IM). First-degree relatives of patients with gastric cancer might be at an increased risk of developing gastric cancer. However, this evidence is based on the scattered individual studies. The aim of this study was to examine the risk of first-degree relatives developing gastric cancer, in comparison with controls that have no family history of gastric cancer, by meta-analyzing all relevant studies. METHODS: Extensive English language medical literature searches for human studies were performed up to the end of November 2009, using suitable keywords. Inclusion and exclusion criteria were identified and in eligible studies data on three parameters, that is, H. pylori prevalence, atrophy and IM, were extracted. Pooled estimates (odds ratio with 95% confidence intervals) were obtained using either the fixed or random-effects model as appropriate. Heterogeneity between studies was evaluated with the Cochran Q test, whereas the likelihood of publication bias was assessed by constructing funnel plots. Their symmetry was estimated by the Egger's regression asymmetry test. RESULTS: Out of 155 initially identified studies, 11 studies, from various countries, fulfilling the inclusion criteria, examined the risk of first-degree relatives developing gastric cancer (n=1500) in comparison with controls (n=2638). For H. pylori prevalence, the pooled odds ratio with 95% confidence interval was 1.925 (1.419-2.611) and the test for overall effect Z was 4.211 (P=0.000). The respective values for atrophy and IM were 2.200 (1.266-3.824), Z=2.797, (P=0.005) and 1.982 (1.363-2.881), Z=3.582 (P=0.000) respectively. CONCLUSION: The results of this meta-analysis showed that first-degree relatives of patients with gastric cancer might be at an increased risk of developing gastric cancer, as judged by significantly higher prevalence of H. pylori, gastric atrophy and IM, in comparison with controls. Consequently, H. pylori detection and prophylactic eradication of the infection should be offered to such individuals. However, follow-up studies are required to prove the above.

Rollán, A., et al. (2014). "[Recommendations of the Chilean Association for Digestive Endoscopy for the management of gastric pre-malignant lesions]." Revista Medica de Chile 142(9): 1181-1192.

An expert panel analyzed the available evidence and reached a consensus to release 24 recommendations for primary and secondary prevention of gastric cancer (CG) in symptomatic patients, with indication for upper GI endoscopy. The main recommendations include (1) Search for and eradicate H. pylori infection in all cases. (2) Systematic gastric biopsies (Sydney protocol) in all patients over 40 years of age or first grade relatives of patient with CG, to detect gastric atrophy, intestinal metaplasia or dysplasia. (3) Incorporate the OLGA system (Operative Link on Gastritis Assessment) to the pathological report, to categorize the individual risk of CG. (4) Schedule endoscopic follow-up according to the estimated risk of CG, namely annual for OLGA III- IV, every 3 years for OLGA I- II or persistent H. pylori infection, every 5 years for CG relatives without other risk factors and no follow-up for OLGA 0, H. pylori (-). (4) Establish basic human and material resources for endoscopic follow-up programs, including some essential administrative processes, and (5) Suggest the early CG/total CG diagnosis ratio of each institution and the proportion of systematic recording of endoscopic images, as quality indicators. These measures are applicable using currently available resources, they can complement any future screening programs for asymptomatic population and may contribute to improve the prognosis of CG in high-risk populations.

Royero, H. (2019). "Detection of gastric preneoplastic lesions according to the olga-olgim systems in the province of Ocaña: Colombia." Turkish Journal of Gastroenterology 30: S364.

Background/Aims: Gastric cancer of the intestinal type can be preceded by atrophy and intestinal metaplasia in the stomach. The follow-up of these findings through OLGA systems (Operative link on Gastritis Assessment) and OLGIM (Operative link on Metaplasia Assessment), can simplify its clinical approach and estimate the surveillance intervals / to determine the prevalence of high-risk lesions for gastric cancer using the OLGA-OLGIM systems simultaneously in the province of Ocaña. Materials and Methods: Retrospective descriptive study, carried out in a reference center in Ocaña, Colombia between January 2011 and April 2019. We included 1380 consecutive patients who had an esophagogastroduodenoscopy indicated, we obtained the information from the endoscopic and histological reports, the inclusion criteria were individuals equal to or older than 18 years, patients with previous gastric surgeries, upper gastrointestinal bleeding, advanced gastric neoplasia and incomplete reports were excluded. Gastric biopsies were taken and analyzed according to the recommendations of the Sydney protocol; Helicobacter Pylori (Hp) positive was considered if it was observed in some of the histological samples. The findings were tabulated in Excel 2007 and the frequencies were analyzed in EPI-INFO, a p<0.05 was considered significant. Results: The female man ratio was 1: 0.67, the average age was 50.65% +/-15.9 (range 18-91 years), the classification of the stadiums by Olga-Olgim was: Stage 0 (1014/1055 ); Stage I (249/216); Stage II (86/81); Stage III (26/23); Stage IV (5/5), the concordance between the two systems was 96.5% (Table 1). The OLGA and OLGIM system found similar findings in high risk patients (III and IV) 2.24% vs 2.03% respectively, of these 93% of the patients with OLGA and 92% with OLGIM, were found in patients older than 45 years (p<0.000), the Hp was diagnosed in 48% of the subjects, being less frequent in stages III and IV (p=0.004 and P=0.039) respectively. Conclusion: Our population has a low prevalence of high-risk lesions (III-IV), presenting mainly in people older than 45 years, only in this group endoscopic surveillance would be recommended. No differences were found in the use of the OLGA-OLGIM system in the stratification of gastritis. (Table Presented) .

Rubio, C. A., et al. (1993). "Gastric intestinal metaplasia eleven years after randomized selective proximal vagotomy for peptic ulcer." Histology and Histopathology 8(2): 243‐245.

Rugge, M., et al. (2011). "Operative link for gastritis assessment vs operative link on intestinal metaplasia assessment." World Journal of Gastroenterology 17(41): 4596-4601.

AIM: To compare the reliability of gastritis staging systems in ranking gastritis-associated cancer risk in a large series of consecutive patients. METHODS: Gastric mucosal atrophy is the precancerous condition in which intestinal-type gastric cancer (GC) most frequently develops. The operative link for gastritis assessment (OLGA) staging system ranks the GC risk according to both the topography and the severity of gastric atrophy (as assessed histologically on the basis of the Sydney protocol for gastric mucosal biopsy). Both cross-sectional and long-term follow-up trials have consistently associated OLGA stages III-IV with a higher risk of GC. A recently-proposed modification of the OLGA staging system (OLGIM) basically incorporates the OLGA frame, but replaces the atrophy score with an assessment of intestinal metaplasia (IM) alone. A series of 4552 consecutive biopsy sets (2007-2009) was retrieved and reassessed according to both the OLGA and the OLGIM staging systems. A set of at least 5 biopsy samples was available for all the cases considered. RESULTS: In 4460 of 4552 cases (98.0%), both the high-risk stages (III + IV) and the low-risk stages (0 +I + II) were assessed applying the OLGA and OLGIM criteria. Among the 243 OLGA high-risk stages, 14 (5.8%) were down-staged to a low risk using OLGIM. The 67 (1.5%) incidentally-found neoplastic lesions (intraepithelial or invasive) were consistently associated with high-risk stages, as assessed by both OLGA and OLGIM (P < 0.001 for both). Two of 34 intestinal-type GCs coexisting with a high-risk OLGA stage (stage III) were associated with a low-risk OLGIM stage (stage II). CONCLUSION: Gastritis staging systems (both OLGA and OLGIM) convey prognostically important information on the gastritis-associated cancer risk. Because of its clinical impact, the stage of gastritis should be included as a conclusive message in the gastritis histology report. Since it focuses on IM alone, OLGIM staging is less sensitive than OLGA staging in the identification of patients at high risk of gastric cancer.

Rugge, M., et al. (2021). "Gastritis: The clinico-pathological spectrum." Digestive and Liver Disease.

The inflammatory spectrum of gastric diseases includes different clinico-pathological entities, the etiology of which was recently established in the international Kyoto classification. A diagnosis of gastritis combines the information resulting form the gross examination (endoscopy) and histology (microscopy). It is important to consider the anatomical/functional heterogeneity of the gastric mucosa when obtaining representative mucosal biopsy samples. Gastritis includes self-limiting and non-self-limiting (long-standing) inflammatory diseases, and the latter are epidemiologically, biologically and clinically linked to the onset of gastric cancer (i.e. "inflammation-associated cancer"). Different biological models of inflammation-associated gastric oncogenesis have been proposed. Helicobacter pylori (H. pylori) gastritis is the most prevalent worldwide, and H. pylori is classified as a first-class carcinogen. On these bases, eradicating H. pylori is mandatory for the primary prevention of gastric cancer. Non-self-limiting gastritis may also be triggered by the immune-mediated destruction of gastric parietal cells, resulting in autoimmune gastritis. In both H. pylori-related and autoimmune gastritis, the non-self-limiting inflammation results in atrophy of the gastric mucosa, which is the main factor promoting gastric cancer. Long-term follow-up studies consistently demonstrate the prognostic impact of the histological staging of gastritis in gastric cancer secondary prevention strategies.

Sadjadi, A., et al. (2012). "Helicobacter pylori infection and development of gastric cancer a 10-year follow-up population-based study in a high incidence area." Gastroenterology 142(5): S630.

Backgrounds & Aim: H. pylori (HP) infection is the most important etiology of gastric cancer (GC) in the world but it causes GC in only a minority of those infected .Eradication of HP can decrease the development of GC only in the subgroup of HP infected subjects without precancerous lesions. Strategies of HP eradication is still not well defined in countries with high mortality rates secondary to GC with almost universal HP infection in adults. The aim of the present study was to investigate the predictors of GC in an adult population with almost universal HP infection in an area with highest rate of gastric cancer in the world. Methods: 1011 healthy subjects 40 years and older, permanent residents of Ardabil and Meshkinshahr districts in northwest Iran, were randomly selected and enrolled in an endoscopic screening study during 2000 to 2001 year. Data on demographics and potential risk factors were collected using a well-structured questionnaire. Upper gastrointestinal endoscopy with multiple biopsy sampling was performed to detect HP infection and endoscopic precancerous lesions.Participants have been followed up until 2011. During followup period data on the occurrence of GC, mortality, and cause of death were obtained from cancer and death registries, and when neccessary by direct contacting to participants, and their families. The cumulative incidence and person-time incidence rate were calculated. The effect of other risk factors in addition to H. pylori infection on the risk of GC development were estimated by fitting multivariate hazard model using Cox proportional regression analysis, and were presented as hazard ratio (HR) and corresponding 96% confidence interval (95%CI). Results: During 10-year follow up, 36 participants (3.6%) developed GC yielding an incidence rate of 3.6 per 1000 person-years. The significant risk factors of GC included age over 50 (HR 4.8; 95%CI 1.4-16.2), a positive family history of stomach cancer (6.4; 3.1-13.1), smoking (5.7; 2.5-12.6), gastric atrophy (2.3; 1.0-5.1), intestinal metaplasia (4.5; 2.3-8.9) and presence of gastric ulcer (4.8; 1.9-11.5). Joint presence of precancerous lesion and one of the other risk factors significantly increased risk of stomach cancer as (46.5; 10.8-98.6) for a positive family history of stomach cancer; (27.6; 6.5-116.4) for smoking and (25.1; 16.3-105.3) for age>50. Conclusion: Combining the information on family history, lifestyle risk factors and the type of precancerous lesion may be helpful in order to identify high risk HP infected patients who need more intensive surveillance for early detection of GC. Key words: Stomach cancer, Precancerous lesions, Risk factors, H. pylori, Ardabil,Iran.

Sadjadi, A., et al. (2016). "Helicobacter pylori associated gastric mucosal changes in high risk area of gastric cancer, northwest Iran prospective cohort study with 10 years follow up." Gastroenterology 150(4): S869.

BACKGROUND Even though the worldwide incidence of gastric cancer is declining, it remains highly prevalent in Asia. Areas with high incidence of gastric cancer have higher prevalence of precancerous lesions. We have shown that the Ardabil province in Northwest Iran is a high-risk area for gastric cancer. The last population-based survey showed very high prevalence of H.pylori infection and gastric mucosal changes predisposing gastric cancer. As the incidence of gastric cancer in declining in the area, we aimed to explore background gastric mucosal changes in a subgroup of the adult population who underwent the first assessment 10 years ago, intended to explain declining trend of gastric cancer. METHODS & PATIENTS: Nine hundreds twenty-eight adult volunteers, randomly selected from general population were assessed endoscopically and histologically for inflammatory and precancerous lesions 10 years ago. We reassessed a subgroup of the same subjects through a systematic investigation by same endoscopic and histological criteria. Biopsies from antral, body and cardiac mucosa were evaluated through pairwise analysis. RESULTS: For the period of 9,096 person-years of 928 participants follow-up, 36 new cases of stomach cancer were detected (incidence rate: 3.96/1,000 persons-years). 325 (42.48%) of 765 alive participants accepted and underwent secondary upper GI endoscopy and biopsy. In baseline examination, 68.7% of volunteers had active chronic gastritis and 27.9% chronic gastritis. Reassessment showed 155/205 (75.6 %) of those with active chronic gastritis in baseline examination were downgraded to chronic gastritis after 10 years without any active intervention. Similar changes from active chronic gastritis to chronic gastritis were found in gastric body mucosa of 86%, and in the cardiac mucosa of 89% subjects. The prevalence of H.pylori infection detected histologically were declines from 78.9% to 51.4%. The declining prevalence of active chronic gastritis was associated with either total or partial disappearance of H.pylori infection. There were no significant changes in the prevalence of either atrophic gastritis or intestinal metaplasia in different biopsies of subjects during study period. CONCLUSION: Improvement of gastric mucosal inflammatory status after 10 years in the study participants who did not receive any active intervention is associated with complete or partial disappearance of H.pylori infection. This favorable event might be related to improvement of dietary and life-style factors and/or unreported H.pylori eradication therapy protecting mucosa from further histological damage.

Sadjadi, A., et al. (2014). "Neglected role of hookah and opium in gastric carcinogenesis: a cohort study on risk factors and attributable fractions." International Journal of Cancer 134(1): 181-188.

A recent study showed an association between hookah/opium use and gastric cancer but no study has investigated the relationship with gastric precancerous lesions. We examined the association between hookah/opium and gastric precancerous lesions and subsequent gastric cancer. In a population-based cohort study, 928 randomly selected, healthy, Helicobacter pylori-infected subjects in Ardabil Province, Iran, were followed for 10 years. The association between baseline precancerous lesions and lifestyle risk factors (including hookah/opium) was analyzed using logistic regression and presented as odds ratios (ORs) and 95% confidence intervals (CIs). We also calculated hazard ratios (HRs) and 95% CIs for the associations of lifestyle risk factors and endoscopic and histological parameters with incident gastric cancers using Cox regression models. Additionally, the proportion of cancers attributable to modifiable risk factors was calculated. During 9,096 person-years of follow-up, 36 new cases of gastric cancer were observed (incidence rate: 3.96/1,000 persons-years). Opium consumption was strongly associated with baseline antral (OR: 3.2; 95% CI: 1.2-9.1) and body intestinal metaplasia (OR: 7.3; 95% CI: 2.5-21.5). Opium (HR: 3.2; 95% CI: 1.4-7.7), hookah (HR: 3.4; 95% CI: 1.7-7.1) and cigarette use (HR: 3.2; 95% CI: 1.4-7.5), as well as high salt intake, family history of gastric cancer, gastric ulcer and histological atrophic gastritis and intestinal metaplasia of body were associated with higher risk of gastric cancer. The fraction of cancers attributable jointly to high salt, low fruit intake, smoking (including hookah) and opium was 93% (95% CI: 83-98). Hookah and opium use are risk factors for gastric cancer as well as for precancerous lesions. Hookah, opium, cigarette and high salt intake are important modifiable risk factors in this high-incidence gastric cancer area.

Safatle-Ribeiro, A. V., et al. (2018). "Probe-based confocal endomicroscopy is accurate for differentiating gastric lesions in patients in a Western center." Chinese Journal of Cancer Research. Chung-Kuo Yen Cheng Yen Chiu 30(5): 546-552.

OBJECTIVE: Probe-based confocal laser endomicroscopy (pCLE) technique may improve the diagnosis of gastric mucosal lesions allowing acquisition of high-resolution in vivo images at the cellular and microvascular levels. This study aims to evaluate the accuracy of pCLE for the differential diagnosis of non-neoplastic and neoplastic gastric lesions. METHODS: Twenty gastric mucosal lesions from 10 patients were evaluated during endoscopic procedure and were examined by pCLE. Diagnostic pCLE was followed by biopsies or endoscopic resection of suspected lesions. A senior pathologist evaluated the specimens and was blinded to the pCLE results. RESULTS: Patients' mean age was 68.3 (range, 42-83) years and six were men. Thirteen suspicious flat or elevated lesions (classified as 0-Is, 0-IIa or 0-IIa + IIc) and seven pre-malignant lesions (atrophy and intestinal metaplasia) were evaluated. One patient was studied during his long-term follow-up after partial gastrectomy and presented severe atrophy, intestinal metaplasia, and xanthomas at the stump mucosa. The location of gastric lesions was in the body (n=10 lesions), the antrum (n=9) and the incisura angularis (n=1). All neoplastic lesions and all but one benign lesion were properly diagnosed by pCLE. pCLE incorrectly diagnosed one small antrum lesion as adenoma, however the final diagnosis was intestinal metaplasia. The final histological diagnosis was neoplastic in 9 and benign lesions in 11. In this small case series, pCLE accuracy was 95% (19/20 lesions). CONCLUSIONS: pCLE is accurate for real time histology of gastric lesions. pCLE may change the management of patients with gastric mucosal lesions, guiding biopsies and endoscopic resection, and avoiding further diagnostic workup or unnecessary therapy.

Saieva, C., et al. (2012). "Classification of gastritis in first-degree relatives of patients with gastric cancer in a high cancer-risk area in Italy." Anticancer Research 32(5): 1711-1716.

BACKGROUND: Screening gastroscopic examinations were performed in a cohort of individuals at high risk for developing gastric carcinoma (GC). PATIENTS AND METHODS: Five gastric biopsies were obtained following the Houston schema. Five histological parameters of gastritis were investigated: acute gastritis, chronic gastritis, and its sequelae; mucosal atrophy, intestinal metaplasia and pseudopyloric metaplasia. RESULTS: Out of 134 patients, 50% (n=67) had Helicobacter pylori (HP) infection. The sum of scores for the first four parameters was significantly higher in HP-positive cases than in HP-negative ones (p<0.0001). The frequency of these histological parameters was similar to other series from Northern and Central Italy. Hence, none of the histological parameters of gastritis explain the high GC risk in this borough of Florence, considering that the incidence rate of GC is higher in Central than in Northern Italy. CONCLUSION: Similarities in the frequency of chronic gastritis and sequelae in Northern and Central Italy substantiate the conviction that the difference in GC risk in these regions might be the result of local environmental or lifestyle factors, rather than HP infection. This knowledge is crucial, considering that environmentally related diseases are theoretically preventable.

Santoro, E., et al. (1998). "Gastric cancer. Clinico-biological updating and analysis of 400 operated cases." Journal of Experimental and Clinical Cancer Research 17(2): 175-185.

Gastric cancer is a rather common disease worldwide. In Italy it still accounts for 15,000 deaths annually. A sharp drop in the incidence rate of Lauren's intestinal histotype has been reported, whereas the frequency of the diffuse histotype is relatively steady. If the histogenesis of the latter is still somewhat obscure, the intestinal type confirms the sequence: atrophic gastritis--intestinal metaplasia--dysplasia--neoplasia. These different stages of development can nowadays be singled out through a series of indicators, the most reliable of which are the pepsinogen I/pepsinogen II ratio, the presence of sulphomucins and Lewis antigens in the gastric juices and NOR (Nucleolar Organizer Regions), cell ploidy and oncogenes determination. The genes involved in the neoplastic transformation are mostly oncosuppressors, the most frequent alterations being those relative to the APC gene, p53 and c-myc. In addition to the by now indispensable pathological staging of the disease, the modern prognostic factors are arising great interest: the most significant are the immunohistochemical examination of the peritoneal washing, and cell ploidy. Surgery is still the only potentially curative treatment: the earlier surgery is performed in the course of disease, the greatest the curative potential. The Authors' experience, which includes 400 operated cases with complete follow-up records, is here reported. The resectability rate turned out to be 84%, overall operative mortality was 6.5% with that due to surgical causes along being 3.7%. Overall survival at 5 years was 36%, while that of the curative operations 47%. Good results were obtained with the association surgery + intraoperative radiotherapy which resulted in a significant decrease in local recurrences of the disease.

Sanz-Ortega, J., et al. (1996). "LOH at the APC/MCC gene (5Q21) in gastric cancer and preneoplastic lesions. Prognostic implications." Pathology, Research and Practice 192(12): 1206-1210.

The APC/MCC gene (Familial Adenomatous Polyposis) at 5q21 plays a role in colon cancer carcinogenesis. LOH at this locus has also been described in gastric cancer and preneoplastic lesions. The APC locus has been recently related to a cell surface adhesion molecule and its alteration may favour metastatic dissemination. LOH at 5q21 has been associated with poor prognosis in other tumors such as lung cancer. Thirty-six gastric cancers were evaluated for LOH at 5q21 with 2 polymorphic markers from microdissected paraffin-embedded material. All tumors were classified by stage, histologic type, degree of differentiation and survival rates. In 4 cases, intestinal metaplasia cells in the adjacent mucosae were also microdissected. Six cases of moderate-severe gastric dysplasia were also added to the study. LOH was determined in 84% of the informative cases of GC, affecting both early and advanced stages of disease. Genomic instability was assessed in 5 cases, 3 of them associated with LOH. The only case of gastric cancer that did not show LOH or instability at 5q21 was a stage II, poorly differentiated intestinal carcinoma without evidence of recurrence after a 36 month follow-up period (the mean survival rate in our series was 28.3% at 36 months). We also found LOH in 2/6 dysplastic lesions and 1/4 intestinal metaplasias. Our data show that LOH at 5q21 is frequent in gastric cancer and is also present in intestinal metaplasia and dysplastic lesions. LOH at this locus is not a prognostic factor in GC in our study, due to the high incidence of LOH that we found.

Saraiva, S., et al. (2018). "Gastric dysplasia in familial adenomatous polyposis-what is the relevance?" United European Gastroenterology Journal 6(8): A180-A181.

Introduction: Familial adenomatous polyposis (FAP) is an inherited autosomaldominant disease characterized by the development of neoplasms in both upper and lower gastrointestinal tract. With the implementation of prophylactic colectomy, the incidence of colorectal cancer has declined and extracolonic manifestations have become more relevant. In what gastric lesions are concerned, FAP patients are known to have an increased risk for gastric dysplasia, although it is unclear if these lesions confer an increased risk of gastric cancer. Aims and Methods: The aim of our study was to characterize gastric dysplastic lesions in patients with FAP. We enrolled 144 patients with germline mutation in the APC gene from 63 FAP families and we retrospectively reviewed 366 Upper Gastrointestinal Endoscopies (UGE) performed during regular surveillance at the Familial Cancer Clinic. Statistic tests: Chi-square, Fisher's Exact Test, Student T test, Mann-Whitney U test, Cox Regression Model Results: From the 144 patients included in the study, 94 (Men: 49/Women: 45, mean age 48.3±14,8 years) underwent UGE at least once during a median follow up period of 12.7±8.9 years. 81.9% of patients had classical FAP and 18.1% presented the attenuated phenotype. 14.9% of patients did not have family history of FAP and only 6.4% had family history of gastric cancer. Gastric dysplastic lesions were detected in 16 patients (17%): 37 endoscopically visible lesions (Paris classification: 0-Ip: 10, 0-IIa: 26, 0-IIa+IIc: 1) and 1 case of dysplasia in random biopsies. Regarding their location, the majority of dysplastic lesions were at the antrum (70.3%) and 18.9% were found within fundic gland polyps (FGP) Mean age was significantly higher in patients with gastric dysplastic lesions compared with those without dysplasia (59.3±15.7 vs. 46.0±13.7 years, p=0.001). Histopathologic findings revealed 28 lesions with low-grade dysplasia (LGD), 8 with high-grade dysplasia (HGD) and 2 adenocarcinomas, both diagnosed in the first UGE performed. In regard to the evolution of dysplasia, 7 patients maintained LGD in the subsequent EGDs; only one patient had progression from LGD to HGD, in a 1 year period. This case involved multifocal dysplasia of the antrum and the patient underwent subtotal gastrectomy. The majority (70.3%) of gastric dysplastic lesions were treated endoscopically (endoscopic mucosal resection: 16; polypectomy: 9; endoscopic submucosal dissection: 1) and surgery was conducted in 2 cases. Gastric dysplasia was positively associated with the presence of gastric polyps and flat lesions (p=0.014 and p<0,001, respectively) and with atrophic gastritis and/or intestinal metaplasia (p=0.001). Gastric dysplasia was not associated with FAP phenotype, Helicobacter pylori infection or the presence/number of FGP. Conclusion: Despite the high prevalence of gastric dysplasia in FAP patients, its course is indolent. This may allow endoscopic surveillance and validate a conservative treatment strategy in the majority of cases.

Satarasinghe, R., et al. (2013). "Prevalence of histological gastric pathologies in gastric biopsies in adult Sri Lankans." Journal of Gastroenterology and Hepatology 28: 502.

Objective: To analyze the histological gastric pathologies in gastric biopsy specimens of a cohort of adult Sri Lankans who had undergone upper gastrointestinal endoscopy for various reasons. Methods: Histology notes of 224 gastric biopsies of patients who had undergone upper gastrointestinal endoscopy for various indications in the principle author's unit at Sri Jayewardenepura General Hospital, Kotte, Sri Lanka from 15th of February 2002 to 15th February 2013 were retrospectively analyzed. Results: Major indications for upper gastrointestinal endoscopy had been dyspepsia, reflux symptoms, abdominal pain, anorexia and haematemasis. in 42.2%, 22.2%, 16.0%, 12.0%, 11.1% and 10.2% of the instances respectively with overlaps. Age range had been 15 to 91 years with a mean age of 51.8 ± 15.5 SD years. Sex distribution, male: female was 2 : 1. Chronic antral gastritis, reactive gastropathy, gastric ulcers, gastric adenocarcinima and intestinal metaplasia were found in 67.4%, 5.3%, 5.3%, 2.2% and 1.8% of the instances respectively. H. pylori had been reported in 25.4% of the biopsies. Lymphocytic gastritis was found in 0.9%. Histological detection of H. pylori in chronic antral gastritis was 37.7%. The demographics for chronic antral gastritis showed a mean age of 50.3 ± 14.8 SD years, sex distribution male: female was 2: 1. Gastric ulcers and gastric carcinomas were found endoscopically in 5.4% and 2.2% patients of the instances respectively. Conclusion: Chronic antral gastritis was the commonest histological abnormality detected in the gastric biopsies. There was less prevalence of H. pylori histologically which could be multi-factorial in origin which could in turn influence the low incidence of gastric ulcer and gastric carcinoma in the cohort. Further multicentre studies are needed for confirmation.

Satoh, K., et al. (1999). "[Changes in the severity of atrophic gastritis after Helicobacter pylori eradication]." Nihon Rinsho. Japanese Journal of Clinical Medicine 57(1): 185-190.

There is a diversity of opinions as to whether Helicobacter pylori eradication leads to the improvement or regression of atrophic gastritis and intestinal metaplasia (IM), which are considered precursor lesions of intestinal type gastric cancer. We have made a 1.5-yr follow-up study after H. pylori eradication, but no significant improvement of atrophy or IM has so far been found. Some other factors than H. pylori may also play an important part in the development and progress of atrophic gastritis. The discrepancy between our data and others may be caused in part by the different methods of assessment of the grade of atrophy and sampling of biopsies.

Saulino, D., et al. (2021). "Characterization of Chronic Gastritis in Lynch Syndrome Patients With Gastric Adenocarcinoma." Gastroenterology Res 14(1): 13-20.

BACKGROUND: Gastric cancer is one of the Lynch syndrome (LS)-associated malignancies. Previous studies have suggested that LS patients with gastric cancer also had chronic atrophic gastritis in the background mucosa, but further histologic characterization was not attempted. This study aims to understand the histologic features of background chronic gastritis in LS patients with gastric adenocarcinoma. METHODS: Eleven LS-associated gastric cancer cases were collected from five institutions. Demographics and clinical features were retrieved by review of medical charts. Pathological material was reviewed for tumor location and histologic type. In addition, non-neoplastic gastric mucosa was assessed for inflammation (chronic and active), atrophy, intestinal metaplasia (IM) in the antrum and body, as well as pyloric gland metaplasia and enterochromaffin-like (ECL) cell hyperplasia in the body. RESULTS: Eleven LS patients with gastric cancer (four male and seven female) with a mean age of 63 years (range: 23 - 83) were included. Ten (90.9%) had personal cancer histories; however none of the patients had family history of gastric cancer. Eight (72.7%) patients underwent gastrectomy and three had endoscopic resection. Nine (81.8%) patients had tumor in the fundus and/or body and two had tumor present in the antrum. Seven (63.6%) cases were intestinal type or mixed type carcinoma, and the remaining four were signet ring cell carcinoma. Eight (of 11, 72.7%) patients had chronic gastritis, five (45.4%) had atrophy, and four (36.3%) had intestinal metaplasia. Four of five patients with both antrum and body mucosa available for evaluation (80%), demonstrated body-predominant chronic gastritis. Four patients had germline MLH1 alterations and all of these patients had chronic gastritis, including one Helicobacter pylori (H. pylori) gastritis and three H. pylori-negative gastritis. CONCLUSIONS: None of LS patients with gastric cancer in our cohort had a family history of gastric cancer. Gastric adenocarcinomas in LS patients were primarily located in the fundus and/or body. Two-thirds of these tumors were of intestinal type and had a background chronic, H. pylori-negative gastritis. These results support a chronic atrophic gastritis with intestinal metaplasia-dysplasia-carcinoma sequence in LS-related gastric tumorigenesis, particularly in MLH1-mutated LS patients.

Saulino, D., et al. (2020). "Characterization of chronic gastritis underlying lynch syndrome-associated gastric cancer." Modern Pathology 33(3): 765.

Background: Gastric cancer is a Lynch syndrome (LS) associated malignancy. Recent studies have attempted to identify the clinical risk factors for LS-associated gastric cancer. Additionally, a few previous studies suggest that there may be underlying immune gastritis in some LS-associated gastric cancers. However, histology of this potential underlying immune gastritis is not well defined. This study aims to characterize the underlying gastritis in LS patients with gastric cancer. Design: A cohort of 12 LS-associated gastric cancer cases were collected via a multicenter collaboration. Our study includes patients diagnosed with LS using clinical criteria and/or genetic confirmation. Clinicodemographics and pathology material were reviewed. The frequency of chronic gastritis and intestinal metaplasia was then compared to a cohort of LS patients without gastric cancer in a previously published study [Renkonen-Sinisalo L et al., 2002]. Results: A cohort of 12 LS patients (4 male and 8 female, mean age 62 years) with gastric cancer were included in this study. Seven of the patients had gastrointestinal symptoms and 5 were evaluated as part of a surveillance program. All patients had a background gastric biopsy available for review and 9 had chronic gastritis. The gastric body was biopsied in 9 cases and 7 had at least moderate chronic gastritis. Additionally, 6 of these cases had atrophy, 5 had multifocal intestinal metaplasia, and 5 had pseudopyloric gland metaplasia. Eight cases had gastric antral biopsies; 2 of these cases had moderate chronic gastritis, 3 had mild chronic gastritis, 1 had reactive gastropathy, and 2 had intestinal metaplasia. Of the 5 cases that had both antral and body biopsies 4 had body predominant gastritis and 1 had similar inflammation in both. H. pylori gastritis was noted in 2 of the 11. Activity was noted in 3 cases including those two with H. pylori infection. Compared to LS patients without gastric cancer from a previously published study; LS patients with gastritis cancer had a higher rate of chronic gastritis (p=0.006), atrophy (p=0.009), and intestinal metaplasia (p=0.038). [Table 1] (Table presented) Conclusions: LS patients with gastric cancer had higher rate of chronic gastritis, atrophy, and intestinal metaplasia compared to a previously published group of LS without gastric cancer. The presence of gastritis may help risk stratify LS patients for gastric cancer. Therefore, future studies are needed to examine the mechanisms of chronic gastritis in LS patients.

Schipper, D. L., et al. (1996). "Correlation of glutathione S-transferases with overall survival in patients with gastric carcinoma." International Journal of Oncology 9(2): 357-363.

Glutathione S-transferases (GST) are enzymes involved in the detoxification of xenobiotics and are divided into four subclasses, Alpha, Mu, Pi, and Theta. Most human gastrointestinal tumors contain increased amounts of GST Pi and GST enzyme activity. The relationship between GST parameters and tumor and patient characteristics, including overall survival, were studied retrospectively in normal and malignant gastric tissue from 49 patients with primary gastric carcinoma. Twelve patients (24%) were alive at the end of the study with a mean follow-up time of 4.1 ± 0.4 years. Levels of GST Alpha, Mu, Pi and GST enzyme activity were not related to tumor stage, localization and diameter of the tumor, number of eosinophils in the tumor, presence of intestinal metaplasia in normal gastric mucosa, or gender and age of the patient. Optimal dichotomization and uni- and multivariate analyses were done with the Cox proportional hazard model. None of the clinicopathological parameters were associated with survival, except the number of eosinophils in the tumor. In contrast, high levels of GST Pi in both normal mucosa (Hazard ratio 3.0, p = 0.02) and in gastric carcinoma (HR 2.2, p = 0.05) and the presence of GST Mu in normal (HR 0.4, p = 0.05) and malignant (HR 0.3, p = 0.009) gastric tissue were found to have a significant prognostic value, independent from the clinicopathological parameters, when added separately to a Cox model. In conclusion, the levels of GST Mu and Pi in both normal or carcinomatous gastric tissue have an independent prognostic impact on overall survival.

Sȩn, N., et al. (2015). "The prevalance of atrophic gastritis and intestinal metaplasia in helicobacter pylori gastritis." Helicobacter 20: 109.

Aim: Atrophic gastritis and intestinal metaplasia (IM) are considered premalignant lesions of gastric cancer.Histological diagnosis for Helicobacter pylori infection allows the recognition of gastric lesions.The aim was to assess the incidence of atrophy and IM associated with H. pylori infection and determine its relation to demographic data. Methods: One-hundred-six adult dyspeptic patients were admitted to Gastroenterology-Outpatient-Clinic and referred to upper gastrointestinal endoscopy at Sifa University Bornova Hospital in March 2014-2015.One-hundredtwo (48M and 54F;mean age 39.2 years) of them were studied.Since biopsy was not seen necessary by gastroenterologists,four patients were excluded.Presence of inflammation, activity, atrophy and IM were evaluated on gastric biopsy specimens stained with haematoxylin-and-eosin (HandE) and classified morfologically by modified Sydney system.Atrophy was evaluated as defined in OLGA system and severity of atrophy was graded according to the modified Sydney system.Toluidine-blue staining was used to evaluate the presence of Helicobacter-like-organisms (HLO) in corpus and antrum biopsy specimens. Results: Sixty-four (62.7%) of 102 patients were HLO positive.Gastric atrophy was observed in 20.3% and 18.4% of the HLO positive and negative patients, respectively.However,IM was observed in 14.1% and 26.3% of the HLO positive and negative patients,respectively. Conclusion: To determine gastritis scoring and to detect the HLO presence is very important for patient treatment and follow-up.As long-term H. pylori infection is the main reason of atrofic gastritis, considered as the major risk factor for the development of gastric cancer.Although atrophic changes appear in the gastric mucosa,many biopsies become negative for a bacterial histology.The disappearance of H. pylori relates to the development of unsuitable environments for H. pylori colonization in metaplastic areas.OLGA staging may contribute the physician's diagnosis process for management of gastritis.

Seo, J. Y., et al. (2013). "Eradication of Helicobacter pylori reduces metachronous gastric cancer after endoscopic resection of early gastric cancer." Hepato-Gastroenterology 60(124): 776-780.

BACKGROUND/AIMS: Although some studies have shown improvement of precancerous lesions and a decrease of metachronous gastric cancer after eradication of H. pylori, this is still controversial. METHODOLOGY: We identified 74 patients with early gastric cancer and who had their H. pylori eradicated after undergoing endoscopic resection between September, 2003 and September, 2010. The endoscopic biopsy specimens, campylobacter-like organism test and urea breath test were reviewed. Relapse of gastric cancer was assessed from medical records. RESULTS: Among the 74 patients, 61 (82.4%) were successfully eradicated. The mean duration of follow-up was 27.2±18.7 months. H. pylori colonization, neutrophil infiltration, mononuclear cell infiltration and intestinal metaplasia decreased after eradication (all p<0.05). For all the patients, metachronous gastric cancer showed a decrease in the eradicated group, but this did not reach statistical significance (odds ratio: 0.36, 95% CI: 0.08-1.70, p=0.189). However, when restricted to those who were followed-up for more than 18 months, metachronous gastric cancer was significantly decreased in the eradicated group (odds ratio: 0.108, 95% CI: 0.016-0.726, p=0.035). CONCLUSIONS: Eradication of H. pylori decreased precancerous lesions, and when following-up for more than 18 months, eradication also reduced metachronous gastric cancer.

Serov, V. V., et al. (1990). "Early stomach cancer: its morphology, histo- and morphogenesis." Arkhiv Patologii 52(5): 70-74.

Macroscopic, histologic and ultrastructural features of an early stomach carcinoma are presented on the basis of literature and the authors' data. Ultrastructural and immunohistochemical data confirm the concept of a common histogenesis of different histologic types of stomach carcinoma, i.e. from reserve cells. Carcinoma, most likely, develops from reserve cells of the foveolate epithelium and metaplastic epithelium of intestinal type (foci of incomplete intestinal metaplasia with sulfomucine secretion). The data are accumulating on the precancerous nature of severe epithelial dysplasia. The development of an early carcinoma from preexisting dysplasia was observed in patients after long follow-up with repeated gastric biopsies.

Serrano, M., et al. (2014). "Advanced endoscopic imaging for gastric cancer assessment: new insights with new optics?" Best Practice & Research: Clinical Gastroenterology 28(6): 1079-1091.

The most immediate strategy for improving survival of gastric cancer patients is secondary prevention through diagnosis of early gastric cancer either through screening or follow-up of individuals at high risk. Endoscopy examination is therefore of paramount importance and two general steps are to be known in assessing gastric mucosa - detection and characterization. Over the past decade, the advent of advanced endoscopic imaging technology led to diverse descriptions of these modalities reporting them to be useful in this setting. In this review, we aim at summarizing the current evidence on the use of advance imaging in individuals at high-risk (i.e., advance stages of gastric atrophy/intestinal metaplasia) and in those harbouring neoplastic lesions, and address its potential usefulness providing the readers a framework to use in daily practice. Further research is also suggested.

Setia, N., et al. (2019). "Endoscopic biopsy followup of gastric intestinal metaplasia is of no clinical benefit in a low risk population." Modern Pathology 32(3).

Background: The significance of gastric intestinal metaplasia in a low risk population is unclear, and guidelines for surveillance of such cases are not available. The aim of this study is to determine the clinical utility of biopsy followup of intestinal metaplasia encountered in routine practice. Design: A retrospective study was performed. Pathology reports of endoscopic gastric biopsies from 2005 through 2014 were reviewed. Of the 13,546 cases, 1,816 biopsies from 717 patients showed intestinal metaplasia. Longitudinal followup was conducted to assess the rate of progression to dysplasia or gastric carcinoma (incident dysplasia/carcinoma). Dysplasia or carcinoma at presentation (prevalent dysplasia/carcinoma) in association with intestinal metaplasia was recorded separately. Results: The mean age of the cohort was 68 years (+/-16.5 years, range 3-98 years), the male: female ratio was 1:1.3 and there was a median followup period of 4 years (range 1-36 years). Intestinal metaplasia was present in 5.1% of the entire cohort. Prevalent high grade dysplasia/carcinoma and prevalent low-grade dysplasia comprised 0.35% and 0.09% cases of the entire cohort, respectively. Incident high grade dysplasia/carcinoma and incident low-grade dysplasia developed in 0.01% cases of the entire cohort. None of the incident low grade dysplasia cases progressed to carcinoma despite a mean followup of 2-3 additional upper GI endoscopies with non-targeted biopsies over a mean of 3 years. Surveillance and operative intervention in the patients with incident high grade dysplasia/carcinoma did not prevent the development or progression of gastric carcinoma. Details of incident high grade dysplasia/carcinoma and followup of the entire cohort are shown in Figure 1. Conclusions: The risk of incident carcinoma developing in the setting of intestinal metaplasia is extremely low, and follow up of cases with intestinal metaplasia does not prevent the development/progression of carcinoma. Prevalent dysplasia/carcinoma accounts for the majority of gastric neoplasia seen in association with gastric intestinal metaplasia in a population with low risk of gastric carcinoma.

Setia, N., et al. (2020). "Gastric cancer in the setting of intestinal metaplasia and surveillance in a low-risk population: Does the end justify the means?" Modern Pathology 33(3): 765-766.

Background: The goal of endoscopic gastric intestinal metaplasia surveillance is to prevent incident gastric cancers. In this study, we reviewed clinicopathologic features of gastric cancers in the setting of gastric intestinal metaplasia to determine if surveillance of gastric intestinal metaplasia is justified in a low-risk population. Design: Gastric cancers with at least one prior endoscopy with intestinal metaplasia, performed >30 days before cancer diagnosis were included in the study. A total of 25 gastric cancers in the setting of intestinal metaplasia were retrospectively identified from six academic institutions after review of 5,771 resected gastric cancers. Carcinomas arising in the setting of Barrett esophagus were excluded. Results: The median age at the diagnosis of gastric intestinal metaplasia was 64 years (range 9-90, +/-17.4), and the median age at the diagnosis of gastric cancer was 72 years (range 16-90, +/-15.9). About 56% (14/25) of patients were male. Race/ethnicity distribution of the cohort was 4: 3.5: 2: 1 - Caucasians: African Americans: Asians: Hispanics. A family history of gastric cancer was present in 15% (3/20) patients, H. pylori gastritis in 27.3% (6/22) patients, and autoimmune gastritis in 22.7% (5/22) patients. The median duration between prior endoscopy and subsequent endoscopic diagnosis of gastric cancer was 18 months (1-125, +/-31). Of all gastric cancers, 72% (18/25) were diagnosed within 3 years of the last endoscopy. Gastric cancers in the setting of gastric intestinal metaplasia were preceded by endoscopic biopsy detection of dysplasia in only 13.6% (3/22) cases. About half of the gastric cancers (45.4%, 10/22) were non-intestinal Lauren type. Conclusions: The extremely low incidence of gastric cancer in the setting of gastric intestinal metaplasia does not support universal (nonrisk adapted) endoscopic surveillance of gastric intestinal metaplasia in a low-risk population. Even targeted endoscopic surveillance in certain high risk racial/ethnic groups may not be justified; however, the cost-effectiveness of these type of surveillance programs needs to be determined. If performed, a surveillance interval of 3 years may be associated with an unacceptable rate of interval gastric cancer.

Shah, S. C., et al. (2020). "Endoscopy for Gastric Cancer Screening Is Cost Effective for Asian Americans in the United States." Clinical Gastroenterology and Hepatology 18(13): 3026-3039.

BACKGROUND & AIMS: Endoscopic screening for gastric cancer is routine in some countries with high incidence and is associated with reduced gastric cancer-related mortality. Immigrants from countries of high incidence to low incidence of gastric cancer retain their elevated risk, but no screening recommendations have been made for these groups in the United States. We aimed to determine the cost effectiveness of different endoscopic screening strategies for noncardia gastric cancer, compared with no screening, among Chinese, Filipino, Southeast Asian, Vietnamese, Korean, and Japanese Americans. METHODS: We generated a decision-analytic Markov model to simulate a cohort of asymptomatic 50-year-old Asian Americans. The cost effectiveness of 2 distinct strategies for endoscopic gastric cancer screening was compared with no screening for each group, stratified by sex. Outcome measures were reported in incremental cost-effectiveness ratios (ICERs), with a willingness-to-pay threshold of $100,000/quality-adjusted life-year (QALY). Extensive sensitivity analyses were performed. RESULTS: Compared with performing no endoscopic gastric cancer screening, performing a 1-time upper endoscopy with biopsies, with continued endoscopic surveillance if gastric intestinal metaplasia was identified, was cost effective, whereas performing ongoing biennial endoscopies, even for patients with normal findings from endoscopy and histopathology, was not. The lowest ICERs were observed for Chinese, Japanese, and Korean Americans (all <$73,748/QALY). CONCLUSIONS: Endoscopic screening for gastric cancer with ongoing surveillance of gastric preneoplasia is cost effective for Asian Americans ages 50 years or older in the United States. The lowest ICERs were for Chinese, Japanese, and Korean Americans (all <$73,748/QALY).

Shah, S. C., et al. (2019). "Upper Endoscopy up to 3 Years Prior to a Diagnosis of Gastric Cancer Is Associated With Lower Stage of Disease in a USA Multiethnic Urban Population, a Retrospective Study." Journal of Preventive Medicine and Public Health. Yebang Uihakhoe Chi 52(3): 179-187.

OBJECTIVES: In the USA, certain races and ethnicities have a disproportionately higher gastric cancer burden. Selective screening might allow for earlier detection and curative resection. Among a USA-based multiracial and ethnic cohort diagnosed with non-cardia gastric cancer (NCGC), we aimed to identify factors associated with curable stage disease at diagnosis. METHODS: We retrospectively identified endoscopically diagnosed and histologically confirmed cases of NCGC at Mount Sinai Hospital in New York City. Demographic, clinical, endoscopic and histologic factors, as well as grade/stage of NCGC at diagnosis were documented. The primary outcome was the frequency of curable-stage NCGC (stage 0-1a) at diagnosis in patients with versus without an endoscopy negative for malignancy prior to their index exam diagnosing NCGC. Additional factors associated with curable-stage disease at diagnosis were determined. RESULTS: A total of 103 racially and ethnically diverse patients were included. Nearly 38% of NCGC were stage 0-Ia, 34% stage Ib-III, and 20.3% stage IV at diagnosis. A significantly higher frequency of NCGC was diagnosed in curable stages among patients who had undergone an endoscopy that was negative for malignancy prior to their index endoscopy that diagnosed NCGC, compared to patients without a negative endoscopy prior to their index exam (69.6% vs. 28.6%, p=0.003). A prior negative endoscopy was associated with 94.0% higher likelihood of diagnosing curable-stage NCGC (p=0.003). No other factors analyzed were associated with curable-stage NCGC at diagnosis. CONCLUSIONS: Endoscopic screening and surveillance in select high-risk populations might increase diagnoses of curable-stage NCGC. These findings warrant confirmation in larger, prospective studies.

Shahinyan, T., et al. (2019). "Effectiveness of Helicobacter pylori eradication standard triple therapy in Armenian children with gastroduodenal disease and functional dyspepsia." Journal of Pediatric Gastroenterology and Nutrition 68: 675.

Objectives and Study: Armenia is a country with high prevalence of peptic ulcer disease and gastric cancer. Taking into consideration our preliminary data on Hp resistance to claritromycin (33.3%) and metronidazole (73.3%) in Armenian children, we aimed to evaluate the efficacy of Hp eradication standard triple therapy in Armenian children with gastroduodenal disease (GDD) and functional dyspepsia (FD). Methods: 150 patients aged 2-18 years (70 males and 80 females, mean age 9.2±3.9y) with GDD (70 patients)-1st group (erosions or ulcer in the stomach and/or duodenum) and FD (80 patients)-2nd group (no lesions in the stomach and duodenum). All patients underwent EGDS with biopsies: 2 from antrum, 1 from duodenal bulb and distal esophagus. Tissues were assessed according to updated Sydney system. One antral biopsy was cultured in Hp selective media. 106 (43 FD and 58 with GDD) Hp positive patients (70.6%) out of 150 received standard Hp eradication therapy: amoxicillin and clarithromycin (CLA) or amoxicillin and metronidazole (METRO) combined with rabeprazole for 10 days. Elimination rate was checked by Hp stool antigen test at least 8 weeks after treatment. Results: 42 (39.6 %) out of 106 patients returned for evaluation by Hp stool antigen test (28 with GDD and 14 with FD). 38 received CLA and 4 METRO based treatment. Compliance to the treatment was high in all of them. Symptoms disappeared in 25 (59.6%) out of 42 patients, condition improved in 13 (30.9%) and remained the same in 4 (9.5%). Clinical data improvement was almost equal in FD and GDD groups. Hp eradication was achieved in 32 (73.8%) out of 42 patients. Eradication rate was 13 (92.8%) in the FD and 19 (67.8%) in GDD group. Endoscopic data analysis of 32 patients with successful Hp eradication showed presence of erosive lesions-in 17 (53.1%) and superficial changesin 13 (40.6%) in the stomach and/or duodenum, 1 had nodular gastritis (3.1%) and 1 stomach ulcer (3.1%). In patients with unsuccessful eradication erosive lesions were observed in 7 (70%), ulcers in 2 (20%), superficial changes in 1 (10%) patient. Comparison analysis of histological pattern of the gastric mucosa of patients from both groups (FD and GDD) with successful and unsuccessful eradication showed: normal stomach mucosa in 2 (6.25%) and 0 (0%), chronic active gastritis in 1 (3.1%) and 1 (10%), chronic non-active gastritis in 23 (71.9%) and 9 (90%), gastric atrophy in 3 (9.3%) and 0 (0%), intestinal metaplasia in 1(3.1%) and 0 (0%), glandular dysplasia in 2 (6.2%) and 0 (0%). Spectrum of histological changes in duodenum were: normal mucosa in 9 (28.1%) and 3 (30%), acute duodenitis in 1 (3.1%) and 0 (0%), chronic active duodenitis in 0 (0%) and 1 (10%), chronic non-active duodenitis in 22 (68.75%) and 6 (60%). In 4 out of 14 patients (28.6%) with FD and in 3 out of 28 patients (10.7%) with GDD gastric atrophy, intestinal metaplasia and glandular dysplasia of the stomach were seen. Conclusions: The efficacy of Hp eradication triple therapy with rabeprazole, amoxicillin, and CLA or METRO in a cohort of Armenian children with FD and GDD was low (73.8%). Hp eradication rate in patients with GDD was higher (92.8%) than in FD group (67.8%). Patients with FD had marked histological changes despite of no endoscopic lesions in comparison to patients with GDD.

Shamaly, H., et al. (2018). "Gastric Mucosa-Associated Tissue (MALT) lymphoma due to Helicobacter pylori infection presents also in teenagers." Journal of Pediatric Gastroenterology and Nutrition 66: 627.

Objectives and Study: Helicobacter pylori (HP) infection in children is a frequent findings. Part of these patients may be asymptomatic and the rest with different gastrointestinal signs and symptoms including abdominal pain, vomiting, nausea, loss of appetite and also extra intestinal manifestations. In endoscopy the presenting signs are nodular gastritis, gastric & duodenal ulcers and gastric cancer In histology with H&E staining we may find helicobacter pylori filaments on epithelial surface, acute and chronic gastritis, intestinal metaplasia changes, Mucosa-associated tissue (MALT) lymphoma cells and cancer cells. These proliferative changes are very rare in children We present three teenagers with recurrent upper abdominal pain which were diagnosed histologically with gastric MALT lymphoma treated against helicobacter pylori infection with disappearance of the bacteria and tumor during follow-up of 3-5 year. Method: Three children aged 13-16 years old suffered from recurrent abdominal pain without vomiting, diarrhea, high grade temperature, sweeting or loss of weight. In endoscopy swelling antral mucosa was present with irregular surface occupying all prepyloric area and part of gastric corpus without nodular gastritis or gastric ulcers. Histologic staining with H&E showed multiple HP elements on epithelial surface, large amount of lymphoma cells & lymphoepithelial lesions, positive for Kappa light chain staining and negative for Lamda light chain staining consistent for MALT lymphoma. Patients were treated for 10 days with triple therapy (Amoxicillin, Clarithromycin and Omeprazole) with disappearance of HP in breath test in 2 patients and after second course with quarter drugs (Amoxicillin, Metronidazole, Clarithromycin, Omeprazole) for 14 days in the third one. Repeated endoscopies and histologic findings were within normal limits during follow-up 3-5 years post first diagnosis Conclusion: MALT lymphoma must be diagnosed and treated also in teenagers.

Sharan, P. and N. Vikneswaran (2013). "Risk of gastric cancer in pernicious anemia." Gastroenterology 144(5): S220.

Background and aims: Pernicious anemia (PA) is a pre-malignant condition associated with an increased risk of gastric carcinoma. A single endoscopic evaluation has been advocated to identify prevalent gastric neoplasia in patients with PA. However, there is no local data available on the risk of gastric cancer in PA. This study characterizes the risk of gastric carcinoma in patients diagnosed with PA in a tertiary care hospital in a multi-ethnic Asian country. Methods: A retrospective review of patients diagnosed with PA in Singapore General Hospital from January 2000 to October 2010 was performed. PA was defined as patients with positive anti-intrinsic factor antibody. Patients were characterized based on baseline demographics and diagnosis of gastric carcinoma. Results: 477 patients with pernicious anemia were identified. 224 patients (47%) underwent OGD with a median follow-up of 742 days (0-3455) and were analyzed further. There were 197 (42.9%) males. Median age at diagnosis of PA was 72.5 (32.8- 93.1) years. 86.6% of the patients were Chinese. There were 6 (2.7%) cases of gastric carcinoma and 76 (33.9%) cases of intestinal metaplasia. There were 2 cases of carcinoid tumor (0.9%). All 6 cases of gastric carcinoma were Chinese (50% males). Median time to diagnosis of gastric carcinoma following diagnosis of PA was 734 days (5-3243) and median age at diagnosis of gastric carcinoma was 76 yrs (66-92). Conclusions: The risk of gastric carcinoma in pernicious anemia is low but the relatively high incidence of neoplastic precursors highlights a need for improved risk stratification.

Sharma, S. and D. Dowling (2018). "The prevalence of gastric intestinal metaplasia in a low-risk Australian cohort aged >50 years." Journal of Gastroenterology and Hepatology 33: 174.

Introduction: Gastric adenocarcinoma is diagnosed in about 2500 Australian adults each year. The gastric adenocarcinoma multistage model suggests a well-defined gastric cancer cascade of chronic gastritis, atrophic gastritis, intestinal metaplasia (IM), dysplasia, and adenocarcinoma. Incomplete IM and extensive IM involving the antrum and body are thought to be associated with the greatest risk of progressing to gastric cancer. In the literature, expert opinion and guidelines from the European Society for Gastrointestinal Endoscopy recommend that patients with incomplete or extensive IM be offered endoscopic surveillance every 3 years. Gastric IM is difficult to detect macroscopically at endoscopy. Individuals most likely to benefit from surveillance can only be identified accurately with biopsy and histology. Aim: We aimed to assess the prevalence and extent of gastric IM in individuals aged >50 years where no macroscopic abnormality of the gastric mucosa was noted at endoscopy. Methods: A prospectively acquired database was established. Data were recorded on a consecutive series of individuals aged >50 years who underwent routine diagnostic gastroscopy between October 2017 and April 2018. All individuals had no macroscopic abnormality of the gastric mu-cosa at endoscopy and were potential candidates for surveillance (i.e. free of major comorbidity) if a diagnosis of IM was made. At the time of endos-copy, two biopsy samples were taken from each of three gastric sites (antrum, incisura, and body). Data recorded included age, sex, presence and extent of IM, and Helicobacter pylori status based on histopathology. We estimated the cost associated with routine biopsies to identify individuals who may potentially benefit from subsequent endoscopic surveillance. Results: Eighty individuals were investigated with gastroscopy. Of these, 46 (58%) were male, and the median age was 66 years. Ten (13%) had evidence of IM. In eight cases, IM was limited to the antrum and in only one of these cases was IM incomplete. In two cases, IM was limited to the gastric body and, in both cases, was complete. H. pylori was present in five (6%) of the cases of antral IM and was absent with IM limited to the gastric body. The prevalence of IM based on age was 1%, 5%, and 6%, respectively, among those aged 50-60, 60-69, and >60 years. Only one individual (incomplete antral IM) was identified in whom ongoing endoscopic surveillance may be appropriate. The cost associated with taking biopsies to identify this single individual was estimated to be $24 000 for 80 cases. Conclusions: Within the population studied, the prevalence of gastric IM was low, and significant lesions which may have led to subsequent ongoing endoscopic surveillance were identified infrequently. The cost of taking biopsies to identify individuals likely to benefit from surveillance was high. Based on these findings, the practice of routinely taking gastric biopsy samples to screen for IM in individuals aged >50 years cannot be recommended.

Shi, Y., et al. (2019). "Telomere Length of Circulating Cell-Free DNA and Gastric Cancer in a Chinese Population at High-Risk." Frontiers in Oncology 9: 1434.

Background: Telomeres have long been found to be involved in cancer development, while little was known about the dynamic changes of telomere length in carcinogenesis process. Methods: The present study longitudinally investigated telomere alterations of cell-free DNA (cfDNA) in 86 gastric cancer (GC) subjects recruited through a 16-year prospective cohort with 2-4 serums collected before each GC-diagnosis from baseline and three follow-up time-points (a total of 276 samples). As the control, 86 individual-matched cancer-free subjects were enrolled with 276 serums from the matched calendar year. Results: In the 73 pairs of baseline serums from GC and control subjects, shortened telomeres showed increased subsequent GC risk [odds ratio (OR) = 9.17, 95% CI: 2.72-31.25 for 1 unit shortening]. In each baseline gastric lesion category, higher risks of GC progression were also found with shortened cfDNA telomeres; ORs per 1 unit shortening were 6.99 (95% CI: 1.63-30.30) for mild gastric lesions, 6.06 (95% CI: 1.89-19.61) for intestinal metaplasia and 15.63 (95% CI: 1.91-125.00) for dysplasia. With all measurements from baseline and follow-up time-points, shortened telomeres also showed significant association with GC risk (OR = 7.37, 95% CI: 2.06-26.32 for 1 unit shortening). In temporal trend analysis, shortened telomeres were found in GC subjects compared to corresponding controls more than 3 years ahead of GC-diagnosis (most P < 0.05), while no significant difference was found between two groups within 3 years approaching to GC-diagnosis. Conclusion: Our findings suggest that telomere shortening may be associated with gastric carcinogenesis, which supports further etiological study and potential biomarker for risk stratification.

Shibukawa, N. (2017). "The predictive marker of early gastric cancer detected after Helicobacter pylori eradication." Journal of Gastroenterology and Hepatology 32: 68.

Background: In 2013, the Japanese government approved national health insurance coverage for antibiotic treatment for Helicobacter pylori (HP) infection in patients with endoscopically diagnosed chronic gastritis. Then, increase of gastric cancer (GC) detected after HP eradication is expected. In 2015, the Kyoto global consensus report on HP gastritis was published. At the same time, endoscopic scores for GC risk were also announced. Aims: We investigated the predictive markers for early GC detected after HP eradication. Methods: A total of 393 patients underwent ESD for early GC at our hospital between June 2006 and January 2017. We analyzed data from 137 patients comprising 63 patients with GC (Group C) and 74 without GC (Group NC) after HP eradication. We retrospectively investigated the background of patients, endoscopic characteristics, and endoscopic scores for GC risk. Results: About Group C and NC, mean follow-up period was 6.9 ± 3.9 and 5.0 ± 4.4 years. The prevalence of male and past history of other malignant disease were significantly higher in Group C than those in Group NC. The median age of Group C tended to be higher than that in Group NC. About endoscopic scores for GC risk, intestinal metaplasia score and atrophy score were significantly higher in Group C than Group NC. The prevalence of gastric xanthoma (GX) was also significantly higher in Group C than Group NC (63.5% vs 18.9%, P < 0.0001). Multivariate logistic analysis revealed that male, intestinal metaplasia score, and the presence of GX were independently related to GC (odds ratio, P: 8.38 [2.04-34.5], 0.003, 3.58 [1.68-7.62], 0.0009, and 3.15 [1.19-8.33], 0.02, respectively). Conclusion: Male sex, intestinal metaplasia score, and the presence of GX were the useful predictive markers for early GC detected after HP eradication.

Shichijo, S., et al. (2017). "Association between gastric cancer and the Kyoto classification of gastritis." Journal of Gastroenterology and Hepatology 32(9): 1581-1586.

BACKGROUND AND AIM: Histological gastritis is associated with gastric cancer, but its diagnosis requires biopsy. Many classifications of endoscopic gastritis are available, but not all are useful for risk stratification of gastric cancer. The Kyoto Classification of Gastritis was proposed at the 85th Congress of the Japan Gastroenterological Endoscopy Society. This cross-sectional study evaluated the usefulness of the Kyoto Classification of Gastritis for risk stratification of gastric cancer. METHODS: From August 2013 to September 2014, esophagogastroduodenoscopy was performed and the gastric findings evaluated according to the Kyoto Classification of Gastritis in a total of 4062 patients. The following five endoscopic findings were selected based on previous reports: atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness. RESULTS: A total of 3392 patients (1746 [51%] men and 1646 [49%] women) were analyzed. Among them, 107 gastric cancers were diagnosed. Atrophy was found in 2585 (78%) and intestinal metaplasia in 924 (27%). Enlarged folds, nodularity, and diffuse redness were found in 197 (5.8%), 22 (0.6%), and 573 (17%), respectively. In univariate analyses, the severity of atrophy, intestinal metaplasia, diffuse redness, age, and male sex were associated with gastric cancer. In a multivariate analysis, atrophy and male sex were found to be independent risk factors. Younger age and severe atrophy were determined to be associated with diffuse-type gastric cancer. CONCLUSION: Endoscopic detection of atrophy was associated with the risk of gastric cancer. Thus, patients with severe atrophy should be examined carefully and may require intensive follow-up.

Shichijo, S., et al. (2016). "Histologic intestinal metaplasia and endoscopic atrophy are predictors of gastric cancer development after Helicobacter pylori eradication." Gastrointestinal Endoscopy 84(4): 618-624.

BACKGROUND AND AIMS: Helicobacter pylori eradication therapy is effective at reducing the incidence of gastric cancer; however, gastric cancer still develops after eradication. We conducted a cohort study to elucidate the risk factors for gastric cancer development after successful H pylori eradication therapy. METHODS: From June 1998 to December 2012 we assessed histologic and endoscopic findings of gastritis and performed H pylori eradication therapy in 748 patients without a history of gastric cancer. Patients were classified according to the distribution of intestinal metaplasia (IM) as follows: no IM (IM group A), IM in the antrum only (IM group B), and IM in the corpus (IM group C). We assessed atrophy endoscopically according to the Kimura-Takemoto classification system. Gastric cancer incidence was assessed. RESULTS: A total of 573 patients underwent follow-up endoscopy; the mean duration of follow-up was 6.2 ± 4.8 years. Gastric cancer developed in 21 (20 intestinal type). The cumulative 5-year incidences of gastric cancer were 3.2% overall; 1.5%, 5.3%, and 9.8% in IM groups A, B, and C; and 0.7%, 1.9%, and 10% in the none/mild, moderate, and severe endoscopic atrophy groups, respectively. Compared with IM group A, the hazard ratio for IM group B was 3.6 (95% confidence interval [CI], 1.2-11), and that for IM group C was 3.7 (95% CI, 1.1-12). Compared with the none/mild endoscopic atrophy group, the hazard ratio for severe atrophy was 9.3 (95% CI, 1.7-174). CONCLUSIONS: Patients with histologic IM or severe endoscopic atrophy were at increased risk of gastric cancer development after H pylori eradication.

Shichijo, S., et al. (2015). "Distribution of intestinal metaplasia as a predictor of gastric cancer development." Journal of Gastroenterology and Hepatology 30(8): 1260-1264.

BACKGROUND AND AIM: Helicobacter pylori, gastritis, and intestinal metaplasia (IM) are known risk factors for gastric cancer. In the present study, we conducted a cohort study to evaluate the predictive value of the distribution of IM for gastric cancer development. METHODS: We conducted a retrospective cohort study at a university hospital. From June 1998 to December 2000, we assessed histological gastritis using biopsy specimens, one from the antrum and one from the corpus, from 1450 patients, among whom 729 revisited for follow-up endoscopy. Patients were classified into three groups according to the distribution of IM at initial endoscopy. IM group A had no IM, IM group B had IM in the antrum only, and IM group C had IM in the corpus. The development of gastric cancer was assessed by endoscopic examination. RESULTS: The mean duration of follow-up was 6.7 ± 4.7 years. The cumulative incidence of gastric cancer at 5 years was 1.5% in total and 0.8%, 3.3%, and 2.7% in IM groups A, B, and C, respectively. The IM group was identified as an independent risk factor by multivariate analysis; compared with IM group A, hazard ratios were 3.6 (95% confidence interval [CI] 1.1-12.1) in IM group B and 3.8 (95% CI 1.01-14.1) in IM group C. In IM group C, the incidence of gastric cancer in patients who received eradication therapy was significantly lower than that in patients who did not receive (P = 0.021, log-rank). CONCLUSION: IM is a good predictive marker for the development of gastric cancer.

Shichijo, S., et al. (2014). "Histological findings of intestinal metaplasia in the gastric corpus is a predictive factor for the development of gastric cancer." Gastroenterology 146(5): S-330.

Background and aim; Helicobacter pylori, gastritis and intestinal metaplasia are known risk factors for gastric cancer. We previously reported a cross-sectional study showing the association between gastric cancer and the distribution of intestinal metaplasia (IM) and neutrophil infiltration (NI) assessed by two stomach biopsy specimens (J Gastroenterol Hepatol 2011). In the present study, we conducted a cohort study to elucidate that histological findings of gastric mucosa could predict development of gastric cancer. Methods; From June 1998 to December 2000, we prospectively assessed histological gastritis by two biopsy specimens (one from greater curvature of the antrum and one from the greater curvature of the corpus) in 1395 patients. The specimens were assessed for the presence of IM and NI. At the enrollment, 71 patients with gastric cancer were excluded. Patients were categorized according to the distribution of IM as follows: IM group A, no IM in either the antrum or corpus; IM group B, IM in the antrum only; and IM group C, IM in the corpus only or in both the antrum and corpus. Patients were recommended to receive annual endoscopy to examine gastric cancer development. A total of 731 patients (377 males and 354 females) were followed up over an average of 6.8±4.9 years. Gastric cancer incidence was analyzed by histological findings, age, and sex. Results; Out of 731 patients, new gastric cancer developed in 15 cases (12 intestinal-type and 3 diffuse-type). 6 developed in IM group C, and these were all intestinal type. Cox proportional hazard model showed IM group C is an independent predictive factor for the development of gastric cancer, especially intestinaltype. Compared with IM group A, the Hazard Ratio for IM group C was 8.4 (95% confidence interval: 2.4-30.8), and that for IM group B was 2.7 (0.6-10.3). All 3 diffuse-type gastric cancers developed in IM group A (2 from patients without NI, and 1 from patients with NI in the antrum only). NI at initial endoscopy did not affect gastric cancer incidence in follow-up period. Conclusion; Patients with intestinal metaplasia in the gastric corpus were at increased risk for the development of intestinal-type gastric cancers. Hazard Ratio for the development of gastric cancer (Table Presented).

Shichijo, S., et al. (2015). "Histological intestinal metaplasia and endoscopic atrophy are predictors of gastric cancer development after helicobacter pylori eradication." Gastroenterology 148(4): S563-S564.

Background and aim; Helicobacter pylori (H. pylori), atrophic gastritis and intestinal metaplasia are known risk factors for gastric cancer. H. pylori eradication therapy was shown to be effective to reduce gastric cancer incidence. However, gastric cancer does develop after eradication therapy. In the present study, we conducted a cohort study to elucidate the risk factor for gastric cancer development after successful H. pylori eradication therapy. Methods; From June 1998 to December 2012, we prospectively assessed histological and endoscopic gastritis, and performed H. pylori eradication therapy in 751 patients. We assessed histological intestinal metaplasia using two biopsy specimens (one from greater curvature of the antrum and one from the greater curvature of the corpus). Patients were classified according to the distribution of IM as follows: IM group A, no IM; IM group B, IM in the antrum only; and IM group C, IM in the corpus. We assessed endoscopic atrophy according to Kimura- Takemoto classification, and patients were classified to three groups; none or mild atrophy (C0-C2), moderate atrophy (C3-O1), and severe atrophy (O2-O3). Patients were recommended to receive annual endoscopy to examine gastric cancer development. Gastric cancer incidence was analyzed by histological and endoscopic findings, age, and sex. Results; A total of 581 patients (323 males and 258 females) revisited for follow-up endoscopy. The mean duration of follow up was 6.0±4.6 years. Out of 581 patients, new gastric cancer developed in 21 cases (20 intestinal-type and 1 diffuse-type). Fifteen were from male, and six were from female. Cumulative incidence of gastric cancer at 5 year was 2.9% in total, 1.5%, 5.2%, and 10% in IM groups A, B, and C, and 0.7%, 1.9% and 11% in mild, moderate, and severe endoscopic atrophy groups, respectively. IM group B, IM group C, and severe endoscopic atrophy were identified as independent predictive factors by multivariate analysis. Compared with IM group A, the Hazard Ratio for IM group B was 4.2 (95% confidence interval: 1.5-13), and that for IM group C was3.5 (1.03-12). Compared with none or mild endoscopic atrophy group, the Hazard Ratio for severe atrophy was 4.5 (1.1-31). Conclusion; Patients with histological intestinal metaplasia or severe endoscopic atrophy were at increased risk for gastric cancer development after H. pylori eradication. These findings may be useful to clarify the high risk patients after H. pylori eradication. (Figure Presented).

Shin, C. M., et al. (2014). "A follow-up of CDX1 and CDX2 MRNA expressions in noncancerous gastric mucosae after helicobacter pylori eradication." Gastroenterology 146(5): S-399.

Objectives: To evaluate the changes in CDX1 and CDX2 expressions after Helicobacter pylori eradication, in relation to the reversibility of intestinal metaplasia (IM). Methods: Time course of CDX1 and CDX2 expressions was investigated in 107 successfully H. pylori eradicated, 25 non-eradicated and 44 H. pylori negative subjects, including 82 controls, 51 with gastric dysplasia and 43 with early gastric cancer. All dysplasia and gastric cancer patients underwent endoscopic resection at the time of enrollment. Expression levels in CDX1 and CDX2 from noncancerous gastric mucosae of corpus, as well as the histologic findings of gastric mucosae, were evaluated during the follow-up. Results: Average followup duration was 33.6 months (range: 2 to 97 months). Expression levels in both CDX1 and CDX2 mRNAs were significantly correlated with IM grade in corpus (ρ = 0.633 and 0.554, respectively, all P < 0.001). Profiles of CDX1 and CDX2 mRNA expression following H. pylori eradication showed only insignificant results. IM grade in antrum and corpus showed a trend toward decrease after H. pylori eradication without statistical significance (P > 0.05). Interestingly, histologic improvement of IM at corpus was found to be correlated with a decrease in CDX2 mRNA expression, but not in CDX1. Conclusion: In this study, eradication of H. pylori did not show beneficial effects on aberrant CDX1/CDX2 expressions or IM. However, at least a portion of subjects showed a histologic improvement in IM irrespective of H. pylori eradication, and reversibility of IM at corpus appeared to be associated with a decrease in CDX2 mRNA expression.

Shin, C. M., et al. (2013). "Changes in aberrant DNA methylation after Helicobacter pylori eradication: a long-term follow-up study." International Journal of Cancer 133(9): 2034-2042.

Changes of DNA methylation in gastric mucosae after eradication of Helicobacter pylori have not been clarified yet. From this background, we investigated time course of DNA methylation following H. pylori eradication in 221 successfully H. pylori eradicated subjects with endoscopic follow-up at least for 6 months, including 114 controls, 53 subjects with gastric dysplasia and 54 patients with early gastric cancer. All dysplasia and gastric cancer patients underwent endoscopic resection at the time of enrollment. The methylation levels in LOX, APC and MOS genes from noncancerous gastric mucosae using quantitative methylation-specific PCR, as well as the histologic findings of gastric mucosae, were compared before and after eradication. Average follow-up duration was 26.0 months (range: 6 to 76 months). H. pylori eradication decreased methylation levels in LOX (p-value for slope < 0.001) but not in APC. In MOS, decrease of its methylation level following H. pylori eradication was significant among controls without intestinal metaplasia (IM) (p-value for slope < 0.05); however, it was not observed among patients with IM or those with dysplasia or gastric cancer. After H. pylori eradication, methylation level in MOS persistently increased in patients with dysplasia or gastric cancer (p < 0.01). In conclusion, H. pylori eradication decreases aberrant DNA methylation with gene-specific manner. Methylation level in MOS is associated with IM and may be used as a surrogate marker for gastric cancer risk, regardless of H. pylori eradication history.

Shin, S. H. and D. H. Jung (2014). "The effect of H. Pylori eradication on metachronous gastric neoplasms after endoscopic resection of gastric dysplasia." United European Gastroenterology Journal 2(1): A589-A590.

INTRODUCTION: Helicobater pylori (H. pylori) infection was closely related in gastric atrophy, intestinal metaplasia (IM), and a progression to dysplasia or cancer. Furthermore, some studies showed that the eradication of H. pylori after endoscopic resection (ER) of early gastric cancer (EGC) was helpful to prevent the development of metachronous gastric cancer.(1.2) However, there are no sufficient data about the role of eradication of H. pylori after ER for gastric dysplasia. AIMS & METHODS: The aim of this study was to investigate the effect of H. pylori eradication would affect the development of the metachronous gastric neoplasms after ER in patients with gastric dysplasia. We retrospectively reviewed 1850 patients who underwent endoscopic resection of gastric dysplasia from January 2007 to February 2012 at Severance hospital. We excluded patients with follow-up period of < 2 years and who had not undergone tests for active H. pylori infection at the time of endoscopy. Total of 289 patients were enrolled in this study. Then divided them into three groups: those without active H. pylori infection (Hp negative group, n=131), those who successfully underwent H. pylori eradication (eradicated group, n=119), and those who failed or did not undergo H. pylori eradication (non-eradicated group, n=39). The rate of metachronous recurrence after ER was compared. RESULTS: Metachronous reccurence was diagnosed in 42 patients, including 25 in the Hp negative, 8 in the eradicated, 9 in the non-eradicated group. Median time to metachronous recurrence was 36 months (range, 6-85 months). The incidence of metachronous recurrence was 5.13 cases per 1,000 person-years in the Hp negative group, 1.57 cases per 1,000 person-years in the eradicated group, and 6.07 cases per 1,000 person-years in the noneradicated group. Patients in non-eradicated group had a higher risk of developing metachronous gastric neoplasms than eradicated group (hazard ratio [HR] 3.974, p=0.005). CONCLUSION: The successful H. pylori eradication may reduce the development metachronous gastric neoplasms after ER in patients with gastric dysplasia. Also regular follow-up of test for H. pylori infection is important to prevent the metachronous recurrence in those high-risk patients.

Shin, W. G., et al. (2012). "Surveillance strategy of atrophic gastritis and intestinal metaplasia in a country with a high prevalence of gastric cancer." Digestive Diseases and Sciences 57(3): 746-752.

BACKGROUND: It is not clear which screening examinations are best suited for gastric cancer prevention, especially in patients with atrophic gastritis and intestinal metaplasia. Therefore, we investigated the gastric cancer screening methods and intervals that are performed in clinical practice in an area with a high prevalence of gastric cancer. METHODS: Eighty-seven physicians voted by keypad and discussed the consistency of endoscopic diagnosis of atrophic gastritis and intestinal metaplasia at the Annual Symposium of the Korean College of Helicobacter and Upper Gastrointestinal Research. Additionally, 100 core members of this academic society were asked via e-mail to complete the questionnaires related to screening strategies for gastric cancer. RESULTS: The most common recommendation for the subjects with intestinal metaplasia was an annual endoscopic follow-up (95.5% vs. 80.4% in the expert and non-expert groups, respectively; P = 0.118). Annual endoscopic follow-up was also the most predominant recommendation for atrophic gastritis (95.5% vs. 76.5%; P = 0.092), regardless of the physicians' endoscopic experience, position, and degree of the hospital. However, the correct answer rate for the diagnosis of normal endoscopic findings was only 16.7 and 14.1% in the expert and non-expert groups, respectively (P = 0.883). CONCLUSIONS: The most common practical screening strategy for patients with atrophic gastritis and intestinal metaplasia in Korea was annual endoscopic examination. However, a new program estimating individualized gastric cancer risk might be needed because of the low inter-observer agreement in the endoscopic diagnosis of atrophic gastritis and intestinal metaplasia.

Shiotani, A., et al. (2005). "Histologic and serum risk markers for noncardia early gastric cancer." International Journal of Cancer 115(3): 463-469.

Corpus dominant gastritis and intestinal metaplasia (IM) are considered markers of increased risk of gastric carcinoma. The aim of our study was to determine serum and histologic risk markers of gastric cancer. Antral and corpus histology, pepsinogen and gastrin 17 levels were compared among patients with history of endoscopic mucosal resection (EMR) for early gastric cancer and controls. Serum pepsinogen (PG) and gastrin 17 levels were measured by RIA. There were 53 gastric cancer patients and 75 controls. The scores for IM in each region and atrophy at the lesser curvature of the corpus were significantly higher in the cancer group than in the H. pylori-positive control group. IM at the greater curvature of the corpus and atrophy at the lesser curvature of the corpus were associated with multiple malignant lesions. Although corpus gastritis was associated with an increased risk of gastric cancer (odds ratio [OR] = 3.4; 95% confidence interval [CI] 1.6-7.0) (p = 0.001), the most important marker was the presence of IM at the lesser curvature of the corpus (OR = 15.1; 95% CI 4.3-52.6) (p < 0.001)). The best cut-off points of serum markers for gastric cancer were a PG I concentration of 45 ng/mL or less and a gastrin 17 >60 pg/mL (sensitivity = 83%; specificity = 68%). IM at the lesser curvature of the corpus and the combination of serum gastrin 17 and PG I identified a group at high risk for development of gastric cancer. Annual endoscopic follow-up is warranted for patients with IM found at the greater curvature of the corpus.

Siciliano, I., et al. (2019). "A cohort study of patients with gastric bypass and simultaneous preventive subtotal gastrectomy of excluded metaplastic stomach." Obesity Surgery 29(5): 664.

Background / introduction: Now Helicobacter pylori and stomach chronic lesions are the factors of gastric cancer development. Since 2016 Maastricht V/Florence consensus, each patient with atrophy/intestinal metaplasia should have a follow-up by endoscopic staging. In such conditions, the sleeve gastrectomy is a frequent option for patients with morbid obesity. Nevertheless, if the patient presents a severe gastroesophageal reflux disease the sleeve resection should be avoided; the one-moment gastric bypass with subtotal gastrectomy may be considered. Objectives: To analyze a treatment option and technical points of simultaneous preventive subtotal gastrectomy of excluded metaplastic stomach after gastric bypass. Clinical setting: A single-center observational study. Methods: A total of 520 patients with a surgical treatment of obesity were treated from 11/2016 to 03/2019. For eight patients was performed an associated gastrectomy with a laparoscopic bypass surgery. All patients had acid reflux with proton-pump inhibitors use. Five patients (62.5%) presented diabetes. Results: The cohort median BMI was 44,9 (38,2 - 55,8), 5 women and 3 man with average age of 54. The technical intraoperational features were evaluated. The hospital stay was from 3 to 7 days (average 4.6). No mortality on day 30 was observed. One patient (13%) had an intraperitoneal hemorrhage associated with an anastomosis leak. Conclusion: The simultaneous preventive subtotal gastrectomy of excluded stomach is a feasible technique. It seems that this unique radical option does not give morbi-mortality for selected patients with obesity under the metaplasia context. More robust studies are needed.

Signorelli, S., et al. (2011). "Surveillance and treatment of premalignant gastric lesions 6 years after helicobacter pylori eradication." Digestive and Liver Disease 43: S204.

Background and aim: Gastric cancer in an important worldwide healt problem and is the fourth most common cancer. H. pylori plays a central role in carcinogenesis. Chronic active gastritis, glandular atrophy, intestinal metaplasia (IM), dysplasia and adenocarcinoma are significantly associated with H. pylori infection. Some of the premalignant condition may regress after H. pylori eradication. The aim of this study is evaluate histological findings and to investigate the reverbibility of these mucosal changes after H. pylori eradication therapy. Material and methods: 223 H. pylori infected patients (pts) with non ulcer dyspepsia were treated for 7 days with omeprazole 20 mg bid, Amoxicillyn 1 gr bid and Claritromicyn 500 mg bid. Every pts underwent to an endoscopic examination and H. pylori status was assessed by histology according to the Sydney system and scored on a 0-3 scale. Treatment success was checked by C-13 Urea Breath Test three months after end of therapy. Mucosal alterations were evaluated before and after eradication therapy. 169 pts were classified as the eradicated group and 54 pts remained H. pylori infected. The pts were followed up by endoscopy with gastric antral biopsy each year. 15 pts dropped out during the 6 years (mean) of follow-up: 9 in eradicated group and 3 in infected group. Results: Histopathological analysis of gastric antral mucosa from H. pylori negative pts revealed a significant decrease in chronic active inflammation (p<0.001), regenerative foveaolar hyperplasia and mucosal-associated lymphoid tissue (p<0.01). Gland atrophy and IM remained unchanged in two groups and had no significant regression. During follow-up one uninfected and four Hp positive pts developed low-grade dysplasia. Two non eradicated subjects (4%) developed gastric cancer but none of the uninfected pts. Conclusions: Very interesting appears the presence of a significant decrease of inflammation activity: atrophy and IM persisted for a long period in both groups. Gastric cancer develops in pts infected with H. pylori, but not in uninfected subjects. H. pylori eradication and follow-up endoscopy and histology seem indicated in pts with premalignant gastric lesions.

Simko, V., et al. (2015). "Gastric intestinal metaplasia - age, ethnicity and surveillance for gastric cancer." Bratislavske Lekarske Listy 116(1): 3-8.

AIM: Determine the prevalence and distribution of gastric intestinal metaplasia (GIM) in a large cohort of patients subjected to esophagogastroscopy (EGD). Evaluate usefulness of grading the severity of gastritis, GIM and the impact of Helicobacter pylori (HP). Define the population at risk for gastric adenocarcinoma (GC) and assess the value of surveillance. METHODS: In the course of 19 years, we performed 11,600 sequential EGDs in male veterans at Brooklyn, New York. Of all patients, 47 % had EGD only one time while 53 % had EGD repeated, 11 % of these had four or more EGDs. Patients with GIM were matched with equal number of controls with no GI symptoms. All gastric biopsies were processed in one laboratory, using the standardized protocol for histological staining and for grading the severity of epithelial changes. RESULTS: Of all patients subjected to EGD, 354 (3.05 %) were diagnosed with GIM. Compared to controls, GIM patients were older, 80 % were over 71. Regarding ethnicity, GIM was 5.4 % more frequent in 177 African Americans than in 159 Caucasians. Distribution of GIM did not differ with respect to age or ethnicity. As many as 6 %of GIM cases were diagnosed with GC. Grading of GIM severity had a predictive value, the average grade of severity in GC was 50 % higher than in non-cancer patients with GIM. Severity of gastritis was also a useful biomarker: patients with GC had more severe gastritis. Surprisingly, HP positivity had no predictive value: HP positive patients had similar distribution of GIM as the HP negative patients. Use of proton pump inhibitors in the past was unknown. CONCLUSION: Prevalence of GC in patients with GIM was more than 200 times higher than reported in normal population. Age more than 70 years and African Americans appeared to be at higher risk. Routine EGD and histological diagnosis, with simple grading of severity of epithelial changes provides a useful predictive information. Individuals with upper GI symptoms undergoing EGD with gastric biopsy benefited from routine clinical screening for GC. Patients with higher severity of GIM should enter surveillance (Tab. 1, Fig. 10, Ref. 45).

Singla, M., et al. (2014). "Topographical mapping in a cohort of patients with gastric intestinal metaplasia ACG fellow award." American Journal of Gastroenterology 109: S45-S46.

Introduction: Gastric intestinal metaplasia (GIM) is a premalignant lesion commonly found on routine biopsies of the gastric mucosa. Progression to cancer in U.S. patients is low; the ASGE recommends surveillance of GIM with topographic mapping (TOMP) only in “high-risk” patients. No prospective studies have been done to evaluate the yield of TOMP in patients with GIM. The aim of our study was to evaluate the use of TOMP for cancer surveillance in patients with GIM. Methods: We prospectively enrolled consecutive adults with GIM found on routine biopsies of the stomach during endoscopy. We collected data on clinical history, ethnicity, family history of gastric cancer, H. pylori infection, and indication for index endoscopy. All patients underwent at least 1 TOMP of the stomach with multiple biopsies of the antrum, angularis, body, and fundus. Repeat TOMP was performed 6 months later, and, if no dysplasia was found, every 2 years and sooner if dysplasia or cancer was identified. Patients were dis-enrolled from the study if they had 2 consecutive TOMPs that were negative for GIM. Results: One hundred-eight adult patients were enrolled with a mean ± SD age of 57.1 ± 14.3 years; 37% were male; 45.4% Caucasians, 22.2% African Americans, 25% Asians, 2.8% Hispanics, and 4.6% others. We performed 276 TOMPs (mean 2.55 studies/patient) over a mean ± SD of 46.5 ± 26.5 months per patient. 71.1% of TOMPs revealed persistent GIM; 44.9% of these revealed incomplete metaplasia. 40.7% of the patients tested positive for H. Pylori; all were treated with triple or quadruple therapy. Six patients had a first-degree relative and 4 patients had a second-degree relative with gastric cancer. Index endoscopy (prior to TOMP) identified 1 patient with low-grade dysplasia (LGD) and 2 patients with high-grade dysplasia (HGD). TOMP revealed 2 additional patients with LGD and 1 patient with an identifiable lesion of gastric adenocarcinoma. Thirty-five patients had GIM that resolved on surveillance. These patients were more likely to be Caucasian than non-Caucasian (71.4% vs. 28.6%, p=0.000). Of the 6 patients with dysplasia or cancer, 2 had a family history of cancer, 2 had H. pylori, and 3 were Asian. There were no significant differences in gender, ethnicity, H. pylori infection, medication use, family history, or type of metaplasia between patients with dysplasia identified and those without. Conclusion: In our prospective cohort study, we report a significantly lower prevalence of gastric cancer and of dysplasia in GIM than previously reported retrospective studies. Our data suggest that surveillance with TOMP in a U.S. population, even of those patients at higher risk for gastric cancer, is of low clinical yield.

Sinha, A., et al. (2019). "GASTRIC CARCINOID IN A PATIENT WITH AUTOIMMUNE POLYENDOCRINE SYNDROME TYPE III." Chest 156(4): A1307-A1308.

SESSION TITLE: Tuesday Fellows Case Report Posters SESSION TYPE: Fellow Case Report Posters PRESENTED ON: 10/22/2019 01:00 PM - 02:00 PM INTRODUCTION: Autoimmune polyendocrine syndromes (APS) are a group of rare diseases which are characterized by autoimmune damage to multiple endocrine organs. We describe a case of Autoimmune Polyendocrine Syndrome Type III with symptomatic vitamin B12 deficiency from pernicious anemia and chronic atrophic gastritis with gastric carcinoid. CASE PRESENTATION: A 46-year-old woman presented with tingling and numbness of the hands and feet. She had a history of hypothyroidism and breast cancer. An initial evaluation for the tingling and numbness showed a hemoglobin (Hb) of 13.3 grams per deciliter, hematocrit of 38.8 %. Mean corpuscular volume (MCV) was 89 Femtoliters. The Vitamin B 12 level was low at 63 picorgrams per milliliter and the serum folic acid level was high at 20 nanograms per milliliter. The methyl-malonic acid level (MMA) was high (9.07 nanomoles per milliliter). Parietal cell antibodies were positive to a ratio of 1:160 and intrinsic factor blocking antibody was negative. She was dosed with intramuscular B12 and a daily dose vitamin b12 extended release tablets. She also received a referral for an urgent gastroenterology evaluation. The patient had an endoscopy with biopsy, and was found to have a well differentiated carcinoid tumor of the cardiac part of the stomach with moderate chronic gastritis with intestinal metaplasia consistent with autoimmune gastritis. Enterochromaffin-like cell hyperplasia was also present. She is now being worked up for an elective removal of the tumor. DISCUSSION: Autoimmune polyendocrine syndromes (APS) are a group of rare diseases which are characterized by autoimmune damage to multiple endocrine organs [1]. The two major APS are type I and type II, both of which include Addison’s disease a component. The rarer entity, APS type III, can be further divided into 3 subcategories: 1) APS IIIA- Autoimmune thyroiditis (ATD) with type I diabetes Mellitus (DM) 2) APS IIIB- ATD with pernicious anemia 3) APS IIIC- ATD with vitiligo and/or alopecia and/or other organ specific autoimmune disease. 10% patients with CAG are predisposed to development of gastric carcinoid tumors and adenocarcinomas [2]. Gastric carcinoid type I which evolve from enterochromaphil like cell dysplasia may develop in about 5% patients with CAG as seen in our patient [3]. Therapy for APS type IIIB consists of targeting the thyroid disease and pernicious anemia. For ATD, thyroid replacement therapy should be administered. For pernicious anemia, supplemental vitamin B12 therapy is the treatment of choice. Patients who are found to have gastric carcinoid on endoscopy and biopsy can follow up with either monitoring with repeat endoscopies or undergo endoscopic resection of the tumor. CONCLUSIONS: Physicians should be aware of the possibility of a APS and gastric carcinoid in the presence of Vitamin B12 deficiency and gastroenterology should be involved early in the course of the disease. Reference #1: Cutolo M. Autoimmune polyendocrine syndromes. Autoimmunity Reviews 2014;13(2):85–89. Reference #2: Kokkola A, Sjoblom SM, Haapiainen R. The Risk of Gastric Carcinoma and Carcinoid Tumours in Patients with Pernicious Anaemia: A Prospective Follow-Up Study. Scandinavian Journal of Gastroenterology 1998;33(1):88–92. Reference #3: Armbrecht U, Stockbrugger RW, Rode J, Menon GG, Cotton PB. Development of gastric dysplasia in pernicious anaemia: a clinical and endoscopic follow up study of 80 patients. Gut 1990;31(10):1105–1109. DISCLOSURES: No relevant relationships by Yizhak Kupfer, source=Web Response No relevant relationships by Namrita Malhan, source=Web Response No relevant relationships by Ravikaran Patti, source=Web Response No relevant relationships by Arjun Saradna, source=Web Response No relevant relationships by Ankur Sinha, source=Web Response No relevant relationships by Parita Soni, source=Web Response

Sipponen, P. (1995). "Helicobacter pylori: A cohort phenomenon." American Journal of Surgical Pathology 19(SUPPL. 1): S30-S36.

Helicobacter pylori infection is an etiopathogenetic cause of chronic gastritis in more than 90% of the cases. In a proportion of infected subjects, gastritis slowly (over years or decades) progresses, for unknown reasons, into atrophic gastritis that affects antral or corpus mucosa, or both (multifocal atrophic gastritis). Some recent improvements have been made in studies of H. pylori gastritis. H. pylori gastritis has shown to associate strongly with peptic ulcer diseases and gastric cancer. The risk for ulcer (excluding the nonsteroidal anti-inflammatory drug related ulcers) is highest in the nonatrophic forms of gastritis and the risk for gastric cancer in the severe forms of atrophic (metaplastic) gastritis. For routine histopathologic practice, the Sydney System has been developed to describe and grade the histopathologic appearances of gastritis, i.e., chronic and acute ('activity') inflammation, atrophy (loss of normal mucosal glands), intestinal metaplasia, and H. pylori in endoscopic biopsy specimens from antrum and corpus. Different phenotypes of H. pylori gastritis can be reliably described and the risks for various gastric diseases reasonably well predicted by the System. Most recent studies from developed countries have indicated that H. pylori acquisition occurs mainly during childhood and that the infection risk is quite low in adulthood. In addition, the acquisition rate has declined in these countries during the past few decades. The observations suggest that H. pylori gastritis is a birth cohort-related phenomenon. The acquisition rate has been high and the subsequent chronic gastritis is a common disease in the cohorts (generations) born in the beginning of this century but both are much less common in cohorts born more recently.

Sipponen, P. and K. Kimura (1994). "Intestinal metaplasia, atrophic gastritis and stomach cancer: trends over time." European Journal of Gastroenterology and Hepatology 6 Suppl 1: S79-83.

BACKGROUND: The pathogenetic association of chronic atrophic gastritis and intestinal metaplasia with gastric cancer implies that the trends seen in these disorders over time should be similar. Both should similarly decrease in incidence with time, and a time-related relationship should occur between the incidence of gastric cancer and the rate of development of atrophic gastritis in the stomach of Helicobacter pylori-infected subjects. AIMS AND METHODS: We reviewed some recent studies from Finland on the time trends seen in chronic gastritis, atrophic gastritis (and intestinal metaplasia) and gastric cancer over a period of 15 years (1977-1992). In addition, using results from earlier studies from Japan and Finland, we formed hypotheses on how the time-dependent evolution and extension of atrophic gastritis may accord with the occurrence of gastric cancer in the stomach. RESULTS: Our investigations showed that the incidence of gastric cancer and the prevalence of H. pylori-associated gastritis, atrophic gastritis and intestinal metaplasia have decreased similarly in outpatient series during the last 15 years. Correspondingly, gastric cancer, atrophic gastritis and intestinal metaplasia are cohort phenomena in the population, and the prevalence rate of atrophic gastritis is correlated with the cohort-specific incidence of gastric cancer; both are high in cohorts born near the beginning of the century but are quite low in those born in recent decades. Since antral and angular areas of the stomach are primary sites for gastric cancer tumours, the earlier investigations indicate that the time-dependent progression of gastritis in grade (development of atrophic gastritis and intestinal metaplasia) and extent (spreading of gastritis by pylorocardial extension) is well correlated with the rate and predisposition of gastric cancer tumours in the distal and angular stomach. CONCLUSIONS: We conclude that atrophic gastritis (or intestinal metaplasia) and gastric cancer are very much alike in time trends and in course. This parallelism favours suggestions that H. pylori-associated gastritis with atrophic and metaplastic sequelae (atrophic gastritis) contribute to the pathogenesis of gastric cancer.

Sipponen, P. and K. Kimura (1995). "Intestinal metaplasia, atrophic gastritis and stomach cancer trends over time." European Journal of Gastroenterology and Hepatology, Supplement 6(1): S79-S83.

Background: The pathogenetic association of chronic atrophic gastritis and intestinal metaplasia with gastric cancer implies that the trends seen in these disorders over time should be similar. Both should similarly decrease in incidence with time, and a time-related relationship should occur between the incidence of gastric cancer and the rate of development of atrophic gastritis in the stomach of Helicobacter pylori-infected subjects. Aims and methods: We reviewed some recent studies from Finland on the time trends seen in chronic gastritis, atrophic gastritis (and intestinal metaplasia) and gastric cancer over a period of 15 years (1977-1992). In addition, using results from earlier studies from Japan and Finland, we formed hypotheses on how the time-dependent evolution and extension of atrophic gastritis may accord with the occurrence of gastric cancer in the stomach. Results: Our investigations showed that the incidence of gastric cancer and the prevalence of H. pylori-associated gastritis, atrophic gastritis and intestinal metaplasia have decreased similarly in outpatient series during the last 15 years. Correspondingly, gastric cancer, atrophic gastritis and intestinal metaplasia are cohort phenomena in the population, and the prevalence rate of atrophic gastritis is correlated with the cohort-specific incidence of gastric cancer; both are high in cohorts born near the beginning of the century but are quite low in those born in recent decades. Since antral and angular areas of the stomach are primary sites for gastric cancer tumours, the earlier investigations indicate that the time-dependent progression of gastritis in grade (development of atrophic gastritis and intestinal metaplasia) and extent (spreading of gastritis by pylorocardial extension) is well correlated with the rate and predisposition of gastric cancer tumours in the distal and angular stomach. Conclusions: We conclude that atrophic gastritis (or intestinal metaplasia) and gastric cancer are very much alike in time trends and in course. This parallelism favours suggestions that H. pylori-associated gastritis with atrophic and metaplastic sequelae (atrophic gastritis) contribute to the pathogenesis of gastric cancer.

Skup, M., et al. (2019). "GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): RISKS ASSOCIATED WITH RECURRENCE IN WESTERN POPULATIONS." Gastrointestinal Endoscopy 89(6): AB498.

Background: ESD is a well-established technique for ensuring en bloc resection. It has gained early prominence in Asian countries in the treatment of gastric advanced benign neoplasm and early gastric cancer. It has been well noted in the surgical literature that there are differences in tumor biology between Eastern and Western gastric cancer. Following R0 resection in ESD, Eastern literature suggests a local recurrence rate of less than 2% and a metachronous lesion rate of less than 5%. Aim: To assess the safety and efficacy of gastric ESD within a Western population and determine the risk factors for disease recurrence or metachronous lesions. Methods: A retrospective study of consecutive gastric ESDs performed by a single endoscopist (G.B.H)between 2008 and 2018 was undertaken. Primary outcomes were en bloc resection rate, R0 resection, histologic evaluation, including vertical and horizontal margins, perineural and vascular invasion. Secondary outcomes were complication rates, recurrence rates, and metachronous lesion rates. Results: A total of 92 gastric ESDs were performed. The average size of the lesion was 37.7 mm. The en-block resection rate was 98% with R0 margins in 89% of cases. There were positive vertical and horizontal margins in 8% and 3% of cases respectively. Gastric cancer was present in 35% of cases. 4% of patients required further surgical resection of their lesions following ESD. The bleeding rate was 5% and the perforation rate was 3%. All complications were managed endoscopically. Patients with recurrent or metachronous lesions all demonstrated a background of extensive intestinal metaplasia. No patient had positive vertical margins. One patient with positive horizontal margins had both a metachronous and recurrent lesion on follow-up endoscopy. Conclusions: Gastric ESD performed in Western centers can achieve a success rate comparable to Asian endoscopists. The incidence of recurrence and metachronous lesions is comparable between both populations. Extensive intestinal metaplasia may be a risk factor for both recurrent and metachronous lesions. [Figure presented][Figure presented]

Slade, J. and S. Jakate (2015). "Is grossly cryptic early gastric carcinoma a distinctive phenotype rather than a stage?" Laboratory Investigation 95: 192A-193A.

Background: The vast majority of gastric carcinomas are advanced. In the WHO classification, early gastric carcinoma (EGC) is not a subtype but carcinoma limited to the mucosa or submucosa regardless of the nodal status. In endoscopic/clinical classifications (Japanese Endoscopic Society, Paris Classification), EGCs are classified by the macroscopic appearance as polypoid, elevated or ulcerated. However, none of these classification schemes apply when EGC is grossly cryptic or extends beyond a small grossly visible lesion. We studied resected grossly cryptic EGCs for their clinical, endoscopic and pathological characteristics. Design: Between 1994 and 2014, 16 cases of EGC were retrieved from the clinical/ pathology archives at our medical center. Only cases with a prior biopsy and subsequent gastrectomy were included. We reviewed each case for clinical presentation, endoscopic appearance, gross appearance of the resected specimen, microscopy of tumor and surrounding stomach, stage and available follow-up. Results: There was a female predominance (68%) and a mean age of 62. The most common clinical presentation were epigastric pain (7), weight loss (5), anemia (2) and gastrointestinal bleeding (2). Endoscopic findings included small mucosal irregularity (9), small shallow ulcer/erosion (3), and normal stomach (4). After biopsy, all cases underwent partial or subtotal gastrectomy. Determining the extent of the tumor was challenging in 15 of 16 cases since the tumor was either grossly unidentified or cryptic tumor extended considerably beyond the confines of a shallow erosion. Eighteen to 58 blocks were required for evaluation. Microscopic invasive tumor was either well to moderately differentiated intestinal (7), poorly differentiated (7) or mixed (2). The stomach in the background showed chronic gastritis (10), intestinal metaplasia (6) and Helicobacter organisms (3). All cases except one (pT1N2) were stage pT1N0. More than 6 months of follow-up was available in 12 cases and ranged from 7 months to 18 years. A disease-free state without recurrent tumor was seen in 8/12 (66%) cases. Conclusions: The grossly cryptic EGCs show female preponderance and have clinical, endoscopic and pathological characteristics that do not conform to any prototypical gastric carcinoma classification schemes. EGCs also show mixed microscopic subtypes and predisposing conditions. Gross evaluation, sampling and sizing of EGC is challenging. Nodal metastasis is rare and prognosis is excellent. Rather than just an early stage, our findings raise the possibility that EGC may signify a distinctive and overlooked phenotype.

Snir, Y., et al. (2017). "Gastric intestinal metaplasia is significantly associated with post endoscopy Non-Cardia gastric cancer." United European Gastroenterology Journal 5(5): A126.

Introduction: Evidence suggests that the presence of gastric intestinal metaplasia (GIM) is involved in the pathogenesis of Non-Cardia Gastric Cancer (NCGC). Yet, the role of GIM in the occurrence of post endoscopy cancer is scarce. Aims & Methods: We aimed to determine the incidence of post endoscopy NCGC and assess whether the presence of GIM is associated with its occurrence. Subjects with no previous cancer undergoing upper endoscopy at a tertiary referral center of the Clalit Health Services (CHS) HMO were included. NCGC was detected through the National Cancer Registry. Demographic data was extracted from the CHS database and pathology data including presence of GIM (with or without dysplasia) and extent (focal/extensive) were reviewed. Covariate data included age, sex, body mass index, smoking status, proton pump inhibitors use, triple therapy for helicobacter pylori, comorbidity index. Cox proportional Hazard Ratios (HR) model along with 95% Confidence Interval (CI) was calculated. Results: Between 01.2004 to 12.2013, 34, 391 subjects (55% females; mean age 60.2±17.5 years) underwent upper endoscopy. At baseline, 1406 (4.1%) had GIM:1360 without dysplasia, 46 with low grade dysplasia (LGD). During a median follow-up of 52 months [interquartile range (IQR) of 28-82 months], 25 cases of NCGC occurred (0.07%):13/32, 985 without GIM, 10/1360 with GIM without dysplasia, and 2/46 with GIM-LGD. The rate (cases/105) of post endoscopy NCGC for subjects with GIM and LGD, GIM without dysplasia, and without GIM was 1031, 163 and 8.5, respectively (P<.001). Eight cancers (32%) occurred within 12 months from endoscopy, 11 cancers (44%) within 12-36 months of endoscopy and 6 (24%) after 36 months. Among subjects with GIM without dysplasia, 7/10 developed NCGC within 36 month. Compared to subjects without GIM, the presence of GIM with and without dysplasia was significantly associated with NCGC at follow-up, HR 73.5 (CI% 16.3-331) and 14.23 (CI 6.1-32.8), respectively. Among subjects with GIM without dysplasia, extensive GIM was associated with NCGC, HR 7.63 (95% CI 1.96-29.8). Conclusion: GIM is significantly associated with post endoscopy NCGC. This finding highlights the importance of GIM as a marker for identifying subjects at risk. Health policy makers may take these finding into consideration in future guidelines regarding biopsies during upper endoscopy and GIM surveillance.

Snir, Y., et al. (2018). "Proton pump inhibitors use, helicobacter pylori infection, anti parietal cell antibodies and smoking are associated with diagnosis of gastric intestinal metaplasia." Gastrointestinal Endoscopy 87(6): AB178.

Objective and aims: Gastric Intestinal Metaplasia (GIM) is a well-defined gastric cancer precursor. Aim: to evaluate the prevalence and factors associated with the diagnosis of GIM among consecutive patients undergoing upper endoscopy at our tertiary referral center. Methods: A retrospective endoscopy-based cohort study was performed within the Clalit Health Services (CHS), Israel. Pathology data were reviewed and classified for the presence of GIM (with or without dysplasia). Demographic data were extracted from the CHS database and included age, gender, body mass index, smoking status, Helicobacter pylori (HP) infection (based on clarithromycin, amoxycillin and PPI prescriptions), presence of anti-parietal cell antibodies (1:80) and proton pump inhibitors (PPI) use. The exposure to PPI was defined as heavy use/light use/no use (12 /1-12 /no prescriptions per 30 days within the 3 years preceding baseline endoscopy, respectively). The main outcome measure was the presence of GIM at endoscopy. Odds ratios (ORs) and 95% CIs were adjusted for patient demographics and baseline risk factors. Results: Between 01.2004-12.2013, 34,391 patients (median age 62 years [IQR 49.4-73.9 years]; women 55.0%), were included. GIM was detected in 1,406 cases (4.1%): 1360 (4%) without dysplasia, 46 (0.1%) with low grade dysplasia (LGD). Factors significantly associated with GIM included PPI use (heavy use OR 1.55 [95% CI 1.33-1.80], light use OR 1.28 [95% CI 1.12-1.45]), HP infection (OR 1.55 [95% CI 1.35-1.74]), presence of anti-parietal cell antibodies (OR 2.65 [95% CI 1.79-3.90]), and smoking status (OR 1.27 [95% CI 1.13-1.42]). Any PPI use was significantly associated with GIM in subjects with and without HP infection (OR 1.31 [95% CI 1.04-1.64], p=0.019, and OR 1.37 [95% CI 1.18-1.60], p<0.001, respectively). PPI use was significantly associated with the presence of GIM-LGD (heavy use OR 5.7 [95% CI 2.1-15.4] and light use OR 3.5 [95% CI 1.35-9.20]). Conclusions: PPI use, HP infection, anti-parietal cell antibodies and smoking are significantly associated with GIM. The association between PPI and GIM, regardless of the presence of HP infection may support recent reports regarding the association between PPI use and risk of gastric cancer.

Sobala, G. M., et al. (1993). "Effect of eradication of Helicobacter pylori on gastric juice ascorbic acid concentrations." Gut 34(8): 1038‐1041.

Sobrino-Cossío, S., et al. (2018). "Efficacy of narrow-band imaging for detecting intestinal metaplasia in adult patients with symptoms of dyspepsia." Revista de Gastroenterología de México 83(3): 245-252.

INTRODUCTION AND OBJECTIVE: Atrophy and intestinal metaplasia are early phenotypic markers in gastric carcinogenesis. White light endoscopy does not allow direct biopsy of intestinal metaplasia due to a lack of contrast of the mucosa. Narrow-band imaging is known to enhance the visibility of intestinal metaplasia, to reduce sampling error, and to increase the diagnostic yield of endoscopy for intestinal metaplasia in Asian patients. The aim of our study was to validate the diagnostic performance of narrow-band imaging using 1.5× electronic zoom endoscopy (with no high magnification) to diagnose intestinal metaplasia in Mexican patients. MATERIALS AND METHODS: A retrospective cohort study was conducted on consecutive patients with dyspeptic symptoms at a private endoscopy center within the time frame of January 2015 to December 2016. RESULTS: A total of 338 patients (63±8.4 years of age, 40% women) were enrolled. The prevalence of H. pylori infection was 10.9% and the incidence of intestinal metaplasia in the gastric antrum and corpus was 23.9 and 5.9%, respectively. Among the patients with intestinal metaplasia, 65.3% had the incomplete type, 42.7% had multifocal disease, and one third had extension to the gastric corpus. Two patients had low-grade dysplasia. The sensitivity of white light endoscopy was 71.2%, with a false negative rate of 9.9%. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of narrow-band imaging (with a positive light blue crest) were 85, 98, 86.8, 97.7, and 87.2%, respectively. CONCLUSION: The prevalence of H. pylori infection and intestinal metaplasia in dyspeptic Mexican patients was not high. Through the assessment of the microsurface structure and light blue crest sign, non-optical zoom narrow-band imaging had high predictive values for detecting intestinal metaplasia in patients from a general Western setting.

Sokolov, L. K., et al. (1990). "Gastroscopy in follow-up studies of patients with chronic atrophic gastritis and diagnosis of early gastric cancer." Klinicheskaia Meditsina 68(11): 108-111.

Visual assessment of gastric mucosa and histological findings in biopsies from the lesions were compared for 1806 patients with chronic atrophic gastritis. The spectrum of the focal lesions appeared wide. Morphological examinations determined basic comparable structural elements typical for atrophic gastritis. 85 patients were diagnosed to have early gastric cancer. All the cancer patients suffered from chronic atrophic gastritis and developed in 88% of cases intestinal metaplasia, in 32% severe epithelial dysplasia. Focal changes in the mucosa characteristic for early gastric cancer in 64% of cases could be considered as variants of chronic atrophic gastritis. In 52 patients cancer was identified during the follow-up, new-onset macroscopic alterations emerging in the last year in 62% cancer subjects. The rest of them had long-lasting macroscopic lesions, among them severe dysplasia of the epithelium in 65% of cases, believed to be histological variants of atrophic gastritis. Early cancer is suggested to develop in the presence of previous lesions rapidly and discretely.

Song, H., et al. (2018). "Family history of gastric mucosal abnormality and the risk of gastric cancer: A populationbased observational study." International Journal of Epidemiology 47(2): 440-449.

Background: An increased prevalence of gastric premalignant abnormalities was reported among relatives of gastric cancer (GC) patients, with rather unexplored clinical significance. Methods: In Swedish computerized pathology registers, we identified, as 'index' persons, 232 681 patients who were born after 1931 and underwent endoscopic examination with stomach biopsy between 1979 and 2014. Through linkage with the Multi-Generation Register, we compiled a cohort consisting of 903 337 first-degree relatives of these biopsied patients. The relatives were grouped according to their 'family histories', defined as the first gastric mucosal diagnosis of the index person or GC family history known before that. Standardized incidence ratios (SIRs) provided comparisons with the matched general population. For internal comparisons with relatives with 'normal/minor changes' mucosal family history, hazard ratios (HRs) were derived from adjusted Cox regression modelling. Results: During follow-up, 1302 relatives developed GC. Crude incidence rates of non-cardia GC were 7.7×10-5 year-1 for the 'normal/minor changes' family history group (SIR=1.0), 11.2 to 12.6×10-5 year-1 for precancerous changes groups (atrophic gastritis/intestinal metaplasia/dysplasia, SIR=1.5 to 1.6), and 18.4×10-5 year-1 for those with a family history of GC (SIR=2.3). HRs derived from Cox models corroborated the family history-related risk pattern, with the most conspicuous trend observed among siblings-a family history of any precancerous changes and GC was associated with, respectively, a 2.5-fold and a 3.8-fold increment in non-cardia GC hazard, compared with siblings of index persons with 'normal/minor mucosal changes'. Conclusions: The precancerous mucosal abnormalities recorded in a person's first-degree relatives may improve GC risk stratification for this person.

Song, H., et al. (2015). "Incidence of gastric cancer among patients with gastric precancerous lesions: observational cohort study in a low risk Western population." BMJ 351: h3867.

OBJECTIVE: To accurately measure the incidence of gastric cancer among patients with gastric precancerous lesions, and to quantify the excess incidence in comparison with people with normal mucosa on endoscopy and a general population. DESIGN: Population based cohort study. SETTING: Population of Sweden using data from its national disease registers. PARTICIPANTS: 405,172 patients who had gastric biopsy samples taken for non-malignant indications between 1979 and 2011. MAIN OUTCOME MEASURES: Incidence of gastric cancer, reported separately for patients with different mucosal changes in biopsy samples. Standardised incidence ratios provided estimation of the relative risk, using the general Swedish population as reference; and hazard ratios were derived from Cox regression modelling for internal comparisons with patients with normal gastric mucosa. RESULTS: After excluding the first two years of follow-up, 1599 cases of gastric cancer were identified. The annual crude incidence of gastric cancer was 20 × 10(-5) for those in the normal mucosa group (standardised incidence ratio 1.0), 42 × 10(-5) for those with minor changes (1.5), 59 × 10(-5) for the gastritis group (1.8), 100 × 10(-5) for the atrophic gastritis group (2.8), 129 × 10(-5) for the intestinal metaplasia group (3.4), and 263 × 10(-5) for the dysplasia group (6.5). Cox regression modelling confirmed that excess risks increased monotonically with progressive severity of gastric lesions, with the highest hazard ratio of 10.9 (dysplasia versus normal mucosa, 95% confidence interval 7.7 to 15.4). The increased incidence was stable throughout the follow-up period, and the gaps between cumulative incidence curves grew continuously. CONCLUSIONS: Among patients who undergo gastroscopy with biopsy for clinical indications, approximately 1 in 256 with normal mucosa, 1 in 85 with gastritis, 1 in 50 with atrophic gastritis, 1 in 39 with intestinal metaplasia, and 1 in 19 with dysplasia will develop gastric cancer within 20 years. These numbers, along with cost-benefit analyses, should guide future surveillance policies for these particular patient groups.

Song, J., et al. (2015). "Risk factors for gastric neoplasm in chronic atrophic gastritis." Helicobacter 20: 108.

Background/Aims: The prevalence of chronic atrophic gastritis is very high in Korea. Atrophic gastritis and intestinal metaplasia is considered as premalignant lesions, but the understandings about natural course of atrophic gastritis are not sufficient. The aims of this study were to evaluate the natural course of chronic atrophic gastritis and to analyze risk factors for gastric neoplasm in atrophic gastritis patients. Methods: A total of 4821 subjects underwent upper gastrointestinal endoscopy for health checkup between 2003 and 2004 were enrolled in this retrospective cohort study. Follow-up endoscopy was performed in 2754 subjects between 2004 and 2014. Atrophic gastritis and intestinal metaplasia were assessed according to the Kimura-Takemoto classification by endoscopy. Helicobacter pylori (Hp) was evaluated by serum IgG antibody. Results and discussion: The number of atrophic gastritis was 1619 (33.6%) in initial endoscopy; 523 showed aggravation of atrophy and 436 showed no change in follow-up (87.8 ± 40.3 month). A total of 62 subjects were diagnosed as gastric neoplasms (26 adenoma, 36 carcinoma). The risk factors for gastric neoplasm were age (OR=1.054, 95% CI 1.011-1.099), extent of atrophic gastritis (OR=2.800, 95% CI 1.165-6.730 in C3-O1, OR=4.686, 95% CI 1.445- 15.198 in O2-O3), and intestinal metaplasia (OR=2.844, 95%CI 1.082-7.476). Hp was a risk factor for aggravation of atrophy (OR=3.785, 95%CI 2.286- 6.266), but not for gastric neoplasm (OR=2.043, 95%CI 0.245-17.025). Conclusions: Extent of atrophic gastritis and intestinal metaplasia were most important risk factors for gastric neoplasm.

Song, J. H., et al. (2015). "Risk factors for gastric neoplasm in chronic atrophic gastritis." Journal of Gastroenterology and Hepatology (Australia) 30: 68.

Background and Aims: The prevalence of chronic atrophic gastritis is very high in Korea. Atrophic gastritis and intestinal metaplasia are considered as premalignant lesions, but the understandings about natural course of atrophic gastritis are not sufficient. The aims of this study were to evaluate the natural course of chronic atrophic gastritis and to analyze risk factors for gastric neoplasm in atrophic gastritis patients. Methods: A total of 4821 subjects that underwent upper gastrointestinal endoscopy for health checkup between 2003 and 2004 were enrolled in this retrospective cohort study. Follow-up endoscopy was performed in 2754 subjects between 2004 and 2014. Atrophic gastritis and intestinal metaplasia were assessed according to the Kimura- Takemoto classification by endoscopy. Helicobacter pylori (Hp) was evaluated by serum IgG antibody. Results and discussion: The number of atrophic gastritis was 1619 (33.6%) in initial endoscopy; 523 showed aggravation of atrophy; and 436 showed no change in follow-up (87.8 ± 40.3months). A total of 62 subjects were diagnosed as gastric neoplasms (26 adenoma and 36 carcinoma). The risk factors for gastric neoplasm were age (OR = 1.054; 95% CI 1.011-1.099); extent of atrophic gastritis (OR = 2.800; 95% CI 1.165-6.730 in C3-O1; OR= 4.686; 95% CI 1.445-15.198 in O2-O3); and intestinal metaplasia (OR= 2.844; 95%CI 1.082-7.476). Hp was a risk factor for aggravation of atrophy (OR = 3.785; 95%CI 2.286-6.266), but not for gastric neoplasm (OR= 2.043; 95%CI 0.245-17.025). Conclusions: Extent of atrophic gastritis and intestinal metaplasia were most important risk factors for gastric neoplasm.

Song, J. H., et al. (2016). "Risk factors of gastric carcinogenesis in underlying gastric mucosal atrophy." Journal of Clinical Oncology 34(4).

Background: Atrophic gastritis and intestinal metaplasia were considered as premalignant lesions. The prevalence of chronic atrophic gastritis is very high in Korea. The aims of this study were to evaluate the risk factors of gastric carcinogenesis in underlying gastric mucosal atrophy. Methods: A total of 10187 subjects underwent upper gastrointestinal endoscopy for health checkup between 2003 and 2004 were enrolled in this retrospective cohort study. Follow-up endoscopy was performed between 2005 and 2014. Atrophic gastritis and intestinal metaplasia were assessed according to the Kimura-Takemoto classification by endoscopy. Helicobacter pylori (Hp) was evaluated by serum IgG antibody. Results: The number of atrophic gastritis was 3716 (36.5%) in baseline endoscopy, and 2146 were undergone follow-up endoscopy (82.8±38.3month); 1139 showed aggravation of atrophy and 1007 showed no change. A total of 71 subjects were diagnosed as gastric neoplasms (34 adenoma, 37 carcinoma). Age (HR = 1.019, 95%CI 1.010-1.028), alcohol intake (HR = 1.002, 95%CI 1.001-1.002), Salt intake (HR = 1.295, 95%CI 1.038-1.617) and Hp infection (HR = 1.584, 95%CI 1.220-2.057) were associated with aggravation of mucosal atrophy. The risk factors for gastric neoplasm in underlying mucosal atrophy were age (HR = 1.041, 95%CI 1.004-1.079), alcohol intake (HR = 1.003, 95% CI 1.001-1.005), Salt intake (HR = 2.553, 95% CI 1.141-5.712), Extent of mucosal atrophy (HR = 2.375, 95% CI 1.201-4.695 in C3-O1; HR = 4.255, 95% CI 1.612-11.229 in O2-O3), and intestinal metaplasia (HR = 2.599, 95% CI 1.286-5.251). Conclusions: Hp was a risk factor for aggravation of atrophy, but not for gastric neoplasm. Salt intake, extent of mucosal atrophy, and intestinal metaplasia were important risk factors for gastric neoplasm.

Song, J. H., et al. (2017). "Risk Factors for Gastric Tumorigenesis in Underlying Gastric Mucosal Atrophy." Gut Liver 11(5): 612-619.

BACKGROUND/AIMS: Atrophic gastritis is considered a premalignant lesion. We aimed to evaluate the risk factors for gastric tumorigenesis in underlying mucosal atrophy. METHODS: A total of 10,185 subjects who underwent upper gastrointestinal endoscopy between 2003 and 2004 were enrolled in this retrospective cohort study. Follow-up endoscopy was performed between 2005 and 2014. Atrophic gastritis and intestinal metaplasia were assessed by endoscopy using the Kimura-Takemoto classification. Helicobacter pylori infection was evaluated based on serum immunoglobulin G antibody levels, the rapid urease test, or the urea breath test. RESULTS: Atrophic gastritis was confirmed in 3,714 patients at baseline; 2,144 patients were followed up for 6.9 years, and 1,138 exhibited increased atrophy. A total of 69 subjects were diagnosed with gastric neoplasm during follow-up (35 adenoma and 34 carcinoma). Age ≥55 years (hazard ratio [HR], 1.234), alcohol consumption (HR, 1.001), and H. pylori infection (HR, 1.580) were associated with increased mucosal atrophy. The risk factors for gastric neoplasm in underlying mucosal atrophy were age ≥55 years (HR, 2.582), alcohol consumption (HR, 1.003), extent of mucosal atrophy (HR, 2.285 in C3-O1; HR, 4.187 in O2-O3), and intestinal metaplasia (HR, 2.655). CONCLUSIONS: Extent of atrophy, intestinal metaplasia, and alcohol consumption are significant risk factors for gastric neoplasm in underlying mucosal atrophy.

Song, Z. (2017). "The epidemiological study of upper gastrointestinal cancer screening in rural areas in Sichuan, China." European Journal of Cancer 72: S74-S75.

Background: Upper gastrointestinal cancers are leading causes of cancer mortality in China. We conducted an upper gastrointestinal cancer screening program from 2006 in Sichuan Province, including esophagus cancer and gastric cancer. This study aims to investigate the effectiveness of the upper gastrointestinal cancer screening program in the last 4 years. Material and Methods: The targeted population are 40-69 years in rural areas and sampled by random cluster sampling. Esophageal and gastric endoscopy were uesd to dectect the lesions in upper gastrointestinal tract. The esophageal precancerous lesions (mild to moderate dysplasia), cardiac and gastric precancerous lesions (severe chronic atrophic gastritis, severe intestinal metaplasia and low grade intraepithelial neoplasm) detected at baseline were followed-up in accordance with precancerous lesions screening program, and patients who diagnosed as high-grade lesion or worse were treated. Results: In total, 88,825 participants were enrolled for primary screening and 2,828 were followed-up. 5,021 (5.65%) mild to moderate dysplasia cases, 1,014 (1.14%) high grade dysplasia or preinvasive carcinoma cases were detected in esophagus baseline screening. 60.86% esophagus mild to moderate dysplasia were followed-up and 75 (4.91%) high grade dysplasia cases were detected. 1,084 (1.22%) atrophic gastritis and low grade intraepithelial neoplasia, 315 (0.35%) high-grade squamous intraepithelial lesion cases were detected in cardiac baseline detection. 55.92% cardiac low-grade lesions cases were followed up and 12 (4.98%) cases of highgrade intraepithelial neoplasia were detected. 2,697 (3.04%) severe chronic atrophic gastritis, severe intestinal metaplasia and low grade intraepithelial neoplasia cases, 298 (0.34%) high-grade intraepithelial neoplasia cases were detected in gastric baseline screening.70.39% enrolled in the followup and 23 (2.16%) high-grade intraepithelial neoplasia or worse cases were detected. The detection rate of high-grade intraepithelial neoplasia cancer increased from 1.53% in 2012-2013 to 2.11% in 2015-2016 (P < 0.001). The high-grade intraepithelial neoplasia and cancer dection rate in follow up group was significantly higher than baseline population (P = 0.001). Conclusion: The quality of the upper gastrointestinal cancer screening program is improving steadily. Improving the quality of follow-up examination could effectively improve the quality of the screening program.

Stemmermann, G. N., et al. (1990). "Impact of diet and smoking on risk of developing intestinal metaplasia of the stomach." Digestive Diseases and Sciences 35(4): 433-438.

A cohort of Hawaii Japanese men was assembled for epidemiologic studies of heart disease and cancer. Diet and tobacco consumption data were obtained from 1965 to 1968 and from 1971 to 1975. Biopsies from sites at maximal, intermediate, and minimal risk of intestinal metaplasia were performed on 350 men. Metaplasia was found in 234 men. Gastric cancer was found in 9/234 with metaplasia (3.8%) and 1/116 men without metaplasia (0.89%). Nitrite-rich salty foods (e.g., cured meats) were directly related to metaplasia at both examinations. Vitamin C intake did not appear to have prevented the development of intestinal metaplasia. Smoking was directly related to the presence of metaplasia, but the association was weaker than was observed for cured meats. The strong association between nitrite-rich salty foods and metaplasia appears to be uniform from one study to another, as is the lack of a consistent relation between metaplasia and either smoking or vitamin C consumption. Heavy smokers were more likely to have metaplasia than were nonsmokers, but these associations were weaker than were those with cured meats.

Sugimoto, M., et al. (2016). "Efficacy of the Kyoto gastritis classification for endoscopic identification of patients at high risk for gastric cancer." Gastroenterology 150(4): S1-S2.

Background: An accurate risk stratification system for gastric cancer related with Helicobacter pylori (H. pylori) infection is important for early identification and treatment. The Kyoto gastritis classification was formulated to categorize endoscopic characteristics of H. pylori infection-associated gastritis and to identify patterns associated with a high risk of gastric cancer by grading of endoscopically-visible risk factors. However, whether or not the Kyoto scoring system can effectively identify high-risk patients is unclear. Therefore, to clarify endoscopic risk factors and efficacy of the Kyoto gastritis classification, we investigated the endoscopic characteristics of gastritis in patients with H. pylori-positive gastritis alone and with early-stage gastric cancer and compared their scores. Methods: A total of 1200 patients with H. pylori-positive gastritis alone (n = 932), early-stage H. pylori-positive gastric cancer (n = 189), and successfully treated H. pylori-negative cancer (n = 79) were endoscopically graded according to the Kyoto gastritis classification for atrophy, intestinal metaplasia, hypertrophy of gastric folds, nodularity, and diffuse redness. Results: The prevalence of OII/ O-III-type atrophy according to the Kimura-Takemoto classification (the grading system of endoscopic gastric mucosal atrophy) in gastric cancer group was 45.1%, which was significantly higher than in subjects with gastritis alone (12.7%, P < 0.001). In the Kyoto gastritis classification, scores of atrophy and intestinal metaplasia in the cancer group were significantly higher than in subjects with gastritis alone (all P < 0.001). No significant differences were noted in the rates of gastric fold hypertrophy, nodularity, or diffuse redness between the two groups. In univariate analysis, among patients aged over 65 years, the risk of gastric cancer significantly increased in the presence of atrophy (odds ratio [OR]: 2.813, 95% confidence interval [CI]: 1.817-4.356) and intestinal metaplasia (OR: 6.303, 95% CI: 4.440-8.950). In multivariate analysis, the risk of gastric cancer increased with atrophy (OR: 1.822, 95% CI: 1.087-3.056), intestinal metaplasia (5.954, 4.157-8.527) and male (1.659, 1.027-2.681). Conclusions: In the time of total eradication in Japanese, the endoscopic critical diagnosis and the endoscopic detecting patients at high risk is important. We demonstrated that the Kyoto gastritis classification provided clinically useful information for identifying patients at elevated risk of gastric cancer development. If patients with H. pyloriinfection had 4.8 of total score according to the Kyoto gastritis classification, they would be needed eradication treatment and intensive follow-up to pick-up any gastric cancer at early phase. These results should be confirmed by future investigations using a multicenter prospective design.

Sugimoto, T., et al. (2015). "Neutrophil infiltration and the distribution of intestinal metaplasia is associated with metachronous gastric cancer following endoscopic submucosal dissection." Canadian Journal of Gastroenterology & Hepatology 29(6): 321-325.

BACKGROUND: Endoscopic submucosal dissection (ESD) of early gastric cancer is a minimally invasive procedure. However, the risk for metachronous cancers after successful cancer treatment remains high and the risk factors for metachronous cancers have not been elucidated. OBJECTIVE: To evaluate the risk factors for metachronous gastric cancers after ESD with a long-term follow-up. METHODS: A total of 155 consecutive patients (119 men, 36 women, mean age 68.9 years) were treated with ESD between September 2000 and September 2009. Biopsy specimens were obtained from the greater curvature of the antrum and middle corpus to evaluate gastric mucosal status, including Helicobacter pylori, intestinal metaplasia (IM) and neutrophil infiltration (NI) before ESD. Follow-up endoscopy after ESD was scheduled at two and six months, one year and annually thereafter. H pylori eradication was recommended when possible. RESULTS: The median follow-up period was 4.2 years. Metachronous gastric cancers were found in 23 of 155 patients (3.5% per year). No local recurrences were observed. The cumulative incidence of metachronous gastric cancer was significantly high in IM and NI in the corpus (P=0.0093 and P=0.0025, respectively [log-rank test]). The ORs for IM and NI in the corpus were 2.65 and 3.06, respectively, according to the Cox proportional hazards model (P=0.024 and P=0.0091, respectively). CONCLUSIONS: The presence of IM and NI in the corpus was closely related to the development of metachronous gastric cancer after ESD.

Publisher: Abstract available from the publisher.

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Sugimoto, T., et al. (2012). "Metachronous gastric cancer risk after endoscopic submucosal dissection." Gastroenterology 142(5): S630.

[OBJECTIVE] Endoscopic submucosal dissection is getting certified as method to treat mucosal gastric cancer. However, after successful treatment of cancer, the residual stomach is known to have the higher risk of metachronous cancers than the stomach which is naÏve for cancer and the risk factor of metachronous cancers is not elucidated. The aim of this study was to evaluate the risk factor of metachronous gastric cancers after endoscopic submucosal dissection (ESD) in a long-term follow-up. [METHODS] A total of 164 consecutive patients (male: female 122: 42, mean age 68.9 yrs) were treated by ESD from September 2000 to September 2009. Biopsy specimens were taken from the greater curvature of the antrum and middle corpus to evaluate the gastric mucosal status, including H. pylori, intestinal metaplasia (IM), and neutrophil infiltration (NI) before ESD. Blood samples were also collected before ESD to measure serum levels of pepsinogen I and II. Follow-up endoscopy after ESD was scheduled at 2 and 6 months, 1year, and annually thereafter. Eradication of H. pylori was recommended when possible. Eradication was confirmed by a negative 13Curea breath test following the completion of eradication therapy for 8 weeks. [RESULTS] The median follow-up period was 3.8 years. We found metachronous gastric cancers in 23 of 164 patients (3.7%/year). There were no local recurrences in this study group. The cumulative incidence of metachronous gastric cancer was statistically higher in IM and NI in the corpus (P=0.013, 0.0058, respectively, log-rank test). The hazard ratios of IM and NI in the corpus, and H. pylori eradication were 2.98, 2.72, 0.52, respectively by Cox proportional hazard model (P=0.022, 0.026, 0.26). [CONCLUSION] The presence of intestinal metaplasia and neutrophil infiltration in corpus were closely related to the development of metachronous gastric cancer after ESD. Not only eradication of H. pylori but annual followup endoscopy may be important to improve the prognosis of metachronous gastric cancer.

Suh, S., et al. (2012). "Changes in prevalence of Helicobacter pylori infection after subtotal gastrectomy." Hepato-Gastroenterology 59(114): 646-648.

BACKGROUND/AIMS: There have been few reports comparing pre and postoperative prevalence of Helicobacter pylori infection and gastritis in patients with gastric cancer surgery. METHODOLOGY: Seventy patients with primary gastric cancer were identified to be infected with Helicobacter pylori preoperatively and tested for Helicobacter pylori infection after subtotal gastrectomy. We analyzed changes in Helicobacter pylori infectivity and histological features of gastric mucosa. RESULTS: The overall spontaneous regression rate of Helicobacter pylori infection was 38.6% (27/70). The mean time between surgery and follow-up tests was 1.02±0.5 years. The activity and chronic inflammation scores were significantly decreased in regression group. In non-regression group, there was no significant difference in activity scores, but the chronic inflammation score was significantly increased. There were no significant changes in atrophic gastritis and intestinal metaplasia scores in either group. The grade of Helicobacter pylori infection was significantly decreased in non-regression group. CONCLUSIONS: The spontaneous regression rate of Helicobacter pylori infection after subtotal gastrectomy was 38.6% (27/70), it occurred in larger scale of patients and it occurred earlier (1.02±0.5 years) than in previous studies. We suggest that further prospective study on spontaneous regression rate of Helicobacter pylori infection after subtotal gastrectomy and its mechanism is needed in the future.

Sun, S. B., et al. (2013). "Clinical pathology and recent follow-up study on gastric intraepithelial neoplasia and gastric mucosal lesions." Hepato-Gastroenterology 60(127): 1597-1601.

BACKGROUND/AIMS: To explore the correlations between endoscopic gastric mucosal lesions and pathological gastric intraepithelial neoplasia (GIN), and to investigate outcomes of gastric intraepithelial neoplasia after treatments. METHODOLOGY: Biopsies of 18,566 Chinese patients undergoing diagnostic gastroscopy were included. Among them, 130 patients were given various treatments, including medication, endoscopic treatment and surgery. RESULTS: There were 433 patients with GIN by initial pathological diagnosis. Among them, 367 low-grade GIN and 66 high-grade GIN, 348 cases accompanied with chronic gastritis, and 85 cases accompanied with localized foci. Eighty cases of Hp-positive patients with low-grade GIN were given anti-Hp therapy. Our results showed that 45 cases of intraepithelial neoplasia disappeared when chronic inflammation left, and 33 cases were given the original diagnoses and two cases developed into high-grade GIN. Surgery was then performed, after which one case was confirmed to have early gastric carcinoma, and the other was diagnosed as advanced gastric carcinoma. Pathological examinations were carried out undergoing EMR or ESD treatment for 18 patients with localized foci accompanied with low-grade GIN. Results showed four cases of chronic inflammation, 11 cases with original diagnoses maintained, and three cases of high-grade GIN. CONCLUSIONS: GIN occurred frequently in patients with more severe pathological inflammations under endoscope, which also had certain correlations with intestinal metaplasia. After treatment, parts of low-grade GIN could be reserved. The effect of endoscopic resection on localized foci accompanied with low-grade GIN was affirmative. However, the limitation of endoscopic biopsy should be fully understood.

Suzuki, S., et al. (2014). "Endoscopic and histological changes of gastric adenoma after Helicobacter pylori eradication." Journal of Gastroenterology and Hepatology (Australia) 29: 233-234.

Objective: Helicobacter pylori infection causes gastric adenoma and gastric cancer through the developments of chronic atrophic gastritis and intestinal metaplasia. The efficacy of Helicobacter pylori eradication for existing gastric neoplasia is unknown. This study investigated the efficacy of Helicobacter pylori eradication therapy for existing gastric adenoma. Methods: We reviewed retrospectively 27 patients with gastric adenoma underwent Helicobacter pylori eradication therapy from April 1997 to December 1997.We evaluated the endoscopic and histological changes of gastric adenoma more than 3 years. We analyzed the relationship between endoscopic and histological changes and the following clinicopathological factors using univariate analysis: follow-up periods, age, gender, serum pepsinogen level, lesion size, lesion location, and phenotypic expression. Results: The total mean follow-up periods were 91.9 months. 12 lesions (44.4%) disappeared in endoscopic findings, and 7 lesions (25.9%) disappeared in both endoscopic and histological findings. The mean period of showing endoscopic disappearances were 21.8 months after Helicobacter pylori eradication therapy. 14 (51.9%) lesions were not shown any endoscopic changes. In these lesions, 6 (22.2%) lesions were diagnosed intramucosal cancer in the follow-up periods, resulting in performed endoscopic treatments. Univariate analysis revealed that gender (p = 0.009), lesion size (p = 0.025), and serum pepsinogen 2 level before Helicobacter pylori eradication therapy (p = 0.041) were significant associated with endoscopic and histological disappearance of lesions. Conclusion: Helicobacter pylori eradication therapy might effect to some of gastric adenoma disappearing. Therefore, Helicobacter pylori eradication therapy can be first therapy for gastric adenoma.

Suzuki, S., et al. (2015). "Morphologic and Histologic Changes in Gastric Adenomas After Helicobacter pylori Eradication: A Long-Term Prospective Analysis." Helicobacter 20(6): 431-437.

BACKGROUND: Helicobacter pylori infection causes gastric neoplasia via development of chronic atrophic gastritis and intestinal metaplasia. The effect of H. pylori eradication on pre-existing gastric neoplasias is still controversial. The aim of this study was to use long-term observation to clarify morphologic and histologic changes in gastric adenomas following H. pylori eradication. MATERIALS AND METHODS: Twenty-seven patients with gastric adenomas (revised Vienna classification category 3 or 4.1) who underwent successful H. pylori eradication between April 1996 and December 1997 were followed up at regular intervals with endoscopic and histologic examination. The association between macroscopic and histologic regressions of the lesions and the following patient and lesion characteristics was assessed with univariate analysis: follow-up period, age, sex, serum pepsinogen level, lesion size, lesion location, and histologic gastritis. RESULTS: The mean follow-up period was 91.9 months (range 44-181 months). Twelve lesions (44.4%) showed macroscopic regression, of which 7 (25.9% of the total) also showed histologic regression, with the mean duration from H. pylori eradication to complete macroscopic and histologic regression being 19.9 months. The other 15 lesions (55.6%) remained stable macroscopically and histologically, of which 6 (22.2% of the total) progressed to malignancy during the follow-up period. Univariate analysis revealed that female sex (p = .005), smaller lesion size (p = .025), higher baseline serum pepsinogen II level (p = .041), and absence of intestinal metaplasia in the greater curvature of the corpus (p = .026) were significantly associated with complete regression. CONCLUSIONS: Helicobacter pylori eradication may induce regression in some gastric adenomas.

Syrjänen, K. J. (2014). "A non-invasive diagnosis of gastric cancer (GC) precursors (Helicobacter pylori infection and atrophic gastritis) by an ELISA-test (GastroPanel®) measuring 4 stomach-specific biomarkers in the blood. the first-line diagnostic tool of dyspeptic patients and for screening of the risk groups of GC." Anticancer Research 34(10): 6192-6194.

Background: It is estimated that 50% of all gastric cancer (GC) cases develop through the “Correa cascade”, progressing from Helicobacter pylori (HP)-associated gastritis to mucosal atrophy, intestinal metaplasia (IM), dysplasia, to invasive adenocarcinoma. The concept on atrophic gastritis (AG) and IM as precancerous conditions is based on long-term prospective cohort studies, demonstrating that the risk of GC is significantly increased among patients with AG, which is currently considered as the single most powerful independent risk factor of GC. Gastroscopy with biopsies is the time-honored method to diagnose and grade these gastric precancer lesions, recently re-classified by WHO as intraepithelial neoplasia (IEN), to circumvent the unsatisfactory inter-rater agreement of previous classifications using the dysplasia (mild, moderate, severe) concept. Recently an ELISA-based assay (GastroPanel®)(GP) was designed (Biohit Oyj, Helsinki) to measure the serum concentrations of four stomach-specific biomarkers: pepsinogen I (PGI) and II (PGII), gastrin-17 (G-17) and HP IgG antibodies (IgG-HP), making it the first non-invasive diagnostic tool for detection of the subjects at risk for GC. Thus, capable of accurately detecting both AG and HP-infection, GP examination provides possibilities for an early detection of the patients at risk for GC and peptic ulcer, respectively. Similarly as long-term PPI medication, AG in the gastric corpus results in an aclorhydric (anacidic) stomach, regularly accompanied by malabsorption of vitamin B12, iron, magnesium, calcium and some drugs, with potentially serious sequels: calcium deficiency causes osteoporosis, and vitamin B12 deficiency may cause Alzheimer's disease, dementia, depression and polyneuropathy, as well as high homocysteine content in the body. The latter in turn is thought to be an independent risk factor for atherosclerosis, heart attacks and strokes. Study Designs: Clinical studies have been designed to assess the performance of GP test in detecting the surrogate intermediate endpoints of GC, i.e., H. pylori infection and AG. Currently, two standard study protocols are freely available, one for the clinical setting with gastroscopy-referral patients, and another one for population-based screening of the subjects at increased risk for gastric cancer (http:// www.biohithealthcare.com/fi/tutkimus/tutkimussuunnitelmia). GP Clinical Trial: A cohort of (n=?) patients (45 years and older, both genders) for the cohort are enrolled among the patients referred for gastroscopy at Hospital X. The GP test contains four biomarkers specific for the gastric mucosa: 1) Pepsinogen I (P-PGI), 2) Pepsinogen II (P-PGII), 3) Gastrin-17 (P-G-17) and 4) H. pylori antibody (P-HpAb). All four ELISA tests will be done in the clinical laboratory of Hospital X. At the same visit, all patients are subjected to gastroscopic examination, with directed biopsies from the antrum and corpus, following the protocol of the Updated Sydney System (USS). Biopsies are examined at the Pathology laboratory of Hospital X, and interpreted using the USS for classification of gastritis. Statistical analyses include calculation of the performance indicators of the GP test for individual study endpoints, including ROC analysis for cut-off values that give the optimal sensitivity/specificity balance. GP Screening: A cohort of 1000 (minimum) patients (45 years and older, both genders) will be enrolled among randomly selected patients attending the Hospital X, with any indication, other than gastroscopy referral patients. Primarily, only the patients testing positive with the GP test will be subjected to gastroscopic examination, with directed biopsies from the antrum and corpus, following the protocol of the Updated Sydney System (USS). To correct for the verification bias, a random sample of 5% of the subjects testing negative with the GP test, will be invited for gastroscopy. Statistical analyses include calculation of the performance indicators of the GP test for individual study endpoints, including ROC analys s for cut-off values that give the optimal sensitivity/specificity balance. Specific Aims: The single most important goal in both study designs is to establish the performance indicators for the GP test in detecting the intermediate surrogate endpoints of GC. These study endpoints include the following: i) atrophic gastritis in the antrum, ii) atrophic gastritis in the corpus, and iii) atrophic gastritis in both antrum and corpus (=atrophic pangastritis). For all these endpoints, test performance indicators: sensitivity (SE), specificity (SP), negative predictive value (NPV), positive predictive value (PPV) and AUC (area under ROC curve) are calculated. ROC analysis can be used to estimate the best SE/SP balance for each single marker against each different endpoint. In the clinical setting with 100% biopsy-confirmation devoid of any verification bias, it is also possible to assess: 1) the rate of unnecessary referrals for gastroscopy (false positive rate; 1-PPV) following a positive GP test; 2) the rate of gastroscopies to be avoided after a negative GP examination (true negative rate; NPV), and 3) the rate of clinically significant diseases (conditions) that are missed by the GP test (i.e., false negative rate; 1-SE). In the screening setting, where only a minor fraction (test positives +random 5% of test-negatives) are subject to examination by the gold standard (gastroscopy), the results must be corrected for the verification bias. Cut-off values of GP test established in gastroscopy-referral patients: Based on several thousand samples derived from Finnish population examined by GP testing (with different indications), validated cut-off values for the 4 biomarkers have been well established. Accordingly, the normal range of P-PGI falls within 30-160 μg/l, that of P-PGII between 3-15μg/l, Gastrin-17 (basal secretion) is <7pmol/l, G-17 (stimulated) 3-30 pmol/l, and H. pylori antibody (P-HpAb) should be <30 EIU. Importantly, the serum levels of all 4 biomarkers reflect the function of stomach mucosa, which, by definition is closely related to mucosal structure. Because of their confinement with specific cell types in gastric mucosa, any disturbance in mucosal structure closely parallels with the serum levels of these biomarkers. Based on these established cut-off values, GP test results (interpreted by GastroSoft software) are classified into one of the following five categories: 1) healthy stomach, 2) HP-infection, 3) atrophic gastritis (AG) of the antrum, 4) AG of the corpus, and 5) AG of both antrum and corpus (pangastritis). When all 4 biomarkers are normal, stomach mucosa is structurally healthy and shows a normal function. When only the H. pylori Ab titres are elevated but all other markers remain normal, the condition is known as superficial (HP) gastritis. In AG of the antrum, HP Ab titre is elevated and antrum-specific (G cells) G-17 levels are decreased below the threshold. This applies to stimulated G-17 as well, which fails to increase because of the specific G cells are disappeared due to mucosal atrophy of the antrum. In AG of the corpus, the specific chief cells secreting PGI and PGII gradually decrease in number and finally disappear, resulting in gradually decreasing serum levels of PGI and PGII. The same applies to PGI/PGII ratio, which is another useful indicator of atrophic gastritis in the corpus. In the most severe condition, mucosal atrophy affects both the antrum and corpus - a condition known as pangastritis- chara cterized by low levels of both the antrum- and corpus-specific markers, while HP Ab titres can be normal or elevated. Such a condition has 90-fold increased risk of future development of GC. Using the above cut-off values, the performance indicators of GP test in the reference material collected from 5 hospitals in Finland (mean age of 57.5 ±14.6 (SD) years), are as follows: Using the moderate/severe AG of the corpus as an endpoint, PGI shows ROC=0.970 (95%CI 0.945-0.996), with SE=85.7% (71.5%-94.6%), SP= 98.1% (96%-99.2%), PPV=83.7% (69.3%-93.2%), and NPV=98.3% (96.4%-99.4%). For GI/PGII ratio, the indicators are only slightly inferior. GP test in hospital-based screening: Several studies are ongoing, where GP test is being evaluated in a screening setting based on hospital patients, including a recently reported cohort of 835 subjects in Kazakhstan (median age 46.8 years; range 13.6-74.8)(1). The distribution of the five GP categories was identical in both sexes (p=0.259). Healthy stomach was detected in only 196 (23.5%) subjects, whereas the vast majority, 62.3% (n=519) had HP-infection (with no AG). In 118 (14.1%) subjects, results were consistent with AG; in antrum (n=72), corpus (n=42) or pangastritis (n=4). Prevalence of AG increased with the patient's age in both sexes. There was no age-related pattern in biomarker levels, and only slight differences between the genders. It was concluded that while capable of detecting the subjects at risk for GC (HP or AG), GP should be the cost-effective means to intervene the current ominous trend in GC incidence in this country. Conclusion: GastroPanel is recommended by an authoritative panel of leading gastroenterologists (2) for diagnosis of stomach health and disease in two primary indications: 1) in the first-line diagnosis of all subjects with dyspeptic symptoms, and 2) in screening of the risk groups of gastric cancer. In both indications, GP test accurately detects the two most important risk conditions for GC: HP-infection and AG. HP infection is a curable disease, whereas AG is not. Due to malabsorption through an atrophic stomach mucosa, AG is associated with several clinically important sequels, which, however are preventable by early diagnosis by the GP test.

Tachibana, S., et al. (2009). "Recovery of RUNx3 expression in long-term follow-up after H. Pylori eradication." Gastroenterology 136(5): A749-A750.

Background: It is clear that H. pylori eradication improves an inflammation of gastric mucosa, but scientific evidence is still insufficient in view of its preventive effect for gastric carcinogenesis. Human runt-related transcription factor gene 3 (RUNX3 ) is known to be a growth regulation factor of gastric epithelial cells. We have disclosed that in the majority of gastric cancers RUNX3 expression is reduced by hypermethylation not only at the cancer but also at the surrounding intestinal metaplasia. RUNX3 expression is therefore supposed to be a surrogate biomarker for gastric premalignant lesion. Aim: To examine RUNX3 expression in gastric mucosa before and after H. pylori eradication therapy, and to compare their histological findings with RUNX3 expression by the risk of gastric cancers. Material and Methods: A retrospective review of 44 patients of H. pylori-positive gastritis (low-risk group) and 16 patients of early gastric cancer who were treated endoscopically (high-risk group) was performed. We classified both of them in short-time follow-up group (less than one year) and long-term follow-up group (from one to twelve years, mean 4.4-year) after H. pylori eradication. Immunohistological analysis was performed on paraffin-embedded tissue samples using RUNX3 monoclonal antibody (given by Prof. YOSHIAKI ITOH in Institute of Molecular and Cell Biology, National University of Singapore). We compared RUNX3 expression in gastric mucosa of low-risk and high-risk groups by immunohistological analysis and methylation specific PCR. Additionally, out of low-risk group, we compared RUNX3 expression in gastric mucosa of 18 gastric ulcers (GU group) and 9 duodenal ulcers (DU group). Results: After H. pylori eradication, RUNX3 expression in gastric mucosa recovered in few cases of short-term follow-up group and most cases of long-term follow-up group (p<0.05). In both groups, milder atrophy and less intestinal metaplasia cases showed more recovery of RUNX3 expression(p<0.01). RUNX3 expression did not recover in most cases of high-risk group after H. pylori eradication in this observation period. Among low risk group, RUNX3 expression barely recovered in GU group compared with in DU group within short-term follow-up. Conclusion: RUNX3 expression recovered long-term follow-up after H. pylori eradication especially in milder atrophy and less metaplasia cases. From the point of view of RUNX3 expression, long-term follow-up may be necessary to prevent the development of gastric cancer after H. pylori eradication. In addition, it was supposed that RUNX3 expressions in high risk group and in GU group were hard to recover by short-term progress.

Tamayo, L., et al. (1995). "Epidemiology of gastric cancer in Tungurahua." Oncologia 4: 33-38.

The investigation is aimed to define risk factors for gastric cancer and to detect premalignant lesions in association with alimentary habits and socio economic status. This study was made in Ambato, Quero y Pilaro, areas of the Province of Tungurahua with high prevalence of gastric cancer. Study design. A sample of 429 subjects older than 35 years to whom a socio economic questionnaire, endoscopy with biopsy and rapid urease test was performed. Results. 21.2% of familial history positive for cancer of the stomach was found. - Urease test was positive in 95.9% in the patient group who had endoscopy. - Premalignant lesions in 20.2% (chronic atrophic gastritis, intestinal metaplasia, polyps) was found. - High consumption of insufficient cooked meat and home made sausage, was noted in the group. - The food is kept without refrigeration and this produce the formation of nitrosoamines. Conclusion. The antecedent of mortality due to digestive tract cancer is high in the poblational group. The prevalence of Helicobacter pylori infection is high (95.9%). The alimentary habits and the method of preservation increase the risk factor. The follow up of premalignant lesions in high risk population is justified in spite of the cost involved.

Tan, M. C., et al. (2019). "MISSED OPPORTUNITIES FOR SCREENING OR SURVEILLANCE AMONG PATIENTS WITH NEWLY DIAGNOSED NON-CARDIA GASTRIC ADENOCARCINOMA." Gastroenterology 156(6): S-522.

Background: There are known risk factors for non-cardia gastric adenocarcinoma, and endoscopic surveillance of preneoplastic lesions has been associated with the early detection of gastric adenocarcinoma. We determined possible missed opportunities for the detection and subsequent surveillance of preneoplastic conditions in a cohort of patients with gastric adenocarcinoma. Method: We conducted a retrospective cohort study among consecutive, newly diagnosed patients with non-cardia gastric adenocarcinoma from 11/2007 to 10/2018 at the Michael E. DeBakey VA Medical Center in Houston, Texas. We performed structured medical record review for gastric adenocarcinoma risk factors (non-White race [i.e., Black, Hispanic, Asian], smoking, alcohol, Helicobacter pylori infection, gastric ulcers, family history of gastric cancer), past endoscopic and gastric biopsy history and histopathological findings. We evaluated the indications for the gastric adenocarcinoma diagnosing endoscopy (diagnostic, surveillance, incidentally found) and identified the proportions of all patients with missed opportunities for screening and surveillance based on risk factors and presence of preneoplastic lesions. Associations between receipt of prior endoscopy and cancer-related outcomes (cancer stage, receipt of treatment, survival) was determined using logistic regression models. Results: Among 91 patients diagnosed with gastric adenocarcinoma, 87 (95.6%) were men and 29 (31.9%) were White, with mean age at diagnosis of 68.0 years (SD 10.8). The cancer diagnosing endoscopy was done for diagnostic indications in 89.0%, surveillance of preneoplastic gastric lesions in 2.2%, and cancers were found incidentally in 8.8%. Dyspepsia (29.6%), iron deficiency anemia (27.2%) and gastrointestinal bleeding (27.2%) were the most common diagnostic indications. Most patients had at least one risk factor for gastric cancer (N=79, 86.8%), and 42 (46.2%) had 2 or more risk factors. The most common risk factors included smoking (76.9%), non-White race (67.0%) and alcohol use (59.3%). Twenty patients (22.0%) had at least 1 endoscopy performed at a median 2.4 years prior to gastric cancer diagnosis. Of 14 patients who had previous gastric biopsies, 7 had high risk lesions (6 intestinal metaplasia; additional 1 gastric ulcer) but only 2 underwent surveillance endoscopy with gastric biopsies. Receipt of prior endoscopy was not associated with significant differences in cancer stage, receipt of treatment, or survival. Conclusion: Most patients with gastric adenocarcinoma had at least 1 known risk factor but never had prior screening/surveillance endoscopy and therefore could represent missed opportunity for prevention or early detection. Among the few with known prior preneoplastic lesions, endoscopic surveillance with gastric biopsies was not consistently performed, representing another missed opportunity.

Tanaka, I., et al. (2018). "Clinical characteristics of multiple metachronous gastric cancers that were endoscopically resected." Journal of Gastroenterology and Hepatology 33: 291.

Background and Aim: Eradication of Helicobacter pylori (H. pylori) significantly reduces the occurrence of metachronous gastric cancer (MGC). However, there are some cases of the recurrent multiple MGC despite eradication of H. pylori. In this study, we examined the clinical characteristics of multiple MGC that was resected by endoscopic submucosal dissection (ESD). Methods: Forty-six early-stage gastric cancers in 11 patients (9 males and 2 females) who received ESD more than three times in the period from January 2003 to April 2018 were reviewed. MGS was defined as a lesion that was not detected previously and was found 1 year or more after last ESD. We classified the cancers into 3 groups (group I: a group of 23 primary cancers, group II: a group of 11 secondary cancers, and group III: a group of 12 tertiary and later cancers). Results: The median age of patients with primary gastric cancer was 74.4 years, and all of the patients had severe atrophy. H. pylori infection status at the first ESD was as follows: 8 patients were positive for H. pylori and 3 patients were negative for H. pylori including 2 patients in whom H. pylori had been eradicated. The mean durations from primary cancer to secondary cancer and to tertiary and later cancer were 3.5 and 6.3 years, respectively. Lesions that were depressed type in the lower third of the stomach were more frequently in groups II and III. Furthermore, MGC often occurred in the areas near the primary cancers. All of the lesions were intramucosal tubular adenocarcinoma surrounded by intestinal metaplasia. Conclusion: Attention should be given to the lower third of the stomach and areas near the primary cancers in follow-up endoscopy after ESD for patients with severe atrophy and intestinal metaplasia.

Tashiro, J., et al. (2007). "Gastric cancer detected after Helicobacter pylori eradication." Digestive Endoscopy 19(4): 167-173.

Background: Helicobacter pylori is associated with progression to gastric cancer. However, it is still unclear whether eradication therapy can prevent the development of gastric cancer. Methods: Subjects were 242 patients in whom success in eradication of Helicobacter pylori had been continuous for more than 3 years. Clinical, endoscopic and histological findings were compared retrospectively between those who developed gastric cancer (cancer group) and those who did not (non-cancer group). Clinical features of each cancer case were also evaluated. Results: Gastric cancer was found in six of the 242 subjects (2.5%) during a mean follow-up period of 4.6 years (range: 3.0-7.0). The mean age of the cancer group tended to be higher than that of the non-cancer group. Endoscopy revealed a more severe grade of gastric corpus atrophy in the cancer group, and histological findings showed that the degree of intestinal metaplasia in the upper corpus was higher in the cancer group. Four of the six cancers were located in the gastric antrum. All were early cancers and five were of 0-IIc type endoscopically. All were intestinal type histologically. Conclusions: Gastric cancer was discovered at a rate of 2.5% during the mean follow-up period of 4.6 years after H. pylori eradication. Careful endoscopic follow up is necessary even after successful eradication, especially in cases characterized by an endoscopically high grade of gastric atrophy and pathologically severe intestinal metaplasia at the upper corpus. © 2007 The Authors.

Tashiro, J., et al. (2009). "Origin of gastric cancer detected after Helicobacter pylori eradication: Retrospective review of endoscopic image taken before eradication." Gastroenterology 136(5): A342.

Background and Am: It has been reported that Helicobacter pylori (H. pylori) eradication prevents gastric cancer, but in some cases, gastric cancer is discovered even after successful eradication. Our previous study showed that careful endoscopic follow-up was necessary after eradication, especially in cases characterized by an endoscopic ally high grade of atrophy and pathologically severe intestinal metaplasia (Tashiro J et al. Digest. Endosc. 2007; 19: 167-173). However, the mechanism of cancer development after eradication is unclear. To elucidate the origin of gastric cancer after eradication, we reviewed the endoscopic images taken before eradication. Methods: A total of 25 cancers (23 cases) after H. pylori eradication had been detected from March 1996 to October 2008 at Toshiba General Hospital. We excluded 10 cases with poor records, and analyzed 13 cancers (13 cases). Four endoscopists retrospectively reviewed the endoscopic images taken before eradication. Cancers were devided into two groups; positive finding group is defined as the case in which some endoscopic findings could be recognized in the same area where cancer was detected after eradication. Negative finding group is defined as the case in which no findings could be recognized. Clinical features of both groups were studied. Results: 1) Positive finding group and negative finding group contain 9 cases (69.2%), and 4 cases (30.8%), respectively. 2) Among positive finding group, three cancers were more than 20mm in diameter, and discovered within a year after eradication. Six cancers were less than 20mm in diameter, all histologically intestinal-type, and review of endoscopic images taken before eradication demonstrated following findings in the area where cancer was detected after eradication: small whitish elevation (1 case), depressed lesion (2 cases), redness (2cases), and erosion (1 case). 3) Among negative finding group, three cancers were histologically diffuse-type. Two of them were discovered from 3 to 4 years after eradication, and invaded deeply under submucosal layer. Conclusion: About 70% of gastric cancers, discovered after H. pylori eradication, had some findings in the same area before eradication. This result indicates most of cancers, which were detected after eradication, developed before eradication. While most of intestinal-type cancers showed findings before eradication, some of diffuse-type cancers did not. Further study will be needed to evaluate the origin of gastric cancer after eradication, especially histologically diffuse-type.

Tatsugami, M., et al. (2012). "Bile acid promotes intestinal metaplasia and gastric carcinogenesis." Cancer Epidemiology, Biomarkers and Prevention 21(11): 2101-2107.

BACKGROUND: Bile acid and Helicobacter pylori (H. pylori) are important toxic factors for gastric mucosal injury. We examined the role of bile acid in promoting histologic gastritis and gastric carcinoma in Japanese patients. METHODS: A total of 767 patients (452 men, mean age 51.1 years) were studied. Gastric juice was collected by gastro-endoscopic examination, and the bile acid concentration was examined by enzymatic method. The grade of histologic gastritis was evaluated by gastric biopsies, and the relationship between the bile acid concentration and the gastritis score was examined. The occurrence of gastric cancer was examined by a retrospective cohort study. CDX2/CINC1 expression in RGM-1 cells was evaluated by real-time PCR. RESULTS: In H. pylori-positive patients, we found significant positive correlation between the bile acid concentration and the grades of atrophy/intestinal metaplasia (P < 0.01). However, we found significant negative associations between the bile acid concentrations and the histologic scores of mononuclear cell/neutrophil infiltrations (P < 0.01). Patients with a high concentration of bile acid developed gastric cancer more frequently than those with a low concentration (P < 0.05). Cholic acid treatment significantly increased CDX2 expression in RGM-1 cells. CINC1 expression in RGM-1 cell was significantly induced by coculture with H. pylori, and the induction was reduced by glycochenodeoxycholic acid treatment. CONCLUSION: The bile acid in gastric juice contributes to the progression of histologic atrophy and intestinal metaplasia without inflammatory cell infiltration, followed by carcinogenesis in H. pylori-positive patients. IMPACT: Bile acid promotes intestinal metaplasia and gastric carcinogenesis without inflammatory cell infiltration.

Tatsuta, M., et al. (1988). "Value of gastric juice carcinoembryonic antigen in identifying high-risk patients for gastric cancer." Oncology 45(1): 30-34.

The relationship of the level of carcinoembryonic antigen (CEA) in the gastric juice to the extent of intestinal metaplasia and gastric cancer, and clinical values of gastric CEA for identifying high-risk patients for gastric cancer were examined. A significant correlation was found between the levels of gastric CEA and the distribution of intestinal metaplasia. Studies were made by the endoscopic Congo red-methylene blue test developed at our hospital. Gastric CEA levels were significantly higher in patients with localized and diffuse intestinal metaplasia than in those with no intestinal metaplasia. The mean levels of gastric CEA in patients with well-differentiated adenocarcinomas were significantly higher than in those with diffuse intestinal metaplasia. They were also significantly higher in patients with poorly differentiated adenocarcinomas than in patients with no intestinal metaplasia, but not significantly higher than in those with diffuse intestinal metaplasia. Endoscopic follow-up examinations show that gastric cancer was detected in only 1 patient with a gastric CEA level of 10 ng/ml or more, but in none of those with gastric CEA of less than 10 ng/ml, during the average observation period of 4.3 years. These results indicate that gastric CEA is produced both by intestinal metaplasia and well- and poorly differentiated adenocarcinomas, and that gastric CEA is useful in identifying high-risk patients for gastric cancer.

Teh, J. L., et al. (2014). "Longer examination time improves detection of gastric cancer during diagnostic upper gastrointestinal endoscopy." Gastroenterology 146(5): S742-S743.

Background: Little is known about the impact of duration of examination during gastroscopy on detection of high-risk gastric pathology. This study aims to determine whether speed of examination affected detection rates of high-risk gastric pathology. Methods: A historical cohort of 2,014 consecutive patients during a three-month period in 2010 undergoing their first-ever diagnostic gastroscopy was utilised. Endoscopists were dichotomised into fast or slow using their mean examination time for performing a normal gastroscopy. Using this stratification, the detection rate of intestinal metaplasia, gastric atrophy, dysplasia and carcinoma between the 2 groups was compared using logistic regression. Results: Mean duration of 224 normal endoscopies was 6.6 minutes. Using a cut off of 7 minutes, 8 endoscopists were classified as fast (mean duration 5.5 ± 2.1 minutes) and 8 classified as slow (mean duration 8.6 ± 4.2 minutes). 92 (11.0%, of which 1.3% were carcinoma, 1.0% dysplasia, 8.7% intestinal metaplasia and/or gastric atrophy) high-risk gastric lesions were detected in the 837 patients included. Endoscopists classified as slow were more than twice as likely to detect a high-risk lesion than those who were classified as fast (OR 2.50, 95% CI 1.52 - 4.12) and thrice as likely to detect a neoplastic lesion (OR 3.42, 95% CI 1.25-10.38). Subset analysis showed that this relationship was true for both staff and trainee endoscopists. Conclusion: Speed of examination may affect the detection rate of high-risk gastric lesions. A prospective validation should be performed to reaffirm the notion that a minimum amount of time is required for a quality gastroscopic examination. Estimating factors associated with detection of a histologically verified high-risk gastric lesion using logistic regression (Table Presented).

Tepeš, B. and N. Zidar (2014). "Recommendations for endoscopic and histological follow-up of patients with chronic gastritis and precancerous gastric lesions." Zdravniski Vestnik 83(2): 93-101.

Gastric cancer is the fourth most common cancer in the world and the second most common cause of cancer-related death. In the year 2009, 469 new cases of gastric cancer were found in Slovenia, 5-year survival rate was 24.5 %. Helicobacter pylori is a class I carcinogen and responsible for 60 %-80 % (by some authors up to 98 %) of all gastric cancers of intestinal and diffuse type, as well as gastric MALT lymphoma. Gastric cancer incidence can be reduced by population- based screening for Helicobacter pylori infection before the age of 30 years. When after several decades of infection chronic multifocal atrophic gastritis with intestinal metaplasia develops in 8 % of infected persons, this is a point of no return. Eradication of infection at this stage cannot entirely prevent gastric cancer development. In those patients, serial biopsies according to Sydney protocol and risk stratification by means of the OLGIM (Operative Link for Gastric Intestinal Metaplasia Assessment) staging system should be performed. Patients with OLGIM stage III and IV should be subject to surveillance endoscopies. The European Society of Gastrointestinal Endoscopy, the European Helicobacter Study Group and the European Society of Pathology have developed evidencebased guidelines on the management of patients with precancerous conditions and lesions of the stomach. Patients with intestinal metaplasia in both corpus and antrum should undergo endoscopic and histological follow-up every three years. If low-grade dysplasia is present, controls should be performed every year. If high grade dysplasia is present, endoscopic and histologic follow-up should be performed every 6 months. All visible endoscopic lesions should be resected (endoscopically or surgically). Helicobacter pylori infection should be searched for with different diagnostic tests and all infected patients should be cured. It is only by this approach that gastric cancer can be diagnosed at an early stage and five-year survival can be improved. These recommendations were accepted by the Slovenian Society for Gastroenterology and Hepatology, and the Slovenian Society for Pathology and Forensic Medicine.

Testino, G. (2004). "[Gastric preneoplastic changes]." Recenti Progressi in Medicina 95(5): 239-244.

Gastric cancer (GC) is the second most common cause of cancer related death worldwide. The 5-year relative survival rate ranges from 10 to 20% of cases. Therefore, it is necessary to diagnose gastric non invasive neoplasia (formerly dysplasia). Correa suggested more than 20 years ago that there was a histological cascade leading to GC: chronic active gastritis --> atrophy (AG) --> achlorydria with nitrocompounds increase --> intestinal metaplasia (IM) type I --> IM type III --> low grade dysplasia (LGD) --> high grade dysplasia (HGD) --> GC. The discovery of Helicobacter pylori infection has imposed a revision of the various pathogenetic stages: 1) GC may arise in the same context as IM and dysplasia, but without any documentable precursor. GC can develop in a context of normochloridria; 2) there are not sufficient data to support endoscopic surveillance for patients with AG; 3) there are doubts about the real necessity to operate histologically a subdivision of IM in subtypes: probably it is more important the extent of IM; 4) dysplasia is the only true histological marker of CG. In fact, LGD is associate or progressed to GC in the 9% of cases, HGD is associated or progressed to GC in the 74% of cases. It emerges the real oncologic risk of dysplasia. Such data are confirmed by immunohistochemical study of the dysplastic lesions. Therefore, an appropriate follow-up of non invasive neoplasia increases the likelihood of CG being detected in its potentially curable stage.

Testino, G. (2006). "Gastric precancerous changes: carcinogenesis, clinical behaviour immunophenotype study and surveillance." Panminerva Medica 48(2): 109-118.

Gastric cancer (GC) is the second most common cause of cancer-related death worldwide. Two-thirds of the GC patients are diagnosed in advanced stages, when surgery can only be a palliative. When the diagnosis is made at an early stage, the surgical treatment results in 10 years survival rates are higher than 85%. From the critical evaluation of the literature data we can affirm that there are some obstacles to an exclusive acceptance of the idea that the relation of Helicobacter pylori (H. pylori) infection with noninvasive (formerly dysplasia) or invasive neoplastic modifications solely develop by means of chronic gastritis with its atrophic evolution and achlorhydria. Intestinal metaplasia as a precursor of GC has been overemphasized and doubts persist about the real necessity to operate histologically a subdivision into subtypes. The extent of the metaplastic process is probably more important that the metaplastic subtype. The evaluation of the clinical behaviour shows how low grade noninvasive neoplasia is associated with or progressed to GC in about 9% of cases, while high grade noninvasive neoplasia is associated with or progressed to GC in about 75% of cases, thus proving to be a real histological marker of GC. The subdivision of the cases according to the TNM classification demonstrates that, in most of the cases, early GC is present (43/45: 95.5%). An appropriate endoscopy follow-up with biopsies according to well defined criteria increases the likelihood of invasive neoplasia being detected in its early stage with a better postsurgical prognosis. Noninvasive neoplasia is characterized by severe alterations of the immunophenotype profile in association with a high proliferation index and frequent p53 mutations. The choice to address the patients to surgical intervention could be made not only on the basis of histochemical techniques, but also with the help of immunohistochemical evaluations.

Testoni, P. A., et al. (1987). "Gastric cancer in chronic atrophic gastritis. Associated gastric ulcer adds no further risk." Journal of Clinical Gastroenterology 9(3): 298-302.

Atrophic gastritis with intestinal metaplasia is generally considered a precancerous lesion. We followed 261 patients with chronic atrophic gastritis and intestinal metaplasia, with and without gastric ulcer, every 12 months for 9 ± 2 years by means of endoscopic and histologic examination. In the presence of dysplasia, however, studies were carried out every 6 months in moderate cases, or every 3 months in severe cases. Patients with gastric ulcer received medical therapy for 8 weeks; if healing did not occur, treatment was continued. Only subjects with healed ulcers were admitted to the follow-up. To date, 205 subjects have been included in the study. Over a 10-year period, 16 patients with recurrent gastric ulcer and 12 patients with cancer in situ or in an early stage, were subjected to surgery. One case of advanced cancer was observed. Cancer has been found in five of 95 cases of atrophic gastritis with gastric ulcer (5.2%), and in 7 of 166 cases of atrophic gastritis without gastric ulcer (4.2%). The difference was not statistically significant. Our results confirm that gastric ulcer per se is not a high-risk condition, but it must be considered as an epiphenomenon on a background of epithelial atrophy.

Tham, T. C. K., et al. (1997). "Long-term semi-quantitative follow-up of Helicobacter pylori associated gastritis." Irish Journal of Medical Science 166(3): 132-134.

Helicobacter pylori infection has been implicated with the development of gastric carcinoma and lymphoma. We studied the long-term effects of H. pylori infection on gastric mucosa. Ten patients with Helicobacter pylori infection underwent repeat endoscopy and antral biopsies 8 years later. Gastric mucosal features (polymorphs, monocytes, intestinal metaplasia, atrophy and lymphoid aggregates) were graded from mild to severe (0 to 3) based on the Sydney system of gastritis classification. At repeat biopsy, 1 patient was negative for H. pylori after eradication therapy. Two patients (20 per cent) had spontaneous disappearance of H. pylori. One of these had intestinal metaplasia which progressed to low grade dysplasia. Polymorphs decreased with eradication of H. pylori (P < 0.05). Lymphoid aggregates increased with continued H. pylori infection but decreased with eradication of H. pylori (P < 0.05). Monocytes, intestinal metaplasia and atrophy remained unchanged. Persistent H. pylori infection appears to increase lymphoid aggregates and may promote its evolution into gastric lymphoma while eradication of H. pylori may result in a reduction of polymorphs and lymphoid aggregates.

Thapa, S., et al. (2019). "Association between Dietary Salt Intake and Progression in the Gastric Precancerous Process." Cancers 11(4).

Gastric cancer is the third leading cause of cancer mortality worldwide. Studies investigating the effect of salt on gastric cancer have mainly used self-reported measures, which are not as accurate as sodium/creatinine ratios because individuals may not know the amount of salt in their food. Using data from a prospective cohort study, we investigated the effect of salt intake on progression to gastric precancerous lesions. Salt intake was estimated by urinary sodium/creatinine ratios, self-reported frequencies of adding salt to food, and total added table salt. We repeated the analyses among groups with and without Helicobacter pylori infection. We did not observe a positive association between salt intake, measured by urinary sodium/creatinine ratio, and overall progression in the gastric precancerous process (adjusted risk ratio (RR): 0.94; 95% confidence interval (CI) 0.76-1.15). We did observe an association between salt intake and increased risk for progression to dysplasia or gastric cancer overall (adjusted risk ratio (RR): 1.32; 95% confidence interval (CI): 0.96-1.81), especially among those who continued to have H. pylori infection at the five-month follow-up (adjusted RR: 1.53; 95% CI: 1.12-2.09), and among those who had persistent H. pylori infection over 12 years (adjusted RR: 1.49; 95% CI: 1.09-2.05). Salt intake may increase the risk of gastric dysplasia or gastric cancer in individuals with H. pylori infection.

Thapa, S., et al. (2019). "Using Machine Learning to Predict Progression in the Gastric Precancerous Process in a Population from a Developing Country Who Underwent a Gastroscopy for Dyspeptic Symptoms." Gastroenterology Research and Practice 2019: 8321942.

BACKGROUND: Gastric cancer is the fourth most common cancer and the third most common cause of cancer deaths worldwide. Morbidity and mortality from gastric cancer may be decreased by identification of those that are at high risk for progression in the gastric precancerous process so that they can be monitored over time for early detection and implementation of preventive strategies. METHOD: Using machine learning, we developed prediction models for gastric precancerous progression in a population from a developing country with a high rate of gastric cancer who underwent gastroscopies for dyspeptic symptoms. In the data imputed for completeness, we divided the data into a training and a validation test set. Using the training set, we used the random forest method to rank potential predictors based on their predictive importance. Using predictors identified by the random forest method, we conducted best subset linear regressions with the leave-one-out cross-validation approach to select predictors for overall progression and progression to dysplasia or cancer. We validated the models in the test set using leave-one-out cross-validation. RESULTS: We observed for all models that complete intestinal metaplasia and incomplete intestinal metaplasia were the strongest predictors for further progression in the precancerous process. We also observed that a diagnosis of no gastritis, superficial gastritis, or antral diffuse gastritis at baseline was a predictor of no progression in the gastric precancerous process. The sensitivities and specificities were 86% and 79% for the general model and 100% and 82% for the location-specific model, respectively. CONCLUSION: We developed prediction models to identify gastroscopy patients that are more likely to progress in the gastric precancerous process, among whom routine follow-up gastroscopies can be targeted to prevent gastric cancer. Future external validation is needed.

Thian, M. Y., et al. (2018). "Long-term outcomes of early gastric cancer treated with endoscopic submucosal dissection (ESD) in a tertiary centre in Singapore." Journal of Gastroenterology and Hepatology 33: 295.

Background and Aim: A retrospective review of a single center's outcome post ESD for treatment of early gastric cancer. Methods: Patients' records from all gastric ESD cases performed in our institution were reviewed from May 2011 till March 2015. A total of 14 cases were performed and 5 cases without follow up endoscopy or low grade dysplasia were excluded. Results: A total of 9 patients were followed up with endoscopy post ESD for a median duration of 35 months (range 20-61 months). The site of lesions treated were antrum (n = 4), incisura (n = 4), body of greater curve (n = 1) with a median size of 25 mm (range 20-40 mm). En bloc resection rate was 89%. Histopathology results showed 56% (5/9) had high grade dysplasia and 44% (4/9) had adenocarcinoma. The majority of cases had associated intestinal metaplasia changes and 22% had Helicobacter pylori which were treated. Among the adenocarcinoma cases, 50% (2/4) had submucosal invasion with one involving resection margins; however, both cases declined surgery. Local recurrence rate was 11% with one recurrence seen at 3 months with adenocarcinoma but declined surgery and with additional ESD treatment had no further recurrence seen endoscopically and on CT imaging at 61 months follow up. No disease specific deaths were noted during the follow up period for the whole cohort. Conclusion: Overall, local recurrence rate remains low with good outcome seen at our center.

Toiyama, Y., et al. (2014). "Angiopoietin-like protein 2, a driver of cancer cell metastasis, is a novel serum biomarker for the diagnosis and prognosis in patients with gastric cancer." Cancer Research 74(19).

Background: Gastric carcinogenesis is regarded as a multistep process with an intestinal metaplasia-dysplasia-carcinoma sequence, which is initiated by Helicobacter pylori infection that causes a chronic active inflammation in the gastric mucosa. Angiopoietin-like protein 2 (ANGPTL2) is known to act as a causative mediator of chronic inflammation and inflammatory carcinogenesis. However, the biological role and clinical significance of ANGPTL2 expression remains poorly understood in human cancer. We investigated the functional role of ANGPTL2 and evaluated the clinical significance of its expression in both primary tumor and matched serum specimens in patients with gastric cancer (GC) Methods: The function of ANGPTL2 in GC was investigated by siRNA using GC cell lines (MKN1 and KATO III). Next, we examined ANGPTL2 expression in GC tissues (n=192) by immunohistochemistry (IHC) to evaluate associations between its expression and various clinicopathological features. Finally, we determined serum ANGPTL2 levels from 32 GC and 23 normal controls (NC), and validated its expression levels using 194 serum samples from GC and 45 from NC to evaluate its utility as a biomarker by ELISA Results: Knockdown of ANGPTL2 resulted in significant induction of anoikis (p<0.05) and inhibition of cell proliferation (p<0.05), invasion(p<0.05) and migration (p<0.05) in GC cells. ANGPTL2 was overexpressed in GC tissues compared to normal gastric mucosa, and high ANGPTL2 expression was significantly associated lymph node metastasis (p=0.0001), distant metastasis (p=0.01), early recurrence (p=0.003) and poor prognosis (p=0.007) in GC patients. Serum ANGPTL2 levels in GC patients were significantly higher compared to NC (p<0.05), and successfully distinguished GC patients from NC with high accuracy (AUC=0.814). Finally, validation of these results in an independent patient cohort revealed that serum ANGPTL2 levels in GC patients were significantly higher compared to NC (p<0.0001), demonstrated high AUC (0.831) values with 73.0% sensitivity and 82.2% specificity to distinguish GC patients from NC. In addition, serum ANGPTL2 levels also discriminated early GC patients (stage I) from NC (AUC=0.8). High ANGPTL2 in serum rather than in tissues were significantly associated with tumor progression, and consequently emerged as an independent predictor of tumor recurrence (HR=5.05, p=0.0004) and prognosis (HR=3.6, p=0.01) in patients with GC. Of interest, serum ANGPTL2 levels closely correlated with IHC scores in matched GC tissues (r= 0.16, p=0.02) Conclusion: Our study first reports that overexpression of ANGPTL2 in GC cells results in increased malignant potential and metastasis. Serum ANGPTL2 expression emerged as a novel, non-invasive biomarker for the earlier diagnosis, recurrence and prognosis in patients with gastric cancer.

Tomizawa, Y., et al. (2020). "PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY (P-CLE) IS USEFUL AS AN ALTERNATIVE “OPTICAL” BIOPSY MODALITY IN DIAGNOSIS OF GASTRIC INTESTINAL METAPLASIA (GIM) IN U.S. POPULATION." Gastrointestinal Endoscopy 91(6): AB587.

Background: Gastric intestinal metaplasia (GIM) is a well-established risk factor for gastric cancer (GC), however optimal surveillance endoscopic modality for GIM is yet solidified in the U.S. Although the updated Sydney System, a comprehensive endoscopic biopsy protocol, has been advocated for GIM mapping, challenges are the heterogeneous distribution of GIM, suboptimal diagnostic accuracy of high definition white light endoscopy to detect GIM, the cost burden of multiple biopsy and bleeding risk from multiple biopsies. The diagnostic yield of blue crest sign using narrow band imaging (NBI) has been reported but the reliability has varied. Probe-based confocal laser endomicroscopy (pCLE), widely used as “optical” biopsy of goblet cells in Barrett’s esophagus, has not been well studies as an alternative optical biopsy modality to detect goblet cell metaplasia in GIM. Our academic institution serves an ethnically diverse high risk population and we have established a unique GIM surveillance cohort with recalling patients in an interval based on each patient’s risk profiles. Aims: To evaluate the diagnostic yield of pCLE for the diagnosis of GIM in U.S. population. Methods: We performed a retrospective review of patients in our cohort who were all pathologically confirmed GIM from 10/1/1997 to 11/30/2019. pCLE was carried out with a GastroFlex UHD probe and intravenous fluorescein. Biopsy was obtained as the gold standard diagnosis of GIM in all EGD sessions. Results: 159 patients (mean age 59 years [SD 13], 52% male) underwent a total of 454 EGDs (median 2 per patient [range 1-11, IQR 1-4]) with median of 1056 days follow-up. Patients’ ethnicity was as follows; Asian in 87 (55%), Caucasian in 25 (16%), Hispanic in 19 (12%), African American in 18 (11%) and others in 10 (6%). 23 (15%) patients had family history (at least one within 2nd degree relatives) of GC. History of Helicobacter Pylori infection was found in 87 (55%) patients and 81 (51%) patients took PPI at the time of EGD. The majority (94 %) of patients showed evidence of GIM at least in the gastric antrum. 29 (18%) patients demonstrated pathologically confirmed atrophy and 8 (5%) patients were histopathologically confirmed autoimmune gastritis. 42 (26%) patients showed at least one focal atypia on pathology and the presence of dysplasia was confirmed in 18% of patients. CLE was applied in 54 (34 %) patients (range 1-2 per patient) with a total of 63 EGD sessions. Accuracy of CLE for the diagnosis of GIM was 87.3%. The overall sensitivity and specificity was 91.1% and 57.1%, and positive predictive value (PPV) and negative predictive value (NPV) was 94.4% and 44.4%, respectively. Conclusion: pCLE demonstrated high sensitivity and PPV for the diagnosis of GIM in vivo, which implies the potential of pCLE as an alternative “optical” biopsy modality for optimal GIM surveillance. [Formula presented] [Formula presented]

Tongtawee, T. (2018). "Expression of cancer stem cell CD44 in patients with chronic gastritis, pre-cancerous and gastric cancer in Thailand." Annals of Oncology 29: VII79.

Background and Aim: CD44 cancer stem cell is another marker of the gastrointestinal cancer, including gastric cancer. The aim of this study was to investigate the expression of CD44 cancer stem cells in tissues from the gastrointestinal or surgical patients, including the association of CD44 cancer stem cell expression and clinical symptoms in patients with chronic gastritis, precancerous and gastric cancer. Materials and Methods: Biopsy specimens were obtained from Esophagogastroduodenoscopy and surgery. The gastric lesions were divided into 3 groups according to the stage of the disease. The first group is the chronic gastritis. The second group is the precancerous gastric lesion, including gastric atrophy and intestinal metaplasia. The third group is gastric cancer. The CD44 cancer stem cell expression was done by using immunohistochemistry techniqe. Results: A total 106 patients were included in this study. 68 male and 38 female. Mean age 57±2, including 33 in group 1, 31 in group 2 and 42 in group 3. CD44 cancer stem cell were expression 6.06% in group 1 22.58% in group 2 and 73.81% in group 3. significant high expression in gastric cancer patients OR=2.98; 95%CI=1.21-4.86; p=0.024. Conclusion: Studies show that the expression of CD44 cancer stem cells is associated with the severity of the inflammation and changes of the gastric tissue to gastric cancer. Some patients in group 1 and group 2 who expression of the CD44 cancer stem cell were at risk or high risk for developing gastric cancer. The information above can be used to develop effective patient care. Close follow up should be recommended for high risk patients.

Trieu, J. A., et al. (2019). "RISK FACTORS FOR DEVELOPING GASTRIC CANCER AMONG PATIENTS WITH GASTRIC INTESTINAL METAPLASIA." Gastrointestinal Endoscopy 89(6): AB497.

Introduction: Gastric intestinal metaplasia (GIM)is characterized by a change from the normal glandular epithelium found in the stomach to a small-intestinal phenotype. Risk factors for development of GIM are currently unclear but suggested to be multifactorial. There continues to be paucity of literature characterizing the epidemiology of GIM in the United States (U.S.). We aim to characterize the patient population at our tertiary care academic center who were found to have GIM and evaluate the incidence of and risk factors for developing gastric cancer. Methods: Pathology database was used to identify patients with GIM from January 2008 to December 2016. Data regarding patient demographics, comorbid conditions, indication for esophagogastroduodenoscopy (EGD), Helicobacter pylori status, and endoscopic findings were noted. Outcomes of patients with GIM were evaluated over a 2 to 10-year follow-up period. Results: A total of 254 patients were identified with GIM. The average age was 60 years and 57% were males. Caucasians constituted 34.6% of the study population, followed by Hispanics (30.3%), African Americans (17.3%), and Asians (1.6%). 54.2% were smokers, while 19.8% were diagnosed with alcoholism. Family history of gastric cancer was present in 3.2% of patients. The most common comorbid conditions associated with GIM are summarized in Table 1. The three most common indications for EGD were abdominal pain, gastroesophageal reflux disease, and anemia. Endoscopically, prevalent findings were gastritis, antral erosions, erythema of gastric mucosa, and nodularity of gastric mucosa. 55.5% of the GIM was located in the antrum. Chronic gastritis was present in 97% of the patients and 25.6% had either a concomitant or previous Helicobacter pylori infection. Mapping was completed on 1.6% patients and only 5.5% had appropriate guideline-based surveillance. Our mean follow-up was 3.2 years after diagnosis of GIM. Gastric adenocarcinoma developed in 1.2% of patients with GIM. After a multivariable analysis, the risk factors associated with the development of gastric adenocarcinoma included history of alcoholism (p=0.041)and concurrent use of histamine-2 receptor blockers (p=0.001). Conclusion: The risk of developing gastric adenocarcinoma in patients with GIM is low in the West. Our study characterizes a patient population with GIM at an academic institution in the U.S. The risk factors for developing gastric cancer in the U.S. may differ from those previously studied in Asian countries. Further large multi-center studies are needed to evaluate the risk of gastric adenocarcinoma in patients with GIM in the U.S. so effective surveillance strategies can be developed. [Figure presented][Figure presented]

Tsuji, N., et al. (2000). "Time trends for small gastric cancer in Japan." Gastric Cancer 3(3): 123-127.

BACKGROUND: Gastric cancer rates in Japan have been declining since the 1970s. The rate of differentiated carcinomas has decreased and that of undifferentiated carcinomas has increased. However, little is known about the time trends of small gastric cancer. The aim of this study was to investigate the trends of small gastric cancer over time in Japan. METHODS: We reviewed cases of small gastric cancer (less than 20 mm in diameter) in two groups of patients who entered the age range of 55-to-67 years 14 years apart: patients in cohort 1 (n = 66) were born between 1899 and 1912, and those in cohort 2 (n = 66) were born between 1926 and 1936. Between-group comparisons were made for macroscopic, microscopic, and histochemical findings. Mucin histochemical analysis was used to investigate gastric and nongastric phenotypes. Helicobacter pylori was also investigated by immunohistochemistry. RESULTS: There were significant decreases in the incidence of elevated carcinoma (20% in cohort 1 vs 6% in cohort 2; P < 0.05) and papillary adenocarcinoma (11% vs 2%; P < 0.05). The incidence of flat carcinomas was significantly increased (3% vs 15%; P < 0.05). The incidence of tumors surrounded by fundic gland mucosa increased (20% vs 29%), whereas that of tumors surrounded by intestinal metaplastic mucosa decreased (52% vs 41%). The rate of H. pylori infection in mucosa surrounding tumors was the same in both groups (35%). The incidence of tubular adenocarcinoma with gastric-type mucin was higher in cohort 2 (64%) than in cohort 1 (51%). CONCLUSION: The rate of tubular adenocarcinomas containing gastric type mucin has increased over time. These tumors had a tendency to develop in the fundic gland mucosa and to show less intestinal metaplasia. The H. pylori infection rate was unrelated to this time trend. In advanced gastric cancer, the differentiated carcinoma rate has decreased; however, in small gastric cancer, the rate of tubular adenocarcinoma containing gastric type mucin has increased. This suggests that tubular adenocarcinoma with gastric type mucin changes into poorly differentiated adenocarcinoma as tumors grow to advanced stages.

Tulassay, Z., et al. (2010). "Twelve-month endoscopic and histological analysis following proton-pump inhibitor-based triple therapy in Helicobacter pylori-positive patients with gastric ulcers." Scandinavian Journal of Gastroenterology 45(9): 1048-1058.

Objective. To evaluate endoscopic and histological findings after Helicobacter pylori eradication therapy in gastric ulcer (GU) patients after 12 months' follow-up. Material and methods. A total of 401 GU patients were randomized to receive either twice-daily (b.i.d.) esomeprazole 20 mgamoxicillin 1000 mgclarithromycin 500 mg (EAC) for 1 week followed by placebo for 3 weeks, EAC followed by once-daily (o.d.) esomeprazole 20 mg for 3 weeks or esomeprazole 20 mg b.i.d. plus placebo antibiotics for 1 week followed by esomeprazole 20 mg o.d. for 3 weeks. Endoscopy with biopsy was performed at baseline, after treatment and at 6 and 12 months' follow-up (healed patients). Results. Endoscopic abnormalities, particularly in the stomach, were common at baseline and remained similar during follow-up, regardless of ulcer status and treatment. Helicobacter gastritis was present (antrum or corpus) in ≈ 20% of patients following eradication therapy (versus ≈ 80% with esomeprazole alone); these effects were sustained during follow-up. Similar trends were observed for other histological variables (granulocyte and lymphoplasmocytic cell infiltration, replacement of gastric surface cells by regenerative epithelium, and mucous depletion). No changes in atrophy or intestinal metaplasia were observed. Eighteen gastric cancer cases were detected: 11 at baseline endoscopy, and seven during treatment and follow-up. Conclusions. Endoscopic abnormalities are common in GU patients and persist after proton-pump inhibitor-based triple therapy for H. pylori eradication, which is associated with large, sustained improvements in histological variables. Follow-up endoscopy and histology may be necessary, even in patients with apparently non-malignant GU, to improve the detection rate of gastric malignancy in populations with a high prevalence of gastric cancer. © 2010 Informa Healthcare.

Turkot, M., et al. (2020). "Revising the paradigm of endoscopic treatment for gastric hyperplastic polyps: Analysis of recurrence rate and malignant progression." United European Gastroenterology Journal 8(8 SUPPL): 21-22.

Introduction: Gastric hyperplastic polyps (GHPs) remain the second most common type of epithelial polyps in the stomach after fundic gland polyps. The rate of dysplasia within GHPs is highly variable among reports and most of the guidelines recommend to resect GHPs ≥1cm due to their potential risk of malignant progression. Unlike neoplastic polyps, GHP may arise as a response to mucosal injury, therefore, complete removal of these lesions do not guarantee a definite cure and recurrent GHPs have been widely reported in the literature. Aims & Methods: In this single-center retrospective study we aimed to assess the rate of GHPs' malignant progression and the recurrence rate after GHP removal. We reviewed the hospital endoscopic database to identify adult individuals with a diagnosis of GHPs. We then used the National Cancer Registry to follow-up those patients until 12.2017 and identify those who developed a subsequent gastric cancer (GC). We then analyzed a subset of GHPs ≥1cm that underwent endoscopic resection to determine the rate of local recurrence and rate of cancerous component in removed lesions. We defined recurrence as the presence of a polyp or number of polyps during the follow-up (FU) which was exceeding the number of polyps at the time of initial polypectomy; or the presence of any remnant tissue within a post-polypectomy scar with biopsies demonstrating GHP. Results: Overall, we identified 675 patients [464 (68.7%) females], of a mean age 63.0(±13.3) with GHPs between 2005 and 2017. Of these, 368 patients (54.5%) had a single lesion, 221 (32.7%) had several GHPs (≤5) and 86 (23.3%) had multiple GHPs (>5). In 89 cases (13.2%), the polyps were present in multiple locations throughout the stomach, and in 202 (29.9%), 258 (38.2%), 61 (9.0%) and 65 (9.7%) they were confined to the antrum, body, fundus and the cardia, respectively. The initial median polyp size was 4mm (IQR 3-8). The background mucosa was assessed in 221 individuals (32.7%) with atrophic gastritis and/or intestinal metaplasia being present in most of the patients (179/221; 81.0%). H.pylori status had been obtained in 304 individuals (45.0%), within those nearly a third were found to be positive (108/304; 35.5%). Among patients with GHP who did not undergo endoscopic treatment (n=197; 29.2%), only two patients (1.0%) were diagnosed with a subsequent GC after a median 5.9 years (range 0.9-11.9 years). We identified 105 (15.6%) patients with GHPs ≥1cm who underwent endoscopic resection. Of these, 15 patients had a local recurrence (14.3%). The majority of the recurrent polyps were initially localized in the antrum (11/15, 73.3%) and most had a sessile morphology (Paris 0-Is; 66.7%). Of all resected GHPs ≥1cm, 3 harboured cancer (2.9%). All of the cancerous polyps had a pedunculated morphology (0-Ip) and a size of ≥2cm Conclusion: GHPs carry a low risk of malignant progression. Given a significant recurrence rate (>14%), endoscopic resection of GHPs ≥1cm, especially when sessile and localized in the antrum, remains debatable. In contrast, bigger (≥2cm) and pedunculated polyps do require complete endoscopic resection as they may harbour cancer.

Uedo, N., et al. (2016). "Long-term changes of extent of chronic atrophic fundic gastritis after h. pylori infection observed in autofluorescence imaging videoendoscopy." United European Gastroenterology Journal 4(5): A519.

Introduction: Long-term infection of H. pylori causes subsequent changes in the gastric mucosa from inflammatory cell infiltration, glandular atrophy, intestinal metaplasia, dysplasia and cancer. Eradication of H. pylori improves inflammatory cell infiltration and, in part, glandular atrophy but whether areas that involved by glandular atrophy and intestinal metaplasia recover or not is unknown. Autofluorescence imaging videoendoscopy (AFI) visualize areas with chronic atrophic fundic gastritis (CAFG) including glandular atrophy and intestinal metaplasia in the gastric corpus as green mucosa in endoscopic images. Aims & Methods: In this study we investigated changes of extent of CAFG after H. pylori eradication. Among consecutive patients with history of endoscopic treatment of early gastric cancer who visited an outpatient clinic between July 2013 and August 2014, those who received endoscopy with AFI more than two times with an interval of 2 years or longer were enrolled in this study. Patients with no evaluable AFI images of the corpus, the lesion in the corpus lesser curvature, history of gastric resection, negative and unknown H. pylori infection status at initial endoscopy were excluded. At least one downward and one retroflex view of AFI images of the corpus were identified for each patient. Extent of CAFG was graded by consensus of two endoscopists according to the Kimura- Takemoto classification as C-1, C-2, C-3, O-1, O-2, and O-3. Results: A total of 101 patients (median age of 73 years old, 81 man and 20 women) with positive H. pylori infection at initial endoscopy were enrolled in this study. 43 patients received successful eradication therapy and 58 patients did not receive eradication therapy. During median (range) follow-up period of 5 (2- 8) years, CAFG reduced in 9 (21%) patients in the eradication group and 7 (12%) in the non-eradication group; CAFG increased in 7 (16%) in the eradication group and 5 (9%) in the non-eradication group; and CAFG did not change in reminders (73%, 74/101) in either group (p=NS). Limitation of this study is retrospective design and inclusion of many patients with severe CAFG at initial endoscopy. Conclusion: In majority of patients in this study, extent of CAFG did not improve significantly after eradication of H. pylori.

Uemura, N., et al. (1997). "Effect of Helicobacter pylori eradication on subsequent development of cancer after endoscopic resection of early gastric cancer." Cancer Epidemiology, Biomarkers and Prevention 6(8): 639-642.

Although epidemiological studies strongly suggest an association between gastric cancer and Helicobacter pylori infection, there has been no clinical report indicating that cure of the infection prevents cancer. We conducted a nonrandomized H. pylori eradication trial in patients whose gastric cancer was removed by endoscopic resection (ER). We investigated the effect of treatment on the histopathology of the gastric mucosa, as well as on the incidence of metachronous gastric cancer during the long-term clinical and endoscopic follow-up. One hundred and thirty-two patients with early gastric cancer underwent ER and had H. pylori infection. Sixty-five (group A) were treated with omeprazole and antibiotics to eradicate the infection, and 67 (group B) were not. All patients were followed for 2 years post ER. After eradication treatment in group A, the disappearance of neutrophil infiltration in the antrum and body of the stomach was observed as was a decrease of the severity of intestinal metaplasia. Endoscopy after ER detected no new gastric cancers in these patients. After 3 years of follow-up, 6 (9%) of the 67 patients in group B had a new early-stage, intestinal-type gastric cancer endoscopically diagnosed. The above results suggest that H. pylori eradication may improve neutrophil infiltration and intestinal metaplasia in the gastric mucosa and inhibit the development of new carcinomas. This finding should be confirmed in a randomized, controlled trial.

Uemura, N., et al. (2002). "H. pylori infection and the development of gastric cancer." Keio Journal of Medicine 51(SUPPL. 2): 63-68.

BACKGROUND: Recently, many study have shown that Helicobacter pylori infection is crucial in development of atrophic gastritis, which is closely associated with gastric cancer. We conducted a long-term endoscopic prospective follow-up study to investigate the development of gastric cancer in H. pylori-positive and -negative patients. METHODS: 1603 patients who underwent endoscopy and were assessed as to the presence of H. pylori infection by histology, rapid urease test and serologic test between April 1990 and March 1993 were entered. We prospectively studied 1246 subjects with and 280 subjects without H. pylori infection for a mean follow-up of 7.8 years (range 1-10.6 years). RESULTS: Gastric cancer of both the intestinal and diffuse type developed in 36 (2.9%) infected patients but in none of the uninfected patients during follow-up. There was an increased risk for gastric cancer in infected patients with severe gastric atrophy and corpus predominant gastritis and intestinal metaplasia. Gastric cancer was detected in 21 (4.7%) of the patients with non ulcer dyspepsia, in 10 (3.4%) of those with gastric ulcer and in 5 (2.2%) of those with gastric hyperplastic polyp, at enrollment. No gastric cancer was detected in duodenal ulcer patients. CONCLUSION: These results suggest that the development of both types of gastric cancer is caused by H. pylori-associated gastritis, and the risk for development of gastric cancer in H. pylori-negative subjects is extremely low. Subjects having H. pylori-positive gastric mucosa with severe atrophy and/or corpus gastritis may be at particularly high risk for gastric cancer.

Uemura, N., et al. (2000). "Changes in Helicobacter pylori-induced gastritis in the antrum and corpus during long-term acid-suppressive treatment in Japan." Alimentary Pharmacology and Therapeutics 14(10): 1345-1352.

BACKGROUND: Several studies have shown that acid-suppressive therapy aggravates corpus gastritis in patients with Helicobacter pylori infection, promoting the development of atrophic gastritis. AIM: To study the effects of long-term use of antisecretory agents on the H. pylori-positive gastric mucosa in Japan, a country with a high incidence of gastric cancer. METHODS: A total of 141 H. pylori-positive patients who had peptic ulcers or reflux oesophagitis were treated for 3 years with either omeprazole (20 mg/day) alone (n=7) or with omeprazole for primary therapy (8 weeks), followed by famotidine (40 mg/day) for maintenance therapy (n=134). Endoscopy was performed before, during, and after treatment. Biopsy specimens were taken from the greater curvature of the antrum and corpus and were examined histologically. RESULTS: The long-term use of famotidine after 8 weeks of treatment with omeprazole distinctly decreased H. pylori density and neutrophil infiltration in the antrum, but did not change H. pylori density in the corpus. The gastritis score increased in patients who had no, or only mild corpus gastritis before treatment (n=74), and significantly decreased in those who had moderate or severe gastritis before treatment (n=60). In four of the seven patients who received long-term treatment with omeprazole alone, neutrophil infiltration and H. pylori density decreased not only in the antrum but also in the corpus. There was no increase in intestinal metaplasia or mucosal atrophy as assessed endoscopically during follow-up. CONCLUSION: Changes in corpus gastritis in response to acid-suppressive therapy depend on the severity of gastritis before treatment. Long-term use of acid-suppressive therapy apparently does not accelerate the development of atrophy or intestinal metaplasia in Japanese patients.

Uemura, N., et al. (2001). "Helicobacter pylori infection and the development of gastric cancer." New England Journal of Medicine 345(11): 784-789.

BACKGROUND: Although many studies have found an association between Helicobacter pylori infection and the development of gastric cancer, many aspects of this relation remain uncertain. METHODS: We prospectively studied 1526 Japanese patients who had duodenal ulcers, gastric ulcers, gastric hyperplasia, or nonulcer dyspepsia at the time of enrollment; 1246 had H. pylori infection and 280 did not. The mean follow-up was 7.8 years (range, 1.0 to 10.6). Patients underwent endoscopy with biopsy at enrollment and then between one and three years after enrollment. H. pylori infection was assessed by histologic examination, serologic testing, and rapid urease tests and was defined by a positive result on any of these tests. RESULTS: Gastric cancers developed in 36 (2.9 percent) of the infected and none of the uninfected patients. There were 23 intestinal-type and 13 diffuse-type cancers. Among the patients with H. pylori infection, those with severe gastric atrophy, corpus-predominant gastritis, and intestinal metaplasia were at significantly higher risk for gastric cancer. We detected gastric cancers in 21 (4.7 percent) of the 445 patients with nonulcer dyspepsia, 10 (3.4 percent) of the 297 with gastric ulcers, 5 (2.2 percent) of the 229 with gastric hyperplastic polyps, and none of the 275 with duodenal ulcers. CONCLUSIONS: Gastric cancer develops in persons infected with H. pylori but not in uninfected persons. Those with histologic findings of severe gastric atrophy, corpus-predominant gastritis, or intestinal metaplasia are at increased risk. Persons with H. pylori infection and nonulcer dyspepsia, gastric ulcers, or gastric hyperplastic polyps are also at risk, but those with duodenal ulcers are not.

Urabe, M., et al. (2018). "Adenocarcinoma of the esophagogastric junction and its background mucosal pathology: A comparative analysis according to Siewert classification in a Japanese cohort." Cancer Med 7(10): 5145-5154.

Adenocarcinoma of the esophagogastric junction (AEG) has heterogeneous carcinogenic process due to its location straddling the esophagogastric junction. We assessed background mucosal pathology and its correlation with clinicopathological features of each Siewert type of AEG. Clinicopathological and immunohistochemical analyses of 103 AEGs and 58 gastric cancers (GCs) were conducted. Background mucosal features were evaluated according to the updated Sydney System. Siewert classification divided 103 AEGs into three type I, 75 type II, and 25 type III tumors, respectively. Two type I, 9 type II AEGs, and none of type III AEGs were Barrett-related and were excluded from further analysis. Background mucosa of type III AEGs more frequently showed moderate to marked degree of atrophy and intestinal metaplasia than those of type II AEGs and was very similar to those of GCs. Among type II AEGs, tumors with atrophic background were significantly associated with higher patient age and intestinal-type histology. Type II AEGs with nonatrophic background, but not those with atrophic background, showed more frequent mismatch repair deficiency, TP53 overexpression, and less frequent intestinal phenotypic markers expression than type III AEG or GC. Type II AEGs with atrophic background involved suprapancreatic nodes more frequently than those without. We demonstrated that chronic atrophic gastritis was a major precancerous condition of AEG in the Japanese population, especially Siewert type III which had background mucosal pathology similar to that of GC. Type II AEGs with and without atrophic background showed some clinicopathological differences, and these observations might represent heterogeneous carcinogenic process within type II AEGs.

Ushiku, T., et al. (2013). "Very well differentiated gastric cancer of intestinal metaplasia-type: A systemic analysis." Laboratory Investigation 93: 185A.

Background: Very well differentiated gastric adenocarcinoma of intestinal metaplasiatype (VWDAIM) is a rare variant characterized by morphologic differentiation towards intestinal metaplasia (IM) and low-grade cytologic atypia. Because it mimics IM, a definite biopsy diagnosis is challenging. Small series have been published, but detailed diagnostic criteria and clinical behavior are not fully established. Design: Slides from the resection specimens of 21 cases of VWDAIM were reviewed and their cytoarchitectural features recorded. Forty histologic pictures of benign IM and VWDAIM were also assessed by a blinded independent reviewer to determine the sensitivity & specificity of the diagnostic features of malignancy. Pre-resection biopsies from 19 cases were also evaluated. Results: Characteristic architectural features of VWDAIM were branching (100%), tortuous (95%), anastomosing (95%), distended (90%), abortive (81%), spiky (76%), and budding (71%) glands. Cytologic atypia was mild in all cases (Figure 1). Sensitivity and specificity of these features for malignancy are shown in Table 1. (Figure Presented) The original preoperative biopsy diagnoses for 19 patients were adenocarcinoma (36%), suspicious for adenocarcinoma (14%), indeterminate for neoplasia (21%), and reactive IM (29%). One patient with a pT4 tumor showing concomitant diffuse-type carcinoma died of disease, while all others were alive and without disease at a mean 13 month follow-up (range 1-56 months). Conclusions: The features that best differentiate VWDAIM from IM are anastomosing, spiky, abortive, and budding glands. However, a preoperative biopsy diagnosis is achieved in only 50% of the cases. Although VWDAIM is typically thought to be a low-grade cancer, rare cases are associated with diffuse-type carcinoma and have aggressive behavior.

Valenzuela, M. A., et al. (2015). "Helicobacter pylori -induced inflammation and epigenetic changes during gastric carcinogenesis." World Journal of Gastroenterology 21(45): 12742-12756.

The sequence of events associated with the development of gastric cancer has been described as "the gastric precancerous cascade". This cascade is a dynamic process that includes lesions, such as atrophic gastritis, intestinal metaplasia and dysplasia. According to this model, Helicobacter pylori (H. pylori ) infection targets the normal gastric mucosa causing non-atrophic gastritis, an initiating lesion that can be cured by clearing H. pylori with antibiotics or that may then linger in the case of chronic infection and progress to atrophic gastritis. The presence of virulence factors in the infecting H. pylori drives the carcinogenesis process. Independent epidemiological and animal studies have confirmed the sequential progression of these precancerous lesions. Particularly long-term follow-up studies estimated a risk of 0.1% for atrophic gastritis/intestinal metaplasia and 6% in case of dysplasia for the long-term development of gastric cancer. With this in mind, a better understanding of the genetic and epigenetic changes associated with progression of the cascade is critical in determining the risk of gastric cancer associated with H. pylori infection. In this review, we will summarize some of the most relevant mechanisms and focus predominantly but not exclusively on the discussion of gene promoter methylation and miRNAs in this context.

van der Post, R. S., et al. (2018). "Outcomes of screening gastroscopy in first-degree relatives of patients fulfilling hereditary diffuse gastric cancer criteria." Gastrointestinal Endoscopy 87(2): 397-404.e392.

BACKGROUND AND AIMS: The aim of this study was to determine the yield of endoscopic screening in first-degree relatives (FDRs) of CDH1-negative hereditary diffuse-type gastric cancer (HDGC) patients. METHODS: In this retrospective observational cohort study, in 2 expert centers in the Netherlands data were collected on FDRs from families fulfilling the international HDGC criteria that underwent endoscopic screening. Extensive inspection of the stomach was performed by gastroscopy, taking random and/or targeted stomach biopsy specimens to identify diffuse-type gastric cancer. RESULTS: Between 2004 and 2016, 90 persons (40% men; mean age, 48 years) from 40 families were offered endoscopic screening. The mean number of endoscopies per person was 3. The mean follow-up time was 46 months and mean endoscopic interval 20 months. Signet ring cell carcinoma foci restricted to the mucosa (pT1a) were identified in 4 persons (4%) from 1 family, which afterward was diagnosed with a germline CTNNA1 mutation. Advanced poorly cohesive gastric carcinoma was diagnosed in 1 person from another family. Intestinal metaplasia was diagnosed in 38 persons (42%) and low-grade dysplasia in 4 persons (4%). Additionally, in 40 persons (44%) scar tissue was observed in the gastric mucosa, which can hinder the endoscopic detection of small white lesions typical for HDGC. CONCLUSIONS: Endoscopic screening in HDGC families without a pathogenic CDH1 mutation may be reasonable, as we detected signet ring cell carcinomas in 6% of persons screened. However, the criteria and frequency of screening may have to be reconsidered.

Van Olphen, S. H., et al. (2014). "SOX2 as a novel marker to predict neoplastic progression in barrett's esophagus." Gastroenterology 146(5): S-112.

Objective: The value of surveillance for patients with Barrett's esophagus (BE) based on histological diagnosis of low grade dysplasia (LGD) remains debated given the lack of discriminative power to stratify BE patients at high risk for neoplastic progression of those at low risk. The use of biomarkers in addition to histological assessment improves risk stratification and has the potential to improve cost-effectiveness of BE surveillance. SOX2 plays a pivotal role in the development of esophageal and gastric epithelium and is down regulated in intestinal metaplasia and gastric cancer. The aim of this study was to investigate the value of SOX2 in BE patients to predict neoplastic progression and to combine the results with our previously reported promising p53 immunohistochemical data within the same cohort. Methods: We conducted a case-control study within a large prospective cohort of 720 BE patients, with a total follow-up time of more than 5600 years. In total 44 BE patients with neoplastic progression defined as development of high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) (cases) and 44 BE patients without neoplastic progression (controls) were selected and matched for age and gender. SOX2 protein was detected by immunohistochemistry in more than 3000 biopsies and was scored independently by two investigators blinded for long-term outcome. The results were combined with p53 immunohistochemical data. Hazard ratios (HRs) were calculated by time-dependent Cox-regression models adjusted for age, gender, BE length and esophagitis. Results: Normal BE epithelium showed homogeneous strong nuclear expression of SOX2, while expression of SOX2 was progressively lost in dysplastic epithelial cells. Loss of SOX2 expression was seen in only 9.5% of biopsy series without dysplasia, in contrast to 36.8% of biopsy series with LGD and 70% of biopsy series with HGD or EAC. Multivariate analysis showed that loss of SOX2 expression (HR 3.3; 95% CI: 1.6-6.6) and aberrant p53 expression (HR 4.5; 95% CI:2.8- 8.9) were independent predictors for neoplastic progression, whereas presence of LGD was no longer predictive. Aberrant expression of SOX2 and p53 strongly increases the risk to develop HGDor EAC in the individual patient (multiplied HR of 14.9). The positive predictive value for neoplastic progression increased from 47% with histological diagnosis of LGD, to 83% with LGD and concurrent aberrant SOX2 expression, to 87% with LGD and concurrent aberrant p53 expression and to 91% with aberrant SOX2 and p53 expression. Conclusion: Loss of SOX2 and aberrant p53 expression are independent predictors for neoplastic progression in patients with BE and more powerful than the histological diagnosis of LGD. SOX2 en p53 immunohistochemistry may be useful as a discriminative test to improve risk stratification of Barrett surveillance.

Van Olphen, S. H., et al. (2014). "SOX2 as a novel marker to predict neoplastic progression in Barrett's oesophagus." United European Gastroenterology Journal 2(1): A74.

INTRODUCTION: The value of surveillance for patients with Barrett's oesophagus (BO) based on histological diagnosis of low-grade dysplasia (LGD) remains debated given the lack of discriminative power to stratify BO patients at high risk for neoplastic progression of those at low risk. The use of biomarkers in addition to histological assessment improves risk stratification and has the potential to improve cost-effectiveness of BO surveillance. SOX2 plays a pivotal role in the development of oesophageal and gastric epithelium and is down regulated in intestinal metaplasia and gastric cancer. AIMS & METHODS: The aim of this study was to investigate the value of SOX2 in BO patients to predict neoplastic progression and to combine the results with our previously reported p53 immunohistochemical data within the same. We conducted a case-control study within a large prospective cohort of 720 BO patients, with a total follow-up time of more than 5600 years. In total 44 BO patients with neoplastic progression defined as development of high-grade dysplasia (HGD) or oesophageal adenocarcinoma (OAC)(cases) and 44 BO patients without neoplastic progression (controls) were selected and matched for age and gender. SOX2 protein was detected by immunohistochemistry in more than 3000 biopsies and was scored independently by two investigators blinded for long-term outcome. The results were combined with p53 immunohistochemical data. Hazard ratios (HRs) were calculated by Cox-regression models adjusted for age, gender, BE length and esophagitis. RESULTS: Normal BO epithelium showed homogeneous strong nuclear expression of SOX2, while expression of SOX2 was progressively lost in dysplastic epithelial cells. Loss of SOX2 expression was seen in 9% of biopsy series without dysplasia, in contrast to 37% of biopsy series with LGD and 70% of biopsy series with HGD or OAC. Multivariate analysis showed that loss of SOX2 expression (HR 2.3; 95% CI:1.1-4.6) and aberrant p53 expression (HR 3.7; 95% CI:1.8-7.8) were independent predictors for neoplastic progression (multiplied HR of 8.5), whereas presence of LGD was no longer predictive. The positive predictive value for neoplastic progression increased from 47% with histological diagnosis of LGD, to 83% with LGD and concurrent aberrant SOX2 expression, to 87% with LGD and concurrent aberrant p53 expression and to 91% with aberrant SOX2 and p53 expression. CONCLUSION: SOX2 is lost during transition from non-dysplastic BO to HGD/OAC. Loss of SOX2 and aberrant p53 expression are independent predictors for neoplastic progression in patients with BO and more powerful than the histological diagnosis of LGD. SOX2 and p53 immunohistochemistry may be useful as a discriminative test to improve risk stratification of Barrett surveillance.

van Zanten, S. V., et al. (2018). "GASTRIC PATHOLOGY FOLLOW-UP STUDY IN CANADIAN ARCTIC COMMUNITIES." Gastroenterology 154(6): S-505.

In northern Canadian Indigenous communities, the estimated prevalence of H. pylori (Hp) infection is substantially higher than in southern Canadian multiethnic populations. Gastric cancer rates are also higher in northern Canada. To address community concerns about Hp-related health risks, the Canadian North Helicobacter pylori Working Group conducts community-based projects in the Northwest Territories (NT) and Yukon (YT) with breathtest screening for Hp infection, treatment, and upper gastrointestinal endoscopy at baseline and follow-up. This analysis describes changes in the prevalence and severity of gastric pathology in community project participants who completed endoscopy at baseline and several years after treatment. During 2008-2013, 310 participants from Aklavik, NT, Fort McPherson, NT and Old Crow, YT completed baseline endoscopy in mobile units set up in the local health centres. Gastric biopsies were taken from antrum and body: in all, 5-6 per participant. One pathologist (SG) assessed all biopsies, grading acute and chronic gastritis, atrophy, intestinal metaplasia and Hp density using the Sydney System. Baseline prevalence was: Hp-positivity, 72% (223/310); acute gastritis, 70% (215/308); chronic gastritis, 75% (234/310); gastric atrophy, 31% (95/309); intestinal metaplasia, 14% (43/309). Hp-positive participants received treatment followed by a breath test at ≥8 weeks post-treatment to assess treatment success. Follow-up endoscopy occurred in 2017. In 2017, 63 participants completed follow-up endoscopy: 27-76 years of age; 63% female; 97% Indigenous; 78% (49/63) Hp-positive at baseline; 70% (44/63) treated and 81% (30/37) negative on post-treatment breath test. In 38 participants with currently available follow-up data, 26% were Hp-positive, substantially lower than the 72% observed at baseline. Of 11 who were Hp-negative at baseline and follow-up, 100% (11/11) remained free of acute gastritis and 73% (8/11) remained free of chronic gastritis (3/11 had mild chronic gastritis in 2017). Of 14 who were initially Hp-positive and negative after treatment, 86% (12/14) remained Hp-negative at follow-up. Of the 12 who remained negative, none had acute gastritis at followup (baseline severity distribution: 1 severe; 4 moderate; 6 mild; 1 none); 11 of 12 had no chronic gastritis at follow-up (baseline severity distribution: 5 severe; 5 moderate; 1 mild) and one changed from moderate at baseline to mild at follow-up. Follow-up prevalence was 18% (7/38) for gastric atrophy (down from 31% at baseline) and 21% (8/38) for intestinal metaplasia (up from 14% at baseline), though follow-up numbers are too small for conclusions about Hp treatment effects on these two outcomes. These results yield evidence that successful H. pylori treatment leads to sustained decreases in the severity of acute and chronic gastritis in Indigenous Arctic Canadians. [Table Presented] [Table Presented]

Vance, R., et al. (2014). "Prevalence and characteristics of patients with gastric intestinal metaplasia and gastric cancer in a population of American Veterans." American Journal of Gastroenterology 109: S54.

Introduction: The prevalence and clinical significance of gastric intestinal metaplasia (GIM), a precursor to gastric adenocarcinoma (GAC), are not well understood in North American patients. Because GAC is so rare in the USA, it is not common practice to perform either endoscopic screening or surveillance for GAC or GIM, in contrast to recommendations in Asia and parts of Europe. As such, there are little data to describe the patients in the USA with GIM. Our aim was to determine the prevalence of GIM and GAC in a population of U.S. veterans and compare the clinical characteristics between patients with GIM, GAC, and controls. Methods: In this retrospective review, we determined the prevalence of GIM and GAC at our institution from 2008-2013 using the pathology and endoscopy databases, and compared the baseline characteristics, clinical features, mortality, and endoscopic surveillance trends between 50 GIM, 50 GAC, and 50 control patients with normal gastric biopsies. Results: Three hundred seventy-seven of 5,587 patients had GIM on gastric biopsy, a prevalence of 6.75%, while 101 or 1.81% had biopsies diagnostic for GAC. Further data analysis revealed that GAC patients had a higher mortality rate (67%), lower BMI, a lower baseline hemoglobin, and were more likely present for endoscopy with anemia or GI bleeding than either GIM or control patients (p<0.05). There was no difference in mortality between GIM patients and controls. Forty-one percent of GAC patients had GIM present either on biopsy or surgical specimen. GAC was diagnosed at the index endoscopy in 78% of patients. Of the GAC patients who previously underwent endoscopy, 22% had the exam within the past 10 years, but only 42% of these patients had endoscopic findings requiring biopsy (erythema, nodularity, ulcer). Of the patients with GAC who had prior EGD, none had previously been diagnosed with GIM on biopsy. GIM patients had a follow-up EGD 44% of the time, compared to 24% of controls with a range from 1 month to 4 years for GIM and 1 month to 6 years for controls. GIM patients were more often diagnosed with Barrett's esophagus (24%) and Helicobacter pylori (36%) than either GAC patients or controls (p<0.05). None of the patients with GIM progressed to gastric cancer on follow-up EGD. Conclusion: Gastric intestinal metaplasia and gastric adenocarcinoma are uncommon in American veterans. A significant number of patients with GAC also had underlying GIM, but most patients diagnosed with GAC have not had prior endoscopy. The majority of patients with the premalignant condition of GIM are not regularly surveyed with endoscopy. Further researchis needed to define the population of patients who might benefit from endoscopic surveillance for GIM and GAC.

Vanderland, M., et al. (2020). "Group d strep; time for colon prep." American Journal of Gastroenterology 115(SUPPL): S1750-S1751.

INTRODUCTION: The association between colorectal cancer (CRC) and S. gallolyticus (GDS) endocarditis is well-established. Other associations include gastric cancer, colon polyps and liver disease. The exact pathophysiology is not understood; however, fecal carriage rate of bacteria may increase with colonic pathology and play a role in oncogenesis. Infection may be the sole indicator of the underlying neoplasia and colonoscopy is recommended, but there are no guidelines regarding intervals for further surveillance. CASE DESCRIPTION/METHODS: A healthy 35-year-old Vietnamese male with no relevant social or family history, presented with 1 month of cough, dyspnea, unintentional 25 pound weight loss and fevers. Labs showed iron deficiency anemia, WBC 11.55K/uL, BNP 1005pg/mL, troponin 0.12ng/mL. Blood cultures grew GDS. Echocardiogram revealed aortic valve vegetations and severe regurgitation. Work up included CEA 1.3ng/mL as well as normal hepatic function panel and CT of the abdomen/ pelvis. Upper endoscopy revealed gastritis with intestinal metaplasia negative for helicobacter pylori. Three 6-8mm tubular adenomas and one 8mm sessile serrated adenoma were excised on colonoscopy. After valve repair, the patient was discharged with antibiotics and GI follow-up. DISCUSSION: Literature states that colonic neoplasia may arise years after GDS bacteremia or endocarditis, suggesting an association with adenoma progression and emphasizing a need for endoscopy. Despite a low suspicion for neoplasia in this patient, endoscopic findings increase his risk for both colon and gastric cancer. Case reports have demonstrated GDS may be related to extracolonic malignancies though nothing suggests that intestinal metaplasia is analogous to adenomatous colon polyps. Based on findings, surveillance colonoscopy is recommended in 3-5 years in accordance with the US Multi-Task Force guidelines on CRC. Being Vietnamese, he is at high-risk for gastric cancer and should undergo repeat upper endoscopy. If repeat endoscopy is negative, there is no guideline for future surveillance specifically regarding GDS and its association with neoplasia. Other than the 2015 European Society of Cardiology guidelines for the management of infective endocarditis suggesting colonoscopy at diagnosis and if no lesion found, annual colonoscopy should be considered, there is no consensus. This case raises questions about the association between extracolonic pre-malignant pathology with GDS and guidelines about endoscopic surveillance once the diagnosis is made.

Vannella, L., et al. (2010). "Risk factors for progression to gastric neoplastic lesions in patients with atrophic gastritis." Alimentary Pharmacology and Therapeutics 31(9): 1042-1050.

BACKGROUND: Atrophic gastritis, involving the gastric body mucosa, predisposes to gastric neoplastic lesions (GNL). However, regular gastroscopic-histological follow-up for GNL is not recommended for patients with atrophic gastritis. AIM: To evaluate risk factors for the progression to GNL in a cohort of patients with atrophic gastritis. METHODS: A total of 300 patients with atrophic gastritis [205 women, aged 54 (18-78) years] underwent gastroscopy with six gastric antrum and body biopsies. All patients had at least one follow-up gastroscopy/histology at an interval of at least 1 year after the atrophic gastritis diagnosis. Baseline clinical and histological features were analysed as risk factors for the development of GNL by Cox-regression. RESULTS: During a median follow-up of 4.3 (1-16.5) years, 15 GNL were detected in 14 of the 300 patients with atrophic gastritis: three were gastric cancer, whereas 12 were non-invasive neoplasia. The annual incidence for GNL was 1%. Cox-regression analysis identified the following risk factors: age over 50 years (HR 8.8, 95%CI 1.2-68.4), atrophic pangastritis (HR 4.5, 95% CI 1.5-14.1) and severe intestinal metaplasia in the gastric body (HR 4.0, 95% CI 1.3-11.8). CONCLUSIONS: Atrophic pangastritis, severe body intestinal metaplasia and/or age over 50 years increase the risk for developing GNL in patients with atrophic gastritis. In this subset of patients, an endoscopic-histological follow-up for GNL surveillance may be worthwhile.

Vargas, J. I., et al. (2017). "Impact of the staging of gastritis with the OLGA system for risk stratification in a Chilean population with high prevalence of gastric cancer." Gastrointestinal Endoscopy 85(5): AB461.

Background: Gastric cancer (GC) is one of the leading causes of death in Chile. Therefore, opportunist screening for pre-malignant lesions during endoscopy through OLGA system (Operative Link on Gastritis Assessment) is recommended in patients over 40-years-old or first-degree gastric cancer relatives according the the recommendations of the Chilean Association for Digestive Endoscopy for the management of gastric pre-malignant lesions (2014). Data are scarce in Latin- American countries about the prevalence of pre-malignant lesions, atrophic gastritis (AG) using OLGA system and intestinal metaplasia (IM). Objective: To assess the impact of staging of gastritis with the OLGA system in a Chilean population with high prevalence of GC. Methods: Single center cross-sectional study. Upper gastrointestinal endoscopies (UGIEs) with Sydney protocol gastric biopsies were collected between January 2015 and August 2016. Biopsy samples were analyzed by 2 experienced pathologists. Descriptive statistics by means with confident intervals and percentages. Statistical analysis by t-test, chi-square, ANOVA, contingency tables with kappa index for concordance between endoscopic and histologic diagnosis were performed. Results: Eight-hundred and sixty-six UGIEs were evaluated in this study and 243 (28%) filled the inclusion criteria with gastric biopsy obtained following Sydney protocol. Mean age of patients included was 56±12.6 years-old, 61% female gender, family history of gastric cancer in 35.4%. OLGA pathological classification showed that 45.6% had stage 0, 25.2% stage I, 16.4% stage II, 9.3% stage III and 3.5% stage IV. Frequency of Helicobacter pylori (HP) infection by histological staining was 43.6%, 36.5% had IM and 3.5% were compatible with autoimmune atrophic gastritis (AAG). Patients with more advanced OLGA stages (III-IV) were older than those without AG (61.6 vs 54.2 years, p=0.013), similarly, patients with IM were older that those without IM (60.3 vs 53.5 years, p <0.001). Age also influenced the presence of HP, been those infected with HP younger that patients HP-negative (53.1 vs 58.4 years, p<0.001). No differences were observed in OLGA stages according to gender, family history of GC or tobacco use. Endoscopic appearance of AG had a low sensitivity (39.7), compared to histological findings, with kappa coefficient of 0.28 (p<0.001). Similarly, endoscopic IM had 31.2% sensitivity and 0.15 kappa coefficient compared to histological diagnosis (p=0.01). Conclusions: Gastric biopsies by OLGA staging system showed a high prevalence of advanced stages of AG and IM, detecting a significant number of patients whom will required endoscopic follow-up for GC prevention. Presence of features of AAG in histology in a subset of patients was an unexpected finding of protocolized gastric sampling. Endoscopy had low accuracy in detecting AG and IM compared to histology.

Venerito, M., et al. (2019). "Review: Gastric cancer—Clinical aspects." Helicobacter 24(S1).

Gastric cancer (GC) was responsible for over 1 000 000 new cases in 2018 and an estimated 783 000 deaths, making it still the fifth most frequently diagnosed cancer and the third leading cause of cancer deaths in both sexes worldwide. Divergent trends for GC incidence were observed in the USA. Incidence rates, particularly for non-cardia GC, were stable or increasing among persons aged <50 years. In an analysis of data from a public hospital database in Hong Kong, treatment of Helicobacter pylori infection was associated with a lower risk of GC, particularly in older subjects who received treatment ≥10 years before. Based on the results of a 16-year endoscopy-based follow-up eradication trial, patients with incomplete-type intestinal metaplasia (IM) should receive endoscopic surveillance upon H. pylori eradication therapy. Updated guidelines on the endoscopic surveillance of preneoplastic conditions of the stomach (MAPS II) have been published. In the RAINFALL trial, the addition of ramucirumab to a backbone chemotherapy as a first-line regimen failed to improve overall survival (OS) of patients with metastatic disease. Also, pembrolizumab did not prolong OS when compared to paclitaxel in the second-line treatment of patients with advanced GC or esophagogastric junction (EGJ) cancer. Trifluridine/tipiracil improved OS by 2.1 months in the third or further treatment line of patients with advanced GC. In a systematic investigation conducted on Chinese patients with GC, CLDN18-ARHGAP26/6 fusion was associated with signet-ring cell content and was prognostic for a worse outcome and predictive for no benefit from oxaliplatin/fluoropyrimidine-based chemotherapy. Organoid cultures represent an appealing model that may be applied for therapy response testing in the near future.

Venerito, M., et al. (2016). "Prevalence of gastric atrophy and intestinal metaplasia among patients with gastric and duodenal ulcers in saxony-anhalt, a region at increased risk for gastric cancer." United European Gastroenterology Journal 4(5): A694.

Introduction: Helicobacter pylori-induced gastric atrophy (GA) and intestinal metaplasia (IM) are risk factors for gastric ulcer (GU) and intestinal-type gastric cancer (GC). Aims & Methods: We aimed to determine the prevalence of GA and IM in patients with GU and duodenal ulcer (DU) in a tertiary hospital of Saxony- Anhalt, Germany, a region at increased risk for gastric cancer. Methods. Histology based on at least 4 gastric biopsies was available in 1073 (62.3%) out of the 1722 patients (male 60%, mean age 65.7 years) with endoscopic GU and DU diagnosed by January 1st 2004 to December 31st 2014. Demographics, intake of aspirin/non-steroidal anti-inflammatory drugs (NSAIDs), and ulcer localization were documented. Patients with positive results for at least one assay among histology, 13C-urease breath test, rapid urease test or serology were considered H. pylori-positive. Results: Overall, 47.3% of patients had GU, 42.2% had DU and 10.5% had ulcers in both localisations. The prevalence of H. pylori infection, aspirin/ NSAID intake and the presence of both risk factors was 35.1%, 38.7% and 13.0% respectively. Prevalence of extensive GA/IM (excluding mild/moderate GA/IM confined to the antrum) was significantly higher in patients with GU compared to DU (20.3% vs. 6.4%, respectively, p<0.0001). Patients with ulcers of the gastric corpus/fundus were more likely to have extensive GA/ IM compared to those with ulcers located in the gastric antrum/duodenum (OR 2.83; 95% CI: 1.868- 4.285). The prevalence of mild GA/IM was higher among patients with H. pylori infection compared to non-infected patients (20.5% vs. 12.5%, p<0.0001), whereas the prevalence of extensive GA/IM was independent of H. pylori infection (13.3% vs. 14.3%). Prevalence of GA/ IM of any grading did not differ between patients with and without aspirin/ NSAID intake (30.1% vs. 29.6%), independently from ulcer location. Conclusion: The high prevalence of GA/IM in patients with GU may account for the increased risk of intestinal-type GC in this population. The more proximal the ulcer location, the higher was the likelihood of having GA/IM. After early exclusion of a malignant ulcer, follow-up endoscopy should be offered to patients with GU and extensive GA/IM.

Venerito, M., et al. (2015). "Preneoplastic conditions are frequent in patients with gastric ulcer." Gastroenterology 148(4): S223.

Background: Helicobacter pylori (H. pylori) and aspirin/non-steroidal anti-inflammatory drugs (NSAIDs) are the most important risk factors in the pathogenesis of peptic ulcer disease (PUD). H. pylori-induced gastric atrophy (GA) and intestinal metaplasia (IM) are risk factors for the development of gastric ulcer (GU) and intestinal-type gastric cancer (GC). Aim: To determine the prevalence of GA and IM in patients with endoscopic GU and duodenal ulcer (DU) in a tertiary hospital of Germany. Methods: Patients with PUD diagnosed by endoscopy by January 1st 2006 to December 31st 2013 were identified in the digital archive of the Otto-von-Guericke University Hospital, Magdeburg. Medical reports were carefully reviewed to identify patients with PUD. Demographics, intake of aspirin/NSAIDs, and ulcer localization were documented. Histopathological features of gastric biopsies were graded according to the updated Sydney system. H. pylori infection was tested by histology, 13C-urease breath test, rapid urease test or serology and subjects with positive results for at least one assay were classified as H. pylori-positive. Results: 1238 patients with PUD were identified (male 60.3%, mean age 66.4 ± 14.6 years). Overall, 47.3% of patients had GU, 42.1% had DU and 10.6% of patients had peptic ulcer in both localizations. The prevalence of H. pylori infection, aspirin/NSAID intake and the presence of both risk factors was 41.4%, 46.4% and 18%, respectively, whereas the proportion of PUD with undefined etiology was 26.9%. Histopathological assessment of gastric mucosa on the basis of at least 4 gastric biopsies was available in 761 patients (61.5%). Overall, the prevalence of GA/IM did not differ between patients with and without H. pylori infection (31.7% vs. 34.6%) and with and without aspirin/NSAID intake (27.8% vs. 29.0%), independently from ulcer location. Prevalence of GA/IM (independent of grading) and extensive GA/IM (i.e. GA/IM in the corpus and antrum or corpus alone, excluding mild to moderate GA/IM confined to the antrum) was significantly higher in patients with GUcompared to DU(36% vs. 17.3% and 20.5% vs. 5.4%, respectively, p<0.0001). Prevalence of GA/IM in both antrum and corpus was significantly higher among patients with GU compared to DU (30.9% vs. 14.7% and 15.2% vs. 4.5%, respectively, p<0.001). These data were confirmed in the subgroup analysis of both patients with H. pylori infection and those on aspirin/NSAIDs (p<0.0001). Conclusions: GA/IM was observed in approximately one third of patients, independent of PUD etiology. Previous H. pylori infection may account for the high prevalence of GA/IM also in patients with aspirin/NSAIDassociated GU. The high prevalence of extensive GA/IM in patients with GU may account for the increased risk for intestinal-type GC in this population in which a scheduled endoscopic follow-up is mandatory.

Venerito, M., et al. (2016). "Prevalence of gastric atrophy and intestinal metaplasia among patients with gastric and duodenal ulcers in saxony-anhalt, a region at increased risk for gastric cancer." Gastroenterology 150(4): S842.

Background: Helicobacter pylori-induced gastric atrophy (GA) and intestinal metaplasia (IM) are risk factors for gastric ulcer (GU) and intestinal-type gastric cancer (GC). Aim: To determine the prevalence of GA and IM in patients with GU and duodenal ulcer (DU) in a tertiary hospital of Saxony-Anhalt, Germany, a region at increased risk for gastric cancer. Methods: Histology based on at least 4 gastric biopsies was available in 1073 (62.3%) out of the 1722 patients (male 60%, mean age 65.7 years) with endoscopic GU and DU diagnosed by January 1st 2004 to December 31st 2014. Demographics, intake of aspirin/non-steroidal anti-inflammatory drugs (NSAIDs), and ulcer localization were documented. Patients with positive results for at least one assay among histology, 13C-urease breath test, rapid urease test or serology were considered H. pylori-positive. Results: Overall, 47.3% of patients had GU, 42.2% had DU and 10.5% had ulcers in both localisations. The prevalence of H. pylori infection, aspirin/NSAID intake and the presence of both risk factors was 35.1%, 38.7% and 13.0% respectively. Prevalence of extensive GA/IM (excluding mild/moderate GA/IM confined to the antrum) was significantly higher in patients with GU compared to DU (20.3% vs. 6.4%, respectively, p<0.0001). Patients with ulcers of the gastric corpus/fundus were more likely to have extensive GA/IM compared to those with ulcers located in the gastric antrum/duodenum (OR 2.83; 95% CI: 1.868- 4.285). The prevalence of mild GA/ IM was higher among patients with H. pylori infection compared to non-infected patients (20.5% vs. 12.5%, p<0.0001), whereas the prevalence of extensive GA/IM was independent of H. pylori infection (13.3% vs. 14.3%). Prevalence of GA/IM of any grading did not differ between patients with and without aspirin/NSAID intake (30.1% vs. 29.6%), independently from ulcer location. Conclusions: The high prevalence of GA/IM in patients with GU may account for the increased risk of intestinal-type GC in this population. The more proximal the ulcer location, the higher was the likelihood of having GA/IM. After early exclusion of a malignant ulcer, follow-up endoscopy should be offered to patients with GU and extensive GA/IM.

Venerito, M., et al. (2015). "Helicobacter pylori and Gastrointestinal Malignancies." Helicobacter 20 Suppl 1: 36-39.

Helicobacter pylori infection is the principal trigger of gastric carcinogenesis and gastric cancer (GC) and remains the third leading cause of cancer-related death in both sexes worldwide. In a big Japanese study, the risk of developing GC in patients with peptic ulcer disease who received H. pylori eradication therapy and annual endoscopic surveillance for a mean of 9.9 years was significantly lower after successful eradication therapy compared to the group with persistent infection (0.21%/year and 0.45%/year, respectively, p = .049). According to a recent meta-analysis, H. pylori eradication is insufficient in GC risk reduction in subjects with advanced precancerous conditions (i.e., intestinal metaplasia and dysplasia). A microsimulation model suggested screening smokers over the age of 50 in the U.S. for serum pepsinogens. This would allow to detect advanced gastric atrophy with endoscopic follow-up of subjects testing positive as a cost-effective strategy to reduce GC mortality. In a Taiwanese study, the anti-H. pylori IgG-based test-and-treat program had lower incremental cost-effectiveness ratios than that with (13)C-urea breath test in both sexes to prevent GC whereas expected years of life lost for GC were higher and the incremental cost-effectiveness ratios of test-and-treat programs were more cost-effective in young adults (30-69 years old) than in elders (>70 years old). With respect to gastrointestinal malignancies other than GC, a meta-analysis confirmed the inverse association between H. pylori infection and esophageal adenocarcinoma. In a Finnish study, H. pylori seropositivity was associated with an increased risk of biliary tract cancers (multivariate adjusted OR 2.63; 95% CI: 1.08-6.37), another meta-analysis showed a slightly increased rate of pancreatic cancer in patients with CagA-negative strains (OR: 1.30; 95% CI: 1.02-1.65), whereas current data suggest that the association between H. pylori and colorectal neoplasms may be population dependent.

Ventayol Garcia, T., et al. (2012). "The clonal origins of gastric adenocarcinoma." Gut 61: A43-A44.

Introduction: We have previously shown that entire fields of dysplasia in the human stomach are derived from a single mutated, metaplastic gland.1 This suggests that intestinal metaplasia (IM) can be considered a field defect among which dysplasia can arise and this would indicate that adenocarcinomas derived from such dysplasia would also be clonal. Recent work published by our laboratory has indicated that familial adenomatous polyposis-associated colorectal adenomas as well as some sporadic lesions2 and dysplasia within Barrett's oesophagus3 are polyclonal. There is therefore a need to ascertain the clonality of gastric adenocarcinomas (GA). Methods: Here we screened a large cohort of GA patients for mutations in genes accounting for nearly 90% of reported mutations in GA in order assess mutation frequencies. The screening was then followed by laser capture microdissection PCR sequencing and loss of heterozygosity (LOH) analysis of the mutated specimens in order to assess clonality of GA from dysplasia and IM. Results: From the 51 patients cohort we have found 18 patients (35.3%) presenting mutations, but only one out of the 51 patients (1.9%) presented two independent mutations in a single cancer. We found 3 mutations in APC (6.3%), one in CDKN2A (2.2%), 13 in TP53 (27.7%), one in CTNNB1 (2.2%) and one in K-RAS (2.4%), but none in PIK3CA or PTEN. Our mutation frequencies are comparable to previous reports, however we observed that most functional mutations occurred as a single event despite screening multiple genes. Analysis of the multiple laser capture microdissected areas revealed multiple genotypes within the same cancer in three out of the five patients. Moreover, current LOH data shows LOH of chromosome 17 in IM and throughout the cancers in all different genotypes, suggesting that chromosome 17 LOH might have been the first hit mutation followed by mutations in TP53, and in one patient a subsequent CTNNB1 mutation. Conclusion: This suggests that cancer progression may have been initiated by LOH in intestinal metaplasia and that GA cells might become genetically diverse as the cells evolve in the tumour. Therefore, IM is likely to represent a field defect for gastric cancer.

Villarreal-Calderon, R., et al. (2012). "Overexpression of β-catenin and EPHB4 in helicobacter pylori infected mexican children with gastritis." FASEB Journal 26.

Chronic inflammation and infection are major gastric carcinogenic risk factors. As Helicobacter pylori (HP) infection is common in children, determining if HP infection is an early event in gastric carcinogenesis identifies a potential therapeutic target for reducing gastric cancer (GC) in these patients. Gastritis activity, atrophy, follicular pathology (FP), intestinal metaplasia (IM) and expression of 9 biomarkers (Ephrin Type-B Receptor 4 [EphB4], Activation-Induced Cytidine Deaminase, Caudal Type Homeobox 2 [Cdx2], p53, Macrophage Migration Inhibitory Factor, Matrix Metalloproteinase 3, α-Methylacyl-CoA Racemase, β-catenin, Ecadherin) involved in gastric carcinogenesis and progression were examined in antral biopsies from 36 HP+ and 46HP- Mexican children (mean age 8.1y) with chronic gastritis. EphB4 expression (p≤0.008), β-catenin staining intensity (p≤0.002), activity, atrophy and FP (p≤0.0002, p<0.0001 and p≤0.0007) significantly correlated with HP+ biopsies. 6 children (3 HP+) demonstrated aberrant Cdx2 expression without histological evidence of IM. Antral biopsies demonstrating preneoplastic markers may identify high risk patients who would benefit from anti-HP therapy and closer follow up surveillance.

Walker, M. M. (2003). "Is intestinal metaplasia of the stomach reversible?" Gut 52(1): 1-4.

Intestinal metaplasia (IM) of the stomach is a risk factor in developing intestinal-type gastric cancer and hence the question of reversibility is vital. There is emerging epidemiological evidence that with long term follow up, IM may be reversible although a combination of antioxidant agents and eradication of H pylori may be necessary to achieve this. The pathogenesis of IM is currently being elucidated and it is likely that a combination of bacterial, host, and environmental factors will be shown to lead to IM. In assessing gastric cancer risk, histochemical typing of IM will most probably be replaced by molecular markers.

Walker, R., et al. (2016). "Cross-disciplinary methods for personalizing screening modalities for early gastric cancer intervention." Cancer Research 76(14).

Background. Up to 80% of patients in the early stages of gastric cancer are asymptomatic, making early diagnosis and hence effective treatment challenging. The poor prognosis of patients with late diagnoses clearly necessitates the identification of markers for early detection and the development of streamlined screening protocols. This is particularly crucial in high-risk populations, for example regions in which Helicobacter Pylori infection and associated chronic inflammation, responsible for over 70% of gastric cancers worldwide, is prevalent. At present, an efficient and personalized program for early detection does not exist. Methods. Specific biomarkers for the progression of gastric cancer have been identified in preliminary studies, including CD44, Lgr5 and CD133. In retrospective tissue samples incremental increases in expression of these markers was observed during the progression from normal gastric tissue to precancerous histologic lesions such as intestinal metaplasia and ultimately dysplasia and carcinoma. We developed a mechanistic mathematical model capable of simulating these marker-positive population dynamics, calibrated using the existing clinical data. The predictive capability of the model is validated by comparison of simulated to actual marker expression patterns in an independent test cohort of endoscopic gastric biopsies taken at sequential points during individual patients' disease progression. Results. Based on clinically obtainable, patient-specific tissue conditions, the computational model can simulate the dynamics of marker-positive cells and, when calibrated and validated with clinical data from specific patient populations, may forecast disease progression and suggest optimal screening schedules for individual patients. Conclusions. The tools of mathematical oncology have the potential to directly inform clinical screening protocols. Verified prognostic factors for disease progression can be incorporated into mathematical models to improve diagnostic accuracy and allow clinically-actionable screening optimization. This can guide personalized screening schedules according to current marker expression on a case-by-case basis to achieve more efficient prognosis and reduced healthcare costs.

Walker, R., et al. (2016). "CD44, CD133 and Lgr5 as biomarkers for early detection of H. Pylori-associated gastric cancer." FASEB Journal 30.

Background Gastric cancer remains the second most common cause of cancer deaths worldwide, yet specific biomarkers for early detection remain elusive. The present work proposes an increase in stem cell prevalence during the progression through the Correa pathway from normal gastric mucosa (NM) to inflammation and intestinal metaplasia (IM), dysplasia (DS) and gastric cancer (GC), and identifies several stem cell biomarkers which demonstrate increased expression throughout this pathway. Methods Retrospective gastric tissue samples were obtained from a cohort of 63 patients from Colombia, a region where virulent CagA+ H. pylori infection and associated gastric cancer is highly prevalent. We measured variations in expression of stem cell markers CD44 (antibody #HPA005785, Sigma Aldrich, St. Louis, MO), CD133 (antibody MAB4399, Millipore, Billerica, MA) and Lgr5 (antibody ab75850, Abcam, Cambridge, MA) during disease progression. Samples were divided as follows: 10 NM; 17 IM; 10 DS and 26 GC. All cases were stained using the Ventana automated immunostainer Discovery XT (Ventana, Tucson, AZ). Scoring was conducted using the Allred scoring system featuring a proportion score and an intensity score to give a total score between 0 and 8. Results A significant increase in expression of all three stem cell markers (CD44, CD133 and Lgr5) was observed during each progression stage (NM to IM, IM to DS, and DS to GC). Statistical analysis of overall correlation between respective biomarker expression and disease stage is provided in Table 1. Expression increase between each individual stage of progression is demonstrated in Figure 1 for all 3 markers: CD44 (green), CD133 (blue) and Lgr5 (red). Statistical significance of increase at each stage is indicated by asterisks: p < 0.05 (∗), p < 0.01 (∗∗), p < 0.001 (∗∗∗). Conclusion Stem cell dynamics as represented by common epithelial stem cell markers may allow early detection of the transition from to GC in patients at increased risk for gastric cancer. (Table presented).

Walker, R., et al. (2016). "H. Pylori infection induces early expression of CD44 during the progression of gastric cancer." Laboratory Investigation 96: 206A.

Background: Poor prognosis of gastric cancer (GC) patients with late-stage diagnosis necessitates the identification of markers for early detection. CD44 is involved in cell adhesion and migration and plays a role in carcinogenesis. We propose CD44 positive (CD44+) cells as a potential biomarker for early detection of GC. Helicobacter pylori (HP) infection is the leading cause of GC worldwide and is a pathogenetic factor involved in progression from normal mucosa (NM) to chronic gastritis, intestinal metaplasia (IM) and ultimately dysplasia (DS) and invasive adenocarcinoma (GC). We measured variations in the number of CD44+ cells during each of these stages of progression both with and without HP infection. We hypothesize that CD44 expression is associated with progression of GC and the presence of HP may contribute to this expression. Design: Number of CD44+ cells was measured and compared in HP(+) gastric samples from Colombia (Cali) and in HP(-) gastric samples from Moffitt Cancer Center (MCC), Florida. We tested 63 samples from Cali [10 NM; 17 IM; 10 DS; 26 GC] and 48 from MCC [11 NM; 9 IM; 9 DS; 19 GC]. Cases were stained for CD44 using a rabbit polyclonal Ab (#HPA005785, Sigma Aldrich, St. Louis, MO and the Ventana automated immunostainer Discovery XT (Ventana, Tucson, AZ). Results: A statistically significant increase in CD44+ cells was noted during all three stages of progression in the Cali HP(+) cohort: NM to IM (p=2.5E-05), IM to DS (p=0.004) and DS to GC (p=4E-05). Interestingly, the number of CD44(+) cells for each stage was significantly higher in the HP(+) samples as compared to the HP(-) samples. In the latter, the increase in CD44+ cells between NM and IM was less prominent (p=0.006) and no increase in CD44+ cells was visible during the transition from IM to DS (p=ns). CD44(+) cells were, however, increased between DS and GC in the HP(-) samples (p=0.003). Conclusions: CD44+ cells may represent a biomarker for early detection of the transition from DS to GC, particularly in patients at increased risk for GC such as those infected with HP. HP infection induces early expression of CD44 during the carcinogenic process of GC and leads to greater CD44 expression at each stage of disease than in comparable cases without HP. (Figure Presented).

Walker, R., et al. (2018). "Toward early detection of Helicobacter pylori-associated gastric cancer." Gastric Cancer 21(2): 196-203.

BACKGROUND: Gastric cancer is typically diagnosed at a late stage, leading to poor prognoses. Helicobacter pylori is responsible for 70% of gastric cancers globally, and patients with this bacterial infection often present with early stages of the carcinogenic pathway such as inflammation or gastritis. Although many patients continue to progress to advanced-stage disease after antibacterial treatment, there are no follow-up screening protocols for patients with a history of H. pylori. METHODS: Several biomarkers (Lgr5, CD133, CD44) become upregulated during gastric carcinogenesis. A logistic regression model is developed using clinical data from 59 patients at different stages of the carcinogenic pathway to identify the likelihood of being at an advanced stage of disease for all combinations of age, sex, and marker positivity. Using these likelihood distributions and the observed rate of marker positivity increase, time to high likelihood (probability >0.8) of advanced disease for individual patients is predicted. RESULTS: A strong correlation between marker positivity and disease stage was found for all three markers. Disease stage was accurately classified by the respective regression models for more than 86% of retrospective patients. Highly patient-specific predictions of time to onset of dysplasia were made, allowing the classification of 17 patients initially diagnosed with intestinal metaplasia into high-, intermediate-, or low-risk categories. CONCLUSIONS: We present an approach designed to integrate pathology, mathematics, and statistics for detection of the earliest precancerous, treatable lesion. Given the simplicity and robustness of the framework, such technique has the potential to guide personalized screening schedules to minimize the risk of undetected malignant transformation.

Wang, J., et al. (2003). "Effect of Helicobacter pylori infection on pathologic changes of gastric mucosa." Chinese Journal of Gastroenterology 8(1): 25-28.

Background: Helicopter pylori (H. pylori) infection has been regarded as an important risk factor of chronic gastritis and peptic ulcer. Eradication of H. pylori can accelerate the healing of peptic ulcer, but whether it can affect the pathologic changes of gastric mucosa needs to be investigated. Aims: To evaluate the effect of eradication of H. pylori on the pathologic changes of gastric mucosa and its precancerous status in patients with chronic gastritis. Methods: Multicentre randomized controlled clinical trial and retrospective cohort study were conducted. All samples were selected from two rural areas of Shanghai, Jinshan and Fengxian districts, with high incidence of gastric cancer. 360 patients endoscopically diagnosed as chronic gastritis and/or duodenal ulcer with H. pylori infection were recruited and randomly divided into two groups. In the treatment group triple therapy (proton pump inhibitor or H2-receptor antagonist plus two antibiotics) was used, and in the control group cisapride was given to patients with chronic gastritis, and cimetidine to patients with duodenal ulcer. All patients were followed-up by endoscopy at the end of 1 and 4 years. Two cohorts were determined basing on the results of positive and negative H. pylori tested histologically. The biopsied specimens of gastric mucosa were reviewed by two pathologists. Results: At the end of 4 years 120 patients were followed up. Among them, 54 patients were H. pylori eradicated and 5 patients were H. pylori positive again, while 45 patients were H. pylori positive and 16 were H. pylori negative. In those who were persistent H. pylori positive, at the end of first year the proportion of active inflammation decreased (P<0.05). At the end of fourth year, the degree of chronic inflammation and intestinal metaplasia, as well as the proportion of active inflammation decreased (P<0.05). In those H. pylori were persistently positive, the degree of chronic inflammation increased at the end of first year (P<0.05), the degree of chronic inflammation, intestinal metaplasia and the proportion of active inflammation increased at the end of fourth year (P<0.05). At the end of fourth year the degree of atrophy was more significant than that at the end of first year (P<0.05). Conclusions: Eradication of H. pylori can mitigate the degree of chronic gastritis and impede the development and progress of intestinal metaplasia.

Wang, L., et al. (2011). "Expression and significance of p53 and mdm2 in atypical intestinal metaplasia and gastric carcinoma." Oncology Letters 2(4): 707-712.

Subtypes of intestinal metaplasia may have different manifestations in the carcinogenesis of gastric mucosa. The present study aimed to investigate expression of murine double minute gene 2 (mdm2) in atypical intestinal metaplasia (AIM) and its relationship to gastric carcinoma. Intestinal metaplasia (IM) specimens were obtained from 58 cases. Using a novel classification of IM, the specimens were classified according to morphological changes exhibited in the gastric mucosa; specifically, atypical intestinal metaplasia (AIM) and simple intestinal metaplasia (SIM). The gatric carcinoma specimens were then compared with types I, II and III IM based on different substances present in the mucous. Envision immunohistochemical technique was applied to the detection of the expression of p53 and mdm2 in 58 IM and 30 gastric carcinoma cases. Expression of both p53 and mdm2 proteins was found to be higher in gastric carcinomas (p53, 56.67%, 17/30 and mdm2, 53.33%, 16/30) and AIM (p53, 51.85%, 14/27 and mdm2, 51.85%, 14/27) as compared to SIM (p53, 25.81%, 8/31 and mdm2, 19.35%, 6/31) (P<0.05). A similar pattern of expression of mdm2 protein was found in type I (36.84%, 7/19), type II (38.46%, 10/26) and type III (23.08%, 3/13) IM and gastric carcinoma (53.33%, 16/30). p53 expression was higher in gastric carcinoma (56.67%) compared to type I IM (26.32%) (P<0.05). However, no differences were evident among type II (42.31%, 11/26), type III (46.15%, 6/13) IM and gastric carcinoma. AIM may reveal the precancerous nature of gastric carcinoma more clearly than SIM or the conventional IM subtypes. Additionally, AIM may be involved as a preneoplastic lesion and therefore be an effective indicator in the clinical follow-up of gastric carcinoma patients.

Wang, M. W., et al. (2003). "Gastroscopy follow-up study of premalignant gastric lesions in senile patients." World Chinese Journal of Digestology 11(9): 1279-1281.

AIM: To discover the incidence of gastric cancer in premalignant gastric lesions and to evaluate the importance of gastroscopy follow-up for gastric cancer at an early stage. METHODS: A total of 1 417 patients received endoscopy. Among them,750 patients who agreed to undergo annual surveillance endoscopy were studied. RESULTS: Among the 1 417 patients who received endoscopy, 64 had gastric cancer (4.5 %). 35.9 % of them were at their early stage. 82 cancers were detected (10.9 %) during the follow up period. 62 % of them were at their early stage (62.2 % vs 35.9 %; P < 0.005). Gastric dysplasia was frequent in gastric cancers than in non-cancer group (37.0 % vs 13.1 %; P < 0.01) Intestinal metaplasia was also more frequent in gastric cancer group than in non-cancer group (67.1 % vs 58.1 %; P < 0.01). CONCLUSION: In patients with intestinal metaplasia or dysplasia, endoscopic surveillance can detect most new tumors at an early stage.

Wang, S., et al. (2013). "SOX2 predicts prognosis and regulates cancer phenotypes via a PTEN-RB pathway in gastric carcinoma." Journal of Gastroenterology and Hepatology 28: 440-441.

Objective: During the ensuing decade transcription factor SOX2 is solidified as one of the hallmark participants throughout the developmental process in stomach. Ectopic SOX2 levels are responsible for exerting confounding impacts that enable normal cells to become tumorigenic and ultimately malignant on multistep evolution of human gastric carcinoma (GC). We thus identify SOX2 expression profiling over the course of a GC lifespan, encompassing the contributions of SOX2 to our understanding of GC tumorigenesis and prognosis. In addition, the essence of transcription factor regulation exhibited by SOX2 has served both to clarify and modulate the original formulation of cancer phenotypes in GC. Here a central role for SOX2 that governs GC establishment and progression reflected on challenges arising in analogous studies and highlighted mechanistic concepts that might be integral to a more rational elaboration of SOX2-associated traits in GC. Methods: To determine SOX2 that might participate in GC progression rather than passive bystanders, the heterogeneity of SOX2 levels was detected by western blot and immunohistochemistry in human gastric specimens stratified by pathological status. Given the correlations between SOX2 expression and clinical progression, we assessed the prognostic roles for SOX2 elaborately for further characterization. To better enumerate SOX2-relevant features, we stably expressed SOX2 in MKN28 human gastric cancer cells. This overexpression ensured SOX2 levels comparable to those in MNN28 cells carrying control vectors. By means of WST-1, we checked the effects of elevated SOX2 on GC cell proliferation in vitro. Apart from in vitro properties, MKN28 cells expressing SOX2 and control cells were injected into intravenous sites of the nude mice, partially for a direct recording of primary tumor growth, and partially for Ki67 staining on primary tumors tissues. Cell cycle and apoptosis analysis of MKN28 cells with and without SOX2 overexpression were conducted to discern any reactive attenuation in vitro, while in vivo apoptotic potential was examined by TUNEL staining on SOX2-expressing tissue specimens from primary mice tumors. The invasive capability was testified by cell invasion and migration assays in vitro and tail vein injection in vivo respectively. To uncover the mechanistic underpinning of SOX2, we applied two highthroughput genome-sequencing analyses - ChIP-DLS and cDNA expression microarray - in SOX2-expressing MKN28 cells to reveal putative targets catering to the same criteria that they not only straight attach to SOX2 promoter but also manage to take on a remarkable expression alteration subsequent to SOX2 overexpression. Guided by bioinformation analysis, we culminate in the acquisition of our favorable candidate. To verify the validity of our prediction, we deployed a series of approaches like ChIP-PCR, EMSA and luciferase report assays. Furthermore, we suppressed the expression of our predicted target with siRNA in SOX2-overexpressing MKN28 cells to re-confirm our deduction that inhibition of the predicted target might compensate a cohort of functional traits subject to SOX2 overexpression, which was supposed to exemplify both in vitro and in vivo attributes of GC cell proliferation, apoptosis, cell invasion and migration. Finally the association of PTEN and p-RB levels with that of SOX2 was assayed with immunohistochemistry in primary human GC and tumor-matched adjacent gastric tissues to answer whether contributions of SOX2, PTEN and p-RB expression correlations are well suited to be a relevant prognostic indicator group during the course of GC progression. Results: The preceding observations demonstrated that SOX2 expressions were specifically diminished with GC progression, which included normal gastric tissues and tissues derived from chronic gastritis, chronic atrophic gastritis (CAG) with intestinal metaplasia, CAG with mild dysplasia of epithelium, gastric adenocarcinoma and metastatic adenocarcinoma from stomach. The association of low SOX2 levels with GC persisted depen ent of both tumor grade and molecular subtype. Such grade and subtype dependence avails SOX2 of being clinically utilized as a prognostic marker for human GC. Furthermore, elevated SOX2 did impede proliferation, invasiveness and metastasis in vitro and in vivo. Also, SOX2 overexpression enhances apoptosis but did not affect cell cycle. These effects were exclusively attributable to the biological activities of SOX2, as indicated by the fact that equivalent overexpression of a control vector failed to impose influences alike. We proved that SOX2's ability to function in GC derived from its potency to up-regulate PTEN expression, which renders RB protein de-phosphorylated. The coordinate differential levels of these 3 functionally relevant contributors afforded the most pronounced clinical implications to GC progression and overall survival. Of note, it is intensely suggested that within this cohort, the full spectrum of reflection on worse survival are elicited via a target signature based on not only a concomitant reduction of SOX2 and PTEN levels but also a concordant identification of an increased p-RB level in human GC. Conclusion: Our compelling body of evidence highlighted that an ever-declining expression of SOX2 acted at early stages of human gastric malignancies. The bestcharacterized alteration of SOX2 profiling in GC can fully recapitulate clinical malignancy and outcome. When GC specimens were stratified based on clinical status, we read that for SOX2 expression in primary tumor tissues of a GC patient was inversely proportional to disease progression, when compared to the SOX2 level in matched adjacent gastric tissues of the same patient; moreover, metastatic GC patients displaying low SOX2 levels in their metastases normally ended up with even worse clinical prognosis such as diminished distant-free survival comparing to non-metastatic GC patients with low SOX2 expression in their primary tumors. The convergence of our findings helps to discover a notion that a subsequent up-regulation of PTEN triggered by SOX2 overexpression in GC cells serves to hyperactive the de-phosphorylation of p-RB protein, by which heterotypic interactions give rise to SOX2-imposed capacities of cell apoptosis promotion and concomitant suppression over cell proliferation and metastasis in human GC.

Wang, X., et al. (2013). "Expression of group IIA phospholipase A2 is an independent predictor of favorable outcome for patients with gastric cancer." Human Pathology 44(10): 2020-2027.

Growing evidence suggests that phospholipase A2 (PLA2) plays a pivotal role in tumorigenesis in human gastrointestinal cancer. One of the well-studied isoforms of PLA2, group IIA PLA2 (PLA2G2A), appears to exert its protumorigenic or antitumorigenic effects in a tissue-specific manner. The present study was designed to determine the expression profile and prognostic value of PLA2G2A in gastric cancer in a large Chinese cohort. By using real-time polymerase chain reaction, the amount of PLA2G2A messenger RNA in 60 pairs of fresh gastric tumors and adjacent noncancerous mucosa was measured. The immunostaining of PLA2G2A in 866 gastric cancers with paired noncancerous tissues was assayed. No expression of PLA2G2A was found in normal gastric mucosa, and focal expression of PLA2G2A was noticed in intestinal metaplasia, whereas significantly increased expression of PLA2G2A was observed in the cytoplasm of gastric cancer cells. Furthermore, the extent of PLA2G2A expression was associated with tumor size (P < .001), tumor differentiation (P = .001), T class (P < .001), N class (P < .001), and TNM stage (P < .001) of gastric cancer. Multivariate analysis showed that PLA2G2A expression was an independent predictor of survival for patients with gastric cancer (P = .024). Expression of PLA2G2A seems to be protective for patients with gastric cancer (hazard ratio, 1.423; 95% confidence interval, 1.047-1.935), and it may be a target for achieving better treatment outcomes.

Warmke, L., et al. (2015). "What is the clinical significance of intestinal metaplasia in stomach biopsies of pediatric patients?" Laboratory Investigation 95: 197A.

Background: Intestinal metaplasia (IM) of the stomach in adults has been associated with an increased risk for gastric cancer. IM is sometimes encountered in pediatrics gastric biopsies but there is very limited information in the literature regarding its clinical significance. The aim of the study was to determine the clinical significance and associations of gastric IM in pediatric patients. Design: We searched our database for IM in gastric biopsies from pediatric patients (<18 years-old) from 2000-2014. The clinical presentation, endoscopic and histologic findings were reviewed. We randomly selected age-, demographics- and clinical presentationmatched control group. Follow-up biopsy findings and clinical presentations were reviewed, when available. Chi-square test statistical analysis was used to evaluate any association. Results: We identified 23 patients with pediatric gastric IM and selected 46 patients in the control group. All IM were in the gastric antrum. 5 patients (21.7%) with IM were <10 years old and 2 (8.7%) were <5 years old. 56.5% of the patients were females; 78.3% were white. Follow-up biopsies in 6 patients (26%) >1year after original IM showed no IM. There was no statistically significant difference (i.e. <.05) in gender (p = 0.73) or race (p = 0.13) in the IM and the control group. (Table Presented) Conclusions: There is no significant difference in the demographics, clinical presentation and medications between the patients with IM and the control group. It appears that IM in pediatric patients does not have the same association or pathway to carcinogenesis as IM in adult. Larger cohort with longer follow-up, perhaps into adulthood may be required to determine the clinical significance, if any of IM in pediatric patients.

Watanabe, H., et al. (1995). "Expression of tumor-associated antigens on gastric biopsy materials." Digestive Endoscopy 7(4): 379-385.

We investigated the expressions of SLX, ST-439 and PLAP, which are regarded as having high specificity for cancer, in borderline lesions of the stomach to ascertain the significance of these potential markers in distinguishing between benign and malignant lesions. SLX, ST-439 and PLAP expressions in gastric biopsy specimens, from 73 patients with gastric lesions, were visualized using avidin-biotin-peroxidase. Although the prevalence of SLX in Group V was 90%, it was also high in intestinal metaplasia (40%) and adenoma (75%). The prevalences of ST-439 in intestinal metaplasia and adenoma grades 1 and 2 were 5, 23, and 17%, respectively. On the other hand, the prevalence of ST-439 was about 60% in adenoma grade 3 and in Groups IV and V. The prevalence and immunostaining range of ST-439 increased concomitantly with increasing grades of cytological and architectural atypia. The prevalence of PLAP in gastric biopsy materials was 30% overall, but was higher among the differentiated types. Moreover, PLAP was highly specific for cancer because of the negative immunostaining observed in benign lesions such as intestinal metaplasia and adenoma. These results suggest the following : 1) SLX is relatively non-specific for cancer and thus not useful in the pathological diagnosis of gastric lesions, and 2) borderline lesions with positive ST-439 mandate careful follow-up. Moreover, lesions with apparently extensive and intense ST-439 immunostaining may be gastric cancer and require urgent attention. Furthermore, 3) PLAP may provide additional diagnostic information useful for distinguishing between well-differentiated adenocarcinoma and borderline lesions including adenoma.

Watari, J., et al. (2019). "DNA methylation silencing of microRNA gene methylator in the precancerous background mucosa with and without gastric cancer: Analysis of the effects of H. pylori eradication and long-term aspirin use." Scientific Reports 9(1): 12559.

The risk of gastric cancer (GC) declines after Helicobacter pylori (H. pylori) eradication and long-term aspirin use. We evaluated the effects of H. pylori eradication (Cohort 1) and aspirin use (Cohort 2) on the methylation of microRNAs (miRNAs), such as miR-34c, miR-124a-3, miR-129-2, and miR-137, in the gastric mucosa with and without GC, i.e., in atrophic mucosal glands without intestinal metaplasia (non-IM) and intestinal metaplastic glands (IM). DNA was isolated from non-IM and IM separately using laser caption microdissection. In Cohort 1, H. pylori eradication was associated with a significant reduction of miR-124a-3 methylation only in non-IM, but not in IM. miR-129-2 methylation in non-IM may be a surrogate marker of GC in H. pylori-infected patients. In Cohort 2, aspirin did not reverse miRNA methylation in either non-IM or IM, irrespective of H. pylori infection. miR-129-2 methylation in non-IM was an independent predictive marker of GC in H. pylori-infected but not -eradicated patients. These results indicate that H. pylori eradication and aspirin use were less effective for improving methylation in IM than in non-IM; thus, these interventions are recommended at an early stage prior to the development of IM to prevent GC development. In addition, the effects of the interventions were not uniform for each miRNA gene.

Watari, J., et al. (2010). "Biomarkers predicting future development of gastric cancer in japanese patients with premalignant lesions after helicobacter pylori eradication." Gastroenterology 138(5): S288.

Background and Aims: Eradication of Helicobacter pylori (H. pylori) appears to reduce the development of gastric cancer. However, it is evident that gastric cancer still occurs to some degree after successful treatment. We evaluated whether two biomarkers related to carcinogenesis expressed in precancerous lesions, i.e., intestinal metaplasia (IM), can predict for gastric cancer development after eradication of H. pylori. Methods: Sixty-five H. pyloripositive patients from Japan were successfully treated and followed for a mean of 51 months with endoscopy. Group CG (n=39) patients had IM with chronic gastritis; Group DYS (n= 26) patients had IM with mucosal cancer and had undergone endoscopic resection. We analyzed them for genetic instability (GIN) and immunoperoxidase assays using a monoclonal antibody for colonic phenotype (mAb Das-1). Microsatellite instability and a loss of heterozygosity as GIN were evaluated at five microsatellite loci based on the Bethesda panel. Results: When GIN and the immunoreactivity in IM from the same patients before and after treatment were compared, these two biomarkers significantly disappeared in both Group CG and Group DYS (GIN and Das-1 reactivity; p<0.005 and p<0.01 in Group CG, p=0.08 and p<0.05 in Group DYS, respectively). By contrast, some patients became positive for both markers following eradication. Three new gastric cancers developed during the follow-up. Interestingly, all those 3 cases occurred from Group DYS, and showed immunopositivity for mAb Das-1. GIN was observed in one. Conclusions: H. pylori eradication changes GIN and the colonic phenotype of IM. IM patients with persistence of Das-1 reactivity after eradication, especially in patients from Group DYS, may have a high risk of developing gastric cancer.

Watari, J., et al. (2020). "Preventing Metachronous Gastric Cancer after the Endoscopic Resection of Gastric Epithelial Neoplasia: Roles of Helicobacter pylori Eradication and Aspirin." Gut Liver 14(3): 281-290.

Whether Helicobacter pylori eradication actually reduces the risk of metachronous gastric cancer (MGC) development remains a controversial question. In this review, we addressed this topic by reviewing the results of clinical investigations and molecular pathological analyses of the roles of H. pylori eradication and aspirin administration in the prevention of MGC. In regard to the clinical studies, the results of meta-analyses and randomized control trials differ from those of retrospective studies: the former trials show that H. pylori eradication has a preventive effect on MGC, while the latter studies do not. This discrepancy may be at least partly attributable to differences in the follow-up periods: H. pylori eradication is more likely to prevent MGC over a long-term follow-up period (≥5 years) than over a short-term follow-up period. In addition, many studies have shown that aspirin may have an additive effect on MGC-risk reduction after H. pylori eradication has been achieved. Both H. pylori eradication and aspirin use induce molecular alterations in the atrophic gastritis mucosa but not in the intestinal metaplasia. Unfortunately, the molecular pathological analyses of these interventions have been limited by short follow-up periods. Therefore, a long-term prospective cohort is needed to clarify the changes in molecular events caused by these interventions.

Waters, K., et al. (2020). "Assessment of surface cell polarity (the "four lines") distinguishes gastric dysplasia from reactive gastropathy: A comprehensive 2 institution 5-year (2008-2012) histologic and clinical review." Modern Pathology 33(3): 800.

Background: Gastric dysplasia is a risk factor for both synchronous and subsequent gastric carcinoma. Assessing dysplasia is challenging as striking nuclear atypia can accompany reactive gastritis. We previously showed that assessment of surface cytologic architecture/cell polarity (4 lines: 1) apical mucin cap, 2) base of mucin cap, 3) cytoplasm, and 4) nucleus) improved the evaluation of dysplasia in Barrett esophagus. We studied the utility of this feature in distinguishing gastric dysplasia from reactive changes and correlated with findings on follow-up (f/u) biopsies. Design: We identified all biopsied cases of incident gastric dysplasia (n=95) at two tertiary care centers over a 5-year period (2008-2012) and compared them to reactive gastropathy cases (n=60) from 2008. Demographic variables and the results of clinical and pathologic f/u were collected. Each biopsy was evaluated by 2 gastrointestinal pathologists for either maintenance or loss of the "4 lines." Results: Patients with dysplasia versus reactive gastropathy were similar in mean age (67 vs 63) and gender (44% vs. 38% male) but patients with dysplasia were more likely to be Hispanic (6% vs. 0%) or Asian (19% vs. 3%). Intestinal metaplasia (67% vs. 5%), autoimmune metaplastic atrophic gastritis (14% vs. 3%), and prevalent or prior H. pylori infection (16% vs. 0%) were more common in the dysplasia group. The "four lines" were lost in all 92 dysplasia cases with evaluable surface; 3 cases lacked surface dysplasia to evaluate. Surface cytologic architecture was maintained in all 57 cases of reactive gastropathy with evaluable surface, but 17 (28%) showed focal loss of the "4 lines" adjacent to erosion in fibrinous exudate. In the dysplasia group, 48% had low-grade dysplasia (LGD), 35% high-grade (HGD), and 16% at least intramucosal carcinoma (≥IMC). On f/u, 14% (4/28) of the LGD cases progressed to HGD and 21% (5/24) of the HGD cases progressed to ≥IMC. Progression was more common in flat lesions (56% 5/9) than polypoid ones (9%; 4/43; p<0.001). Dysplasia arising in fundic gland polyps did not progress (0/15). No cases of reactive gastritis with f/u biopsy progressed to dysplasia over 100 person-years. Conclusions: Surface cell polarity is a useful tool to differentiate gastric dysplasia from reactive gastritis and the loss of the "four lines" was associated with dysplasia and progression. This feature cannot be relied on in dysplastic cases without evaluable surface and adjacent to erosions in reactive gastropathy.

Williams, G. T. and K. Rogers (1984). "Elevated gastric juice enzymes - a marker for increased gastric cancer risk?" Clinical Oncology 10(4): 319-323.

Measurement of β-glucuronidase and lactic dehydrogenase in the fasting gastric juice of dyspeptic patients is a useful test for gastric cancer, but about 10% of patients tested have positive results without a demonstrable carcinoma. We have compared the histological features of multiple endoscopic gastric biopsies from 17 such patients with apparently false positive enzyme tests with gastric biopsies from 17 age and sex matched patients with negative enzyme tests. Epithelial dysplasia, a precancerous lesion, was found in 3 patients with positive enzyme tests but was not found in those with negative enzyme tests. Sulphomucin-containing intestinal metaplasia, another lesion which is associated with carcinoma of the stomach, was found in 8 patients with a positive enzyme test (including all 3 with dysplasia) but in only one patient with a negative enzyme test. These findings suggest that patients with positive gastric juice enzyme tests who do not have an established carcinoma form a group who are at increased risk of developing gastric cancer in the future and who may be worthy of long-term follow-up.

Wong, B. C., et al. (2004). "Helicobacter pylori eradication to prevent gastric cancer in a high-risk region of China: a randomized controlled trial." JAMA 291(2): 187‐194.

Wong, B. C. Y. (2012). "Eradication of Helicobacter pylori for prevention of gastric cancer." Journal of Gastroenterology and Hepatology 27: 5-6.

Gastric cancer remains an important issue worldwide. Prevention of gastric cancer can be achieved through eradication of Helicobacter pylori and possible chemoprevention in future. There is a strong association between Helicobacter pylori (H. pylori) and gastric cancer. Several studies were designed to address if eradication of H. pylori could reverse premalignant lesions. Correa et al treated the subjects (chronic atrophic gastritis, intestinal metaplasia, dysplasia) with anti-Hp therapy and/or b-carotene and/or vitamin C vs. placebo and showed a significant regression of pre-malignant lesions. More recent trials used gastric cancer as the endpoint, and the strategy changed to include eradication of H. pylori as the primary treatment. In our prospective randomized placebo controlled study in China, after a follow-up of 7.5 years, the overall gastric cancer incidence was reduced by 37% after eradication of H. pylori (P = 0.33)[1]. In the subgroup of patients with no baseline precancerous lesions (intestinal metaplasia or dysplasia), there is a significant reduction in the risk of developing gastric cancer (P = 0.02). We conclude that H. pylori eradication prevents the development of gastric cancer in subjects without preexisting precancerous lesions. In subjects already having precancerous lesions, the effect of H. pylori eradication may not be apparent at this time interval. For those with precancerous lesions that increased the risk of gastric cancer, we randomized them to receive celecoxib, anti-H. pylori treatment, or both, versus placebo. The two year treatment with celecoxib or anti-H pylori treatment increased the rate of regression of precancerous lesions compared with placebo. The combined treatment however did not show any significant improvement. [2]The indication for mass screen and treat for H pylori to prevent gastric cancer is still not listed in most international guidelines. A large population based study is still in need to address various issues of the effectiveness, feasibility, adverse effect and patient selection etc. In conclusion, although we have fairly good evidence that eradication of H pylori can reduce the incidence of gastric cancer, a lot of questions on feasibility and effectiveness need to be addressed before we can adopt this into the national policy.

Wong, B. C. Y., et al. (2004). "Helicobacter pylori Eradication to Prevent Gastric Cancer in a High-Risk Region of China: A Randomized Controlled Trial." Journal of the American Medical Association 291(2): 187-194.

Context: Although chronic Helicobacter pylori infection is associated with gastric cancer, the effect of H pylori treatment on prevention of gastric cancer development in chronic carriers is unknown. Objective: To determine whether treatment of H pylori infection reduces the incidence of gastric cancer. Design, Setting, and Participants: Prospective, randomized, placebo-controlled, population-based primary prevention study of 1630 healthy carriers of H pylori infection from Fujian Province, China, recruited in July 1994 and followed up until January 2002. A total of 988 participants did not have precancerous lesions (gastric atrophy, intestinal metaplasia, or gastric dysplasia) on study entry. Intervention: Patients were randomly assigned to receive H pylori eradication treatment: a 2-week course of omeprazole, 20 mg, a combination product of amoxicillin and clavulanate potassium, 750 mg, and metronidazole, 400 mg, all twice daily (n = 817); or placebo (n = 813). Main Outcome Measures: The primary outcome measure was incidence of gastric cancer during follow-up, compared between H pylori eradication and placebo groups. The secondary outcome measure was incidence of gastric cancer in patients with or without precancerous lesions, compared between the 2 groups. Results: Among the 18 new cases of gastric cancers that developed, no overall reduction was observed in participants who received H pylori eradication treatment (n = 7) compared with those who did not (n = 11) (P = .33). In a subgroup of patients with no precancerous lesions on presentation, no patient developed gastric cancer during a follow-up of 7.5 years after H pylori eradication treatment compared with those who received placebo (0 vs 6; P = .02). Smoking (hazard ratio [HR], 6.2; 95% confidence interval [CI], 2.3-16.5; P<.001) and older age (HR, 1. 10; 95% CI, 1.05-1.15; P<.001) were independent risk factors for the development of gastric cancer in this cohort. Conclusions: We found that the incidence of gastric cancer development at the population level was similar between participants receiving H pylori eradication treatment and those receiving placebo during a period of 7.5 years in a high-risk region of China. In the subgroup of H pylori carriers without precancerous lesions, eradication of H pylori significantly decreased the development of gastric cancer. Further studies to investigate the role of H pylori eradication in participants with precancerous lesions are warranted.

Wu, C. Y., et al. (2013). "Incidence of gastric adenocarcinoma among patients with intestinal metaplasia." United European Gastroenterology Journal 1(1): A572.

INTRODUCTION: Gastric intestinal metaplasia (IM) has been known as a premalignant lesion, but how harmful is the presence of IM for the development of gastric cancer (GCA) is not fully determined. AIMS&METHODS: We conducted a hospital-based cohort study based on 7,059 patients who were diagnosed for the first time between 1992 and 2010 with IM by endoscopic biopsy. The cumulative incidence and standardized incidence rate (SIR) were determined. RESULTS: The total follow-up person-year was 42,325 and the median followup duration was 5.1 years. Eighty-one patients developed GCA during the follow-up period. The 5-year and 10-year cumulative incidences of GCA were 0.9% (95% confidence interval [CI], 0.6-1.1%) and 2.0% (95% CI, 1.5-2.6%), respectively. Compared with the general population, IM patients had significantly higher risk of GCA (SIR, 2.46; 95% CI, 1.96-3.06). The SIRs of GCA decreased steadily with increasing age (3.61, 3.82, 2.39, 2.01, for age <54, 55-64, 65-74, and >75 years, respectively). Compared with patients without dysplasia (SIR, 2.01; 95% CI, 1.54-2.57), patients with dysplasia had significantly higher risk of GCA (mild-to-moderate dysplasia, SIR, 7.82; 95% CI, 3.75-14.39; severe dysplasia, SIR, 35.23; 95% CI, 15.17-69.41). CONCLUSION: IM is a risk factor for GCA with moderate increased risk, but the existence of dysplasia significantly increase the risk of GCA.

Wu, J. (2013). "Clinical pathology and recent follow-up study on gastric intraepithelial Neoplasia and gastric mucosal lesions." United European Gastroenterology Journal 1(1): A443.

INTRODUCTION: Our aim was to explore the correlations between endoscopic gastric mucosal lesions and pathological gastric intraepithelial neoplasia, and to investigate outcomes of gastric intraepithelial neoplasia after various treatments. AIMS&METHODS: A total of 18566 Chinese patients undergoing diagnostic gastroscopy, and biopsies were taken from every patients. Typing and grading of endoscopic and pathological diagnosis were performed. Among them, 130 cases of patients were given various treatments, including medication, endoscopic treatment and surgery. Three months later, re-gastroscopy was carried out, and biopsies were taken to evaluation the efficiency. RESULTS: There were 433 patients with GIN by initial pathological diagnosis. Among them, there were 367 LGIN and 66 HGIN, 348 cases accompanied with chronic gastritis, and 85 cases accompanied with localized foci. Eighty cases of Hp-positive patients with LGIN were given anti-Hp therapy. Three months later, re-gastroscopy was carried out and biopsies were taken. Our results showed that 45 cases of intraepithelial neoplasia disappeared with only chronic inflammation left. and also, 33 cases were given the original diagnoses and two cases developed into intraepithelial neoplasia of higher grade. Surgery was then performed, after that, one case of them was confirmed to have early gastric carcinoma, and the other case was diagnosed as advanced gastric carcinoma. Pathological examinations were carried out undergoing EMR or ESD treatment for 18 cases of patients with localized foci accompanied with LGIN. Results showed four cases of only chronic inflammation, 11 cases with original diagnoses maintained, and three cases of HGIN. Three months later, re-gastroscopy was carried out and biopsies were taken, the results revealed no intraepithelial neoplasia. Surgery and pathological examinations were performed for 32 cases of patients with HGIN. Our result showed that 15 cases maintained the original diagnoses, 12 cases of early gastric carcinoma and five cases of advanced gastric carcinoma. Three months later, re-gastroscopy was carried out and no relapse of foci was observed. CONCLUSION: There were various endoscopic findings of gastric intraepithelial neoplasia, which occurred frequently in localized foci and atrophic gastritis. NBI magnifying endoscopy had a value of targeted biopsy. Meanwhile, GIN occurred frequently in patients with more severe pathological inflammations under endoscope, which also had certain correlations with intestinal metaplasia.

Xiao, S. Y., et al. (2018). "Helicobacter pylori and risk of metachronous recurrence after endoscopic resection for early gastric cancer: A systematic review and metaanalysis." Journal of Digestive Diseases 19: 91.

Objective Endoscopic resection (ER) is widely accepted as the curative treatment for early gastric cancer (EGC), but risk of metachronous gastric lesions in the remnant stomach is higher than after gastrectomy. However, the impact of Helicobacter pylori (H. pylori) eradication on the development of metachronous lesions remains controversial. We conducted a systematic review with meta-analysis to evaluate H.pylori status and the incidence risk of metachronous cancer. Methods Two reviewers independently searched the following electronic databases for identifying potential studies: Pubmed, Embase, the Cochrane Library and Web of Science until the end of March 2018. Reference list of all primary studies and review articles were checked for additional reference. The risk ratio (RR) and 95% confidence interval (CI) of each study were reported as the measure of effect size. Preplanned subgroup meta-analysis was performed with regard to study design (RCT or Cohort study) and primary outcome (either dysplasia and gastric cancer or gastric cancer only). Fixed-effects meta-analysis was conducted for those with heterogeneity I2<40%. Heterogeneity test, publication bias test and sensitivity analysis were also performed. Results 20 eligible studies were identified in systematic review, 17 out of 20 studies were further included in meta-analysis. All included studies for meta-analysis were considered as high or moderate quality by using Cochrane risk of bias tool for RCT and Newcastle-Ottawa scale for cohort studies. Eradication of H.pylori was associated with overall 50% lower odds of metachronous events (including gastric cancer and dysplasia) (RR=0.50; 95%CI, 0.41-0.61) and 54% lower incidence of metachronous gastric cancer (RR=0.46; 95%CI, 0.35-0.60). Similarly, meta-analysis of prospective and retrospective studies respectively also suggested a preventive role of H.pylori eradication for metachronous recurrence. Heterogeneity and publication bias were not observed across the above studies, and sensitivity analyses showed consistent results. Furthermore, random effect meta-analysis of 7 studies (I2=73.2%, P=0.001) involving eradicated group and H.pylori noninfection population showed that occurrence of metachronous lesions after H.pylori eradication was comparable to those without H.pylori infection at the time of gastric cancer or dysplasia diagnosis (RR=0.85; 95%CI, 0.43-1.68). Four of above seven studies whose primary outcome was metachronous gastric cancer were further analyzed within fixed-effect model (I2=0.0%, P=0.776), indicating that the incidence risk of metachronous cancer was higher in the negative group than in the eradicated group though the significance was not observed (RR=0.48; 95%CI: 0.28-0.82). Publication bias was also not detected in these two groups. Conclusions Eradication of Helicobacter pylori can provide partial protection against secondary gastric neoplasm, metachronous risk was comparable between H.pylori eradication group and noninfection population. The quantitative benefit of H.pylori eradication among high-risk populations seemed greater than among asymptomatic individuals. Background gastric mucosa with intestinal metaplasia or severe atrophy and genetic or environmental coeffectors also share the determining risk factors in the occurrence of metachronous events. Studies evaluating when the eradication therapy should be performed in such patients are warranted to magnify the impact of H.pylori eradication on overall reduction in metachronous gastric lesions.

Xu, C.-p. and W.-w. Liu (1985). "Follow-up observations on chronic gastritis, intestinal metaplasia and dysplasia." Chinese Medical Journal 98(5): 347-348.

We collected 448 cases of chronic gastritis (421 chronic atrophic gastritis) from 15 institutes in different areas of China. A study on the dynamic changes in intestinal metaplasia (530 slides), dysplasia (146 slides) and gastric gland atrophy was made over a period of 2 to 10 years. In patients followed up for 5 to 10 years, the severity of glandular atrophy (Table 1) and intestinal metaplasia (Table 2) increased with age. Although in a few cases, partial remission of both disease processes occurred even after a long course (Figs 1,2). On the contrary, regression of dysplasia occurred at any age. Dysplasia regression frequency ranged from 41.54% to 78.94% in different age groups (Fig 3). Nine cases of gastric cancer were found in these patients. Four of them were found in the first 3 years of observation and 5 within 3-6.5 years (Table 3). Three cases of cancer were found in 315 patients (0.95%), with intestinal metaplasia and 6 in 112 patients (5.36%) with both intestinal metaplasia and dysplasia. It appears that dysplasia and intestinal metaplasia are closely related to gastric cancer, especially when they are moderate or severe.

Ya-Lin, Z., et al. (1997). "Mucin-histochemical study on the relationship between the intestinal metaplasia of gastric mucosa and stomach carcinoma." Chinese Journal of Clinical Oncology 24(11): 838-840.

Mucin-histochemical technics were used to analyse the mucin secretion in 117 cases of gastric carcinomas and 62 cases of chronic gastritis accompanied by intestinal metaplasia. According to the difference of the mucin secretion, the gastric carcinomas were divided into intestinal type and gastric type, and, the intestinal metaplasia was divided into large intestinal type and small intestinal type. The result showed that the positive prevalence of intestinal type of gastric carcinomas was significantly higher than that of the gastric type of gastric carcinoma (P< 0. 01). Large intestinal type metaplasia was more common in metaplastic mucosa next to intestinal type of gastric carcinoma than that in metaplastic mucosa next to gastric type of gastric carcinoma or in chronic gastritis accompanied by intestinal metaplasia (P<0.01). The origination of intestinal type of gastric carcinomas is related to the intestinal metaplasia of gastric mucosa, especially to large intestinal type of metaplasia. Follow-up of the patients with large intestinal type of metaplasia will be of value in the discovery of early gastric carcinoma.

Yamaguchi, H., et al. (2017). "A case of gastric cancer without H pylori infection and mucosal atrophy." Digestive Endoscopy 29: 59.

AIMS: We have experienced a case of an intestinal type of gastric cancer without background of mucosal atrophy. So called gatric type of cancer is rare, so we report this case. METHODS: The patient was 63 years old male. Endoscopic examination in a health center revealed an ulcerative lesion in the upper site of the stomach, however pathological examination did not show malignancy. Follow up endoscopic examination found another lesion in the lower site of the stomach and pathological examination revealed it was an intestinal type of cancer. Still we suspected the famer lesion was malignant, so we performed diagnostic ESD for the previous lesion. At the same time, we tried lifting up of the later lesion. We could not lift it up by sub-mucosal injection, so we judged there was no indication of ESD. More over pathological result for the famer lesion said it was an intestinal type of cancer and invaded muscle layer. We finally performed laparoscopic total gastrectomy. RESULTS: In this patient, H. pylori infection was negative and atrophic area of gastric mucosa was restricted at the antrum. H. pylori, class-I carcinogen for gastric cancer, causes atrophic gastritis, and most of gastric cancer are developed with a background of atrophic mucosa. Some of gastric cancer is developed without H. pylori infection, mainly in cardiac area. In this case, both of lesions were located at non-atrophic area. So we supposed these were so called gastric type of cancer, and developed without intestinal metaplasia. CONCLUSIONS: Gastric type of cancer is rare. We will report this rare case with the results of mucus staining.

Yang, H. B., et al. (2009). "H. pylori eradication prevents the progression of gastric intestinal metaplasia in reflux esophagitis patients using long-term esomeprazole." American Journal of Gastroenterology 104(7): 1642‐1649.

Yang, H. J., et al. (2020). "Diabetes mellitus is associated with an increased risk of gastric cancer: a cohort study." Gastric Cancer 23(3): 382-390.

BACKGROUND: Diabetes mellitus (DM) has been considered a potential risk factor for gastric cancer, but the evidence is conflicting. We evaluated the association of DM with incident gastric cancer in a large cohort of men and women with endoscopic assessment at baseline and during follow-up. METHODS: We performed a retrospective cohort study of 195,312 adult men and women who underwent upper endoscopy at baseline and during follow-up between 2003 and 2014. DM was defined as fasting serum glucose ≥ 126 mg/dL, self-reported history of DM or current use of antidiabetic medications. Gastric cancer was confirmed histologically. RESULTS: The prevalence of DM at baseline was 3.0% (n = 5774). Over 865,511 person-years of follow-up, 198 participants developed gastric cancer. The fully adjusted hazard ratio (HR) for incident gastric cancer comparing participants with and without DM at baseline was 1.76 [95% confidence interval (CI) 1.04-2.97; P = 0.033). When we evaluated DM as a time-varying covariate, the fully adjusted HR was 1.66 (95% CI 1.04-2.68; P = 0.036). The association between DM and incident gastric cancer did not differ by the presence of intestinal metaplasia (P for interaction = 0.61). CONCLUSIONS: In this large cohort with endoscopic follow-up, DM was independently associated with increased gastric cancer incidence. The increased risk was independent of mucosal atrophy and intestinal metaplasia and was consistent in participants with newly developed DM during follow-up. Patients with DM may require more intensive endoscopic follow-up for gastric cancer screening.

Yang, H. J., et al. (2018). "Novel risk stratification for metachronous recurrence after curative endoscopic submucosal dissection for early gastric cancer." Gastrointestinal Endoscopy 87(2): 419-428.e413.

BACKGROUND AND AIMS: This study stratified the risk of developing metachronous gastric cancer (MGC) after curative endoscopic submucosal dissection (ESD) of early gastric cancer (EGC) to enable customization of endoscopic surveillance for MGC. METHODS: A total of 1115 patients who underwent curative ESD based on the expanded criteria for differentiated EGC from 2005 to 2014 at a single tertiary hospital were enrolled in this retrospective cohort study. They were followed up with annual endoscopy for a median of 50.1 months. Helicobacter pylori and histologic intestinal metaplasia (IM) were evaluated. The Kaplan-Meier method and Cox regression analysis were used for risk stratification. RESULTS: Three risk groups were identified: group 1 comprised patients with a synchronous neoplasm; group 2 comprised male patients with corpus IM; and group 3 comprised male patients without corpus IM or female patients. The 5- and 7-year cumulative risks (95% confidence interval [CI]) for metachronous recurrence were 15.1% (95% CI, 7.7-22.5) and 26.1% (95% CI, 14.9-37.3), respectively, in group 1; 5.6% (95% CI, 3.1-8.1) and 9.3% (95% CI, 5.4-13.2), respectively, in group 2; and 3.8% (95% CI, 1.6-6.0) and 4.9% (95% CI, 2.4-7.4), respectively, in group 3 (P < .001 by log-rank test). The incidence of MGCs increased constantly even after 5 years in groups 1 and 2 but not in group 3. There was not enough evidence to show an association between H pylori eradication and metachronous recurrence in the data. CONCLUSIONS: Meticulous annual endoscopic surveillance for MGC for more than 5 years is recommended for patients with synchronous neoplasm. Endoscopic surveillance may also be extended beyond 5 years in male patients with corpus IM.

Yang, H. J., et al. (2018). "Surveillance strategy according to age after endoscopic resection of early gastric cancer." Surgical Endoscopy 32(2): 846-854.

BACKGROUND: Whether surveillance strategy after curative endoscopic submucosal dissection (ESD) for early gastric cancer (EGC) differs in young patients is unclear. This study aimed to evaluate the risk of metachronous and extragastric recurrence in young patients with EGC after curative ESD. METHODS: We retrospectively enrolled 1237 consecutive patients who underwent curative ESD for EGC from 2005 to 2014 at a single tertiary hospital. The patients were divided into group 1 (<50 years of age, n = 86), group 2 (age 50-74, n = 985), or group 3 (≥75 years of age, n = 166). The clinical characteristics and outcomes were compared among the three age groups. RESULTS: Group 1 had more frequent Helicobacter pylori infection (P < 0.001), less frequent intestinal metaplasia (P = 0.021), and more frequent undifferentiated tumors (P = 0.039). Although the 5-year risk of developing metachronous recurrence appeared to be lower in group 1 (2.7%) than in groups 2 (8.6%) or 3 (8.7%), the risk became quite similar at the 7-year follow-up (6.4, 12.7, and 8.7% for groups 1, 2, and 3, respectively; P = 0.409 by log-rank test). Extragastric recurrences developed in only 2 cases in group 2 (0.2%). CONCLUSIONS: Surveillance for metachronous and extragastric recurrence after curative ESD in patients <50 years of age should not be different from that in patients ≥50 years of age. Endoscopic surveillance for metachronous recurrence should be continued for longer than 5 years, even in young patients.

Yang, I., et al. (2015). "Different gastric microbiota compositions in two populations with high and low gastric cancer risk in Colombia." International Journal of Medical Microbiology 305: 123.

Among the inhabitants of the Colombian state of Nariño, stomach cancer rates in the Andean region around Túquerres are strikingly higher than in the coastal region around Tumaco. This is in contrast to the very similar levels of H. pylori infection, but is associated with differences in human and bacterial ancestries. In order to investigate whether bacteria other than H. pylori contribute to the differences in susceptibility between the inhabitants of the two regions, we analysed the composition of the gastric microbiota of individuals from both regions (n=20 each). In spite of very high within-population variability, we found significant differences in stomach microbiota between the two populations. We identified operative taxonomic units (OTUs) and phylogenetic clades with significant abundance differences between the two towns. This included two OTUs significantly more abundant in Túquerres, which were identified as Leptotrichia wadei and as a member of the genus Veillonella, respectively, and 16 OTUs significantly more abundant in Tumaco. Tumaco-specific OTUs included an OTU identified as a member of the genus Staphylococcus which was found in 35% of the Tumaco samples. Additionally, we identified OTUs correlated with patient characteristics such as diagnosis of intestinal metaplasia of the stomach epithelium. We also tested for correlation of the microbiota composition with the population, ancestry and cagPAI status of the infecting H. plyori strains. Follow-up studies to test candidate bacterial strains for their accelerating or protective effect on the development of H. pyloriinduced preneoplastic lesions in animal models are under way.

Yang, J. J., et al. (2019). "SCREENING UPPER ENDOSCOPY IS USEFUL FOR DETECTION AND PREVENTION OF UPPER GASTROINTESTINAL CANCERS IN LYNCH SYNDROME PATIENTS." Gastroenterology 156(6): S-179-S-180.

Background: Lynch Syndrome (LS) is the most common cause of hereditary colorectal cancer and is associated with extracolonic cancers including a 6-19% lifetime risk of gastric cancer. Gastric cancers in LS tend to be of the intestinal type that often begin as chronic gastritis and progress to intestinal metaplasia, dysplasia, and ultimately cancer. Current guidelines for gastric cancer screening in LS are conditional and based on low quality evidence. We evaluated the effectiveness of screening upper gastrointestinal (GI) cancer in LS patients at a tertiary cancer center who undergo routine screening esophagogastroduodenoscopy (EGD) every 2-5 years. Methods: We retrospectively reviewed charts from LS patients who had an EGD at our center over the past 21 years (1996-2017). Patients were included if they met one of the following criteria for a diagnosis of LS: 1) germline mutation in one of the DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS2) or the EPCAM gene; 2) LS-related cancer demonstrating deficiency in one of the DNA mismatch repair proteins or microsatellite instability; or 3) meet Amsterdam or Bethesda criteria; and underwent at least 2 screening EGDs. Patients who first presented with an upper GI cancer without prior screening EGDs were excluded. Patient characteristics, EGD and pathology reports were reviewed. Results: We identified 302 LS patients who had an EGD at our center over 21 years, but 149 patients were excluded for not meeting study criteria. The remaining 153 patients underwent a total of 606 screening EGDs with a mean of 3.96 (1-16) EGDs per patient, and a mean duration of follow-up of 9.9 years (0.31–20.1). Chronic gastritis was detected in 62 patients. Intestinal metaplasia was detected in 14 patients. Of the 62 patients with chronic gastritis, 12 (19.4%) were associated with H. pylori infection on gastric biopsy,12 showed progression to intestinal metaplasia on subsequent EGDs, but only 1 of them had both H. pylori infection and progression to intestinal metaplasia. Precancerous upper GI lesions were detected in 13 patients, including 19 duodenal adenomas, 4 ampullary adenomas and 5 gastric adenomas (1 gastric adenoma with high-grade dysplasia). One gastric cancer was detected on the second screening EGD 4.9 years after the baseline EGD. Two interval small bowel cancers (a distal duodenal and a jejunal adenocarcinoma) developed in 2 individual patients who underwent 1 preceding screening EGD 1.3 and 2.3 years prior to diagnosis. These two small bowel cancers may not be routinely seen on EGD. No interval gastric cancers developed. Conclusions: This is the largest study investigating using screening EGD in LS patients. Our data suggest that screening EGD can detect precancerous and cancerous upper GI lesions in LS patients. Further studies are needed to determine the appropriate screening interval and its cost-effectiveness. Screening EGD and pathology results [Table Presented]

Yao, J., et al. (2009). "Expressions and clinical significance of cyclooxygenase-2 and p16 in gastric cancer and its precancerous lesions." Chinese Journal of Gastroenterology 14(1): 31-34.

Background: Monitoring gastric precancerous lesions is the key point for the prevention and early diagnosis of gastric cancer. Aims: To investigate the expressions of cyclooxygenase-2 (COX-2) and p16 in gastric cancer and its precancerous lesions, and to appraise the significance for the early diagnosis of gastric cancer. Methods: Expressions of COX-2 and p16 in tissues of 20 normal gastric mucosa, 60 intestinal metaplasia, 60 gastric intraepithelial neoplasia and 60 gastric cancer were determined by immunohistochemical staining, and the relationship between the two parameters was analyzed. Results: Expression of COX-2 was increased whereas expression of p16 was decreased stepwisely with the progression of gastric lesions, in the order of normal gastric mucosa, intestinal metaplasia, intraepithelial neoplasia and cancer. The positive expression rates of COX-2 and p16 in high-grade intraepithelial neoplasia, early and advanced gastric cancer were significantly different from those in normal gastric mucosa and intestinal metaplasia (P<0.05), whereas no significance difference was found between either the former three or the latter two. The positive expression rates of COX-2 and p16 were not statistically different between small intestinal metaplasia, complete and incomplete colonic metaplasia, between early and advanced gastric cancer, while statistically significant difference was found between low-grade and high-grade intraepithelial neoplasia (P<0.05). There was a negative correlation between the expression of COX-2 and that of p16 (P<0.001). The percentage of patients with positive expression of COX-2 accompanied by negative expression of p16 in early gastric cancer was significantly more than that in high-grade intraepithelial neoplasia (P<0.05). Conclusions: The detection of COX-2, p16 or the two combined is useful for the monitoring and follow-up of gastric precancerous lesions, as well as for the screening of high-risk population of gastric cancer, which may provide an important detection method for the early diagnosis of gastric cancer.

Yeh, J. M., et al. (2010). "Cost-effectiveness of treatment and endoscopic surveillance of precancerous lesions to prevent gastric cancer." Cancer 116(12): 2941-2953.

BACKGROUND: Although surveillance for Barrett esophagus and other gastrointestinal precancerous conditions is recommended, no analogous guidelines exist for gastric lesions. The objective of this study was to estimate the clinical benefits and cost-effectiveness of treatment and endoscopic surveillance to prevent gastric cancer. METHODS: The authors developed a state-transition decision model for a cohort of US men with a recent incidental diagnosis of gastric precancerous lesions (dysplasia, intestinal metaplasia, or atrophy). Strategies included 1) no surveillance or treatment and 2) referral for surveillance and treatment, and varied by surveillance frequency (none, every 10 years, every 5 years, or every year) and treatment modality for dysplastic and cancerous lesions (surgery or endoscopic mucosal resection [EMR]). The term "post-treatment surveillance" was restricted to surveillance of individuals after treatment. Data were based on published literature and databases. Outcomes included lifetime gastric cancer risk, quality-adjusted life expectancy, lifetime costs, and incremental cost-effectiveness ratios. RESULTS: For a cohort of men with dysplasia aged 50 years, the lifetime gastric cancer risk was 5.9%. EMR with annual surveillance reduced the lifetime cancer risk by 90% and cost $39,800 per quality-adjusted life year (QALY). Addition of post-treatment surveillance every 10 years provided little incremental benefit ( approximately 5%) but cost >$1 million per QALY. Results were most sensitive to surgical risks and the proportion of lesions completely removed with EMR. For intestinal metaplasia, surveillance every 10 years reduced lifetime cancer risk by 61% and cost $544,500 per QALY. CONCLUSIONS: EMR with surveillance every 1 to 5 years for gastric dysplasia was promising for secondary cancer prevention and had a cost-effectiveness ratio that would be considered attractive in the United States. Endoscopic surveillance of less advanced lesions did not appear to be cost-effective, except possibly for immigrants from high-risk countries.

Yep-Gamarra, V., et al. (2017). "Prevalence of pre-malignant lesions in biopsies taken from gastric mucosa endoscopically normal or with gastritis." United European Gastroenterology Journal 5(5): A364-A365.

Introduction: Pre-malignant conditions and lesions of the stomach (PCLS): atrophy, intestinal metaplasia and dysplasia are risk factors for the development of stomach cancer; therefore, its diagnosis is very important to identify patients with greater probability of this malignant neoplasm. The Clinical Guidelines recommend that during endoscopy procedure, to avoid an under diagnosis, biopsies of different areas of the stomach should be taken even when no lesion is evident in order to identify PCLS that are generally multi-focal. The initial identification of patients with this type of lesions and their subsequent stratification with the OLGA and OLGUIM systems allows defining the subgroup of patients that merit follow-up because they have a higher risk of developing gastric cancer. However, there is a discrepancy between endoscopists, because it is now preferred to take biopsies directed at the lesions and not to do them systematically at fixed sites, so that no lesion is observed. Aims & Methods: We aimed to evaluate and compare the prevalence of PCLS in biopsies taken from gastric mucosa with or without lesion during the endoscopic examination. A retrospective, cross-sectional study was performed on 356 dyspeptic patients. We reviewed the reports of esophagogastroduodenoscopies at the Trujillo Regional Teaching Hospital-Perú from October 2016 to March 2017. This study included reports which were consigned diagnosis with biopsies of different areas from the stomach. These biopsies were sent in different vials. Permission was obtained from the Hospital's research committee. Those reports that had a diagnosis of stomach cancer, gastrectomy, and those with not biopsy or those in which the biopsies were still taken from the different anatomical areas were sent in a single vial were excluded. Results: Only 148 patients were admitted to the study. The mean age was 49.7+/ ≥3 years, 60% were female (CI: 52-67, 95%). 264 vials were sent with biopsies of the different areas of the stomach distributed as follows: 148 of antrum, 54 of angle and 62 of body. Only 48 (32.4%) patients had biopsies of antrum, angle and body. From 148 patients, 116 (78.4%) had an endoscopic diagnosis of normal gastritis or mucosa and 32 (21.6%) had endoscopic diagnosis of PCLS. From 116 patients with endoscopic diagnosis of gastritis or normal mucosa, LCPM was identified in 46 patients (39.6%) (p<0.001) and 1 of them were low-grade dysplasia. From 32 of patients with suspected endoscopic PCLS, the diagnosis was confirmed with histology in 26 patients (81.2%). A total of 72 patients had PCLS vs. 32 who were initially suspected (p<0.01), with a total prevalence of 48% (CI 40.7-56.6, 95%). Conclusion: Pre-malignant conditions and lesions of the stomach (PCLS) can show as normal mucosa or gastritis during endoscopic procedure. 39.9% of patients who underwent endoscopic procedure with presumptive gastritis had PCLS. PCLS may be under-diagnosed if random biopsies are not taken. Therefore, taking biopsies from areas without suspected PCLS causes a change in the clinical management of patients, both for the initial diagnosis and for the staging according to OLGA and OLGUIM systems.

Yoon, H., et al. (2016). "Risk Factors for Metachronous Gastric Neoplasms in Patients Who Underwent Endoscopic Resection of a Gastric Neoplasm." Gut Liver 10(2): 228-236.

BACKGROUND/AIMS: To identify the risk factors for metachronous gastric neoplasms in patients who underwent an endoscopic resection of a gastric neoplasm. METHODS: We prospectively collected clinicopathologic data and measured the methylation levels of HAND1, THBD, APC, and MOS in the gastric mucosa by methylation-specific real-time polymerase chain reaction in patients who underwent endoscopic resection of gastric neoplasms. RESULTS: A total of 257 patients with gastric neoplasms (113 low-grade dysplasias, 25 highgrade dysplasias, and 119 early gastric cancers) were enrolled. Metachronous gastric neoplasm developed in 7.4% of patients during a mean follow-up of 52 months. The 5-year cumulative incidence of metachronous gastric neoplasm was 4.8%. Multivariate analysis showed that moderate/severe corpus intestinal metaplasia and family history of gastric cancer were independent risk factors for metachronous gastric neoplasm development; the hazard ratios were 4.12 (95% confidence interval [CI], 1.23 to 13.87; p=0.022) and 3.52 (95% CI, 1.09 to 11.40; p=0.036), respectively. The methylation level of MOS was significantly elevated in patients with metachronous gastric neoplasms compared age- and sex-matched patients without metachronous gastric neoplasms (p=0.020). CONCLUSIONS: In patients who underwent endoscopic resection of gastric neoplasms, moderate/severe corpus intestinal metaplasia and a family history of gastric cancer were independent risk factors for metachronous gastric neoplasm, and MOS was significantly hypermethylated in patients with metachronous gastric neoplasms.

Yoon, H., et al. (2017). "Helicobacter pylori Eradication Downregulates Cellular Inhibitor of Apoptosis Protein 2 in Gastric Carcinogenesis." Gut Liver 11(1): 79-86.

BACKGROUND/AIMS: To evaluate the expression of cellular inhibitor of apoptosis protein 2 (cIAP2) during gastric carcinogenesis after Helicobacter pylori (HP) infection and after HP eradication. METHODS: We divided non-cancer patients into four groups according to the status of HP infection and atrophic gastritis (AG)/intestinal metaplasia (IM). We compared cIAP2 mRNA expression among these four groups and patients with HP-positive early gastric cancer (EGC) by using real-time polymerase chain reaction (PCR). We evaluated the expression of cIAP2 messenger RNA (mRNA)/protein by using real-time PCR/immunohistochemistry and the degree of apoptosis with a terminal deoxynucleotidyl transferasemediated nick end labeling assay before and 12 months after endoscopic submucosal dissection (ESD) in HP-positive EGC patients, regardless of whether they had undergone eradication therapy. RESULTS: The expression of cIAP2 mRNA was significantly higher in the groups with HP(+), AG/IM(+), and HP-positive EGC than in the control, HP(+), and AG/ IM(-) groups (p<0.005). In the HP eradication group, the expression of cIAP2 mRNA/protein significantly decreased (p=0.006) and apoptosis increased at the 12-month follow-up after ESD. In the HP noneradication group, the aforementioned changes were not found during the same follow-up period. CONCLUSIONS: The expression of cIAP2 increased during gastric carcinogenesis after HP infection; HP eradication in the patients who had undergone ESD for EGC reversed overexpression of cIAP2 and suppressed cell apoptosis.

Yoon, K., et al. (2017). "Dynamic Changes in Helicobacter pylori Status Following Gastric Cancer Surgery." Gut Liver 11(2): 209-215.

BACKGROUND/AIMS: Helicobacter pylori eradication is recommended in patients with early gastric cancer. However, the possibility of spontaneous regression raises a question for clinicians about the need for "retesting" postoperative H. pylori status. METHODS: Patients who underwent curative gastrectomy at Seoul National University Bundang Hospital and had a positive H. pylori status without eradication therapy at the time of gastric cancer diagnosis were prospectively enrolled in this study. H. pylori status and atrophic gastritis (AG) and intestinal metaplasia (IM) histologic status were assessed pre- and postoperatively. RESULTS: One hundred forty patients (mean age, 59.0 years; 60.7% male) underwent subtotal gastrectomy with B-I (65.0%), B-II (27.1%), Roux-en-Y (4.3%), jejunal interposition (0.7%), or proximal gastrectomy (4.3%). Preoperative presence of AG (62.9%) and IM (72.9%) was confirmed. The mean period between surgery and the last endoscopic follow-up was 38.0±25.6 months. Of the 140 patients, 80 (57.1%) were found to be persistently positive for H. pylori, and 60 (42.9%) showed spontaneous negative conversion at least once during follow-up. Of these 60 patients, eight (13.3%) showed more complex postoperative dynamic changes between negative and positive results. The spontaneous negative conversion group showed a trend of having more postoperative IM compared to the persistent H. pylori group. CONCLUSIONS: A high percentage of spontaneous regression and complex dynamic changes in H. pylori status were observed after partial gastrectomy, especially in individuals with postoperative histological IM. It is better to consider postoperative eradication therapy after retesting for H. pylori.

Yoon, K., et al. (2019). "Correlation between macrophage migration inhibitory factor and autophagy in Helicobacter pylori-associated gastric carcinogenesis." PloS One 14(2): e0211736.

The role of macrophage migration inhibitory factor (MIF) and autophagy in gastric cancer is not clear. We determined H. pylori infection status of the subjects and investigated the expression of MIF and autophagy markers (Atg5, LC3A and LC3B) in human gastric tissue at baseline. Then H. pylori eradication was done for H. pylori positive patients and MIF and Atg5 levels were investigated on each follow-up for both H. pylori-eradicated and H. pylori negative patients. Baseline tissue mRNA expression of MIF, Atg5, LC3A and LC3B was measured by real-time PCR in 453 patients (control 165, gastric dysplasia 82, and gastric cancer 206). Three hundred three patients (66.9%) had H. pylori infection at the time of enrollment. Only within H. pylori-positive group, MIF level was significantly elevated in patients with cancer than in control or dysplasia groups (P<0.05). LC3A and LC3B levels also showed significant differences within H. pylori-positive subgroups. H. pylori-positive dysplasia subgroup showed significantly lower (LC3A) (P<0.05) and higher (LC3B) mRNA levels (P<0.05) than in other subgroups. On follow-up, within H. pylori-eradicated group, Atg5 expression increased sequentially from control to dysplasia and cancer subgroups. Multiple linear regression showed autophagy markers (LC3A, LC3B, and Atg5) directly predicted MIF level (adjusted R2 = 0.492, P<0.001). Serial follow-up showed longitudinal increase in Atg5 level in general, with constantly higher levels in H. pylori-eradicated group than in -negative group. Intestinal metaplasia (IM) group initially showed higher Atg5 expression than the IM-negative group. However, it was reversed between the groups eventually because of the lower rate of increase in IM group. These results suggest a role of MIF and autophagy markers and their interaction in H. pylori-associated gastric carcinogenesis.

You, W. (2009). "Association between genetic variants of DNA base excision repair genes and evolution of precancerous gastric lesions." Gastroenterology 136(5): A300.

Base excision repair pathway may play an important role in repairing DNA damage related to Helicobacter pylori-induced inflammatory process. To evaluate the association between genetic polymorphisms of X-ray repair cross-complementing group 1 (XRCC1, Arg194Trp and Arg399Gln), adenosine diphosphage ribosyl transferase (ADPRT, Val762Ala), 8-oxoguanine DNA glycosylase (OGG1, Ser326Cys) and apurinic/apyrimidinic endonuclease 1 (APE1, Asp148Glu), and evolution of H. pylori-associated precancerous gastric lesions, a population-based cohort study was conducted in Linqu County, a high-risk area of gastric cancer in China. Genotypes were determined by PCR-based denaturing high-performance liquid chromatography and PCR-restriction fragment length polymorphism analysis in 1281 H. pylori infected subjects completing a 4.5-year follow-up. We found that subjects carrying the XRCC1-194Trp allele had an elevated chance of regression of gastric lesions [adjusted odds ratio (OR) 1.44; 95% confidence interval (CI) 1.06-1.96], whereas XRCC1-399Gln allele had a decreased chance of regression (OR 0.68; 95% CI 0.49-0.92). Stratified analysis indicated that an increased risk of progression was observed in subjects carrying XRCC1-399Gln allele (OR 1.60; 95% CI 1.09-2.36) or OGG1-326Cys allele (OR 1.95; 95% CI 1.03-3.71) with intestinal metaplasia or dysplasia at baseline, or carrying the XRCC1-399Gln allele and smoking (OR 1.58; 95% CI 1.02-2.45). Furthermore, a joint effect was observed in subjects carrying one or two hazard alleles of XRCC1-399 or OGG1-326, the ORs were 2.83 (95% CI 1.32-6.08), 2.22 (95% CI 1.24-3.98), and 2.27 (95% CI 1.26-4.10), respectively. These findings suggest that genetic polymorphisms in XRCC1-Arg194Trp, XRCC1-Arg399Gln and OGG1-Ser326Cys may play important roles in the evolution of H. pyloriassociated gastric lesions in this high-risk population.

You, W. C., et al. (1999). "Evolution of precancerous lesions in a rural Chinese population at high risk of gastric cancer." International Journal of Cancer 83(5): 615-619.

The pathogenesis of gastric cancer (GC), particularly of the intestinal type, is thought to involve a multistep and multifactorial process. Our objective was to determine the rates of transition from early to advanced gastric lesions in a population in Linqu County, China, where the GC rates are among the highest in the world. An endoscopic screening survey was launched in 1989-1990 among 3,399 residents aged 34-64 years with precancerous lesions diagnosed from biopsies taken from 7 standard locations in the stomach and from any suspicious sites. The cohort was subsequently followed, with endoscopic and histopathologic examinations conducted in 1994. Logistic regression analysis was used to estimate odds ratios (ORs) of progression to advanced lesions of various levels of severity as a function of age, sex and baseline pathology. The rates of progression were higher among older subjects, among men and among subjects with more extensive gastric lesions. 34 incident GCs were identified during the follow-up period. The ORs of GC, adjusted for age and sex, varied from 17.1, for those with baseline diagnoses of superficial intestinal metaplasia (IM), to 29.3, for those with deep IM or mild dysplasia (DYS) or IM with glandular atrophy and neck hyperplasia, to 104.2, for those with moderate or severe DYS, as compared with subjects with superficial gastritis (SG) or chronic atrophic gastritis (CAG) at baseline. Our prospective study of a high-risk population revealed sharp increases in the risk of GC and advanced precursor lesions according to the severity of lesions diagnosed at the start of follow-up.

You, W. C., et al. (2005). "Etiology and prevention of gastric cancer: a population study in a high risk area of China." Chinese Journal of Digestive Diseases 6(4): 149-154.

A series of studies has been carried out in Linqu County, Shandong Province, China, a high-risk area for gastric cancer, to investigate the risk factors associated with gastric cancer, precancerous lesions and the prevention of gastric cancer. Our studies showed that sour pancakes (a popular local food), salted foods, cigarette smoking, and family history of gastric cancer were risk factors, whereas fresh vegetables, and intake of vitamin C and calcium were inversely associated with the risk of gastric cancer. The prevalence of chronic atrophic gastritis was approximately 20% in an adult population in Linqu County, intestinal metaplasia was approximately 50%, and dysplasia was approximately 20%. A follow-up study showed that the relative risk of developing gastric cancer increased with the severity of gastric lesions, and was associated with dietary factors, cigarette smoking and H. pylori infection in this population. The findings strongly support the idea that gastric cancer is primarily determined by environmental factors and develops in a multistep progression of precancerous lesions.

Yu, Y., et al. (2018). "Risk factors for gastric intraepithelial neoplasia in Chinese adults: A case–control study." Cancer Management and Research 10: 2605-2613.

Background: Gastric carcinoma (GC) is the third most frequent malignancy and the second most common cancer-related cause of death cause worldwide. Gastric intraepithelial neoplasia (GIN) is a well-documented precancerous lesion of GC. In this case–control study, we comprehensively explored the clinical and pathological characteristics of GIN, with the aim to identify its potential risk factors. Patients and methods: A total of 630 consecutive patients who underwent endoscopic submucosal dissection or mucosal resection for GIN were initially included. The detailed characteristics of all eligible patients and well-matched healthy controls were recorded and analyzed. Both univariate and multivariate logistic regression analyses were performed and presented with odds ratio (OR) and 95% confidential interval (CI), with additional subgroup analyses based on lesion location. Results: A total of 485 GIN-eligible patients were selected, among which 156 had proximal GIN. After follow-up, 434 patients with GIN and 310 age- and gender-matched healthy controls were included in the comparative analyses. Family cancer history (FCH); alcohol abuse; tobacco abuse; intake of high sodium, preserved food, spicy food, and less fruit; Helicobacter pylori (Hp) infection; and atrophic gastritis with intestinal metaplasia were more frequent in GIN patients. Thus, FCH (OR =3.485, 95% CI: 2.031–5.981), high sodium intake (OR =2.830, 95% CI: 1.645–4.868), less fruit intake (OR =4.082, 95% CI: 2.515–6.625), Hp infection (OR =2.307, 95% CI: 1.417–3.755), and atrophic gastritis with intestinal metaplasia (OR =15.070, 95% CI: 8.999–25.237) were independent risk factors for GIN. Further subgroup analyses demonstrated that the specific independent risk factor for proximal GIN was age (OR =2.001, 95% CI: 1.003–3.994), whereas that for distal GIN was intake of high sodium (OR =3.467, 95% CI: 1.896–6.338). Conclusion: This study reported a comprehensive overview of the clinical and pathological characteristics of GIN. FCH, high sodium intake, less fruit intake, Hp infection, and atrophic gastritis were identified as the independent risk factors for GIN.

Yue, H., et al. (2018). "The significance of OLGA and OLGIM staging systems in the risk assessment of gastric cancer: a systematic review and meta-analysis." Gastric Cancer 21(4): 579-587.

BACKGROUND: Despite extensive research on the criteria for the assessment of gastric cancer risk using the Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastritis/Intestinal-Metaplasia Assessment (OLGIM) systems, no comprehensive overview or systematic summary on their use is currently available. AIM: To perform a systematic review and meta-analysis to assess the efficacy of the OLGA and OLGIM staging systems in evaluating gastric cancer risk. METHODS: We searched various databases, including PubMed, EMBASE, Medline, and Cochrane's library, for articles published before March 2017 on the association between OLGA/OLGIM stages and risk of gastric cancer. Statistical analysis was performed using RevMan 5.30 and Stata 14.0, with the odds ratio, risk ratio, and 95% confidence interval as the effect measures. RESULTS: A meta-analysis of six case-control studies and two cohort studies, comprising 2700 subjects, was performed. The meta-analysis of prospective case-control studies demonstrated a significant association between the OLGA/OLGIM stages III/IV and gastric cancer. The Newcastle-Ottawa Scale (NOS) score reflected heterogeneity in the case-control studies on OLGA. Subgroup analysis of high-quality (NOS score ≥ 5) studies showed an association between OLGA stage III/IV and increased risk of gastric cancer; the association was also high in the remaining study with low NOS score. The association between higher stages of gastritis defined by OLGA and risk of gastric cancer was significant. CONCLUSIONS: This correlation implies that close and frequent monitoring of such high-risk patients is necessary to facilitate timely diagnosis of gastric cancer.

Yun, G. W., et al. (2015). "What are the risk factors for residual tumor cells after endoscopic complete resection in gastric epithelial neoplasia?" Surgical Endoscopy 29(2): 487-492.

BACKGROUND: In early gastric cancer (EGC) and gastric adenoma, residual tumors may develop despite complete endoscopic resection (ER). To improve the chance of curative resection, we investigated the risk factors of residual tumor development in completely resected gastric epithelial neoplasia after ER. METHODS: In total, 3,879 gastric epithelial neoplasms showing complete resection after ER were examined; 46 (1.2 %) residual tumors were found upon follow-up endoscopy. Clinicopathological characteristics were evaluated between those with and without residual tumors. RESULTS: For gastric adenoma, high-grade dysplasia and severe intestinal metaplasia (IM) in the background mucosa were significantly associated with residual tumors. For EGC, poorly differentiated adenocarcinoma (PD), signet ring cell carcinoma (SRC), having a minimum lateral safety margin of <3 mm, and localization in the upper third of the stomach were significantly associated with residual tumors. Multivariate analysis revealed that a lateral safety margin of <3 mm (OR 13.8; p < 0.001), PD (OR 16.3; p = 0.014), and SRC (OR 9.8; p = 0.009) among EGC patients, and severe IM in the background mucosa (OR 9.0; p = 0.024) among gastric adenoma patients, were significantly associated with residual tumors. CONCLUSIONS: For neoplasms with undifferentiated histology (PD or SRC), short-term endoscopic follow-up may help to detect residual tumors that form after complete resection via ER. For EGC, the lateral margin may be considered safe if greater than 3 mm. However, the possibility of satellite lesions should be investigated when the gastric adenoma to be resected is surrounded by severe IM.

Zerbib, F., et al. (2000). "Long-term effects of Helicobacter pylori eradication on gastric antral mucosa in duodenal ulcer patients." European Journal of Gastroenterology and Hepatology 12(7): 719-725.

OBJECTIVES: The aim of this study was to assess the consequences of prolonged Helicobacter pylori eradication on gastric antral mucosa in duodenal ulcer patients. PATIENTS AND METHODS: Forty-three duodenal ulcer patients with confirmed H. pylori eradication after one year of follow-up were included in this retrospective study. Before H. pylori eradication and during the follow-up, four antral prepyloric biopsy samples were taken for histopathological examination and culture. Histopathological lesions were graded semi-quantitatively according to the updated Sydney System for activity, chronic inflammation, glandular atrophy and intestinal metaplasia (IM), as well as presence of lymphoid follicles. RESULTS: After a mean follow-up of 43 +/- 23 months, H. pylori eradication statistically improved all gastritis scores, including the atrophy score and the lymphoid follicle score but excluding the IM score. H. pylori eradication resulted in normalization of gastric mucosa in 51.2% of patients and a significantly lower proportion of patients with non-atrophic gastritis and atrophic gastritis without IM. Atrophy totally disappeared in 16/29 patients (55.2%) in whom IM was absent. No predictive factor for regression of atrophy or normalization of gastric mucosa was identified. CONCLUSION: In duodenal ulcer patients, prolonged absence (more than one year) of H. pylori can lead to normalization of the antral mucosa and the disappearance of mucosa-associated lymphoid tissue, as well as the regression of antral atrophy. Long-term studies involving selected patients with atrophy and IM which persist after H. pylori eradication are needed to determine the potential benefits of treating H. pylori gastritis with regard to gastric cancer prevention.

Zhang, H. Y., et al. (2018). "Risk factors for development of gastric cancer in chronic atrophic gastritis: A long-term follow-up study." World Chinese Journal of Digestology 26(31): 1812-1817.

AIM To identify the risk factors for the development of gastric cancer (GC) in atrophic gastritis patients during a long-term follow-up. METHODS This study enrolled 522 chronic atrophic gastritis patients who underwent gastroscopy and pathological diagnosis and completed endoscopic follow-up for more than 5 years in the Affiliated Hospital of Qingdao University from 2003 to 2007. The following parameters were collected: age, gender, degree of gastric mucosal lesions, survival time, and survival status. Baseline clinical and histological features are analyzed as potential risk factors for the development of GC by Cox regression analysis. RESULTS After an average follow-up period of 7.57 years ± 1.74 years, 23 of 522 patients with chronic atrophic gastritis were diagnosed with GC, with an incidence of 4.41% (23/522), of whom 11 had poorly differentiated adenocarcinomas, 7 had moderately differentiated adenocarcinomas, 2 had well differentiated adenocarcinomas, 2 had neuroendocrine carcinoma, and 1 had malignant lymphoma. Male gender (P = 0.030, HR = 2.464), age > 55 years (P = 0.021, HR = 2.584), CAG with intestinal metaplasia (P = 0.014, HR = 6.261), CAG with mild to moderate atypical hyperplasia (P = 0.020, HR = 6.504), and CAG with severe atypical hyperplasia (P = 0.015, HR = 22.314) were identified to be risk factors for the development of GC in patients with chronic atrophic gastritis. CONCLUSION Male gender, age > 55 years, and the degree of gastric mucosal lesions are risk factors for GC in underlying mucosal atrophy. Patients with chronic atrophic gastritis with severe dysplasia are at the highest risk, and early endoscopic treatment is recommended after diagnosis.

Zhang, L., et al. (2018). "Occurrence of gastric cancer in patients with atrophic gastritis during long-term follow-up." Scandinavian Journal of Gastroenterology 53(7): 843-848.

BACKGROUND: Additional data on the incidence of gastric neoplasia in the Chinese atrophic gastritis (AG) population during long-term follow-up are needed and the influence of the endoscopic surveillance interval on gastric neoplasia occurrence remains unknown. AIMS: Retrospectively investigated the occurrence of gastric cancer (GC) and precancerous lesions in AG patients during long-term follow-up and assessed risk factors, such as the endoscopic surveillance interval for the development of gastric neoplasia. METHODS: This study enrolled 332 AG patients who underwent initial gastroscopy from 2002 to 2005. Following parameters were collected: age, gender, smoking history, H. pylori infection, location of atrophy and intestinal metaplasia (IM), surveillance interval, follow-up duration, and neoplasia occurrence. RESULTS: Gastric neoplasia was diagnosed in 16 patients. The annual incidence rates per person-year of total gastric neoplasia, gastric high-grade intraepithelial neoplasia (HGIN), early GC and advanced GC were 0.53%, 0.07%, 0.20% and 0.33%, respectively. A multivariate Cox analysis not accounting for the extent of AG and/or IM showed that the risk factors for GC development among AG patients included the presence of AG and/or IM involving both antral and corporal (p<.001, HR 2.898) and H. pylori infection (p=.018, HR 3.946). In the extensive AG and/or IM group, a 2- to 3-year surveillance interval might be instructive in early detection of GC (p=.008, HR 0.015). CONCLUSIONS: Our data reveal an annual incidence rate of 0.53% per person-year for GC and HGIN in AG patients. A 2- to 3-year surveillance interval may be suitable for patients with extensive AG and/or IM.

Zhang, L. Y., et al. (2018). "Efficacy and safety of using premedication with simethicone/Pronase during upper gastrointestinal endoscopy examination with sedation: a single center, prospective, single blinded, randomized controlled trial." Digestive Endoscopy 30(1): 57‐64.

Zhang, M., et al. (2016). "[Analysis of the efficacy of gastric cancer screening in rural population in Henan Province]." Zhonghua Zhong Liu Za Zhi. Chinese Journal of Oncology 38(1): 73-77.

OBJECTIVE: To analyze the efficacy of endoscopic screening for gastric cancer in rural population in high risk areas of upper gastrointestinal cancer in Henan province. METHODS: Subjects aged 40-69 years in the high risk areas were selected to participate in the endoscopic screening based on the cluster sampling, and screening-positive subjects were sampled for pathological examination. The data of screening were summarized and the detection rates of severe chronic atrophic gastritis, severe intestinal metaplasia, low grade intraepithelial neoplasia, high grade intraepithelial neoplasia, early and middle-late cancer were calculated, and the constituent ratio of early cancer cases was calculated. The detection rates and early diagnosis rates for the first round screening and follow-up screening were compared. RESULTS: In the 5 years, a total of 88 263 subjects were endoscopically examined in the first round screening and 4 004 subjects were diagnosed with low grade intraepithelial neoplasia or above (the detection rate was 4.54%), in which 3 256 cases were with low grade intraepithelial neoplasia (the detection rate of 3.69%), 366 cases with high grade intraepithelial neoplasia (the rate of 0.41%), 199 cases with early cancer (the rate of 0.22%) and 183 cases with middle-late cancer (the rate of 0.21%). The number of cases of high grade intraepithelial neoplasia and early cancer was 565 and the early diagnosis rate was 75.53%. 1 894 subjects with severe chronic atrophic gastritis, severe intestinal metaplasia and low grade intraepithelial were followed up with a compliance of 66.32%. A total of 45 cases of early cancer were diagnosed, with a detection rate of 2.38% and early diagnosis rate of 100%. The detection rate and early diagnosis rate in the follow-up screening were both statistically significantly higher than that in the first round screening (P<0.01 for both). CONCLUSION: The efficacy of endoscopic screening for gastric cancer is significant in high risk areas of upper gastrointestinal cancer, and improving the quality of follow-up screening will achieve a better performance of the screening.

Zhang, Y., et al. (2014). "Methylation status of blood leukocyte DNA and risk of gastric cancer in a high-risk Chinese population." Cancer Epidemiology, Biomarkers and Prevention 23(10): 2019-2026.

BACKGROUND: To evaluate the relationship between methylation status of blood leukocyte DNA and risk of gastric cancer, a population-based study was conducted in Linqu County. METHODS: Methylation levels of IGFII and N33 were determined by quantitative methylation-specific PCR. The temporal trend of methylation levels during gastric cancer development was investigated in 133 gastric cancer cases from two cohorts with pre- and/or post-gastric cancer samples. As the references of pre-GCs, 204 intestinal metaplasia (IM) or dysplasia (DYS) subjects who did not progress to gastric cancer during the follow-up period were selected. Meanwhile, 285 subjects with superficial gastritis/chronic atrophic gastritis (SG/CAG) were also selected as controls. RESULTS: IGFII median methylation level was significantly higher in gastric cancer cases than those with SG/CAG (61.47% vs. 49.73%; P < 0.001). IGFII and N33 methylation levels were elevated at least 5 years ahead of clinical gastric cancer diagnosis comparing with SG/CAG (63.38% vs. 49.73% for IGFII, 9.12% vs. 5.70% for N33; all P < 0.001). Furthermore, the frequency of hypermethylated IGFII was markedly increased in IM or DYS subjects who progressed to gastric cancer in contrast to those who remained with IM and DYS, and adjusted ORs were 12.52 [95% confidence interval (CI), 3.81-41.15] for IM and 10.12 (95% CI, 2.68-38.22) for DYS. Similar results were also found for N33 in subjects with IM (OR, 3.77; 95% CI, 1.20-11.86). CONCLUSIONS: Our findings suggested that hypermethylated IGFII and N33 in blood leukocyte DNA were associated with risk of gastric cancer in a Chinese population. IMPACT: IGFII and N33 methylation status may be related to gastric carcinogenesis.

Zheng, Y., et al. (2010). "Expression of p53, c-erbB-2 and Ki67 in intestinal metaplasia and gastric carcinoma." World Journal of Gastroenterology 16(3): 339-344.

AIM: To compare two types of classification of intestinal metaplasia (IM) of the stomach and to explore their relationship to gastric carcinoma. METHODS: Forty-seven cases of gastric IM were classified into type I, type II or type III according to mucin histochemical staining and compared with a novel classification in which the specimens were classified into simple IM (SIM) or atypical IM according to polymorphism in terms of atypical changes of the metaplastic epithelium. Forty-seven IM and thirty-seven gastric carcinoma samples were stained for p53, c-erbB-2 and Ki67 proteins by Envision immunohistochemical technique. RESULTS: There were no significant differences in the expression of p53 and c-erbB-2 among type I, type II, type III IM and gastric carcinomas. The positive expression rate of Ki67 was significantly higher in gastric carcinomas than in type I IM while no significant Ki67 expression differences were observed among type II, type III IM and gastric carcinomas. The expression of p53, c-erbB-2 and Ki67 proteins in 20 SIM, 27 Atypical IM and 37 gastric carcinomas showed significant differences between SIM and gastric carcinomas while no significant differences were observed between Atypical IM and gastric carcinomas. CONCLUSION: Atypical IM may better reveal the precancerous nature of IM and could be a helpful indicator in the clinical follow up of patients.

Zheng, Z. X., et al. (2013). "Intestinal stem cell marker LGR5 expression during gastric carcinogenesis." World Journal of Gastroenterology 19(46): 8714-8721.

AIM: To investigate the differential expression of leucine-rich repeat-containing G protein-coupled receptor 5 (LGR5) in gastric cancer tissues and its significance related to tumor growth and spread. METHODS: Formalin-fixed biopsy specimens of intestinal metaplasia (n = 90), dysplasia (n = 53), gastric adenocarcinoma (n = 180), metastases in lymph nodes and the liver (n = 15), and lesion-adjacent normal gastric mucosa (controls; n = 145) were obtained for analysis from the Peking University Cancer Hospital's Department of Pathology and Gastrointestinal Surgery tissue archives (January 2003 to December 2011). The biopsied patients' demographic and clinicopathologic data were retrieved from the hospital's medical records database. Each specimen was subjected to histopathological typing to classify the tumor node metastasis (TNM) stage and to immunohistochemistry staining to detect the expression of the cancer stem cell marker LGR5. The intergroup differences in LGR5 expression were assessed by Spearman's rank correlation analysis, and the relationship between LGR5 expression level and the patients' clinicopathological characteristics was evaluated by the χ(2) test or Fisher's exact test. RESULTS: Significantly more gastric cancer tissues showed LGR5(+) staining than normal control tissues (all P < 0.01), with immunoreactivity detected in 72.2% (65/90) and 50.9% (27/53) of intestinal metaplasia and dysplasia specimens, respectively, 52.8% (95/180) of gastric adenocarcinoma specimens, and 73.3%% (11/15) of metastasis specimens, but 26.9% (39/145) of lesion-adjacent normal gastric mucosa specimens. Comparison of the intensity of LGR5(+) staining showed an increasing trend that generally followed increasing dedifferentiation and tumor spread (normal tissue < dysplasia, < gastric adenocarcinoma <InvalidTagstasis; all P < 0.001), with the exception of expression level detected in intestinal metaplasia which was higher than that in normal gastric tissues (P < 0.001). Moreover, gastric cancer-associated enhanced expression of LGR5 was found to be signiﬁcantly associated with age, tumor differentiation, Lauren type and TNM stage (I + II vs III + IV) (all P < 0.05), but not with sex, tumor site, location, size, histology, lymphovascular invasion, depth of invasion, lymph node metastasis or distant metastasis. Patients with LGR5(+) gastric cancer specimens and without signs of metastasis from the original biopsy experienced more frequent rates of recurrence or metastasis during follow-up than patients with LGR5(-) specimens (P < 0.05). CONCLUSION: Enhanced LGR5 is related to progressive dedifferentiation and metastasis of gastric cancer, indicating the potential of this receptor as an early diagnostic and prognostic biomarker.

Zhou, L., et al. (2018). "HELICOBACTER PYLORI ERADICATION THERAPY TO PREVENT GASTRIC CANCER IN CHINA POPULATION: A META-ANALYSIS." Gastroenterology 154(6): S-1065.

Background China is a country with high incidence of gastric cancer. An estimate of 952,000 new cases of gastric cancer occurred worldwide in 2012, more than two fifths of which happened in China. As the major cause of gastric cancer, eradication of Helicobacter pylori(H.pylori) has been proved to reduce the risk of gastric cancer by randomized controlled trials. However, there is no meta-analysis addressing the role of H.pylorieradication in preventing gastric cancer in Chinese population. Objective Toexplore whether H. pylori eradication therapycould decreasethe risk of gastric cancer in Chinese population. Methods Chinese and English electronic database and trial registries were searched through August 2017, including China National Knowledge of Infrastructure (CNKI), Chongqing VIP, Wanfang Data, SinoMed, PubMed, Embase, Cochrane, Medline et al. Studies were selected according to criteria: a) RCT, quasi-RCT, Cohort Studies or Observational studies, b) Subjects were from Chinese mainland and Hong Kong, Macao and Taiwan region, and were H. pylori positive before the Study, c) H.pylori eradication therapy was performed and follow-ups for 2 or more years were conducted, d) the cases/incidence of gastric cancer, or OR(odd ratio)/RR(risk ratio) was reported. Additionally, subgroup analyses were conducted. Results A total of 3657 articles were found and eventually 6 were enrolled intothis meta-analysis. In all 6 studies a total of 6727 subjects were included, 3304 of which were in eradication group and 3423 in control. After a follow-up of 2 or more years, 33 gastric cancers occurred in eradication group versus 60 in control (RR: 0.56; 95%CI: 0.31 to 0.98). 3 studies described the pathological state at baseline, in which 1012 subjects with no precancerous lesions (chronic atrophic gastritis, intestinal metaplasia or dysplasia) were analyzed and the gastric cancer incidence was 0/609 (eradication group) versus 7/403 (control)(RR: 0.11; 95% CI: 0.01 to 0.89),1656 subjects with precancerous lesions were analyzed, the incidence was 12/726(eradication)versus 12/930(control)(RR: 1.30; 95% CI: 0.37 to 4.61). 6 studies were divided into two subgroups based on the regional gastric cancer incidence and the analysis results showed that for areas with very high gastric cancer incidence (more than 50/100,000), the effect of H. pylori eradication on preventing gastric cancer was maximized than those with a relatively lower incidence (RR 0.22 versus RR 0.73). Conclusion H. pylori eradication therapy can decrease the risk of gastric cancer in Chinese population, especially for those with no precancerous lesions and from areas with very high gastric cancer incidence

Zhou, L., et al. (2003). "A five-year follow-up study on the pathological changes of gastric mucosa after H. pylori eradication." Chinese Medical Journal 116(1): 11-14.

Objectives. To investigate the relationship between H. pylori infection, gastric cancer and other gastric diseases through the changes in gastric mucosa and the status of different gastric diseases within 5 years after H. pylori eradication in H. pylori-positive subjects in a high incidence region of gastric cancer. Methods. One thousand and six adults were selected from the general population in Yantai, Shandong province, a high incidence region for gastric cancer in China. Gastroscopy and Campylobacter-like organism (CLO) testing were performed on all subjects. Biopsy samples from the gastric antrum and body were obtained for histology and assessment of H. pylori infection. All H. pylori-positive subjects were then randomly divided into two groups: treatment group receiving Omeprazole Amoxicillin Clarythromycin (OAC) triple therapy and placebo as controls. These subjects were endoscopically followed up in the second and fifth year. We compared the endoscopic appearance and histology of the biopsy specimens from the same site obtained at the first and last visits. Results. All 552 H. pylori-positive subjects were randomly and evenly divided into treatment group or control group. During the five-year follow-up, the numbers of patients who continued to be negative or positive for H. pylori were 161 and 198, respectively. Statistical analysis revealed that: 1 At the initial visit, there were no significant differences in the severity and activity of inflammation, atrophy and intestinal metaplasia between the biopsy specimens from the antrum and body respectively in both groups. 2 The severity and activity of inflammation in both the antrum and body were markedly reduced after H. pylori eradication ( P = 0.000). 3 Within five years after H. pylori eradication, intestinal metaplasia in the antrum either regressed or had no progression, while the proportion of intestinal metaplasia in the H. pylori-positive group increased significantly ( P = 0.032). 4 After H. pylori eradication, the atrophy in both the antrum and body had no significant regression. The P value was 0.223 and 0.402, respectively. Conclusions. H. pylori eradication results in remarkable reduction in the severity and activity of chronic gastritis, marked resolution of intestinal metaplasia in the antrum. On the other hand, continuous H. pylori infection leads to progressive aggravation of atrophy and intestinal metaplasia.

Zhou, L. Y., et al. (2014). "Relationship of Helicobacter pylori eradication with gastric cancer and gastric mucosal histological changes: A 10-year follow-up study." Chinese Medical Journal 127(8): 1454-1458.

Background Helicobacter pylori (Hp) is a common and potentially curable cause of gastric mucosa lesion. This study investigated the relationship of Hp infection with histological changes in gastric mucosa and gastric cancer in Hp-positive patients compared with Hp-eradication patients followed up for ten years. Methods From an initial group of 1 006 adults, 552 Hp-positive subjects were randomly assigned to a treatment group (T; n=276) or a placebo group (P; n=276). In the randomized, double-blind, placebo-controlled, parallel trial, T group subjects received oral doses of omeprazole, amoxicillin and clarithromycin for 1 week; those in the P group received a placebo. One month after treatment ended, a 13C urea breath test was performed, and Hp was undetectable in 88.89% of the T group. All subjects were followed at 1, 5, 8, and 10 years after treatment, with endoscopy and biopsies for histological examination. Results Gastric mucosa inflammation was significantly milder in the T group than that in the P group one year after Hp eradication and this persisted for 10 years. Glandular atrophy and intestinal metaplasia (IM) had deteriorated in both groups during ten years. However, the increased score of glandular atrophy at both the gastric antrum and corpus, and IM only at the gastric antrum, in the P group was more obvious than that in the T group. During the 10 years, 9 patients were diagnosed with gastric cancer (2 in the T group; 7 in the P group; P=0.176). When mucosal atrophy was absent at the gastric antrum and corpus when entering the study, the incidence of gastric cancer in the P group (n=6) was much higher than that in the T group (n=0, P=0.013). Conclusions Hp eradication may significantly diminish and help halt progression of gastric mucosal inflammation and delay the development of IM and atrophy gastritis. Hp eradication is helpful for reducing the risk for gastric cancer, especially in the early stage of Hp infection.

Zhou, L. Y., et al. (2003). "[Changes of gastric mucosa histopathology after Helicobacter pylori eradication]." Zhonghua Nei Ke Za Zhi. Chinese Journal of Internal Medicine 42(3): 162-164.

OBJECTIVE: To investigate the relationship between Helicobacter pylori (Hp) infection and gastric cancer through the changes of gastric mucosa histopathology within 5 years after Hp eradication in Hp-positive subjects in the high incidence region of gastric cancer. METHODS: One thousand and six adults were selected from general population in Yantai, Shandong Province, the high incidence region of gastric cancer. Gastroscopy and CLO test were performed in all subjects. Biopsy samples from the gastric antrum and body were obtained for histology and assessment of Hp infection. All the Hp-positive subjects were then randomly divided into two groups: treatment group receiving OAC triple therapy and placebo as controls. These subjects were endoscopically followed up in the second and fifth year. In this article, we compared the endoscopic appearance and histology of the biopsy specimens from the same site obtained at the first and final visit. Statistical analysis was done by chi(2) test. RESULTS: All the 552 Hp-positive subjects were randomly divided into treatment group or control group, 276 in each. During the five-year follow-up, the number of patients who continued to be negative or positive for Hp was 161 and 198, respectively. Statistical analysis revealed that: (1) At the initial visit, there were no significant differences in the severity and activity of inflammation between the biopsy specimens from the antrum (P = 0.105) and body (P = 0.084) in both groups. But the proportion of atrophy and intestinal metaplasia in the antrum was much higher than that in the body (P = 0.000). (2) The severity and activity of inflammation in both the antrum and body were markedly reduced after Hp eradication (P = 0.000). (3) Within the five years after Hp eradication, intestinal metaplasia in the antrum regressed or had no progression, while the proportion of intestinal metaplasia in the Hp-positive group increased significantly (P = 0.032). (4) After Hp eradication, the atrophy in both the antrum and body had no significant regression. P value was 0.223 and 0.402, respectively. CONCLUSIONS: Hp eradication results in remarkable reduction in the severity and activity of chronic gastritis, marked resolution of intestinal metaplasia in the antrum. On the other hand, continued Hp infection leads to progressive aggrevation of atrophy and intestinal metaplasia.

Zhu, F., et al. (2017). "Helicobacter and other risk factors in a prospective cohort in Singapore undergoing surveillance for gastric cancer." Helicobacter 22: 14.

Background/Objectives: The Gastric Cancer Epidemiology and Molecular Genetics Program (GCEP) is a prospective multi-centre study initialized in 2004 to identify predictive risk factors for gastric cancer in the Singapore Chinese population. Method: Chinese subjects aged >50 years were recruited and offered endoscopy surveillance for a minimum of 5 years. All subjects gave informed consent. Outcome measure is the detection of early gastric neoplasia (EGN), including high-grade dysplasia or adenocarcinoma. Risk factors (RF) satisfying P<.15 in univariate analysis were entered in backwards regression modelling. Area under receiver-operating curve (AUC) in identifying EGN was calculated. Results: 2980 Chinese with mean age 59±7 years were recruited and completed 5 years of surveillance in January 2016. Twenty-one EGNs were detected during surveillance. Helicobacter pylori (Hp) was detected in 1278 subjects (43%) and eradicated in 1229 of them. Eight RFs including age, education, smoking, alcohol consumption, Hp seropositivity, serum pepsinogen index (PGI), atrophic gastritis, and intestinal metaplasia were selected for backward regression. We identified a risk prediction model including age >70, smoking, serum PGI and Hp, with AUC of 0.74 (95%CI 0.63-0.85). The model identified a high-risk group with >2 of 4 RF comprising 25% of the cohort and were at 13-fold increased risk of EGN compared to those with no RF, and included 57% of EGN. Conclusions: Individuals with >2 of 4 RF (age >70, smoking, serum PGI, Hp) comprised 25% of the cohort and were at 13-fold increased risk of EGN. These criteria could be useful to risk-stratify high-risk individuals for endoscopic surveillance to detect EGN.

Zhu, F., et al. (2015). "Identification of individuals at high risk of gastric cancer for targeted endoscopic screening." Journal of Gastroenterology and Hepatology (Australia) 30: 82.

Background: Endoscopic screening for gastric cancer is useful for detection of early gastric neoplasia (EGN); however, there is scant data to guide selection of individuals at increased risk. A prospective multicenter cohort study was initialized in 2004 to identify predictive risk factors for gastric cancer in the Singapore Chinese population. Objectives: The aim of the study is to identify individuals at high risk of gastric cancer. Method: Chinese subjects aged >50 years were recruited and endoscopic surveillance offered for at least 5 years. The outcome measure is the detection of EGN, including high grade dysplasia or adenocarcinoma. Risk factors (RF) were identified by univariate analysis; those satisfying P<0.15 were entered in backward regression model. Receiver operating characteristic analysis was performed. Results: Three thousand thirty-three Chinese with mean age 59 ± 7 years were recruited. The study is still in progress and will be completed by 2015. Of subjects, 2649 with complete data were analyzed. The most parsimonious model in risk prediction included four RF: age >70 years, smoking, serum pepsin-ogen index (PGI), and intestinal metaplasia (IM) with adjusted odds ratios (95% CI) of 3.17 (1.19-8.47), 3.49 (1.45-8.41), 3.80 (1.33- 10.91), and 4.167(1.20-14.50), respectively. The area under curve (AUC) in identifying EGN was 0.76 (95% CI 0.64-0.87). Of the cohort, 64% and 91% of EGN had at least one of these 4 RFs. The cohort was grouped into high risk (HR), moderate risk (MR), and average risk (AR) based on RF >2, 1, and 0, respectively. Prevalence of EGN in the HR, MR, and AR groups was 2.3%, 0.5%, and 0.2%, respectively. Subjects in the HR group had 11.33-fold (95% CI 2.55-50.40) increased prevalence of EGN compared with those with no RF. Conclusions: In our study, individuals with >2 of 4 RFs (age >70 years, smoking, serum PGI, and IM) comprised 21% of the cohort and were at 11-fold increased risk of EGN. These criteria could be useful to risk-stratify high-risk individuals for endoscopic surveillance to detect EGN.

Zhu, F., et al. (2009). "Genetic factors associated with intestinal metaplasia in a high risk Singapore-Chinese population: a cohort study." BMC Gastroenterology 9: 76.

BACKGROUND: Intestinal metaplasia (IM) is an important precursor lesion in the development of gastric cancer (GC). The aim of this study was to investigate genetic factors previously linked to GC risk for their possible association with IM. A total of 18 polymorphisms in 14 candidate genes were evaluated in a Singapore-Chinese population at high risk of developing GC. METHODS: Genotype frequencies were compared between individuals presenting with (n = 128) or without (n = 246) IM by both univariate and multivariate analysis. RESULTS: Carriers of the NQO1 609 T allele showed an association with IM in individuals who were seropositive for Helicobacter pylori (HP+; OR = 2.61, 95%CI: 1.18-5.80, P = .018). The IL-10 819 C allele was also associated with IM in HP+ individuals (OR = 2.32, 95%CI: 1.21-4.43, P = 0.011), while the PTPN11 A allele was associated with IM in HP- individuals (OR = 2.51, 95%CI: 1.16-5.40, P = 0.019), but showed an inverse association in HP+ subjects (OR = 0.46, 95%CI: 0.21-0.99, P = 0.048). CONCLUSION: Polymorphisms in NQO1, IL-10 and PTPN11, in combination with HP status, could be used to identify individuals who are more likely to develop IM and therefore GC.

Zhu, S., et al. (2002). "The interventional effect of folic acid on the development of gastric and other gastrointestinal cancers - Clinical trial and follow-up for seven years." Chinese Journal of Gastroenterology 7(2): 73-78.

Aims: To evaluate the interventional roles of folic acid and β-carotene in chemoprevention of gastric and other gastrointestinal cancers. Methods: In a randomized, double-blind, placebo-controlled trial, a total of 216 patients with atrophic gastritis were assigned to one of the four groups: 1 folate (20 mg per day plus vitamin B12 1 mg i.m. per month for one year, then folate 20 mg twice a week plus vitamin B12 1 mg per three months for the next year); 2 natural β-carotene (N-βC, 30 mg per day in the first year, then 30 mg twice a week for the next year); 3 synthetic β-carotene (S-βC, administered as in N-βC); 4 placebo. All patients were followed-up from 1994 to 2001. Results: A total of 5 new cases of gastrointestinal cancers were diagnosed in the placebo group (3 gastric cancer, 1 colonic cancer and 1 esophageal cancer). There was one gastric cancer in each of N-βC group and S-βC group, but none in folate group. Taking gastric cancer as the end point, each of the three interventional groups did not reach statistical significance, but the combined interventional group almost reached (P=0.06). Taking gastrointestinal cancer as the end point, there was a significant decrease of gastric cancer in folate group as compared with placebo group (P=0.04), a similar trend was observed in both N-βC group and S-βC group (P=0.07ε0.08) and a highly significant decrease was found in the combination of the three interventional groups (P=0.04). A lower relative risk (odds ratio 0.12, 95% confidence interval 0.03 ε 0.51) of gastrointestinal cancer was obviously observed. In folate group the gastric mucosal inflammation and the reversed atrophic lesion were stable. (P=0.04), the reverse of intestinal metaplasia approached to 'significant' (P=0.06). Dysplasia was significantly reversed at 12 months after treatment (P=0.017). Two cases were found to have yellowish discoloration of skin in β-carotene groups during follow-up and no side effects were observed in folate group. Conclusions: This study suggests that folate is effective in the intervention of gastrointestinal cancer, and β-carotene has a similar trend of effectiveness. Folate may be used for atrophic gastritis to revert the gastric precancerous lesions.

Zhu, S., et al. (2003). "The effect of folic acid on the development of stomach and other gastrointestinal cancers." Chinese Medical Journal 116(1): 15-19.

Objective. To evaluate the roles of folic acid and β-carotene in the chemoprevention of gastric and other gastrointestinal (GI) cancers. Methods. In a randomized, double-blind, placebo-controlled trial, a total of 216 patients with atrophic gastritis were. randomly assigned to one of the four groups: 1 folate (FA, 20 mg per day plus vitamin B12 1 mg, intramuscularly, per month for one year, then 20 mg two times a week plus 1 mg per three months for the next year); 2 natural β-carotene (N-βC, 30 mg per day for first year, then 30mg two times a week for the next); 3 synthetic β-carotene (S-βC, administered as in N-βC); and 4 placebo. Follow-ups continued from 1994 to 2001. Results. A total of 7 new cases of gastrointestinal cancers were diagnosed with 3 stomach, 1 colon and 1 esophageal cancers occurring in the placebo group; 1 stomach cancer in both of the N-βC and S-βC groups, and no cancer occurring in FA group. In terms of GI cancers, there was a significant reduction in the FA group, compared with the placebo group (P = 0.04). A similar trend was observed in both N-βC and S-βC groups (P = 0.07-0.08). Taken together, the three intervention groups displayed a highly significant decrease in occurrence (P = 0.004, vs placebo), and a lower risk for GI cancers (OR = 0.12; 95% confidence interval, 0.03-0.51). For development of gastric cancer, any one of the three active-treated groups did not reach statistically significant reduction. The FA group showed obvious improvement of the gastric mucosal lesions with more patients displaying lesions reversed or stable atrophy and inflammation (P = 0.04), reversed intestinal metaplasia ( P = 0.06) at the end of follow-up, and reversed displasia (P = 0.017) at 12 months. Two cases of false jaundice were found in β-carotene groups with no influence on administration, and no side-effects were reported in FA group. Conclusions. This trial revealed the interventional effect of folic acid on the development of GI cancers, a similar effect of β-carotene was also detected. Also, folic acid may be of use to treat atrophic gastritis by preventing or reversing the precancerous lesions.

Zullo, A., et al. (2013). "Intestinal metaplasia surveillance: Searching for the roadmap." World Journal of Gastroenterology 19(10): 1523-1526.

Atrophic gastritis and intestinal metaplasia (IM) of the stomach are common and are associated with an increased risk for gastric cancer. In the absence of guidelines, a pragmatic management has been performed in Western countries in patients with these premalignant conditions. Recently, formal European guidelines have been delivered on this topic. Basically, it has been recommended that patients with extensive atrophic gastritis (AG) and/or extensive IM should be offered endoscopic surveillance every 3 years. On the contrary, no scheduled endoscopic/histological control has been advised for those patients with precancerous conditions confined to the antrum. In this commentary, we highlighted some potential weaknesses in the management formally recommended by the new guidelines. In detail, we discussed that AG and IM patients do not share the same gastric cancer risk, at least in Western countries, deserving a different approach. Some factors significantly associated with gastric cancer risk, such as IM type, first-degree family history of gastric cancer, and smoking habit have not been considered in tailoring the endoscopic follow-up. Finally, some data would suggest that a 3-year follow-up in patients with extensive gastric precancerous conditions could result in an inadequate secondary prevention. © 2013 Baishideng. All rights reserved.

Zullo, A., et al. (2012). "Follow-up of intestinal metaplasia in the stomach: When, how and why." World Journal of Gastrointestinal Oncology 4(3): 30-36.

Gastric cancer remains the second most frequent cause of cancer-related mortality in the world. Screening programs in some Asian countries are impractical in the majority of other countries worldwide. Therefore, follow-up of precancerous lesions is advisable for secondary gastric cancer prevention. Intestinal metaplasia (IM) is recognized as a precancerous lesion for gastric cancer, increasing the risk by 6-fold. IM is highly prevalent in the general population, being detected in nearly 1 of every 4 patients undergoing upper endoscopy. The IM prevalence rate is significantly higher in patients with Helicobacter pylori (H. pylori) infection, in first-degree relatives of gastric cancer patients, in smokers and it increases with patient age. IM is the "breaking point" in the gastric carcinogenesis cascade and does not appear to regress following H. pylori eradication, although the cure of infection may slow its progression. Gastric cancer risk is higher in patients with incomplete-type IM, in those with both antral and gastric body involvement, and the risk significantly increases with IM extension over 20% of the gastric mucosa. Scheduled endoscopic control could be cost-effective in IM patients, depending on the yearly incidence of gastric cancer in IM patients, the stage of gastric cancer at diagnosis discovered at surveillance, and the cost of endoscopy. As a pragmatic behavior, yearly endoscopic control would appear justified in all IM patients with at least one of these conditions: (1) IM extension > 20%; (2) the presence of incomplete type IM; (3) first-degree relative of gastric cancer patients; and (4) smokers. In the remaining IM patients, a less intensive (2-3 years) could be proposed.

Zullo, A., et al. (2020). "Management of precancerous conditions and lesions in the stomach (MAPS II): ESGE, EHMSG, ESP, and SPED guideline update 2019." Giornale Italiano di Endoscopia Digestiva 2020(1): 97-100.

Identification and follow-up of precancerous lesions on gastric mucosa are the only applicable procedures aimed to reduce mortality and, possibly, incidence of gastric cancer in those areas where screening programs are not cost-effective. The first European guideline was published on this topic in 2012 and it was recently updated. Among the updates, at least three have a direct impact on clinical practice. Based on the higher diagnostic consistence (at both histology and enhanced endoscopy) and a higher neoplastic potential as compared to atrophy, it was suggested that intestinal metaplasia could be the real target of screening. For the first time, some adjunctive factors increasing gastric cancer risk in those patients with atrophic/metaplastic pangastritis were considered. These included first-degree family history of gastric cancer, incomplete intestinal metaplasia, and persistent H. pylori infection, the presence of which impacts on follow-up timing. Finally, whenever available and after proper training, enhanced endoscopy should be used, particularly for dysplasia confirmation and in the follow-up of preneoplastic lesions.

Zullo, A., et al. (2020). "ONSET AND PROGRESSION OF PRECANCEROUS LESIONS ON GASTRIC MUCOSA OF PATIENTS TREATED FOR GASTRIC LYMPHOMA." Digestive and Liver Disease 52: S55.

Background and aim: Patients with primary gastric lymphoma are at increased risk of developing gastric cancer. Data on gastric precancerous lesions development in these patients are scanty. We aimed to assess the onset and progression o these lesions in a cohort of patients. Materials and methods: Data of patients with primary gastric MALT-lymphoma or diffuse large B-cell lymphoma (DLBCL) were analyzed. Multiple (>10) biopsies were performed on gastric mucosa at each endoscopic control, beyond macroscopic lesions. Presence and distribution of intestinal metaplasia (IM) at entry, the onset at follow-up, and progression through the stomach or transformation in the incomplete IM type were assessed. The onset neoplastic lesions was recorded. Results: Data of 50 patients (Mean age of 63.6 ± 10.7 years; M/F: 25/25), including 40 MALT-lymphoma and 10 with DLBCL, with median follow-up of 30.5 months (range: 9-108) and a median of 6 endoscopic controls (range: 3-14) were evaluated. At entry, IM was present in 12 (24%), and it developed in other 21 (55.3%) patients at a median follow-up of 6 (range: 3-40) months. Overall, progression of IM was observed in 7 (21.2%) cases, including extension in the stomach (N=5) or transformation into the incomplete type (N=2). Moreover, low-grade dysplasia developed in 4 (12.2%) patients with IM. In one of these patients, dysplasia further progressed to high-grade and gastric adenocarcinoma of the fundus. Conclusions: Our data found a frequent onset and rapid progression of precancerous lesions on gastric mucosa of lymphoma patients. This observation could explain the increased incidence of metachronous gastric cancer in these patients.

Zullo, A., et al. (2020). "Onset and progression of precancerous lesions on gastric mucosa of patients treated for gastric lymphoma." Journal of Gastrointestinal and Liver Diseases 29(1): 27-31.

Background & Aims: Patients with primary gastric lymphoma are at an increased risk of developing gastric cancer. Data on gastric precancerous lesions development in these patients are scanty. We assessed gastric precancerous lesions in a cohort of patients with primary lymphoma. Methods: Data of patients with primary gastric lymphoma [mucosa-associated lymphoid tissue (MALT)-lymphoma or diffuse large B-cell lymphoma (DLBCL)] were analysed. Multiple (>10) biopsies were performed on gastric mucosa at each endoscopic control, beyond macroscopic lesions. Presence and distribution of intestinal metaplasia (IM) at baseline, the onset at follow-up, and progression through the stomach or transformation in the incomplete IM type were assessed. The onset of neoplastic lesions was recorded. Results: Data of 50 patients (mean age of 63.6 ± 10.7 years; M/F: 25/25), including 40 with MALT-lymphoma and 10 with DLBCL, with median follow-up of 30.5 months (range: 9-108) and a median of 6 endoscopic controls (range: 3-14) were evaluated. At entry, IM was present in 12 (24%), and it developed in other 22 (57.9%) patients at a median follow-up of 6 (range: 3-40) months. Overall, progression of IM was observed in 7 (21.2%) cases, including extension in the stomach (n=5) or transformation into the incomplete type (n=2). Low-grade dysplasia was detected in 4, and indefinite dysplasia in other 7 patients. In one patient, low-grade dysplasia had progressed to high-grade and gastric adenocarcinoma of the fundus. Conclusions: Our data found a frequent onset and rapid progression of precancerous lesions on gastric mucosa of lymphoma patients. This observation could explain the increased incidence of metachronous gastric cancer in these patients.

**Excluded after the** **second screening:**

1 Buckle, A., et al. (2018). "Prevalence and associations of gastric intestinal metaplasia in a multicultural Australian cohort." Journal of Gastroenterology and Hepatology 33: 119-120. conference abstract

Background: Gastric intestinal metaplasia (GIM) is a premalignant lesion in the Correa cascade to gastric cancer. Its prevalence varies globally, with an intricate relationship with Helicobacter pylori infection. The prevalence of GIM in Australia is not well established, which has significant implications for screening and surveillance recommendations. Aims: Our aims were to (i) assess the prevalence of GIM and H. pylori infection at a large tertiary Australian health service; (ii) describe the demo-graphics of those with GIM; and (iii) assess current GIM management practice. Methods: This study included 1000 sequential gastric pathology specimens from January 2012 onward. Forty were excluded as tissue other than endo-scopic gastric biopsies, and one was excluded due to insufficient sampling. The remaining 959 samples were assessed for GIM, and demographic data including age, sex, and country of birth were collected. Patients who were GIM-positive were followed longitudinally for up to 6 years to determine rates of dysplasia progression and to audit current management. Results: A total of 401 men (41.8%) and 558 women (58.2%) were included. There was a comment on GIM in 100% of histopathology reports as per standard protocol at our center (including or excluding); 108 patients had GIM identified (11.3%; 63 female [58.3%]). GIM subtype was reported in only 40% of cases (complete in 28 reports and incomplete in 15 reports, with no comment in the remainder). Focal GIM was recorded in 70 patients (65%), and extensive GIM in 10 patients (9%). There were 97 patients who had histopathological H. pylori infection (10.1% of total). H. pylori infection was associated with GIM (21 patients had both; RR, 2.15). Age over 50 years was a significant risk factor for both GIM (RR, 5.14) and H. pylori infection (RR, 2.39). Country of birth data were available for 100% of patients, with 102 of the 959 (10.6%) born in Asia. Of these, 16 had GIM (15.7%) and 18 had H. pylori infection (17.6%). For those born elsewhere, 92 (10.7%) had GIM and 79 (9.2%) had biopsy-proven H. pylori. The distribution of GIM was found in patients born in 33 different countries (Fig. 1). Of the 108 patients with GIM, 19 had repeat endoscopy including gastric biopsy at our service over 59.0 person-years. Only 11 of the 19 (57.9%) had GIM on repeat biopsy. None of the 19 had dysplasia or gastric cancer identified. Conclusion: In a cohort of 959 sequential patients with endoscopic gastric biopsies for all indications, the rate of GIM was 11.3%. In keeping with previous studies, there was an association between GIM and both age and H. pylori infection, with higher rates in those born in Asian countries. A significant finding of this study is the heterogeneity in histopathological reporting of GIM, impeding accurate risk stratification clinically. Notably, only 19 of the 108 patients who had GIM identified at index endoscopy had follow-up endoscopy at our service. This study further emphasizes the extent of GIM in the multicultural Australian population and the need for both prospective studies and the development of consensus management guidelines.

2 Cao, Z. M., et al. (1993). "[A long-term follow-up study with endoscope in chronic gastritis]." Zhonghua Nei Ke Za Zhi. Chinese Journal of Internal Medicine 32(11): 743-745. conference abstract

A 10 to 17 years endoscope follow-up was performed to 138 cases of chronic gastritis. The result showed that 118 cases still proved to be chronic gastritis, and the increase of chronic atrophic gastritis (CAG) in numbers. 15 cases developed into peptic ulcer. 5 cases to carcinoma (4 cases were early carcinoma). The time of cancerization differed from 2 to 12 years. The rate of cancerization of CAG reached 7.46%. The rate of cancerization of intestinal metaplasia (IM) were 8.20%. 13 cases of IM were mucus histo-chemical stained, and five of them contained sulfuric acid mucus, one of the 5 cases cancerized. 3 of 14 cases with atypical hyperplasia (ATP) turned into stomach cancer. We believe that chronic gastritis, especially CAG with ATP and IM, or with sulfuric acid mucus of IM had a high possibility of cancerization with the increase of age, and should be followed up for a long time.

3 Chapelle, N., et al. (2019). "Evolution of gastric preca ncerous lesions: A long term follow-up single center study in France." United European Gastroenterology Journal 7(8): 26. conference abstract

Introduction: International guidelines recommend surveillance of gastric precancerous lesions (GPL), but there are limited data on the evolution of these lesions, especially in countries of low gastric cancer incidence. Our objective was to study the evolution of GPL in France. Aims & Methods: From the cohort of 507 patients diagnosed with GPL [atrophic gastritis (AG), or intestinal metaplasia (IM), or low grade dysplasia (LGD), or high grade dysplasia (HGD)]in our center between 2000 and 2015, the patients fulfilling the following criteria were identified: 1) at least one follow-up endoscopy performed after a minimal period of 6 months, 2) at each endoscopy, random gastric biopsies obtained, at least 3 from antrum and 2 from corpus, 3) all biopsy material available for histological review. The biopsy specimens were retrieved from the hospital tissue bank and analysed prospectively by an expert pathologist for the presence of GPL and their extent (according to OLGA and OLGIM score). The type of IM (complete or incomplete) was also evaluated. The evolution of the lesions was assessed by comparing the initial and the final histology. Additionally, for the patients with multiples endoscopies during the follow-up, a precise evaluation of the evolution on individual level was performed. Results: Seventy nine patients (35 men, median age 61 years), were included. At initial endoscopy, the GPL found were, by order of severity: AG in 5 patients (OLGA 1, n=4; OLGA 2, n=1), IM in 73 patients (OLGIM 1, n=39; OLGIM 2, n=28; OLGIM 3, n=6) and LGD in 1 patient. Thirty-seven patients (47%), were H. pyloripositive by histology. Among the 73 patients with IM, 59 had IM in the antrum, 8 in the corpus, and 6 both in the antrum and in the corpus. Sixty patients had complete IM and 13 incomplete IM. The mean (±SD) follow-up period was 66 ±48 months (Min=7, Max=208), the mean (±SD) number of endoscopies per patient was 4±2 (Min= 2, Max = 14), and the total number of endoscopies performed in all patients was 341. At final endoscopy, the GPL found were AG in 2 patients, LGD in 4 patients, HGD in 1 patient, adenocarcinoma (ADK) in 2 patients, IM in 58 patients and normal gastric mucosa (+/-superficial gastritis) in 12 patients. Six patients (7%) were H. pyloripositive by histology. The comparison between the initial and final endoscopy, showed stability of GPL in 56 patients (71%), progression to more severe lesion in 10 patients (13%) (from AG to IM in 4 patients, from IM to LGD in 3 patients, from IM to HGD in 1 patient, and from IM to ADK in 2 patients), and the regression in 13 patients (16%). Both patients who progressed to ADK had incomplete type of antrum IM, one OLGIM 2 and one OLGIM 3. Altogether, among 10 patients who progressed to more severe lesions, 6 (60%) had incomplete type of IM. Among the 13 patients in whom the regression to the normal (+/-gastritis) gastric mucosa was observed, 9 had initially antrum limited OLGIM 1 complete IM and 4 had antrum limited complete OLGIM 2 IM. Conclusion: This study shows that: 1) Most of the GPL remain stable over time, 2) Antrum-limited IM, especially of incomplete type, has the highest risk of progression to dysplasia and cancer, 3) Regression of IM is possible, especially for low grade (OLGIM 1) and for complete type.

4 Conchillo, J. M., et al. (2001). "Is type III intestinal metaplasia an obligatory precancerous lesion in intestinal-type gastric carcinoma?" European Journal of Cancer Prevention 10(4): 307-312. cross-section study

This retrospective study was performed to assess whether type III intestinal metaplasia is an obligatory precancerous lesion of intestinal-type gastric carcinoma and to determine its possible use as a marker of enhanced cancer risk. From 48 consecutive patients with gastric cancer who underwent a gastrectomy over a 3-year period (mean age 72.0 years; 29 M/19 F), at least two sections from antrum, corpus and tumour-surrounding mucosa were obtained for the examination of presence and subtypes of intestinal metaplasia (IM). It was found that 77.1% of the carcinomas were of the intestinal type and 22.9% of the diffuse type. The intestinal-type was more often found in males (P = 0.01); the mean age at diagnosis in this type was higher than in the diffuse cancer group (P = 0.004). There was a high prevalence of total IM in both the intestinal (75.7%) and diffuse group (88.9%). Type I IM was predominant in antrum and corpus of patients from both groups. Type III IM was only found among patients with intestinal-type carcinoma. However, its prevalence was rather low (26.3%). Therefore the absence of this lesion in patients with other risk factors cannot be used as an argument for lowering the degree of surveillance and its presence seems to be sufficient indication for long-term follow-up. © 2001 Lippincott Williams & Wilkins.

5 Dinis-Ribeiro, M., et al. (2004). "A follow up model for patients with atrophic chronic gastritis and intestinal metaplasia." Journal of Clinical Pathology 57(2): 177-182. insufficient data

AIM: To devise a follow up model for patients with gastric cancer associated lesions, such as atrophic chronic gastritis (ACG) and intestinal metaplasia (IM). METHODS: Cohort study of 144 patients, followed for a minimum of one year, in whom at least two upper gastrointestinal endoscopic biopsies in flat gastric mucosa provided a diagnosis of ACG, IM, or low grade dysplasia (LGD). RESULTS: Of those diagnosed with ACG at first endoscopic biopsy (entry biopsy), 12% progressed to LGD in outcome biopsy, as did 8% of those with type I IM, 38% with type II or III IM, and 32% with LGD. Type of IM at entry independently predicted progression to LGD and cancer. Type II and III IM had a higher rate of progression to LGD than type I IM, which showed an indolent behaviour similar to ACG. Patients with type II or III IM were at higher risk for development of dysplasia, and 7% of patients with type III IM at first biopsy progressed to high grade dysplasia (HGD), whereas no cases of ACG or type I/II IM progressed to HGD during the first three years. CONCLUSION: Patients with ACG or IM could possibly be allocated to different management schedules, based on differences in rate and proportion of progression to LGD or HGD. Less intensive follow up (two/three yearly with "serological evaluation" (pepsinogen)) may suit those with ACG or type I IM. Patients with type III IM may benefit from six to 12 monthly improved endoscopic examination (magnification chromoendoscopy).

6 González, C. A., et al. (2011). "Helicobacter pylori cagA and vacA genotypes as predictors of progression of gastric preneoplastic lesions: a long-term follow-up in a high-risk area in Spain." American Journal of Gastroenterology 106(5): 867-874. insufficient data

OBJECTIVES: There are no established predictive markers of progression of gastric preneoplastic lesions. The aim of this study was to analyze the relationship between Helicobacter pylori cagA and vacA genotypes and progression of gastric preneoplastic lesions. METHODS: This was a follow-up study that carried out in a province of Spain with a high risk of gastric cancer. A total of 312 patients who underwent upper endoscopy with gastric biopsy in 1988-1994 with diagnoses of normal mucosa, non-atrophic gastritis (NAG), non-metaplastic multifocal atrophic gastritis (MAG), and complete or incomplete intestinal metaplasia (IM), and who accepted to undergo a new biopsy during 2005-2007 or had an end point during follow-up, were included in this study. Detection and characterization of H. pylori cagA and vacA genotypes was performed directly in baseline paraffin-embedded gastric biopsy specimens by PCR followed by reverse hybridization onto a line probe assay. Inter- and intra-observer variability of histological diagnosis was assessed. Analysis was done using unconditional logistic regression. RESULTS: The mean age of patients was 48.5 years (45% males) and the mean of follow-up was 12.8 years. H. pylori strains harboring cagA, vacA s1, and vacA m1 genotypes were more frequently found in patients with more advanced gastric preneoplastic lesions. Infection with cagA-positive, vacA s1, and vacA m1 strains was associated with progression of gastric preneoplastic lesions (multivariate odds ratio (OR)=2.28, 95% confidence interval (CI) 1.13-4.58; OR=2.90, 95% CI 1.38-6.13; and OR=3.38, 95% CI 1.34-8.53, respectively). Infection with strains that are simultaneously cagA positive and vacA s1/m1 was associated with progression of gastric precancerous lesions with an OR of 4.80 (95% CI 1.71-13.5) in relation to those infected with cagA-negative/vacA s2/m2 strains. CONCLUSIONS: H. pylori genotyping may be useful for the identification of patients at high risk of progression of gastric preneoplastic lesions and who need more intensive surveillance.

7 González, C. A., et al. (2013). "Spanish follow-up multicentric study on phenotypic, epigenetic, genetic and H. pylori virulence factors associated with the progression of gastric cancer precursor lesions." Helicobacter 18: 111. conference abstract

Background: Surveillance of patients at risk of progression from precursor lesions (PL) to gastric cancer (GC) is recommended but more research is needed to identify markers of progression. Aims: (1) To evaluate the risk of progression to GC in patients with PL (atrophic gastritis, complete/incomplete intestinal metaplasia); (2) To assess the effect of virulence factors of H. pylori infection (cagA and s1/m1 vagA alleles), the effect of polimorphisms of candidate genes, the effect of epigenetic variants, and (3) To elaborate an score of different markers of risk to allow identification of patients with high risk of progression to GC. Design: A follow up study is ongoing including about 900 patients of 25- 69 years, diagnosed with PL between 1995 and 2004, in nine participating hospitals. Endoscopy and biopsy is being repeated during 2011-2013, and fresh gastric mucosa is being collected. A sample of saliva and a questionnaire with medical information and habits is also being collected. SNPs of candidate genes will be evaluated in DNA from saliva. Genotyping of virulent factors by PCR is being analysed from DNA of paraffin blocks. Patterns of methylation is being analysed by the Infinium 450 K methylation arrays which allows to interrogate more than 485 0,0,0 CpGs of the whole genome and validation of candidates genes is tested by pyrosequencing. Occurrence of all GC cases is being identified during follow-up. Incidence of GC and progression/regression of PL according to different factors will be analysed by multiple regression models. Results: According to a preliminary analysis, 40.3% of patients had chronic atrophic gastritis, 37.1% complete intestinal metaplasia, 13.2% incomplete intestinal metaplasia and 9.4% dysplasia. The mean time of follow-up was 12.8 years (SD 1.8). More results will be available in September and will be included in the poster.

8 González, C. A., et al. (2014). "Incomplete type of intestinal metaplasia has the highest risk to progress to gastric cancer: Results of the Spanish follow-up multicenter study." United European Gastroenterology Journal 2(1): A51. conference abstract

INTRODUCTION: In high or moderate risk population, periodic surveillance of patients at risk of progression from gastric precursor lesions (PL) to gastric cancer (GC) is recommended, as it represents the most effective strategy for reducing the burden of GC. The incomplete type of intestinal metaplasia (IM) may be considered as the best candidate, but more research is needed to confirm it, and to identify other markers of progression. AIMS & METHODS: 1)To evaluate the risk of progression to GC in patients with PL and 2)To assess the effect of virulence factors of H. pylori infection, the effect of polimorphisms of candidate genes, and the effect of epigenetic variants. Results regarding the first aim are described in this presentation. A multicenter follow-up study was carried-out including 649 patients, diagnosed with PL between 1995 and 2004, in 9 participating hospitals from Spain, which repeated the endoscopy and biopsy (following the Sidney protocol) during 2011- 2013. Fresh gastric mucosa, a sample of saliva, and a questionnaire on medical information and habits of life were collected. DNA from paraffin blocks of recruitment biopsy was used for analysis of H. pylori by PCR, and for the analysis of methylation patterns by the Infinium 450 K methylation arrays. Based on morphology, IM was sub-classified as complete (small intestinal type, CIM) and incomplete (colonic type, IIM). Analysis was done using Cox proportional hazards risk (HR) models. RESULTS: At baseline, 24% of patients had atrophic gastritis, 38% CIM, 34% IIM, and 4% dysplasia. The mean of follow-up was 12 ys. 24 patients (3.7%) developed a gastric adenocarcinoma during follow-up. The incidence rate of GC was 2.76 and 5.76 per 1,000 person-years, for those with CIM and IIM respectively. The HR of progression to CG was 6.4 (95%CI 0.8-49.6) and 2.4 (0.3-19.8) for those with IIM and CIM at baseline, compared with those with chronic atrophic gastritis, after adjusting for sex, age, family history of GC and use of NSAIDs. CONCLUSION: Patients with IIM have the highest risk of progression to GC.

9 González, C. A., et al. (2014). "Incomplete type of intestinal metaplasia has the highest risk to progress to gastric cancer: Results of the spanish follow-up multicenter study." Helicobacter 19: 161. conference abstract

Introduction: In high or moderate risk population, surveillance of patients at risk of progression from gastric precursor lesions (PL) to gastric cancer (GC) is recommended. The incomplete type of intestinal metaplasia (IM) may be considered as the best candidate, but more research is needed. Aims: (i) To evaluate the risk of progression to GC in patients with PL; and (ii) To assess the effect of virulence factors of H. pylori infection, the effect of polimorphisms of candidate genes, and the effect of epigenetic variants. Results regarding the first aim are described in this presentation. Methods: Multicenter follow-up study including 649 patients, diagnosed with PL between 1995 and 2004, in 9 Spanish hospitals, which repeated the endoscopy and biopsy (Sidney protocol) during 2011-2013. Fresh gastric mucosa, saliva sample, and questionnaire on habits of life were collected. DNA from paraffin blocks of recruitment biopsy was used for analysis of H. pylori (PCR) and of methylation patterns (Infinium-450-K-methylation-arrays). Based on morphology, IM was sub-classified as complete (small intestinal type, CIM) and incomplete (colonic type,IIM). Analysis was done using Cox-proportional hazards- risk (HR) models. Results: At baseline, 24% of patients had atrophic gastritis, 38%CIM, 34% IIM, and 4% dysplasia. Mean follow-up was 12 years. 24 patients (3.7%) developed a gastric adenocarcinoma during follow-up. The incidence rate of GC was 2.76 and 5.76 per 1000 person-years, for those with CIM and IIM respectively. The HR of progression to CG was 6.4(95% CI = 0.8-49.6) and 2.4 (0.3-19.8) for those with IIM and CIM at baseline, compared with those with chronic atrophic gastritis. Conclusion: Patients with IIM have the highest risk of progression to GC.

10 Kang, K. P., et al. (2009). "Role of intestinal metaplasia subtyping in the risk of gastric cancer in Korea." Journal of Gastroenterology and Hepatology 24(1): 140-148.

cross-section study

BACKGROUND AND AIM: Gastric cancer is believed to develop by a multistage process. Intestinal metaplasia (IM) is regarded as a premalignant condition; it is classified into subtypes I, II and III. The aim of this study was to evaluate whether the subtypes of IM were associated with progression to gastric cancer. METHODS: The study cohort consisted of 861 subjects, categorized as controls, gastric ulcers, dysplasia and cancer. The IM was scored histologically using the Sydney classification for the antrum and the body of the stomach. The biopsies were stained with high iron diamine and alcian blue (pH 2.5) (HID-AB2.5), and the IM was subtyped as I, II or III. RESULTS: The proportion of IM subtypes I, II and III were 14.5%, 47.2% and 38.3% in the antrum, and 28.1%, 57.8% and 14.1% in the body of the stomach, respectively. These distributions did not show significant differences depending on disease or Helicobacter pylori positivity. In cases that were H. pylori-positive, the prevalence of IM subtype II in the cancer and dysplasia groups was higher than in the control group in the body of the stomach (P < 0.05). The proportion of IM subtype III in the antrum increased in proportion with age (P = 0.036). CONCLUSIONS: IM subtyping was not found to play a major role in the prediction of gastric cancer development in Korea. IM subtype III was associated with aging, and IM subtype II appeared to be related to gastric carcinogenesis in the presence of H. pylori infection.

11 Lin, C. K., et al. (2001). "Cathepsin E and subtypes of intestinal metaplasia in carcinogenesis of the human stomach." Zhonghua Yi Xue Za Zhi. Chinese Medical Journal (Taipei) 64(6): 331-336. cross-section study

BACKGROUND: Cathepsin E is found mainly over the gastric surface and foveolar epithelial cells, and it also is found in the metaplastic pyloric glands and cancer cells. The exact function of cathepsin E in gastric mucosa remains unclear. The colonic type (type III) of intestinal metaplasia (IM) is strongly associated with intestinal-type gastric carcinoma. IM is considered to be a precancerous lesion. The aim of this study was to find out the role of cathepsin E in IM, dysplasia and cancer of stomach. METHODS: Sixty nine biopsy specimens with IM and dysplasia and 33 gastrectomy specimens with gastric carcinoma were fixed, sectioned and stained with PAS-alcian blue stain, high iron-diamine alcian blue stain to classify IM and immunohistochemical stain to localize cathepsin E. Those patients with dysplastic gastric lesions received regular endoscopic follow-up. RESULTS: Fifteen of 69 patients with gastric dysplasia developed cancer in a median 10.5 months follow-up. Severe dysplasia developed carcinoma significantly higher than mild dysplasia (12/20 vs. 1/25, p < 0.001), and type III intestinal metaplasia seemed to have significantly predilection for severe dysplasia and gastric cancer. Cathepsin E was stained in intestinal metaplasia with dysplastic change in 44/69 specimens (63.8%), and carcinoma in 28/48 (58.3%) specimens, there was no significant difference between intestinal type and diffuse type carcinoma in cathepsin E staining. The positive staining for cathepsin E decreased significantly in severe dysplastic gastric mucosa. CONCLUSIONS: Type III IM is commonly associated with severe dysplasia and cancer; it may be a precancerous lesion. The positive staining of cathepsin E decreased with the severity of gastric dysplasia, representing dedifferentiation of the cells.

12 Llach, J., et al. (2020). "Clinical characterization and screening strategies in familial gastric cancer: Preliminary results of the first Spanish Multicenter study." United European Gastroenterology Journal 8(8 SUPPL): 227-228. conference abstract

Introduction: Approximately 10% of gastric adenocarcinomas (GC) show familial aggregation, and a hereditary cause is determined in up to 5% (hereditary GC). Familial GC (FGC) is characterized by an autosomal dominant inheritance pattern of GC, without a responsible germline mutation. The clinical characteristics of FGC, the prevalence of GC and GC-Precursor Lesions (GCPL) and the effectiveness of preventive strategies, have been poorly studied. Aims & Methods: Objective: To describe the clinical and pathological characteristics of FGC, the screening strategies used and estimate the risk of GC and GCPL in this scenario. Methodology: a multicenter nationwide study with retrospective inclusion of individuals with FGC was performed. FGC was defined as: a) Criterion A: ≥ 2 first-degree relatives (FDR) or second-degree relatives (SDR) affected by GC (≥ 1 diagnosed < 50 years), or b) Criterion B: ≥ 3 FDR or SDR with GC at any age. Clinical data, oncological personal and family history (FH), endoscopic and pathological reports, were collected. Results: A total of 69 patients (50 families) were included from 11 Spanish centers: the median age was 59 years (range 46-71) and 37 (53.6%) were women. The criterion A of inclusion was fulfilled by 37,7% of the cases and criterion B was present in the remaining 62.3% individuals. Prevalence of smoking history and chronic alcohol consumption was 38% and 9.4%, respectively. In 14 (20%) cases, personal history of extra-gastric malignancies was reported (3 breast, 2 colorectal, 2 prostate, 2 melanoma, 2 leukemia, 3 other cancers). Twenty-one (30.4%) patients, corresponding to 18 families, developed GC at a median age of 63 years (range 47-73) and 2 (9.5%) of them were diagnosed during screening endoscopy. Diffuse histology was reported in 10 (47.6%) cases and 13 (62%) tumors were detected in advanced stages (III/ IV). Gastrectomy was performed in 14 (66.6%) patients: 9 (64%) total and 5 (36%) partial gastrectomy. Eight (38%) patients died due to this neoplasia. Regarding screening, gastroscopy was performed in 47 (68.1%) individuals, with a total of 176 explorations: in 42 (89.3%) cases random biopsies were taken [(Sydney protocol in 7 (14.9%) and Cambridge protocol in 4 (8.5%)], in 31 (66%) helicobacter pylori (HP) infection was tested and no biopsies were taken in the remaining 5 (10.7%) cases. Median age at first screening endoscopy was 50.5 (range 36-56) years, with a median of 3 (range 1-5) procedures and a median surveillance of 4 (range 1-12) years. Overall, HP was investigated in 39 (56.5%) individuals, being positive in 24 (61.5%). During endoscopic screening, 19/47 (40.4%) GCPL were detected (if more than one in the same patient, the most advanced lesion is specified): complete or incomplete intestinal metaplasia in 6 (12.7%) and 5 (10.6%), respectively; extensive atrophic gastritis in 4 (8.5%), low and high-grade dysplasia in 3 (6.3%) and 1 (2.1%), respectively. Moreover, invasive GC was detected by screening gastroscopy in 2 (4.2%) patients, both in an early stage (I and II). Conclusion: Despite previous family history, the majority of GC within a cohort of individuals of FGC, were diagnosed at advanced stage. Whereas endoscopic screening was performed in nearly 70% of individuals with FGC, HP infection was investigated in just over half. Up to 45% individuals of FGC under endoscopic screening were diagnosed with GC-precursor lesions and early stages GC. Definitive results of our study could improve the characterization of FGC in order to determine the best prevention measures for these patients.

13 Maric, L., et al. (2016). "Gastric intestinal metaplasia: Is it a worrisome finding warranting surveillance endoscopy with repeat biopsies." American Journal of Gastroenterology 111: S485. no diagnosis of IM subtype

Introduction: Gastric cancer is the third leading cause of cancer-related mortality worldwide. The incidence of gastric cancer within United States is low, which has led to lack of screening and surveillance in clinical practice. Gastric intestinal metaplasia (IM) occurs in response to different mucosal injuries, some of which lead to increased risk for gastric cancer, whereas others may not. The process of gastric carcinogenesis appears to be triggered by chronic gastritis (with Helicobacter pylori playing a pivotal role in causing chronic active gastritis). The background in which IM arises has not been systematically investigated. Intestinal metaplasia (IM) of the gastric mucosa is considered a pre-cancerous lesion in the gastric carcinogenesis cascade. While the risk of developing gastric cancer in an individual with IM in United States has remained significantly lower than elsewhere (ex. East Asia), the actual progression to gastric adenocarcinoma is related to conditions that induce the metaplastic changes, its extent and histologic subtype, patient's ethnicity, diet and Helicobacter status. The significance of IM in the absence of more worrisome pre-neoplastic features on gastric biopsy is not entirely elucidated in the United States. In fact, national consensus guidelines are not yet available for the diagnosis and management of gastric intestinal metaplasia. Longitudinal studies are needed to determine not only if these patients have increased risk for gastric cancer, but also need to determine future follow-up and surveillance or whether it can be safely assumed that they are at no greater risk compared to the general population. This study aims to determine what changes are typically seen on the follow-up gastric biopsies obtained on patients with initial biopsy findings consistent with intestinal metaplasia. Methods: This was a retrospective study of 411 patients identified using the Cleveland Clinic Co-Path® data base system with confirmed diagnosis of intestinal metaplasia on initial gastric biopsy. Patients were included from year 1998 to 2014. In addition to findings of IM on tissue biopsy, some patients were also found to have inflammation, low-grade dysplasia (LGD), high-grade dysplasia (HGD), intramucosal carcinoma (IMC) or invasive carcinoma (IC). Out of the 411 cases, 107 patients underwent surveillance endoscopy with biopsies. However, 18 out of the 107 patients were excluded from the study, as they were found to have HGD, IMC, or IC on the initial gastric biopsies. Therefore, a total of 89 patients met the inclusion criteria of IM on gastric biopsy, and were evaluated with surveillance endoscopy with repeat biopsies. No distinction was made between incomplete and complete IM in these patients. Results: Eighty four out of the eighty nine patients were found to have IM and inflammation only on repeat gastric biopsies. Five out of the eighty nine patients were found to have LGD in addition to the presence of IM. The time interval for follow-up surveillance biopsies of 89 patients included in the study ranged from 0.1 to 144 (30.1) months. There was no HGD, IMC or IC on surveillance biopsies at interval follow-up. Fifty four patients were found to have persistent IM, and thirty five patients were found to have no IM on repeat gastric mucosal biopsies. Among the patients with LGD, one had persistent LGD, three had persistent IM and one patient lacked evidence of both on three and a half year follow-up surveillance. Conclusion: 60% of patients with initial gastric biopsy findings consistent with IM alone or LGD were found to have persistent IM on repeat gastric biopsies. None of the patients with IM or IM/LGD were found to have progression to HGD or carcinoma on follow-up surveillance endoscopy between 30.1 and 41 months. Important factors that govern the rate of histological progression are age, Helicobacter pylori status (and if positive, whether or not it was eradicated or remains persistent), ethnicity (with special considerations placed on Asian and Northern Latin American population), smokin history and alcohol use, first-degree relative with gastric cancer, in addition to histological findings of IM extension (>20% being significant) and presence of incomplete type IM. Yearly endoscopic surveillance appears justifiable in all IM patients with presence of at least one of the risk factors. For patients without risk factors, 30.1 month interval endoscopic surveillance for those with IM/LGD, and 41 month follow-up for those with IM alone would be more appropriate. (Figure Presented).

14 Masci, E., et al. (1997). "Subtypes of intestinal metaplasia in patients helicobacter pylori positive and gastric cancer risk index." Giornale Italiano di Endoscopia Digestiva 20(3): 115-119. cross-section study

The follow-up of preneoplastic gastric lesions (PGL) is a controversal problem, because only few patients with chronic atrophic gastritis (CAG) and intestinal metaplasia (IM) develop cancer. Recently a simple score has been proposed to detect Helicobacter pylory (Hp) infected patients with an increased risk for gastric cancer (GC). The aim of our study was to compare three groups of patients: 36 with CAG ant type I IM, 25 with type III IM and 41 with duodenal ulcer (DU), characterized by Hp infection, to assess the difference of lymphocytes/plasmacells and neutrophiles infiltration in corpus and antrum and to calculate gastric carcinoma risk index according to the different features to discriminate the groups of patients with different cancer risk, without considering IM. Patients with PGL had not a higher lymphocytes/plasmacells and neutrophiles infiltration in the corpus when compared to the antral infiltration. Subjects with CAG and type III IM had higher infiltration for lymphocytes/plasmacells and neutrophiles, in the gastric corpus, than DU patients (40% vs 14.63%, 44% vs 14.63%; p<0.05); in contrast, subjects with GAC and type I IM showed, in the corpus, higher infiltration only for lymphocytes and plasmacells than DU patients (41.67% vs 14.63%; p<0.008). The higher degree and activity of gastritis in the corpus when compared to the antral infiltration as considered as 1 point of the score. Odds-ratios are as following: type I IM vs DU: 4.32 (95% CI: 1.21- 15.36); type III IM vs DU: 5.71 (95% CI: 1.49-21.84). In conclusions the overlapping of the results in subjects with type I and III IM demonstrate the two istological features in corpus are not sufficient to recognize patients with an increased risk for the development of gastric cancer. This index is not applicable to follow-up patients with PGL; at present, type III IM is assumed to be the only marker of increased risk of gastric cancer.

15 Piazuelo, M. B., et al. (2017). "Gastric intestinal metaplasia type III and prospective risk of gastric cancer in Colombia." Gastroenterology 152(5): S473. conference abstract

Background: In the Correa model of gastric carcinogenesis, Helicobacter pylori causes chronic gastritis, which over time may progress through the premalignant stages of atrophic gastritis, intestinal metaplasia (IM), and dysplasia, to finally gastric cancer (GC). Extension and types of IM have been associated with differential GC risk. Our study evaluated the association between type III IM (a subtype of incomplete IM with sulfomucin-positive columnar cells) and prospective risk of GC in a cohort of individuals from a high-risk area in Colombia. Methods: 795 subjects with gastric precancerous lesions were randomized to anti-H. pylori treatment or placebo at enrollment. Gastric biopsies at baseline were scored according to our validated histopathology scoring system. Ten individuals developed GC during 16 years of follow-up (median time to GC, 8 years, interquartile range, 3-12). Three controls were selected for each GC case, matched for age, sex, histopathology score at baseline, anti-H. pylori treatment at baseline, and length of follow-up. Sections from all biopsies with IM were stained with high-iron diamine/Alcian blue (HID-AB). IM was initially classified into complete and incomplete types, assessing percentages of epithelium replaced with either IM type. The percentage of epithelium containing sulfomucin-positive columnar cells was assessed in HID-AB sections. All evaluations were performed semiquantitatively by a pathologist blinded to clinical information. The maximum value obtained in a single biopsy across the set of biopsies for each subject was considered for the analyses comparing GC cases and controls. To assess differences in anatomic location of IM, biopsies were grouped into antrum (including incisura) and corpus. Conditional logistic regression models were used to estimate odds ratios (OR). Results: All individuals who developed GC had IM at baseline. As a result of the case-control matching, there were no statistically significant differences in extension of complete-type (p=0.86) or incomplete-type (p=0.43) IM. Notably, greater expression of sulfomucins at baseline, was associated with increased GC risk (adjusted OR= 1.29, 95% CI, 1.02-1.63 for each increment in 5% on the expression of sulfomucins). In anatomic location-specific analyses, mean extensions of sulfomucins, total and subtype IM were greater in the antrum as compared to the corpus: 6% vs. 1% for sulfomucins (p= 0.003), 53% vs. 22% (p<0.001) for total 7% vs. 19% for complete-type (p=0.01), and 17% vs. 3% for incomplete-type (p<0.001), regardless of case-control status. Conclusions: All IM lesions were more extensive in the antrum. Assessment of sulfomucin expression in gastric IM is useful for the identification of patients at higher risk of GC. This strategy could prove useful to determine which individuals with IM may benefit from closer endoscopic surveillance.

16 Pittayanon, R., et al. (2012). "Risk of gastric cancer in the Thai patients with Gastric Intestinal Metaplasia (GIM)." Journal of Gastroenterology and Hepatology 27: 338-339. conference abstract

Background: Gastric cancer is the second leading cause of cancer related death in the world and gastric intestinal metaplasia (GIM) is a well-known premalignant condition. The objective of this study was to determine the risk factors for gastric cancer in the Thai GIM patients in order to propose appropriate recommendation for Thai population. Material and method: Fifty patients with previously diagnosed GIM between 1997 and 2011 were recruited for surveillance EGD every 6 to 12 months interval until completing a 5-year follow-up or until gastric cancer was observed. The probable risk factors of gastric cancer including sex, age, smoking, alcohol consumption, status of H. pylori infection, type of GIM, serum pepsinogen (PG), IL-1RN and IL-1B were recorded. Results: There were 58% male patients. The median age was at 63 year. 50% of these patients had H. pylori infection. One-third of the patients had a significant history of smoking whereas only 16% had a history of alcohol consumption. Most of them (90%) had complete-type of GIM. In addition, the mean of PG I/II ratio was not less than 3 (12.7 ± 7.9) and IL-1RN and IL-1B was predominate in 1/1 and C/C locus, respectively. The mean and mode of follow-up period was 3.3 and 5 years, respectively. Of those, only 1 GIM patient was diagnosed gastric cancer as well-differentiated adenocarcinoma at the 4th year of follow-up. Conclusion: This preliminary report cannot propose the predictive score for gastric cancer in GIM patients because of the limited number of gastric cancer arising from our GIM patients. On the other hand, this study suggests that the intensive follow-up every 6-12 months in complete-type GIM patients may not be necessary in the Thai population. However, we need to include more GIM patients in order to determine risk factors make further recommendation.

17 Quach, T. D., et al. (2010). "A practical model to stratify dyspeptic patients based on the risk of gastric cancer." Journal of Gastroenterology and Hepatology 25: A21.

cross-section study

Background The severity of endoscopic gastric atrophy (EGA), highstage OLGA gastritis (i.e. stage III-IV), and extensive intestinal metaplasia (IM) with incomplete subtype have been separately reported as high risk factors of gastric cancer (GC). Aims To evaluate the associations among these characteristics and to develop a stratification model for GC risk. Methods A cross-sectional study was conducted on 280 patients with non-ulcer dyspepsia. Biopsies were taken according to the updated Sydney system. EGA was assessed according to the Kimura-Takemoto classification and gastritis stage was assessed according to the OLGA system. Results Moderate-to-severe EGA was significantly associated with highstage OLGA gastritis, extensive IM, and incomplete IM subtype (p < 0.001). Extensive IM was also associated with incomplete IM subtype (p > 0.01). Consequently, a classification could be established as illustrated in table 1. Conclusion This model could stratify patients with non-ulcer dyspepsia into 4 groups with different risk levels of developing GC and potentially help to individualize the follow-up strategies. (Table prested).

18 Rokkas, T., et al. (1991). "Detection of an increased incidence of early gastric cancer in patients with intestinal metaplasia type III who are closely followed up." Gut 32(10): 1110-1113. without a comparator

Because early gastric cancer is associated with a much better prognosis than advanced disease, its diagnosis is important. Over a 12 year period (1976-87), a progressive increase in the incidence of early gastric cancer was observed. Twenty four of the 718 (3.3%) consecutive gastric resections for gastric cancer in this period were in patients with early gastric cancer. Six of the 24 were diagnosed in the first six year period (1976-81) and 18 in the second six year period (1982-87) (p less than 0.01). This increase was observed during the prospective phase of the study, when all patients diagnosed on initial biopsy specimen as showing type III intestinal metaplasia underwent follow up endoscopy and biopsy at six to 12 month intervals. Eleven of the 18 with early gastric cancer detected in this period were diagnosed as a direct result of this follow up. We conclude that early gastric cancer can be diagnosed with increasing frequency if patients with type III intestinal metaplasia are closely followed endoscopically.

19 Shah, S., et al. (2016). "Prevalence of precursor lesions at diagnosis of gastric cancer in a multi-ethnic cohort at an academic center in NYC." American Journal of Gastroenterology 111: S486-S487. cross-section study

Introduction: The prevalence of pre-neoplastic gastric lesions (atrophic gastritis (AG), intestinal metaplasia (IM), dysplasia) during the assessment of risk for gastric cancer (GC) in the US is uncertain, (Figure Presented) especially among races/ethnicities considered to be at higher risk for GC. We aimed to characterize the precursor histologic lesions amongst a multi-racial/ethnic cohort of patients with GC in NYC. Methods: We performed a retrospective analysis of patients with histologically and endoscopically confirmed non-cardia GC from 2008-2016 at a NYC academic center. Age at diagnosis, race/ethnicity, smoking status, and Helicobacter pylori status were recorded. Statistical analysis was performed in STATA. Results: 108 patients [67.6% men/32.4% women] met inclusion criteria. Median age at diagnosis was 71.5 (range 41-92) years. Racial/ethnic breakdown was: Hispanic/Latino(n=27), Asian(n=19), African- American (n=18), European/Russian (n=21), non-European/Russian white (n=5), and unknown (n=18). At presentation, 13% were Stage 0, 31.5% Stage 1, 8.3% stage 2, 7.5% Stage 3, 19.4% Stage 4, and 20.4% not specified. 27.8% were moderately- (n=30/103) and 54.6% poorly-diff erentiated (n=59/103). There was associated AG in 33.6% of GC cases, IM in 98%, and dysplasia in 36.5% (27.9% high-grade, 3.8% lowgrade only). Among cases with type of IM specified (n=38), 42% had complete IM only, 29% incomplete IM only, and 29% both. IM type was not associated with GC grade/stage. H. pylori was present in only 7.4% (n=8/108) and was not significantly associated with the presence of any precursor lesion. There was no difference in associated pathologic lesions, GC grade, or stage between the racial/ethnic groups (p=NS). Current/former smoking status was significantly associated with multifocal IM (p=0.009), but was not associated with GC grade/stage at presentation. Patients who underwent endoscopy at any time prior to GC diagnosis (n=22), had similar age at presentation, GC grade, and stage compared to those patients who did not. Conclusion: Precursor lesions for GC occur at comparable rates among different ethnic/racial groups thought to be at higher GC risk within the overall low-prevalence US. Despite a high prevalence of precursor lesions, H. pylori infection in this cohort at GC diagnosis was low. Endoscopy prior to GC diagnosis was not associated with improved disease characteristics. Factors contributing to the progression of pre-neoplastic lesions among different races/ethnicities need to be clarified in larger series.