

HISTOLOGICAL PARAMETERS

ADDITIONAL FILE FOR THE MANUSCRIPT:

Peritoneal Negative Pressure Therapy Prevents Multiple
Organ Injury in a Chronic Porcine Sepsis and
Ischemia/Reperfusion model

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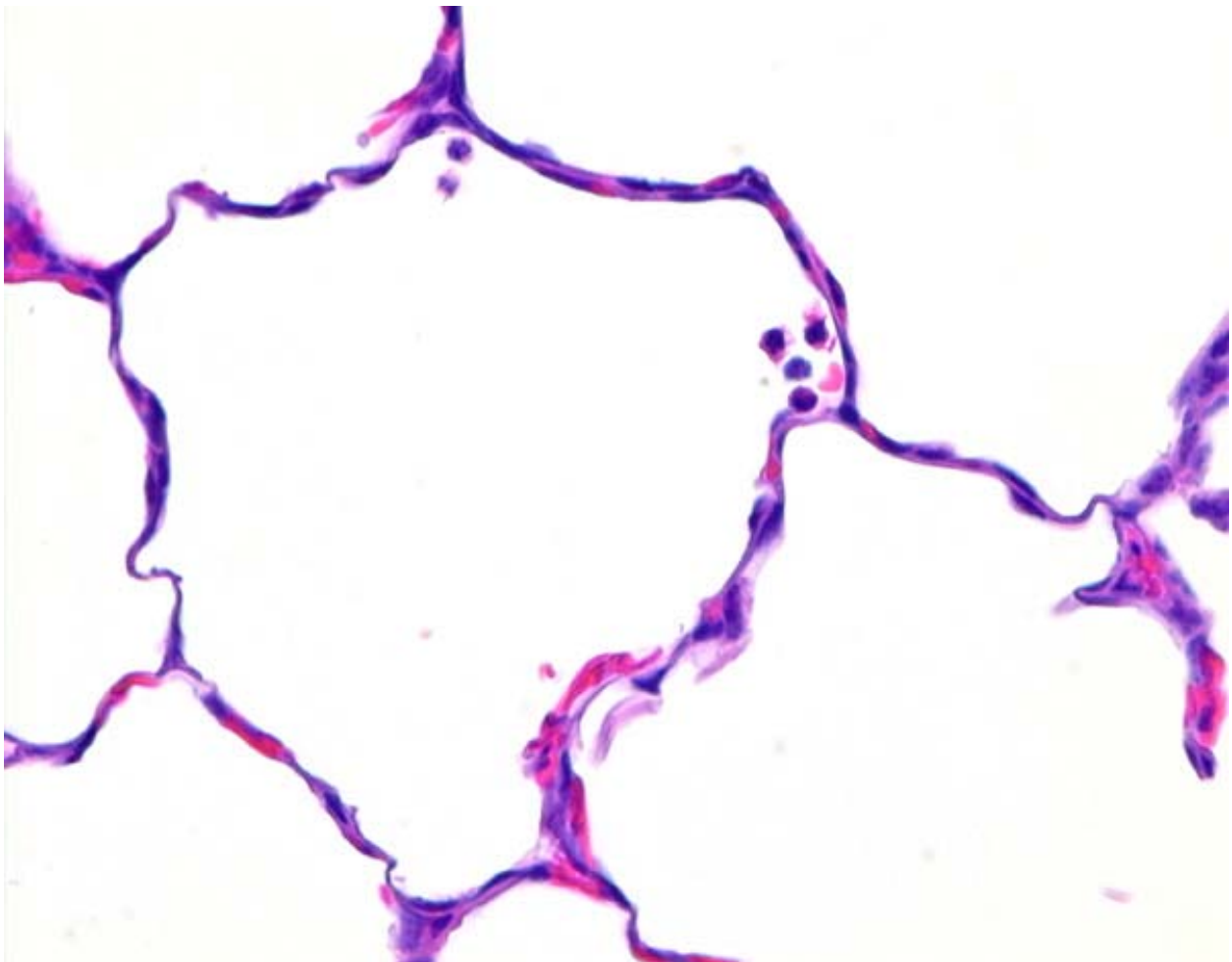
HISTOLOGICAL ASSESSMENT OF THE LUNG

List of Parameters:

- ▶ Atelectasis
- ▶ Fibrinous Deposits
- ▶ Hemorrhage in Air Compartment
- ▶ Vessel Congestion
- ▶ Alveolar Wall Thickness
- ▶ Leukocyte Infiltration

LUNG: NO LESIONS

- No atelectasis
- No fibrinous deposits (hyaline membrane) in air spaces
- No hemorrhage in air spaces
- No congestion of alveolar capillaries
- Alveolar walls are one-cell thick
- Less than 10 leukocytes per sample area (215x165 μm)

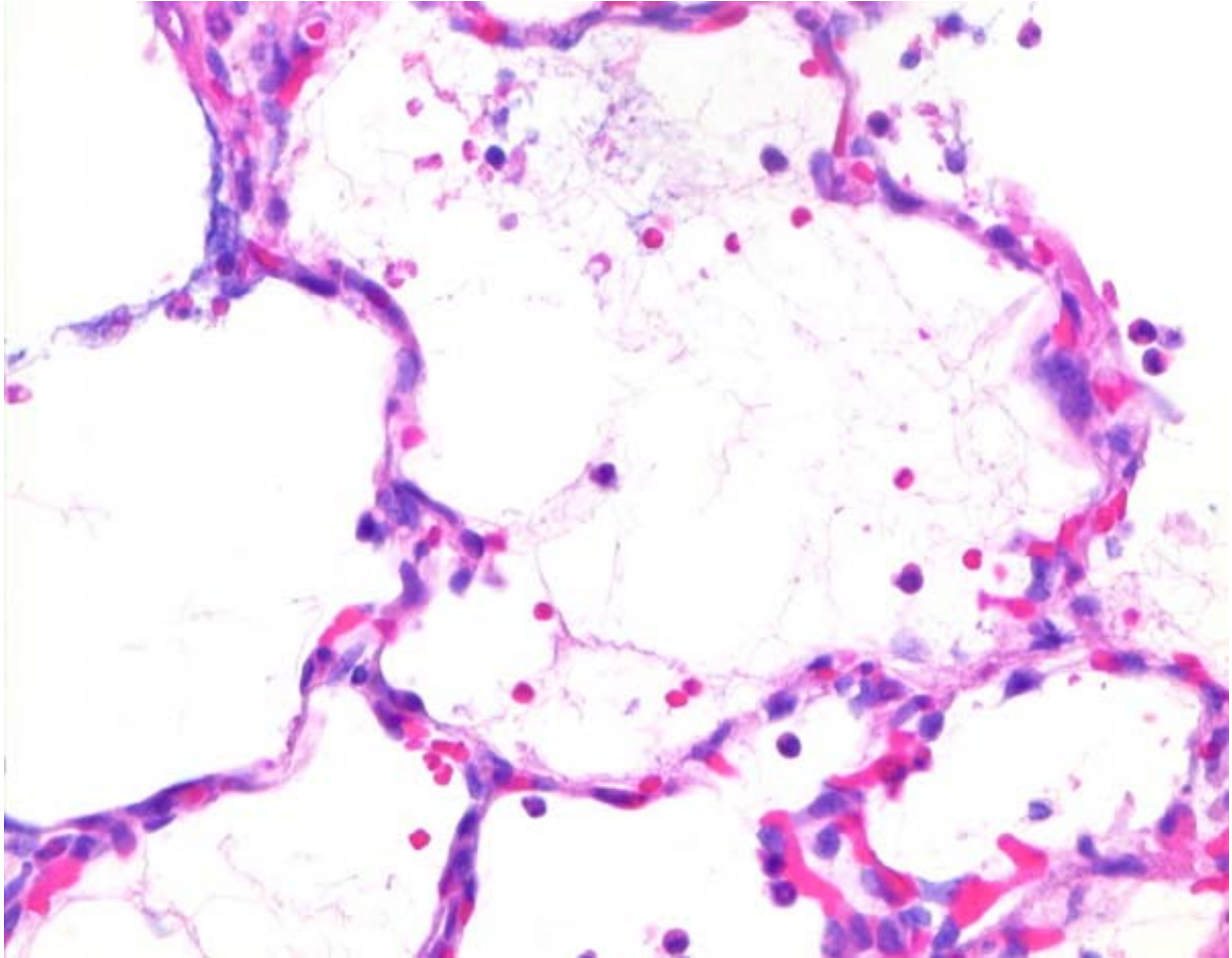


SCORING:

Scores of zero in all categories

LUNG: FIBRINOUS DEPOSITS

Fibrin strands (hyaline membrane) visible within air spaces



SCORING:

The photomicrograph was divided into four quadrants and quantified using the following scoring system:

- 0 = no deposits
- 1 = deposits in one quadrant
- 2 = deposits in two quadrants
- 3 = deposits in three quadrants
- 4 = deposits in all quadrants

LUNG: HEMORRHAGE IN AIR SPACES

Erythrocytes present within alveolar lumen



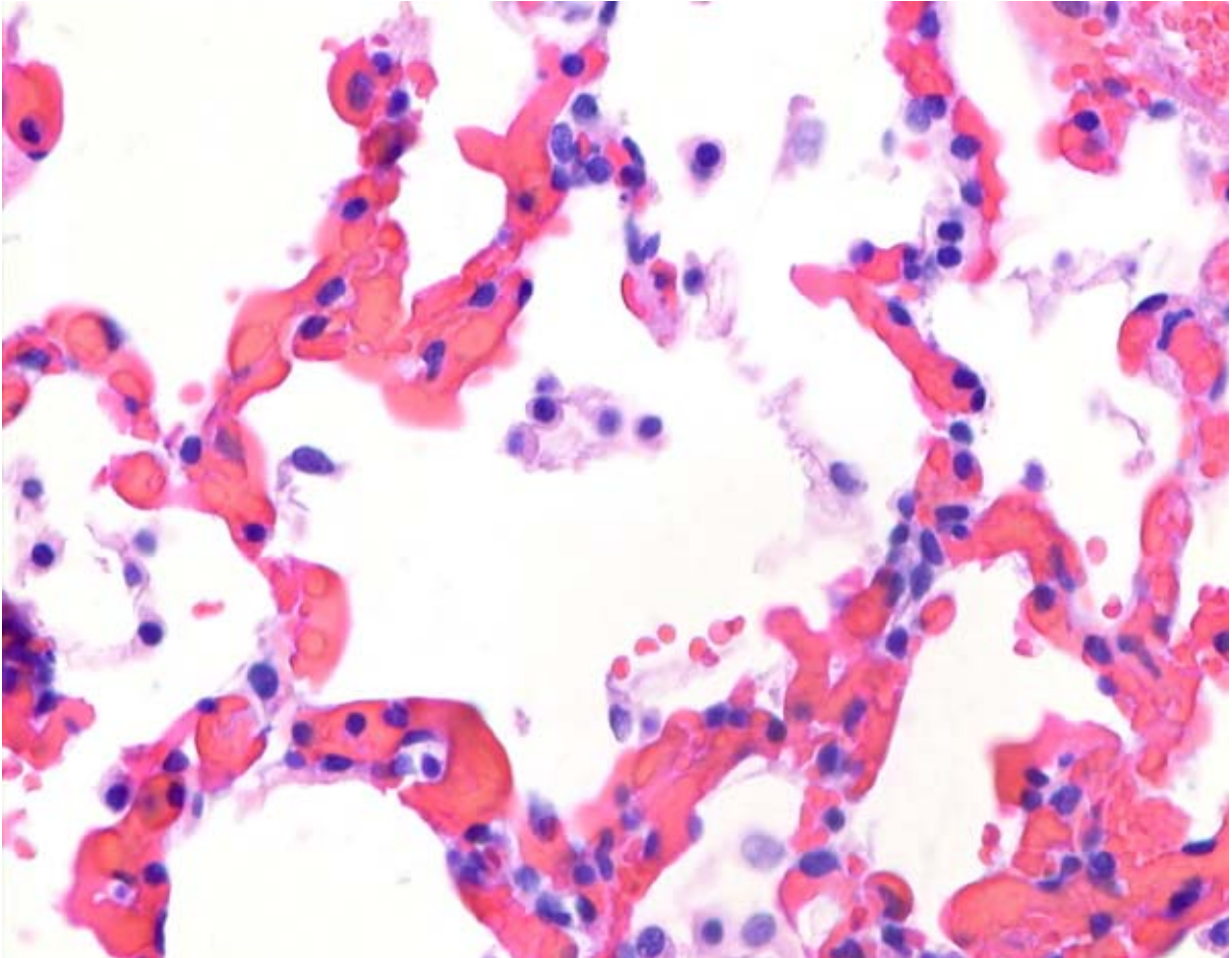
SCORING:

The photomicrograph was divided into four quadrants and quantified using the following scoring system:

- 0 = no hemorrhage
- 1 = hemorrhage in one quadrant
- 2 = hemorrhage in two quadrants
- 3 = hemorrhage in three quadrants
- 4 = hemorrhage in all quadrants

LUNG: VESSEL CONGESTION

Alveolar capillaries filled with blood protrude into air space



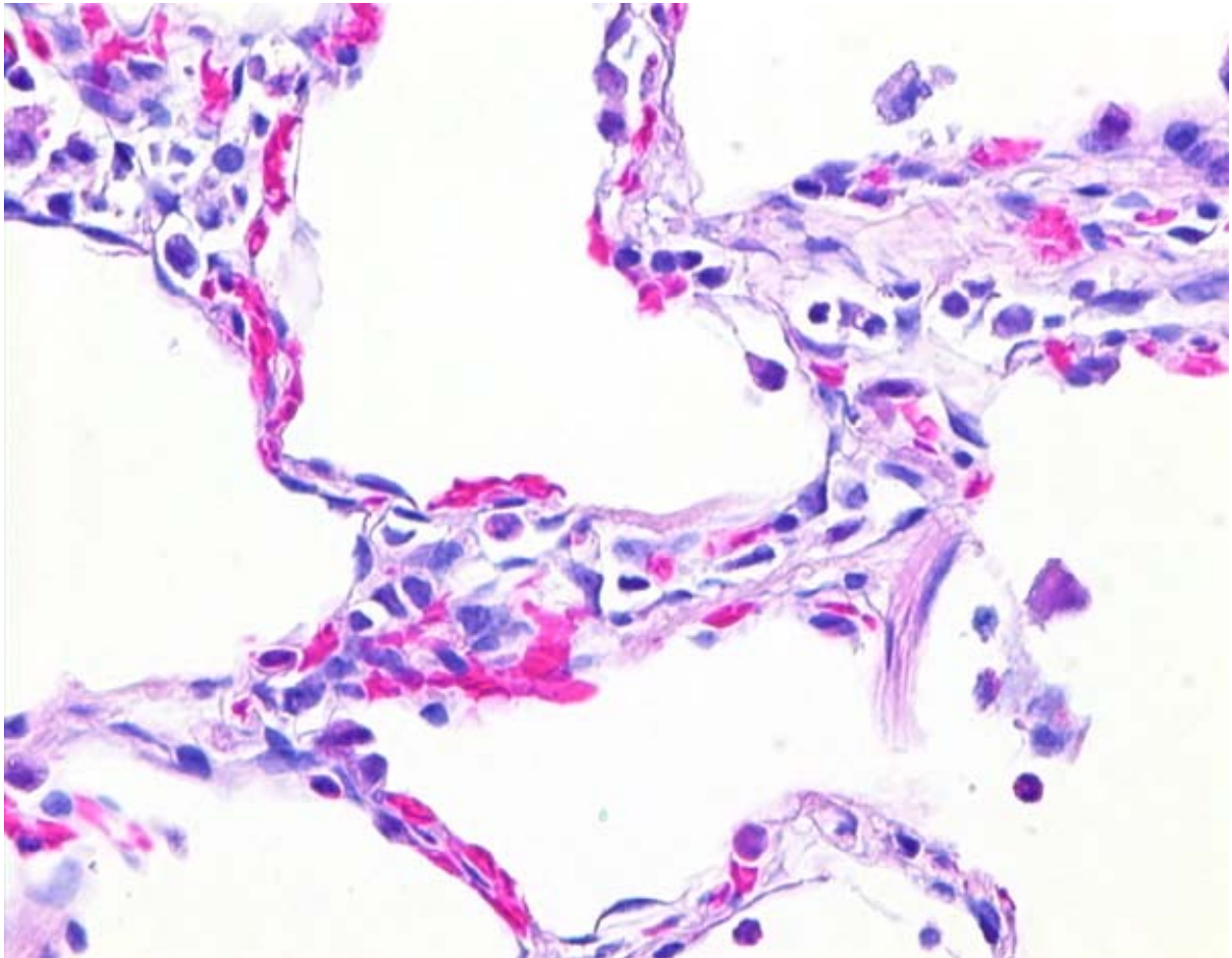
SCORING:

The photomicrograph was divided into four quadrants and quantified using the following scoring system:

- 0 = no congested capillaries
- 1 = congestion in one quadrant
- 2 = congestion in two quadrants
- 3 = congestion in three quadrants
- 4 = congestion in all quadrants

LUNG: ALVEOLAR WALL THICKNESS

Alveolar wall thickness exceeds one cell



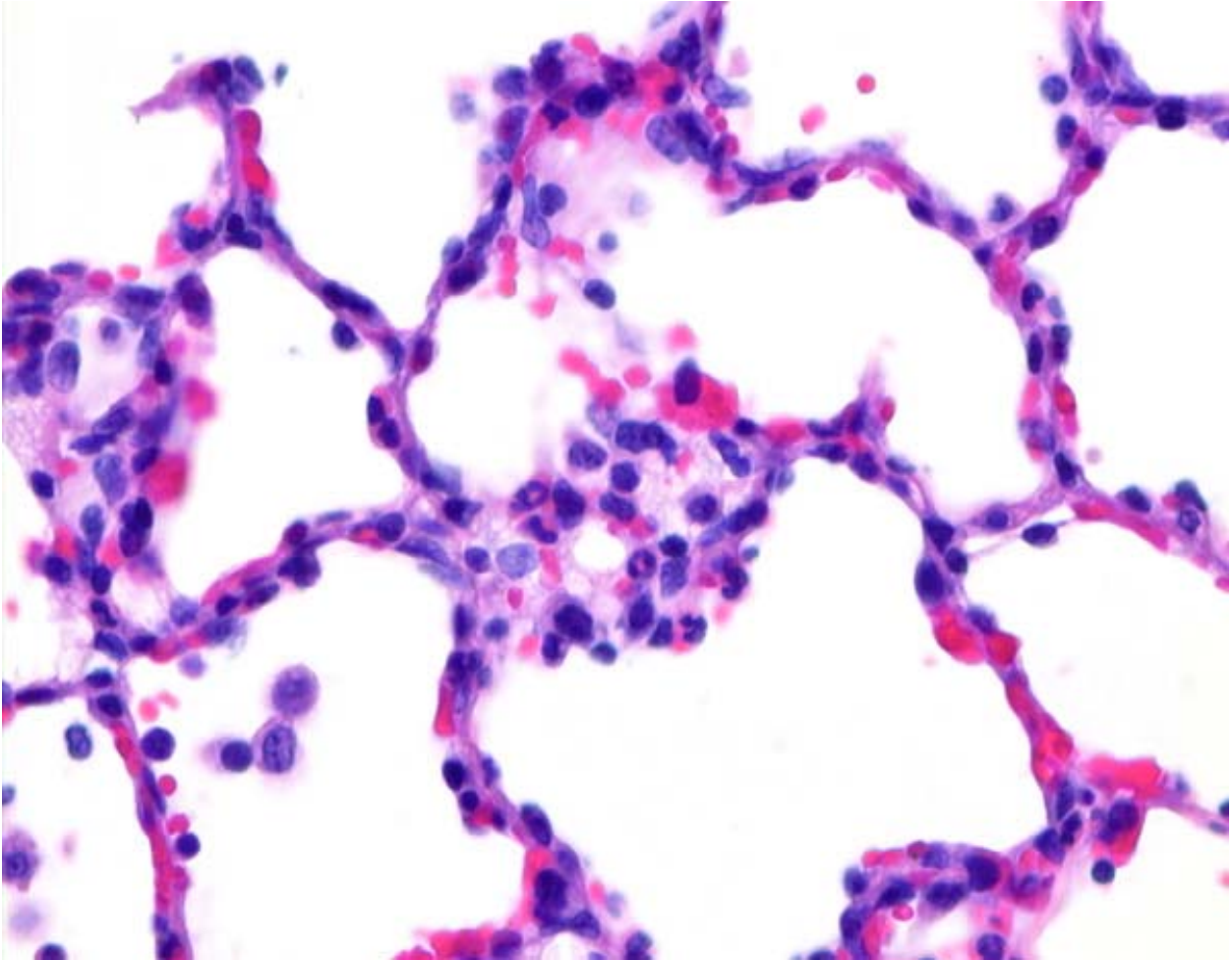
SCORING:

The photomicrograph was divided into four quadrants and quantified using the following scoring system:

- 0 = no thickened alveolar walls
- 1 = thickened walls in one quadrant
- 2 = thickened walls in two quadrants
- 3 = thickened walls in three quadrants
- 4 = thickened walls in all quadrants

LUNG: LEUKOCYTE INFILTRATION

Hematogenous (inflammatory?) wandering cells per sample area (215x165 μm)



SCORING:

The number of wandering cells in the photomicrograph was quantified using the following scoring system:

- 0 = less than 10 cells
- 1 = at least 10 cells
- 2 = at least 25 cells
- 3 = at least 50 cells
- 4 = over 75 cells

HISTOLOGICAL ASSESSMENT OF KIDNEY CORTEX

Histological changes were quantified in the renal cortex according to 5 parameters:

- ▶ Interstitial Edema
- ▶ Epithelial Changes
- ▶ Tubular Degeneration
- ▶ Capillary Congestion
- ▶ Leukocyte Infiltration

(1) Interstitial Edema, present as either of the following:

- (1a) - Edematous vessel cuffs
- (1b) - Peritubular edema
- (1c) - Lymphatic vessel dilation

(2) Epithelial Changes, present as either of the following:

- (2a) - Paracellular spaces
- (2b) - Loss of brush border
- (2c) - Tubular dilation (cell shortening)
- (2d) - Tubular cell apoptosis

(3) Tubular Degeneration, present as either of the following:

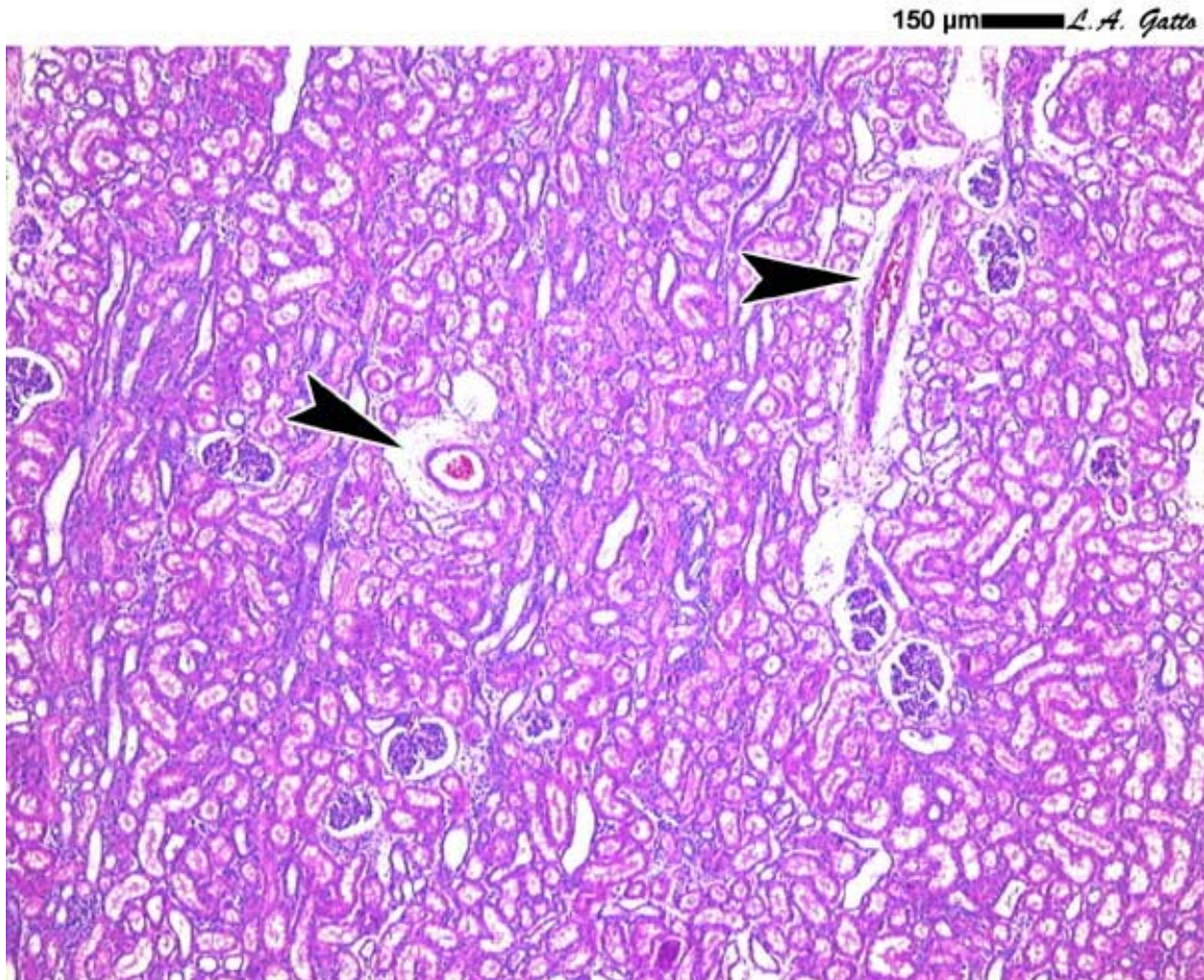
- (3a) - Detached basement membrane
- (3b) - Loss of cellular definition
- (3c) - Epithelial sloughing
- (3d) - Loss of tubular architecture
- (3e) - Tubular necrosis

(4) Capillary Congestion

(5) Leukocyte Infiltration

The pages that follow illustrate and describe morphological examples (a, b, c ...) of each parameter (1 through 5).

Interstitial Edema: (1a) Edematous Vessel Cuffs



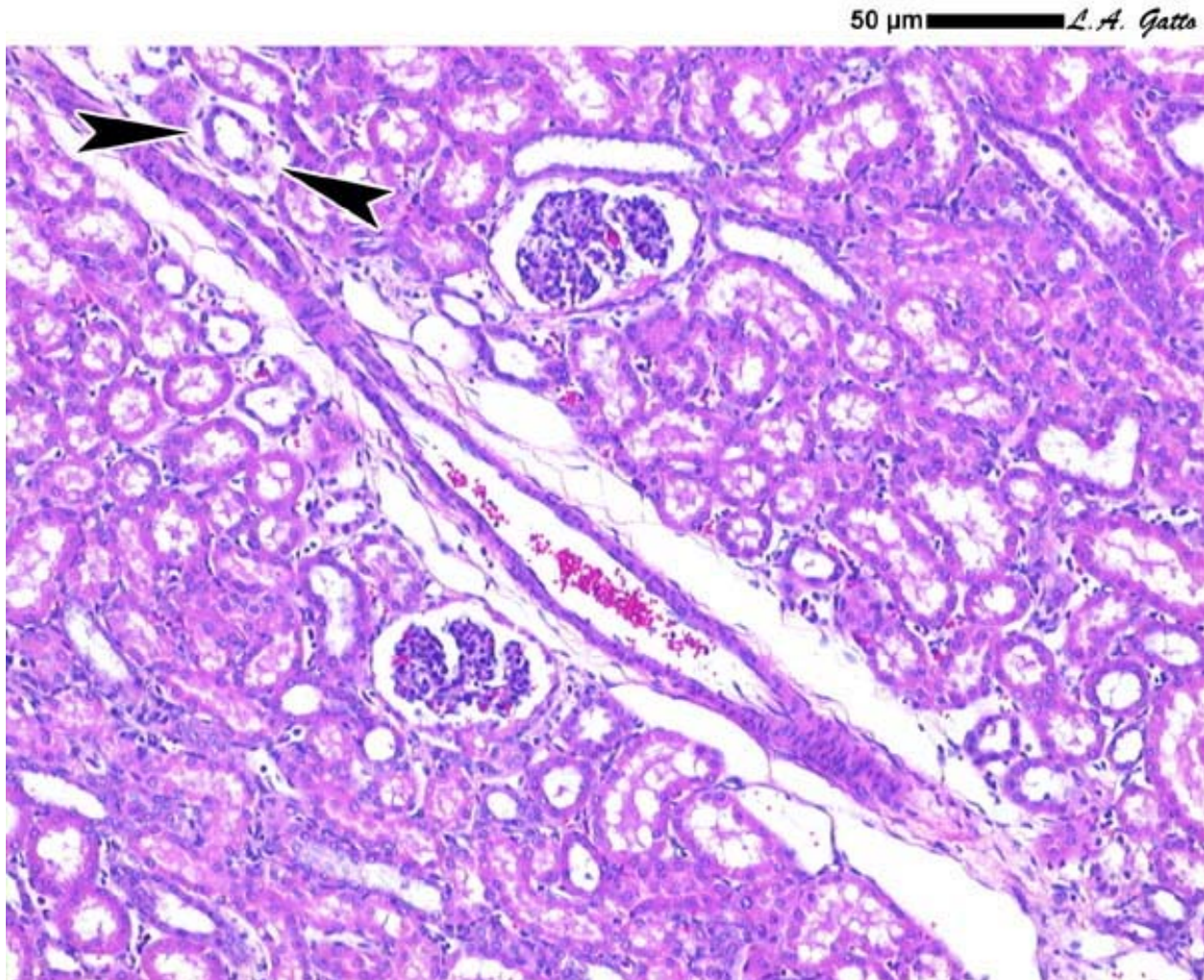
Interstitial edema is most evident in the connective tissue compartments that carry vessels and nerves. Since the kidney has no prominent septa, the most obvious connective tissue occurs around vessels. In an edematous state, the connective tissue forms a prominent cuff around the vessel (**arrowhead**). Frequency of occurrence is highest when vessels of all sizes exhibit cuffs.

Scoring System: 0 to 4

- 0 = cuffs not present in the photo
- 1 = sporadic occurrence of cuffs
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

[NOTE: scoring does not quantify size of cuff]

Interstitial Edema: (1b) Peritubular Edema



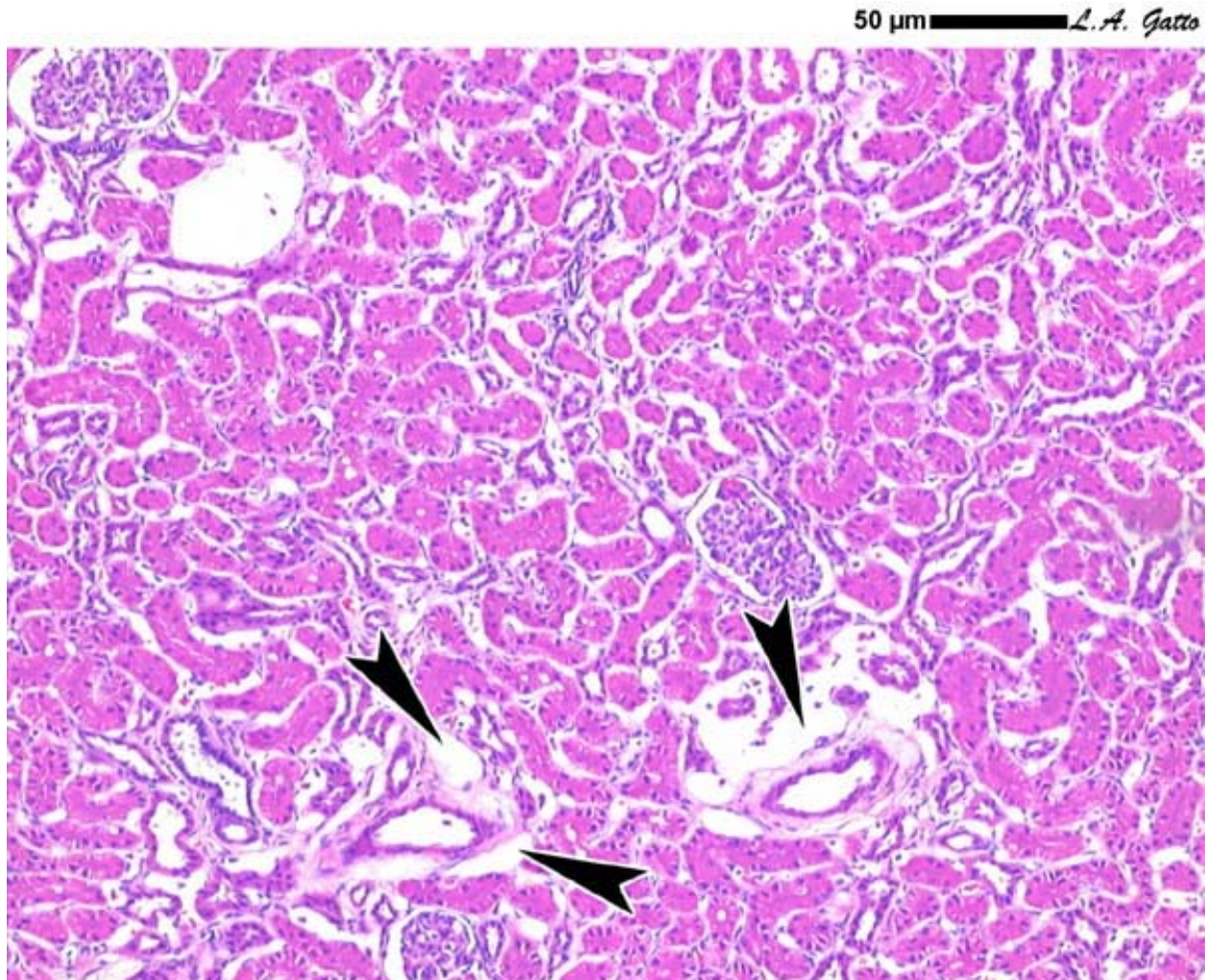
The generalized presence of interstitial edema would expand the connective tissue framework (stroma) and separate all the tubules evenly. Notably, peritubular edema may be prominent around some tubules but not others. In this photo, peritubular edema (**arrowhead**) is conspicuous around some distal convoluted tubules.

Scoring System: 0 to 4

- 0 = peritubular edema not present in the photo
- 1 = sporadic occurrence of peritubular edema
- 2 = incidence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

[NOTE: Scoring does not quantify grouping or anatomical distribution]

Interstitial Edema: (1c) Lymphatic Vessel Dilation

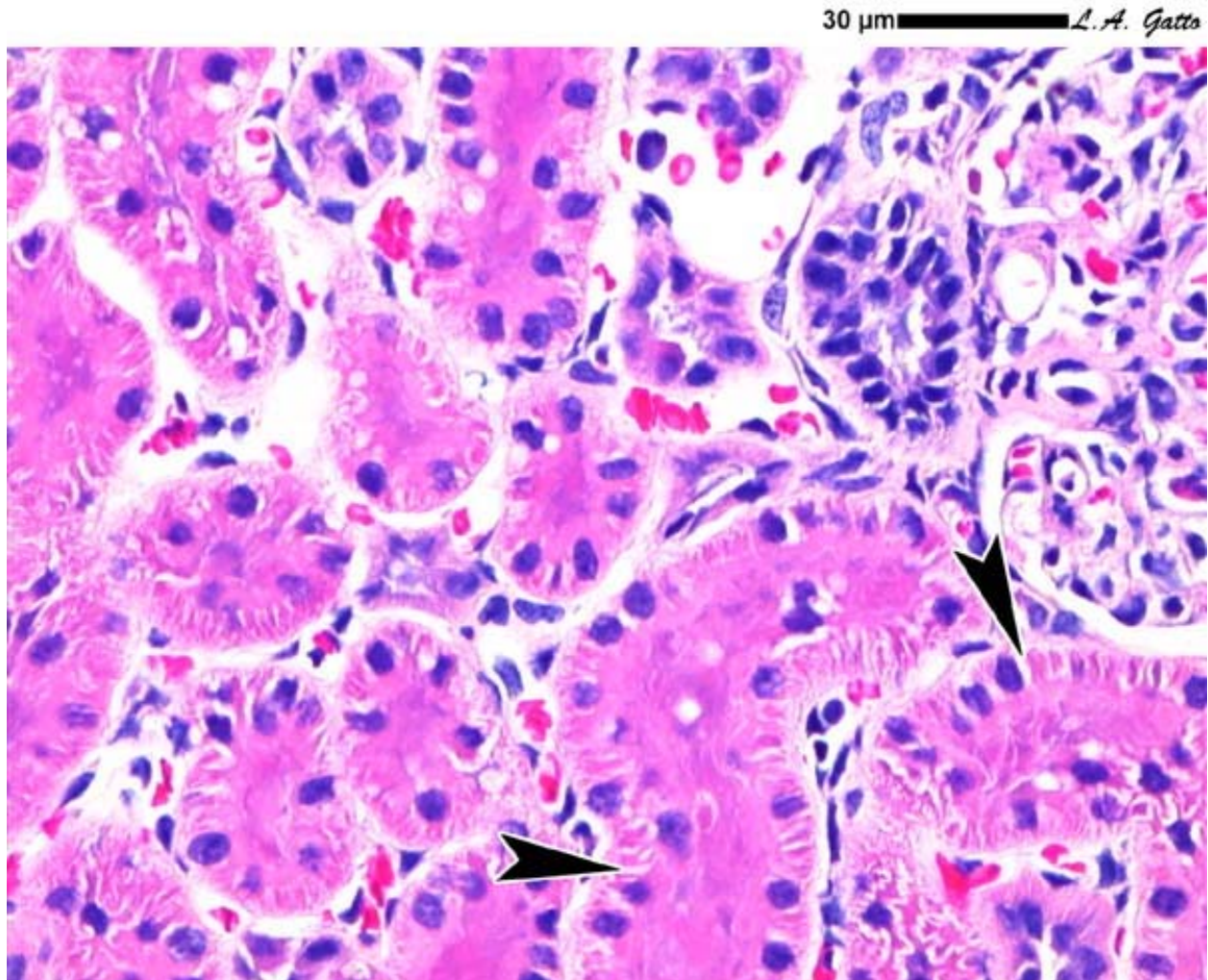


Lymphatic vessels are ordinarily collapsed and inconspicuous. Dilated lymphatic vessels, however, stand out as prominent open areas bound only by very slender endothelium (**arrowheads**). Lymphatic capillaries occur among renal tubules, while larger lymphatic vessels generally extend along connective tissue compartments shared with blood vessels and nerves.

Scoring System: 0 to 4

- 0 = no dilated lymphatics in the photo
- 1 = dilated lymphatics in one quadrant of the photo
- 2 = dilated lymphatics in two quadrants of the photo
- 3 = dilated lymphatics in three quadrants of the photo
- 4 = dilated lymphatics in four quadrants of the photo

Epithelial Changes: (2a) Paracellular Spaces

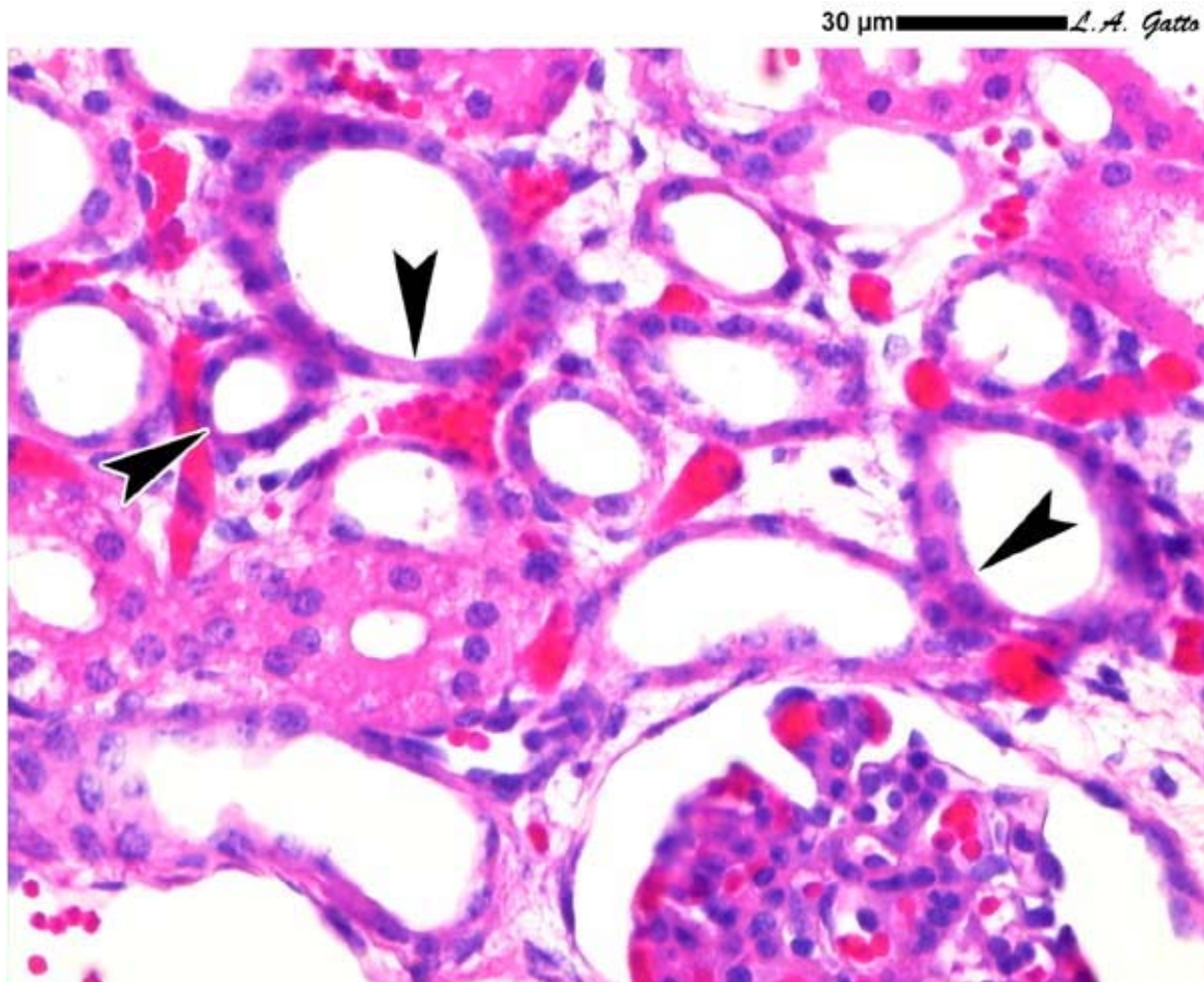


Spaces within the tubular epithelium (**arrowheads**) indicate failure of gap junctions between adjoining cells. Impaired junctional complexes lead to loss of epithelial barrier function.

Scoring System: 0 to 4

- 0 = paracellular gaps not present in the photo
- 1 = sporadic occurrence of paracellular gaps
- 2 = presence amounts to half of the photo
- 3 = paracellular gaps present in up to 3/4 of the photo
- 4 = paracellular gaps prevalent throughout the photo

Epithelial Changes: (2b) Loss of Brush Border

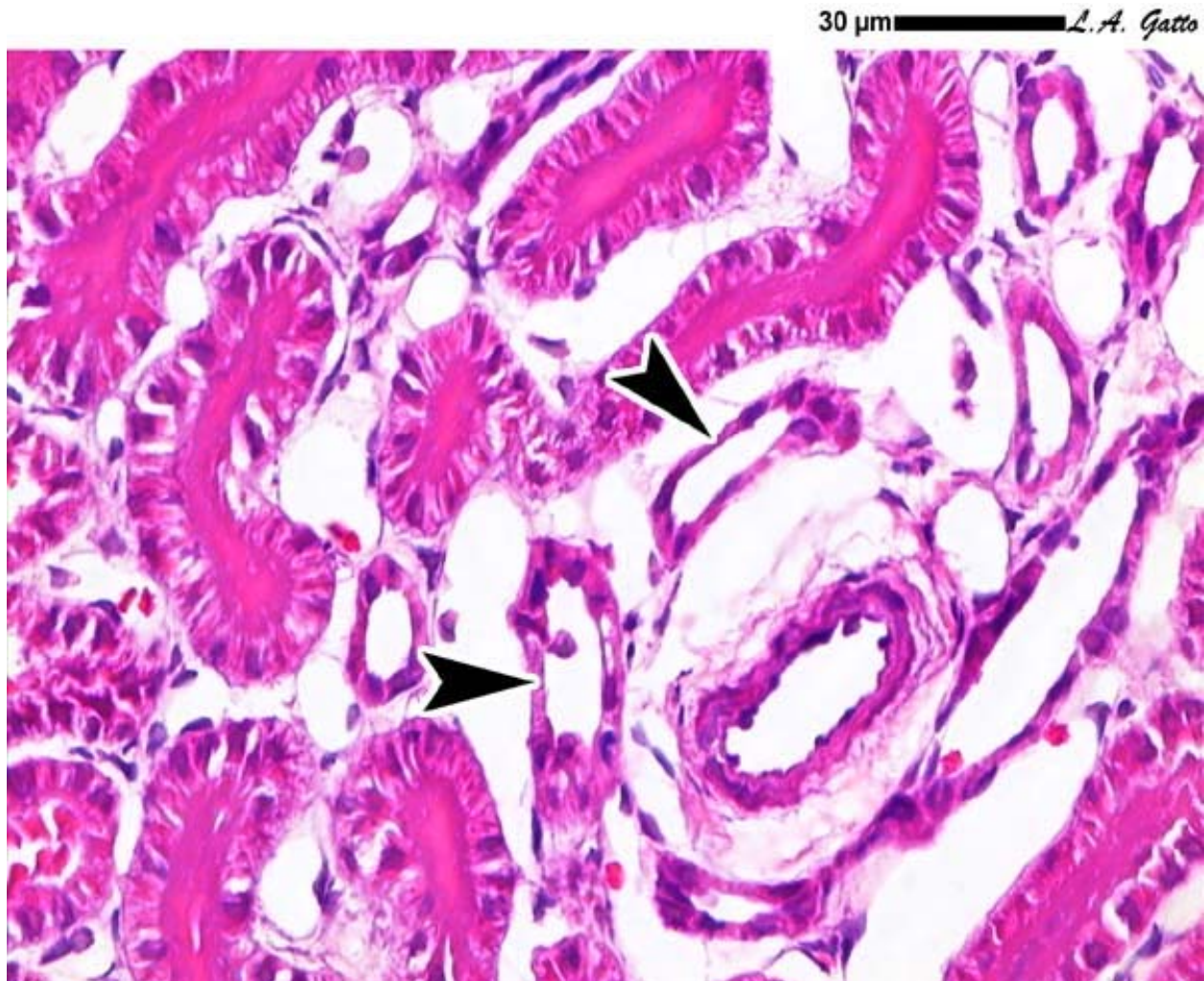


Absorptive activity varies along the nephron and, accordingly, nephron tubule cells exhibit varying amounts of apical microvilli. Cortical tubules have prominent microvilli which can be seen at the level of the light microscope in the form of a brush border. Distal convoluted tubules have very discernable brush borders, even at medium magnification. Tubules that have lost their brush border (**arrowheads**) have the outer diameter of their normal counterparts, but their apical cytoplasm appears truncated.

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

Epithelial Changes: (2c) Tubular Dilation (Cell Shortening)

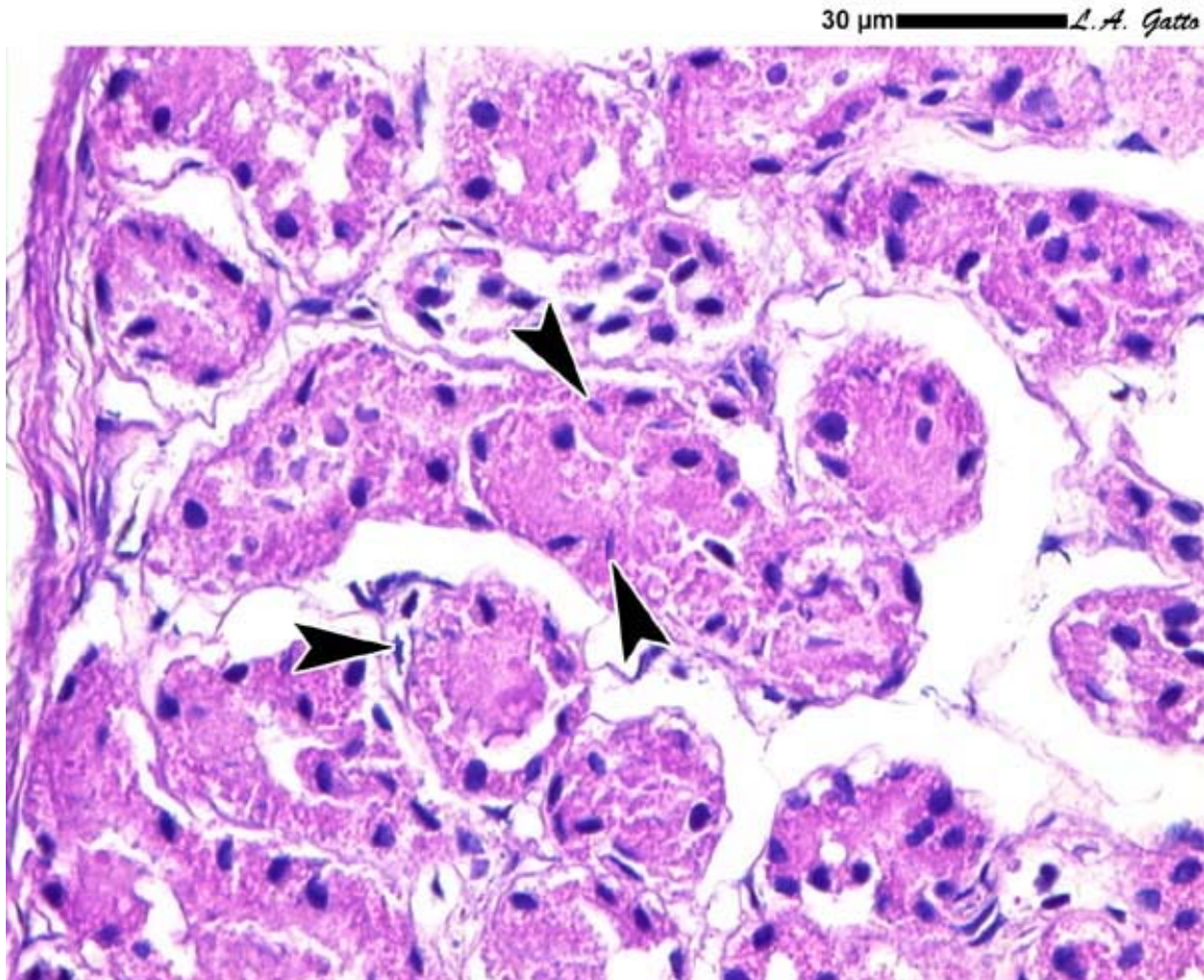


Loss of cytoplasmic mass by the cells of the renal tubule causes architectural changes described in the literature as tubular dilation (**arrowheads**). Close inspection, however, shows that the apparent dilation is caused by a shortening of the cell, as the inner diameter increases without a corresponding increase of the outer diameter of the tubule.

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

Epithelial Changes: (2d) Tubular Cell Apoptosis

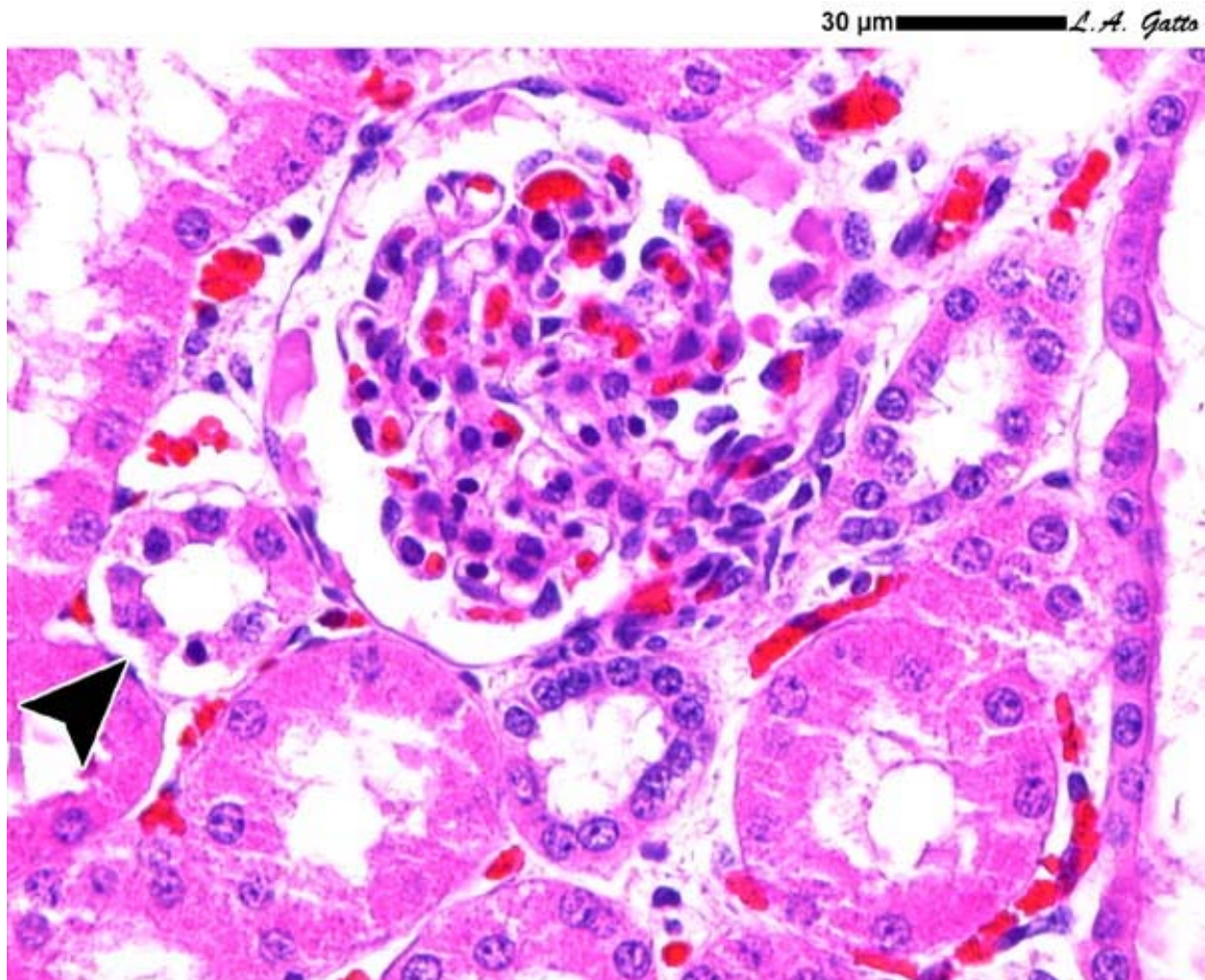


Apoptosis can be determined in routine histological preparations by the identification of morphological characteristics such as cellular rounding and shrinkage. At higher magnifications, morphological criteria include chromatin compaction and formation of apoptotic bodies. The apoptotic nuclear appearance is distinctive with rounded, margined, crescentic nuclear chromatin in condensed or fragmented nuclei (**arrowheads**).

Scoring System: 0 to 4

- 0 = apoptosis not present in the photo
- 1 = sporadic occurrence of apoptosis
- 2 = presence amounts to half of the photo
- 3 = apoptosis present in up to 3/4 of the photo
- 4 = prevalent apoptosis throughout the photo

Tubular Degeneration: (3a) Detached Basement Membrane



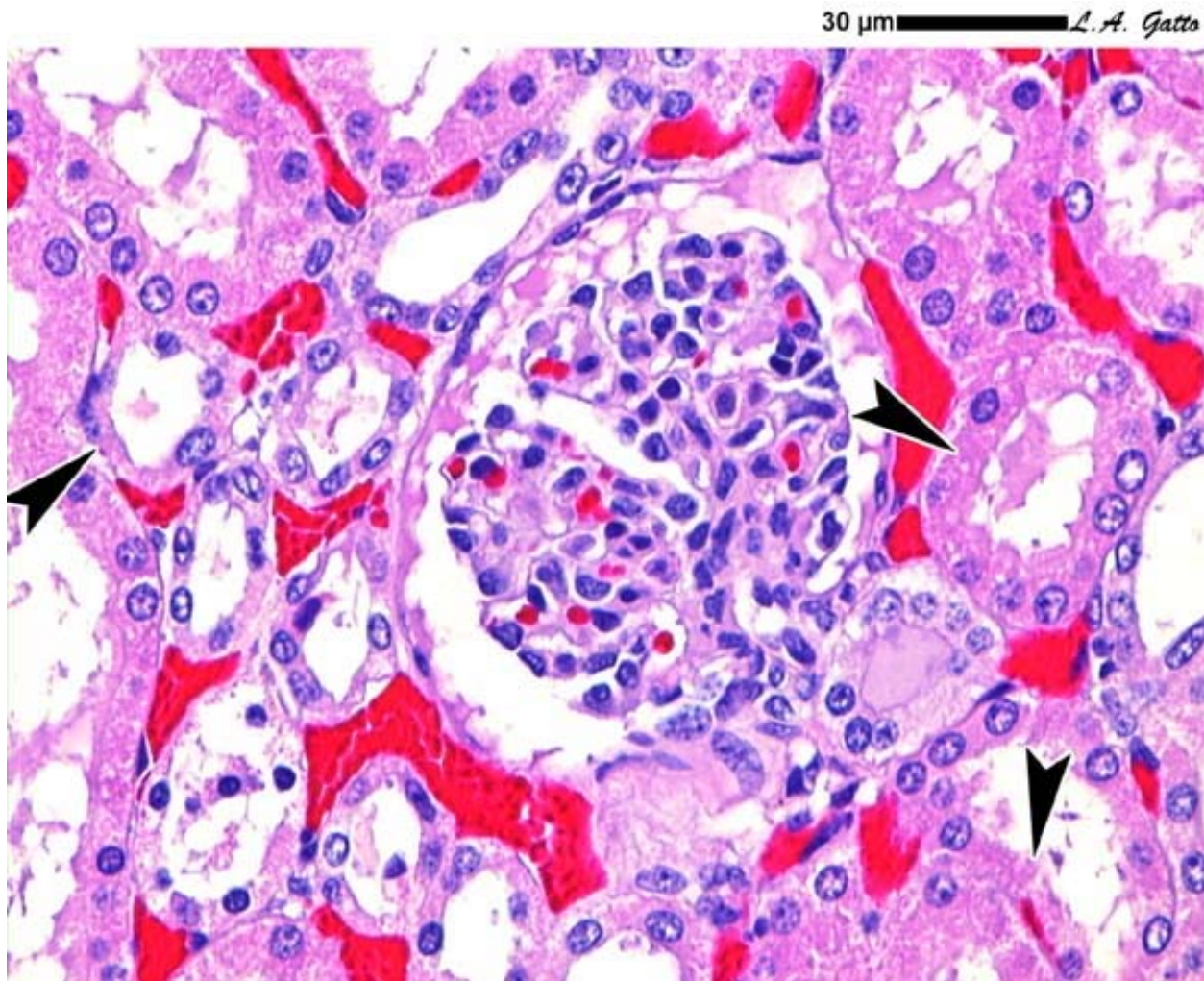
The designation "Tubular Degeneration" refers to morphological changes which alter the basic architecture of the tubule and generally involve more than one cell.

Detachment of the cell from its basement membrane (**arrowhead**) may occur in conjunction with intercellular gaps and may indicate loss of epithelial barrier function.

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

Tubular Degeneration: (3b) Loss of Cellular Definition

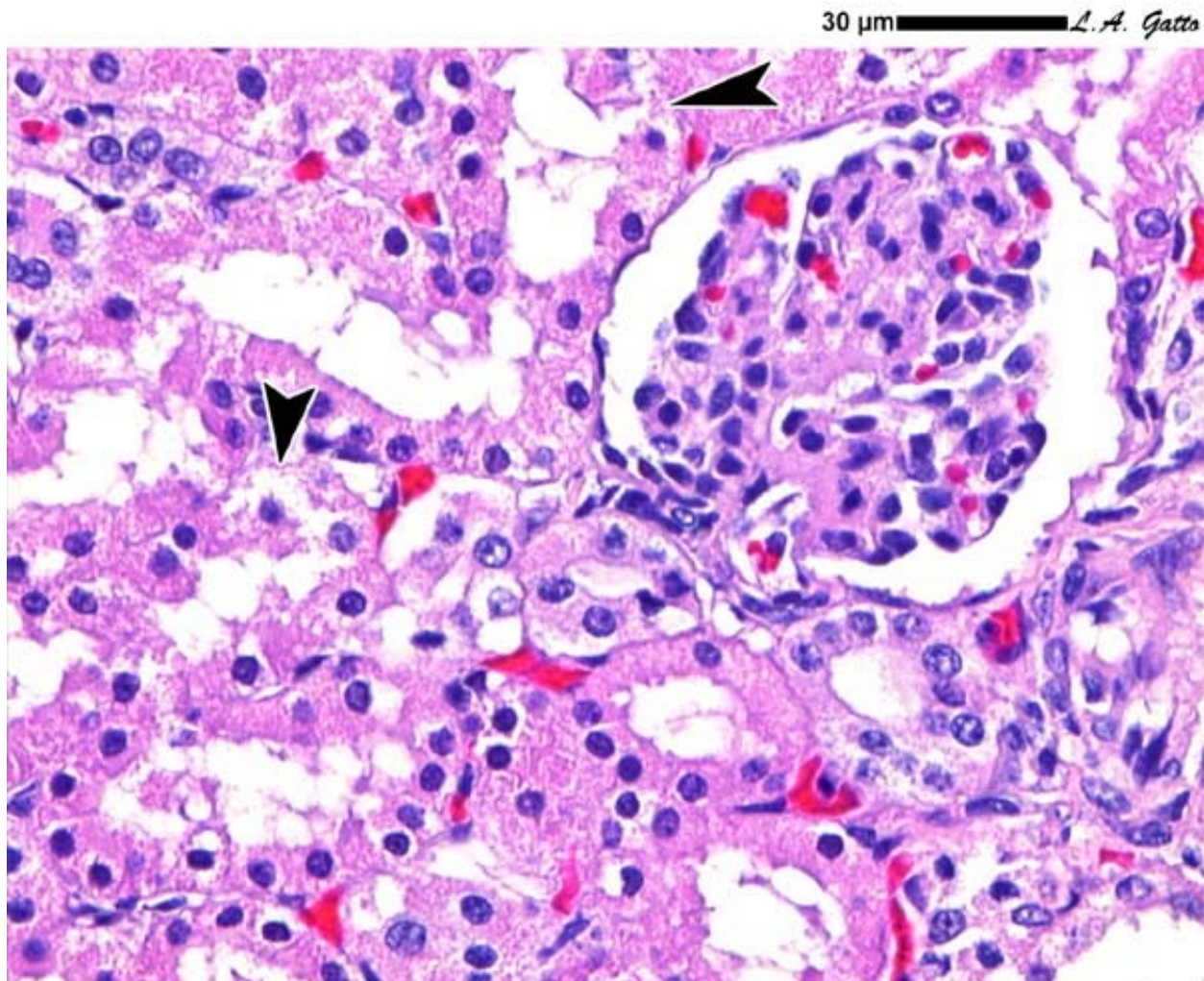


Loss of cellular definition in the tubular epithelium is marked by morphological distortion that renders cytoplasmic features indistinct, blurring the boundaries between cells and leaving portions of the tubule with a scanty, anuclear cytoplasmic presence (**arrowhead**).

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

Tubular Degeneration: (3c) Epithelial Sloughing

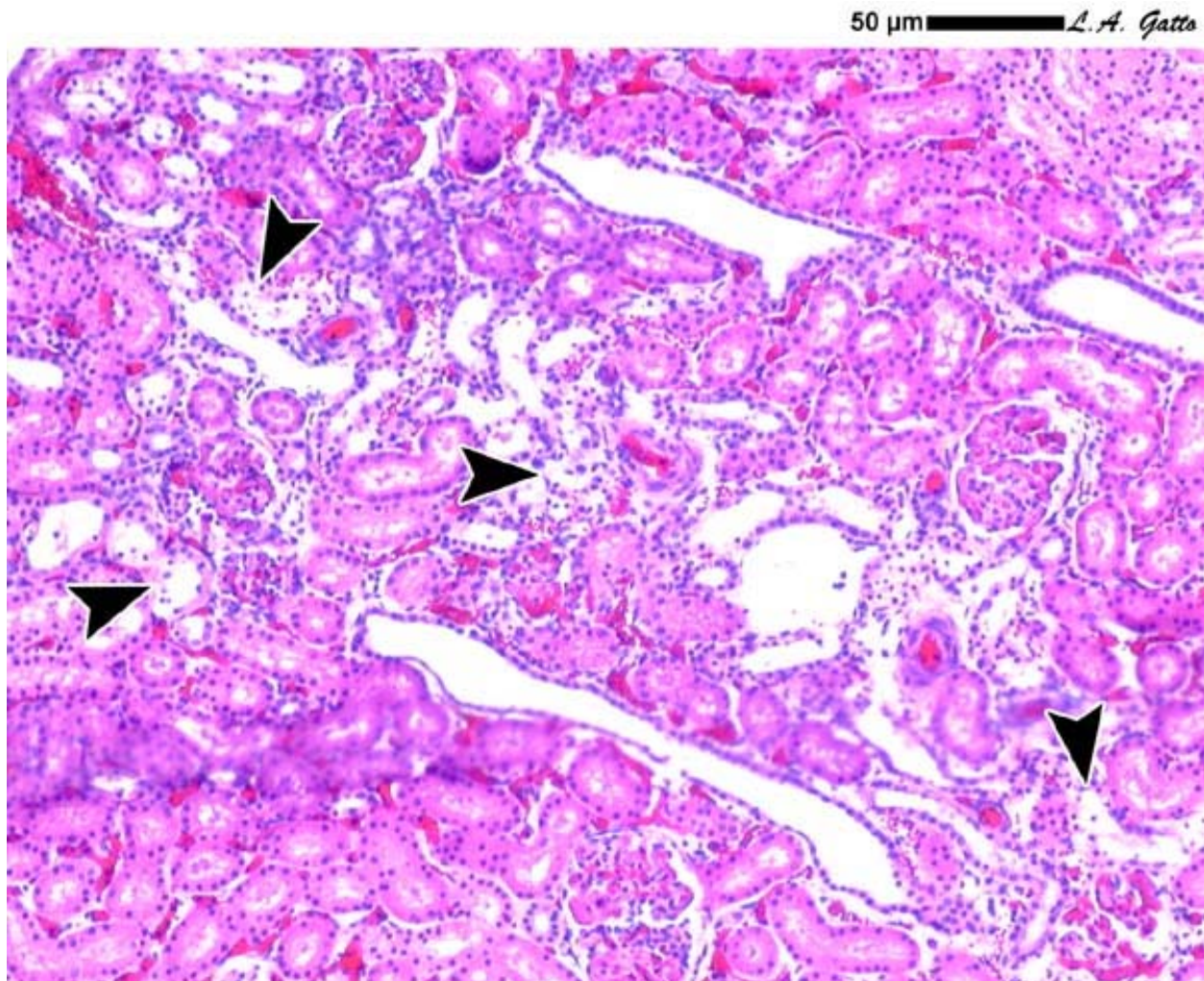


Acute loss of tubular epithelium involves shedding of cytoplasmic material into the tubular lumen (**arrowhead**). Epithelial sloughing leaves portions of the nephron tubule denuded, thus devoid of functional epithelium.

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

Tubular Degeneration: (3d) Loss of Tubular Architecture

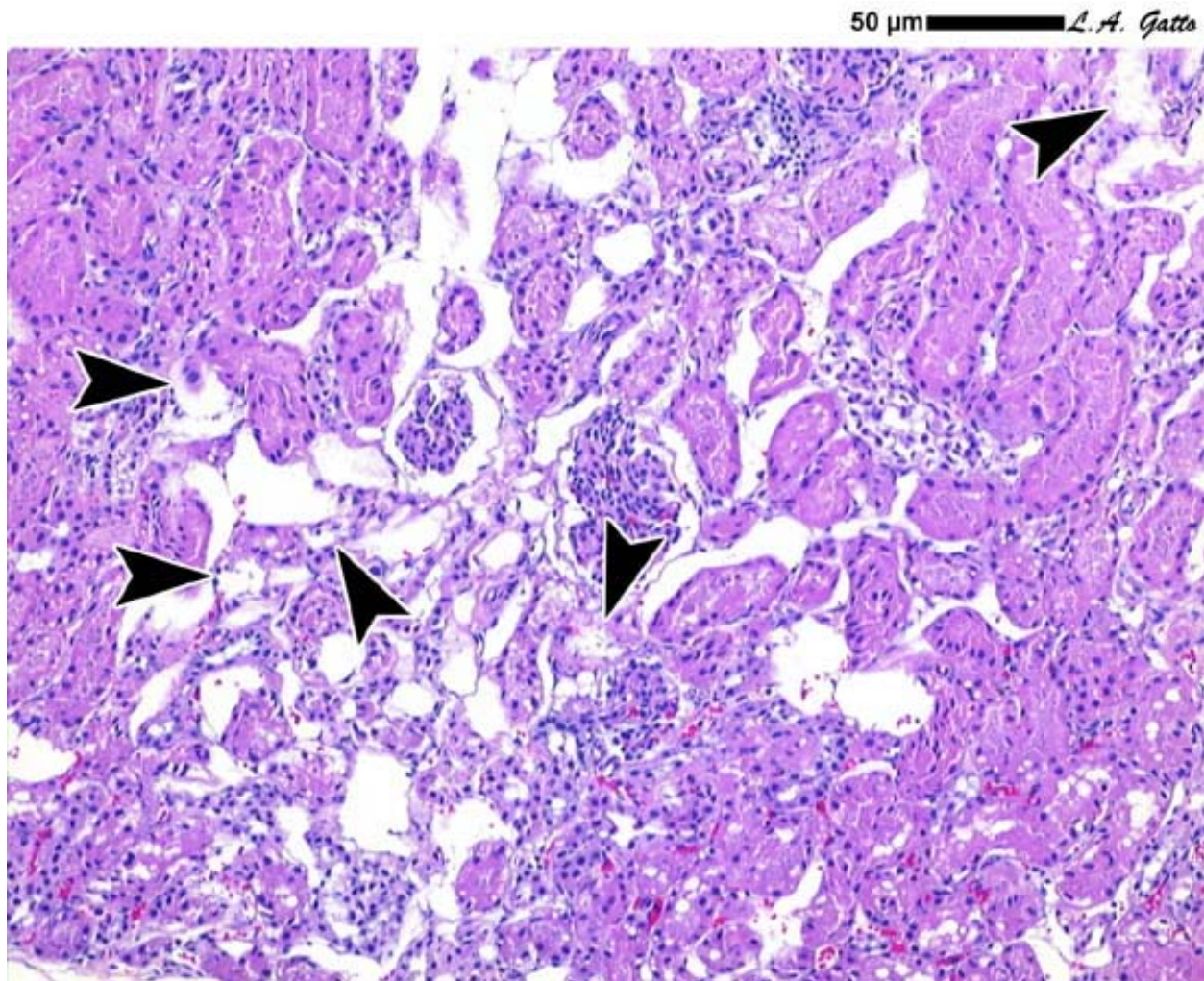


A gross degenerative change is the loss of basic tubular architecture as evidenced by interruptions in the otherwise continuous epithelial wall (**arrowheads**).

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

Tubular Degeneration: (3e) Tubular Necrosis

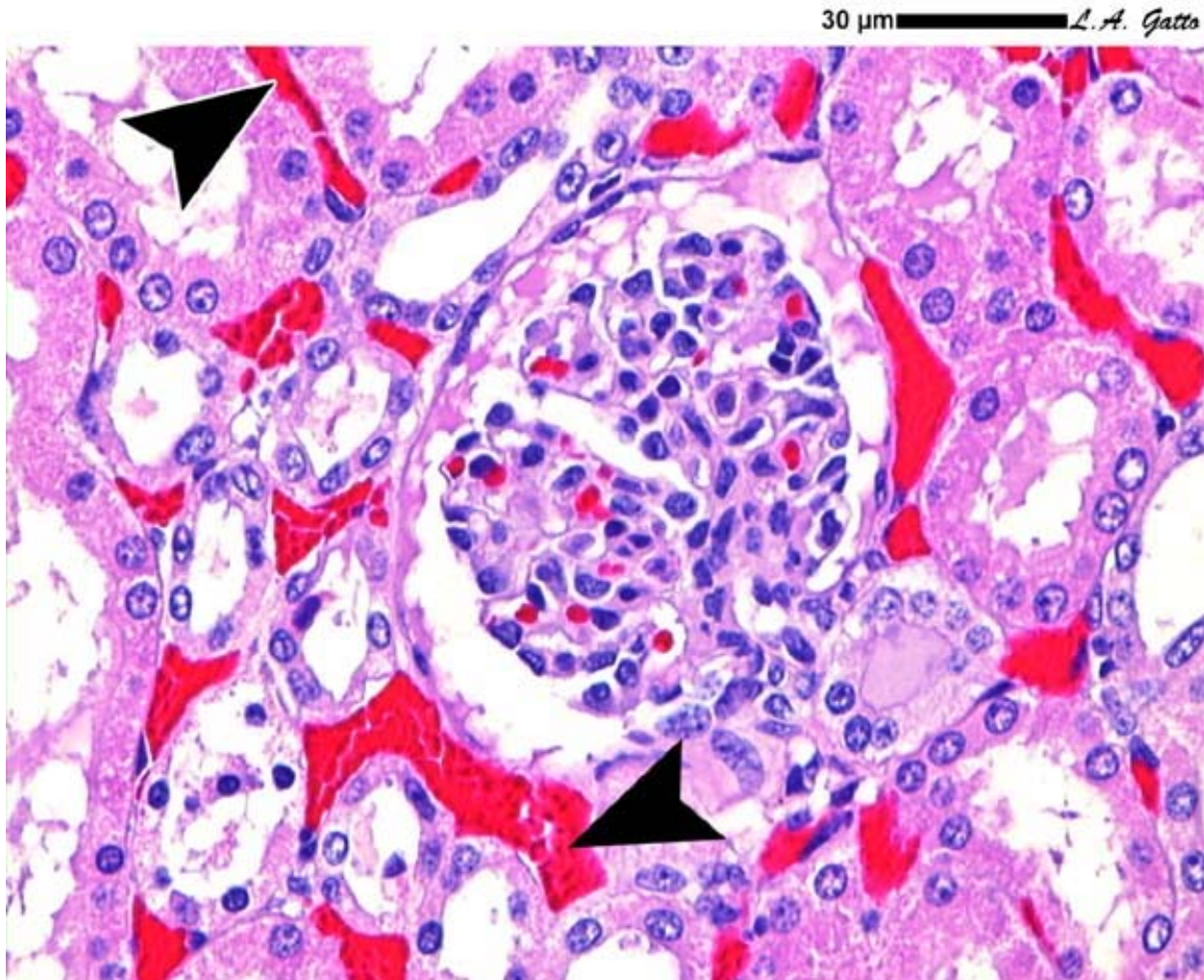


In tubular necrosis the structure (**arrowhead**) amounts to a ghost of the tubule, where the area may remain circumscribed by a basement membrane although the cellular components are either inadequate or altogether missing. There is no infrastructure to carry out the functions of the tubule.

Scoring System: 0 to 4

- 0 = lesion not present in the photo
- 1 = sporadic occurrence of the lesion
- 2 = presence amounts to half of the photo
- 3 = present in up to 3/4 of the photo
- 4 = prevalent throughout the photo

(4) Capillary Congestion



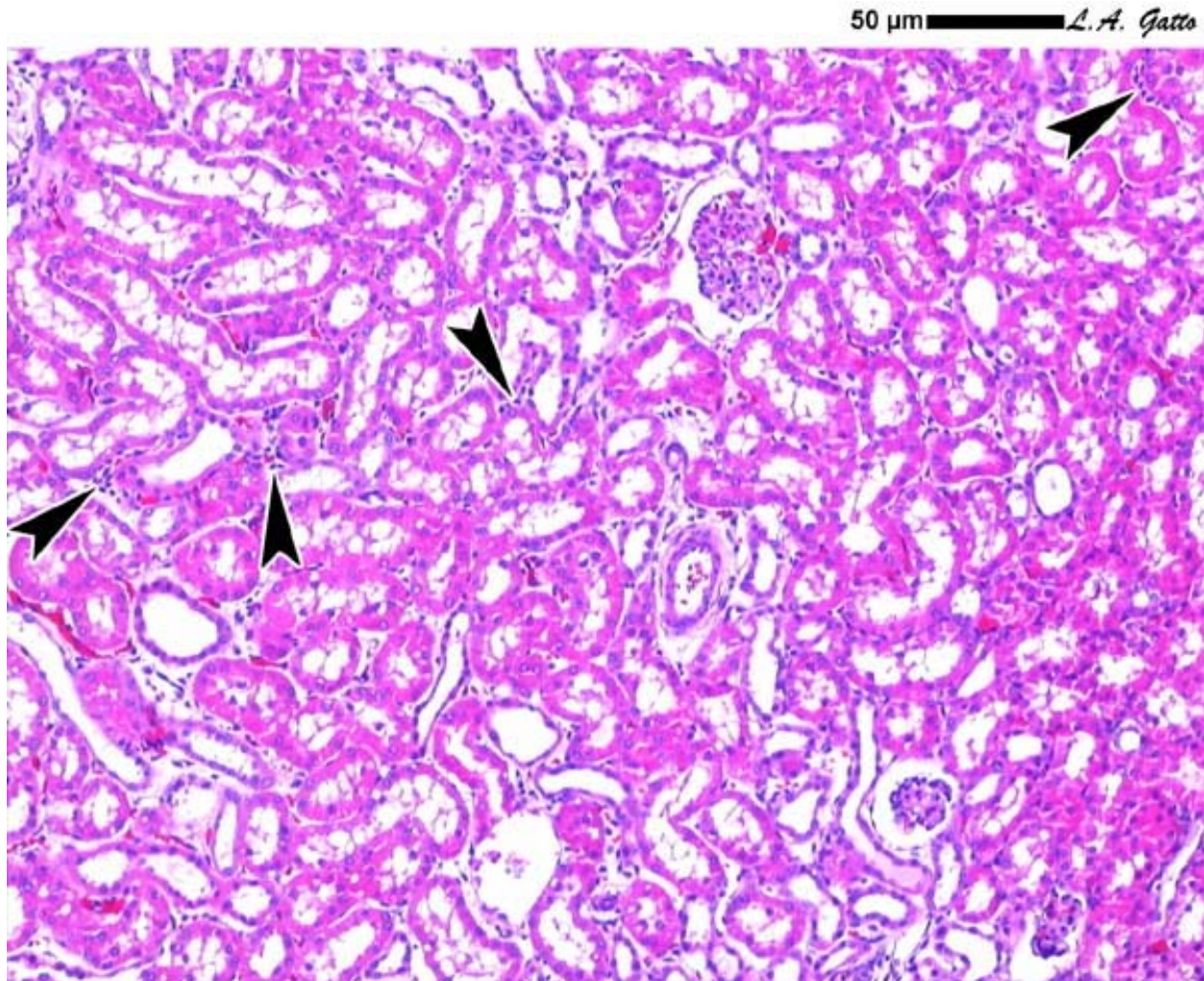
Congested capillaries (**arrowhead**) are blood filled and are also distended. Capillary congestion indicates impaired flow in the end-capillary bed.

Scoring System: 0 to 4

- 0 = congestion not present in the photo
- 1 = sporadic occurrence of congestion
- 2 = presence amounts to half of the photo
- 3 = congestion present in up to 3/4 of the photo
- 4 = congestion is prevalent throughout the photo

[NOTE: Scoring system does not quantify distension of the vascular compartment]

(5) Leukocyte Infiltration



Wandering inflammatory cells represent diverse sources such as local populations of tissue macrophages, lymphoid tissue, or systemic blood. Specific identification is uncertain since expression of markers varies during maturation and activation. For example, expression of a marker may be weak in a circulating monocyte but strong after extravasation. The denomination "leukocyte" denotes white blood cell and is used as an umbrella term to designate wandering cells (**arrowheads**), probably of hematogenous origin.

Scoring System: 0 to 4

- 0 = absent or infrequent
- 1 = sporadic, scattered and ungrouped
- 2 = focalized in dense groups
- 3 = dense foci + scattered presence
- 4 = dense infiltration throughout

HISTOLOGICAL ASSESSMENT OF THE LIVER

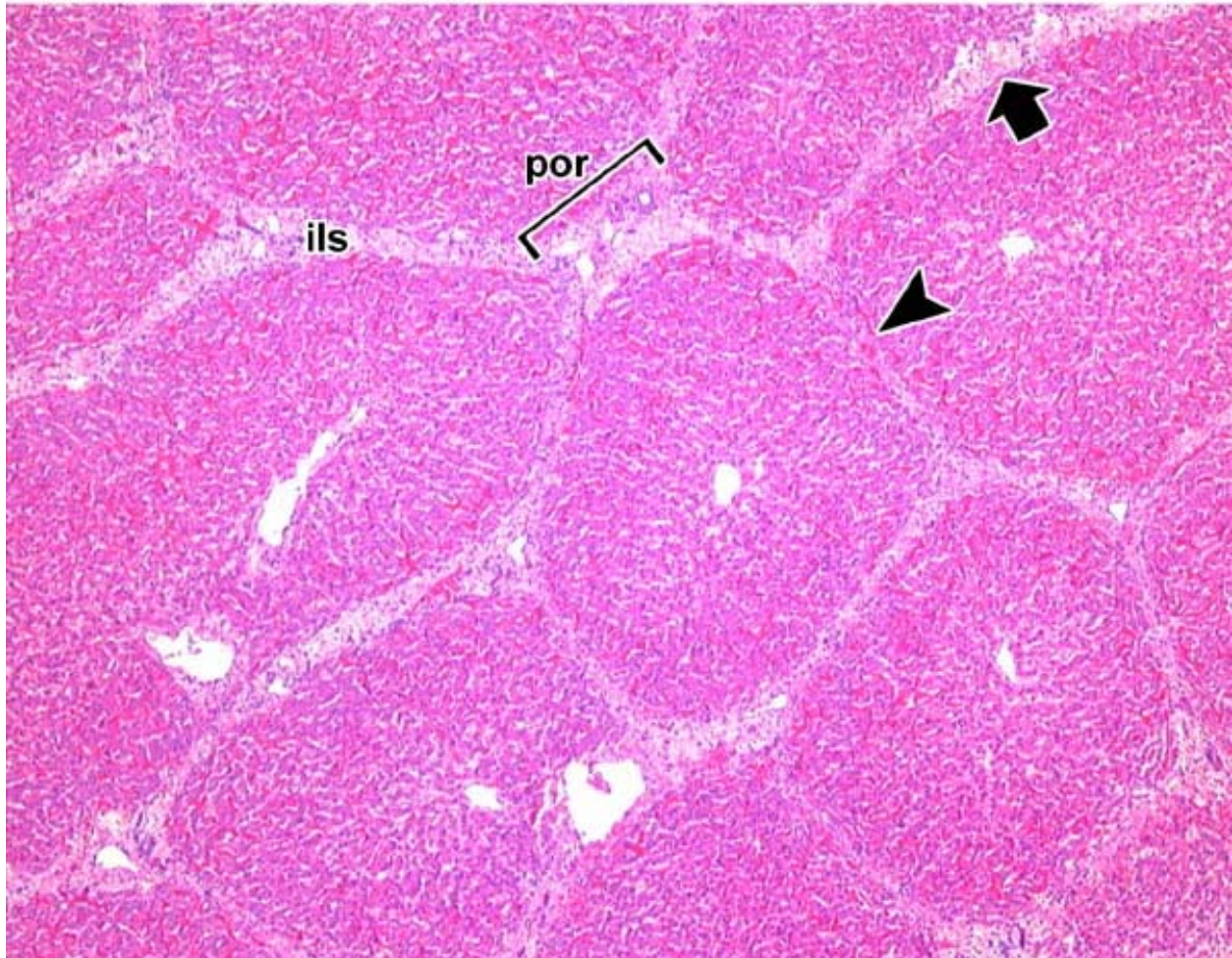
List of Parameters:

- ▶ Interstitial Edema
- ▶ Sinusoid Congestion
- ▶ Hepatocellular Necrosis
- ▶ Hepatocyte Vacuolation
- ▶ Leukocyte Infiltration

Lesion Description: Interstitial Edema

Interstitial Edema in Liver

150 μ m  L.A. Gatto



Edema deposition is accompanied by an acute swelling of the connective tissues of the stroma, which is characterized by a rapid-onset enlargement of the matrix without a concurrent increase in numbers of cells or fibers. Histologically this process results in connective tissue areas of lower optical density. Edematous connective tissues can occur within interlobular septa (*ils*) and portal tracts (*por*).

Since occurrences of interstitial edema may range from prominent (*arrow*) to sparse (*arrowhead*) in adjacent areas, they lend themselves to quantification on a per-lobule basis using a scoring system.

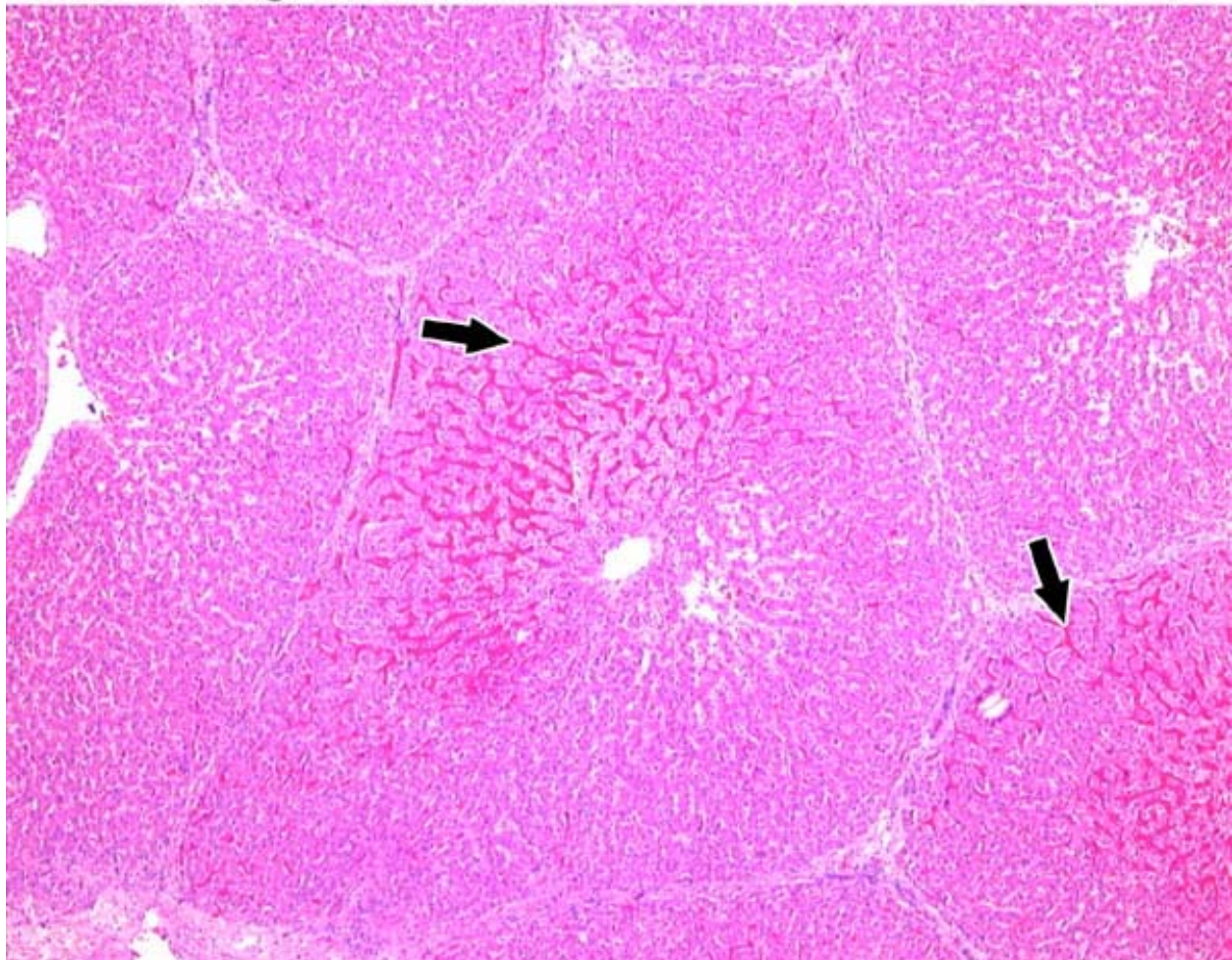
SCORING RUBRIC: Quantification of edematous swelling of interlobular septum in lobule under survey. The perimeter of the lobule was divided into 4 quadrants and the septum was rated according to the incidence of *prominent enlargement* of the matrix (*arrow*) as follows:

- 0 = Slender septum (*arrowhead*) all around this lobule
- 1 = Enlarged septum in one quadrant of this lobule
- 2 = Enlarged septum in two quadrants of this lobule
- 3 = Enlarged septum in three quadrants of this lobule
- 4 = Enlarged septum in all 4 quadrants of this lobule

Lesion Description: Capillary Sinusoid Congestion

Sinusoid Congestion in Liver

150 μ m  L. A. Gatto



The capillary sinusoids of the liver lobule can exhibit congestion, which is morphologically unequivocal since the vessels are conspicuously dilated and filled with blood (**arrows**).

The physiological significance of this histological change rests with general hemodynamic implications of blood irrigation and perfusion of the capillary bed, paucity of venous drainage, and poor oxygenation of the hepatic parenchyma. Since the incidence of congestion is not uniform, this parameter is readily quantifiable per lobule with the use of a scoring system.

SCORING RUBRIC: Quantification of incidence of capillary sinusoid congestion within the liver lobule under survey.

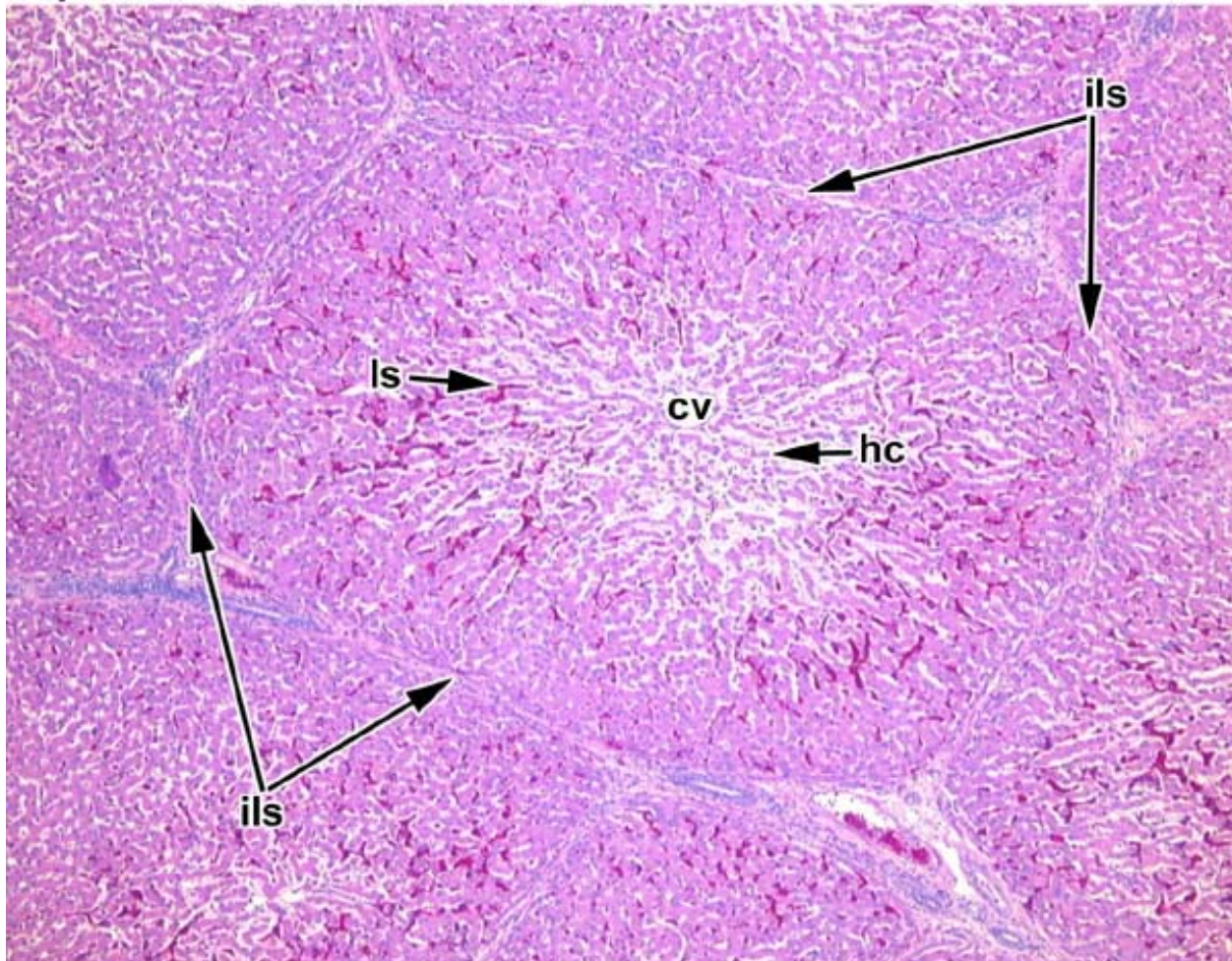
The identified lobule was divided into 4 quadrants and it was rated according to the incidence of capillaries appearing dilated and filled with blood (**arrows**) as follows:

- 0 = No congested capillaries present in this lobule
- 1 = Congested capillaries present in one quadrant of this lobule
- 2 = Congested capillaries present in two quadrants of this lobule
- 3 = Congested capillaries present in three quadrants of this lobule
- 4 = Congested capillaries present in all four quadrants of this lobule

Lesion Description: Hepatocellular Necrosis

Hepatocellular Necrosis in Liver

150 μ m  L.A. Gatto



The center of the photomicrograph shows a liver lobule bound by its interlobular septum (*ils*). Within the lobule, rows of hepatocytes (*hc*) alternate with liver sinusoids (*ls*) which drain into the central vein (*cv*).

Hepatic lobules featuring hepatocellular necrosis are marked by degenerating hepatocytes with less cytoplasmic mass, and this occurrence may be focalized near the center of the lobule. Since the extent of necrotic change is particular to individual lobules, this parameter can be quantitatively assessed on a per-lobule basis.

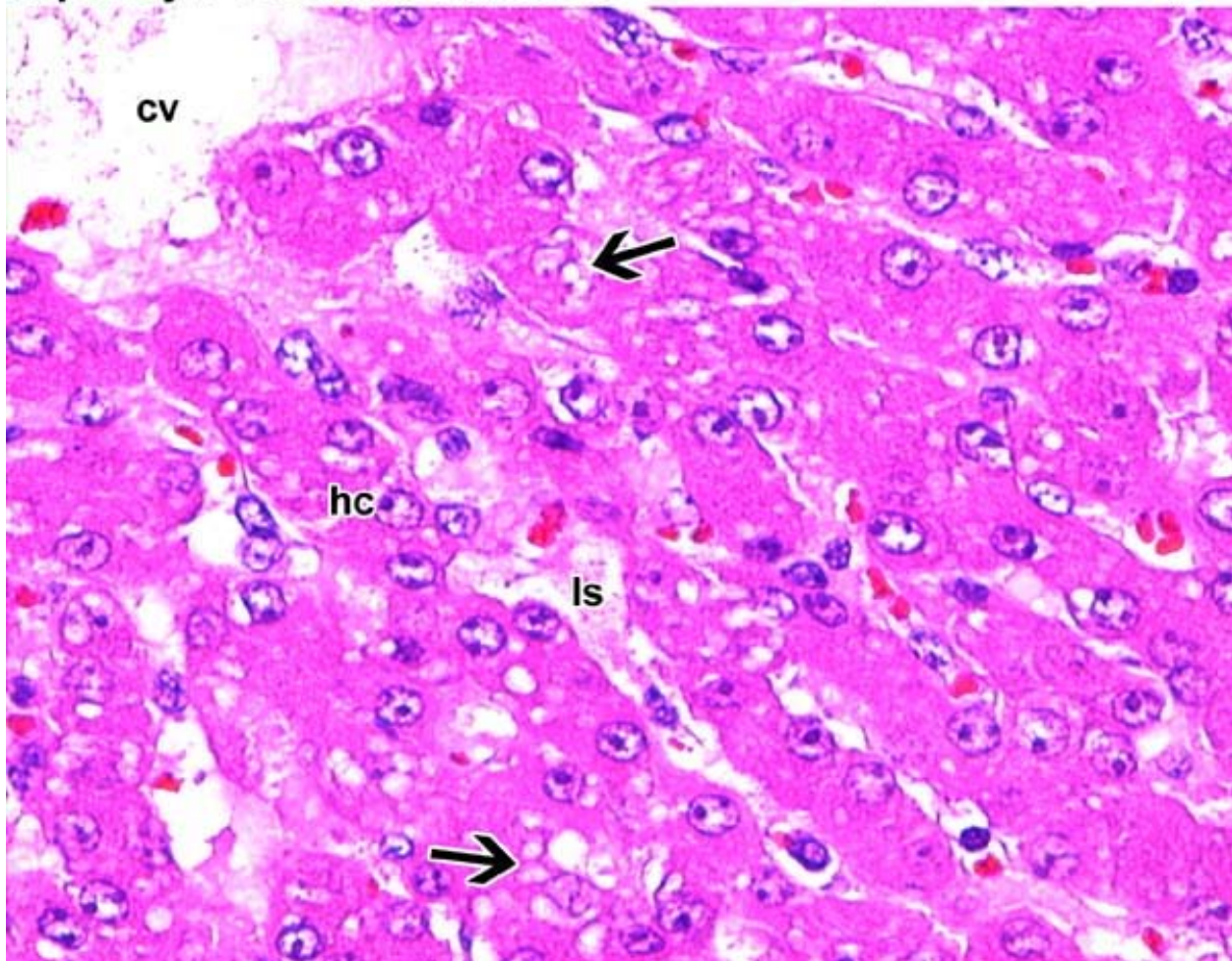
SCORING RUBRIC: Quantification of hepatocellular necrosis within the liver lobule under survey. The identified lobule was rated according to the extent of the area exhibiting hepatocellular necrosis as follows:

- 0 = No hepatocellular necrosis present in this lobule
- 1 = Hepatocellular necrosis present in one-fourth of this lobule
- 2 = Hepatocellular necrosis present in two-fourths of this lobule
- 3 = Hepatocellular necrosis present in three-fourths of this lobule
- 4 = Hepatocellular necrosis present throughout this entire lobule

Lesion Description: Hepatocyte Vacuolation

Hepatocyte Vacuolation in Liver

30 μ m  L. A. Gatto



Diffuse hepatocyte vacuolation is considered an indicator of metabolic change or distress, and consists of clear cytoplasmic vesicles (**arrows**) located within the hepatocyte (**hc**). It should be noted that some small clear openings are bile canaliculi, although these are not cytoplasmic but lie within the intercellular junction between adjoining hepatocytes. Other clear areas in the lobule are much larger and extracellular, and represent the lumina of liver sinusoids (**ls**) which drain into the central vein (**cv**).

If the presence of vesicles is less diffuse and more focalized it may constitute microvesicular steatosis, which is common in the periportal areas and represents evidence of acute metabolic changes. In more severe instances of vacuolation, hepatic cells may display vacuolar degeneration with conspicuous loss of cytoplasmic architecture and failure of junctional complexes, leading to loss of liver lobule structure.

SCORING RUBRIC: Quantification of hepatocyte vacuolation within the liver lobule under survey. The identified lobule was rated according to the extent of the area exhibiting hepatocyte vacuolation as follows:

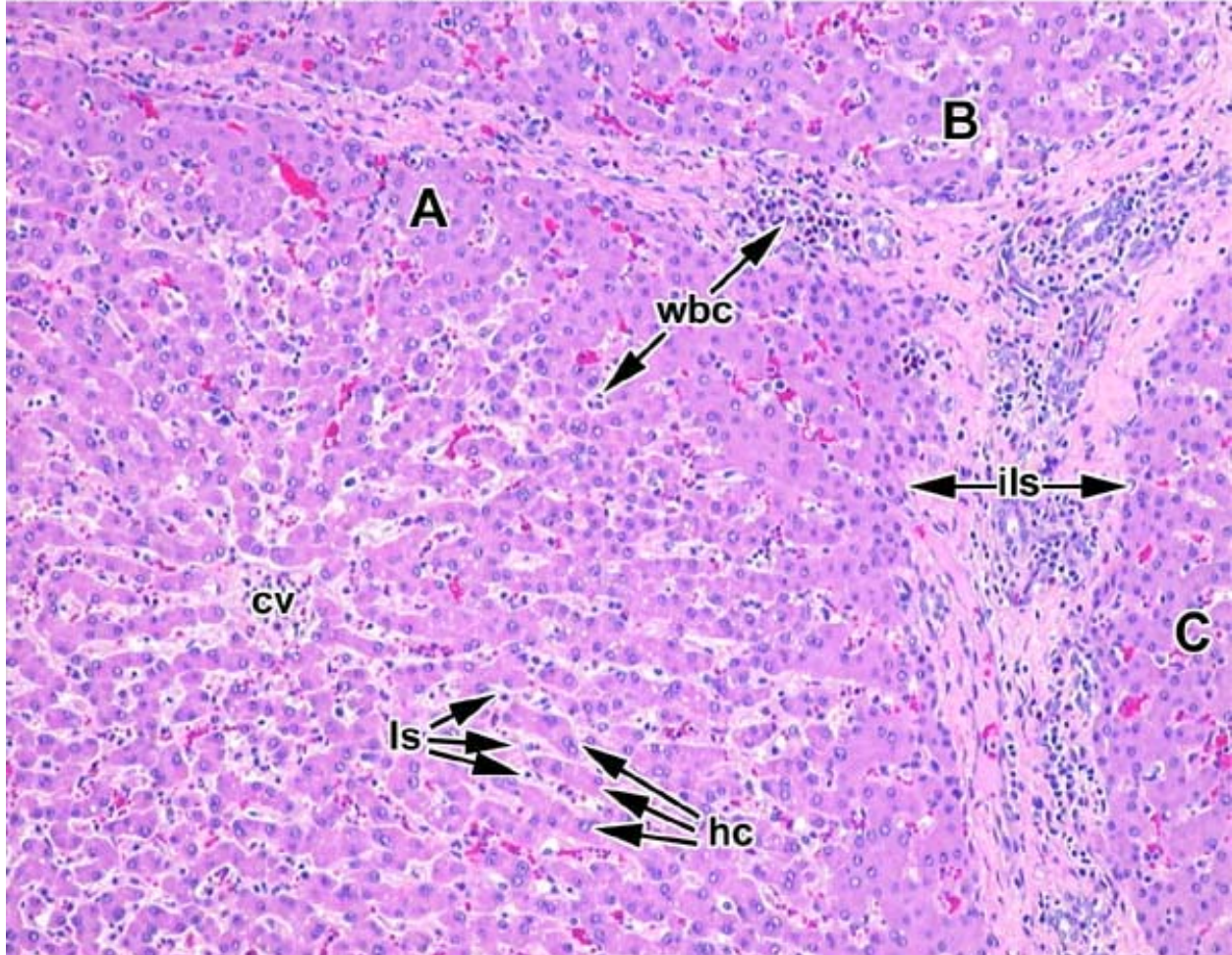
- 0 = No hepatocyte vacuolation present in this lobule
- 1 = Hepatocyte vacuolation present in one-fourth of this lobule
- 2 = Hepatocyte vacuolation present in two-fourths of this lobule
- 3 = Hepatocyte vacuolation present in three-fourths of this lobule
- 4 = Hepatocyte vacuolation present throughout this entire lobule

Lesion Description: Leukocyte Infiltration

- Parenchymal Leukocyte Infiltration
- Interstitial Leukocyte Infiltration

Leukocyte Infiltration in Liver

50 μ m  L.A. Gatto



The photomicrograph shows portions of three adjacent hepatic lobules (**A**, **B** and **C**) separated by interlobular septa (**ils**). Within the lobules, medium magnification shows the close architectural relationship between rows of hepatocytes (**hc**) and the intervening liver sinusoids (**ls**) which drain into the central vein (**cv**).

Leukocyte infiltration refers to the accumulation of white blood cells (**wbc**). Within the lobule, leukocyte infiltration is manifested as high incidence of white blood cells in the liver sinusoids. In the interstitium, leukocyte accumulation takes place as extravascular accumulation of leukocytes in the connective tissues of the liver stroma. Prominent leukocyte infiltration underscores the septic nature of the model.

SCORING RUBRIC: Semiquantitative assessment of leukocyte infiltration within either *the parenchyma* (liver sinusoid) or *the interstitium* (interlobular septa) of the liver lobule under survey. Estimated leukocyte density was rated as follows:

- 0 = Less than 10% of the nuclei in the *sinusoid/septa* of this lobule were from leukocytes
- 1 = Between 10% and 1/4th of the nuclei in the *sinusoid/septa* of this lobule were from leukocytes
- 2 = Between 1/4th and one-half of the nuclei in the *sinusoid/septa* of this lobule were from leukocytes
- 3 = Between one-half and 3/4th of the nuclei in the *sinusoid/septa* of this lobule were from leukocytes
- 4 = Leukocyte nuclei filled the area corresponding to *sinusoid/septa* in this lobule

SMALL INTESTINE HISTOLOGICAL ASSESSMENT

EIGHT PARAMETERS ("►") RECEIVED 0-4 SCORES:

- Shortened or Flat VILLI (*loss of slender villi extending into the lumen*)

EPITHELIAL BARRIER: Between intestinal lumen and intestinal wall

- Gruenhagen Spaces (*subepithelial spaces / lifting of surface epithelium*)
- Lesion to Epithelium (*paracellular spaces / focal loss of epithelial architecture*)
- Denuded Surface (*lamina propria directly exposed to lumen*)

UPPER LAMINA PROPRIA: Core and base of villi, and opening of glands into lumen

- Sloughing (*connective tissue disintegrating into intestinal lumen*)
- Congested Capillaries (*blood-filled vessels near base of villi*)

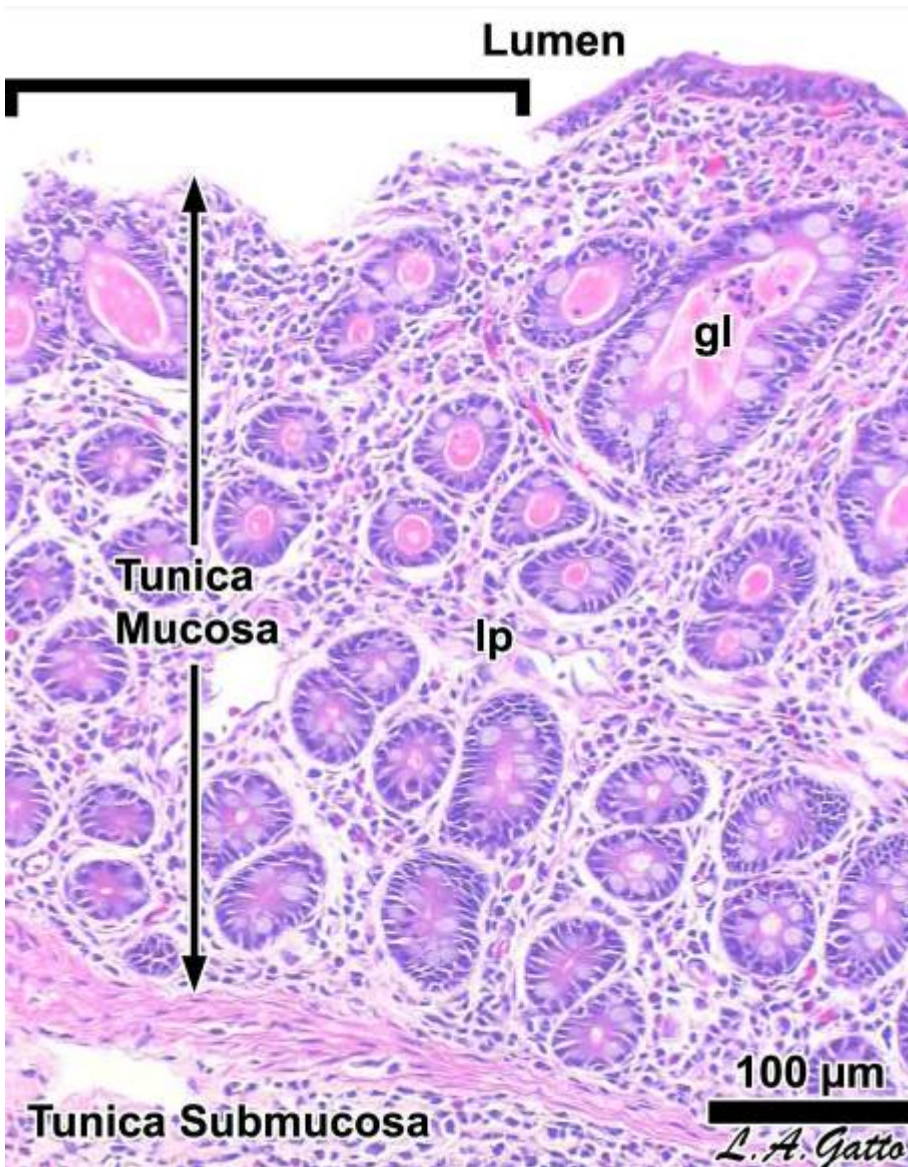
LOWER LAMINA PROPRIA: Base of tunica mucosa with bottom of intestinal glands

- Lesion to Gland (*loss of epithelial barrier or loss of tubule architecture*)
- Congested Capillaries (*blood-filled vessels near base of lamina propria*)

*The pages that follow present
a pictorial description of each parameter*

► Shortened or Flat VILLI

(loss of slender villi extending into the lumen)



In the more severely injured specimens, villi were missing (**bracket**), leaving the connective tissue of the lamina propria directly exposed to the lumen.

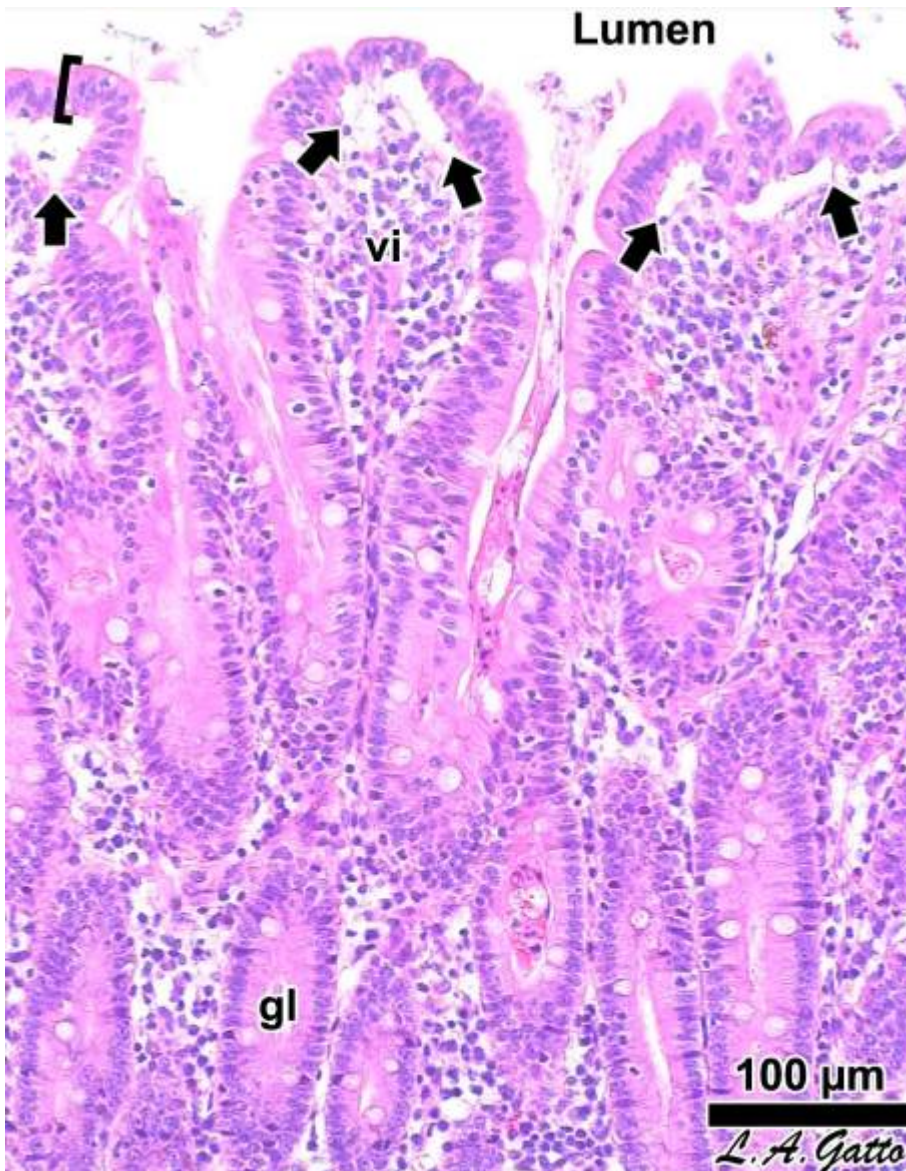
The photomicrograph illustrates transverse sections of intestinal glands (**gl**) within the lamina propria (**lp**).

Scoring rubric for shortened or flat villi per photomicrograph:

- 0 - All villi were slender
- 1 - Shortened or flat villi present in 1/4 of the lumen width
- 2 - Shortened or flat villi present in 2/4 of the lumen width
- 3 - Shortened or flat villi present in 3/4 of the lumen width
- 4 - Shortened or flat villi present throughout the lumen width

► Gruenhagen Spaces

(subepithelial spaces / lifting of surface epithelium)



The least severe histological disruption of the surface epithelial barrier was in the form of subepithelial spaces of Gruenhagen (**arrows**).

In general, the lifting of the surface epithelium (**bracket**) was the only indication of tissue change in areas exhibiting Gruenhagen spaces. Villi (**vi**) remained slender and intestinal glands (**gl**) were not disrupted.

Note that scores of zero occurred in undamaged tissue, as well as in completely denuded areas since subepithelial spaces entail the presence of epithelia.

Scoring rubric for Gruenhagen spaces per photomicrograph:

- 0 - Gruenhagen spaces not present
- 1 - Gruenhagen spaces present in 1/4 of the lumen width
- 2 - Gruenhagen spaces present in 2/4 of the lumen width
- 3 - Gruenhagen spaces present in 3/4 of the lumen width
- 4 - Gruenhagen spaces present throughout the lumen width

► Lesion to Epithelium

(paracellular spaces / focal loss of epithelial architecture)



Loss of epithelial barrier between the intestinal lumen and the organ wall was least extensive when presented in the form of paracellular spaces or gaps between or beneath the cells (**arrowheads**).

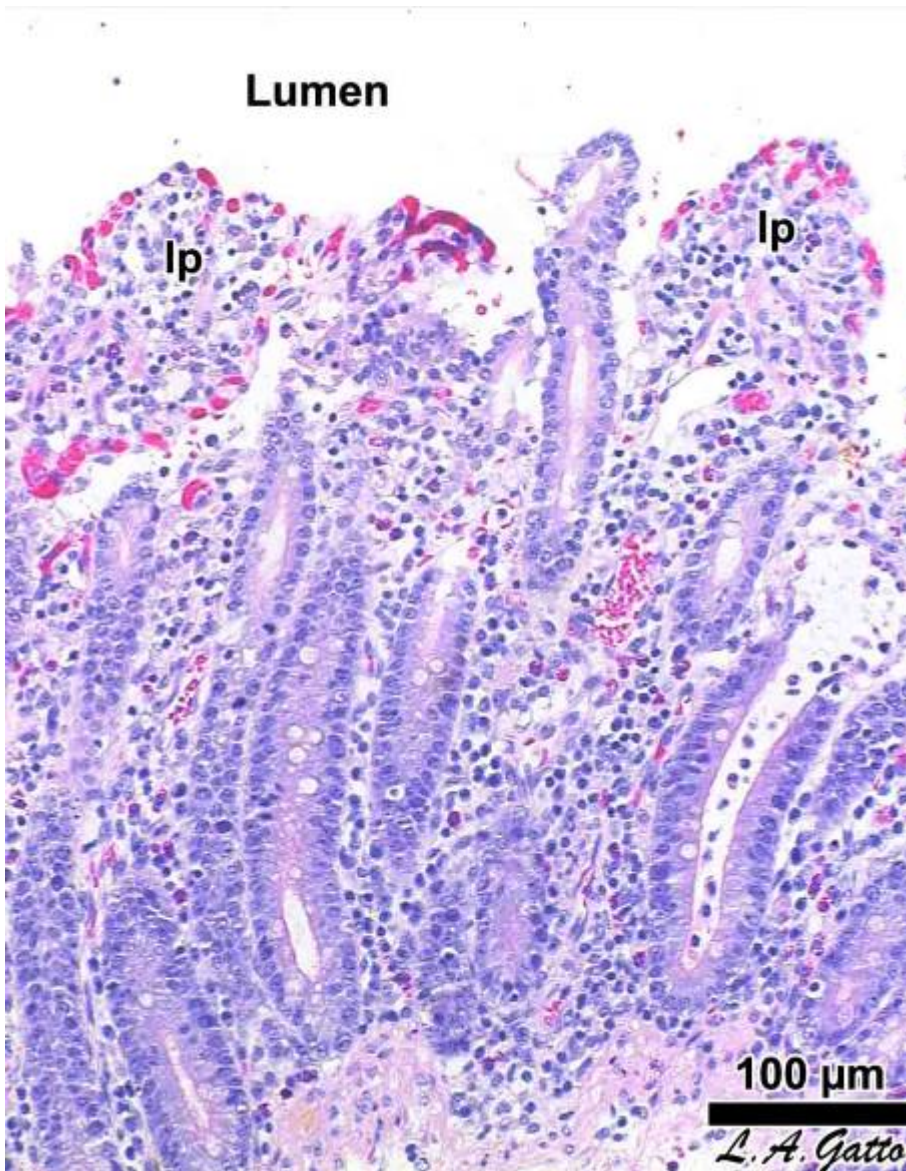
This was deemed a low level histological disruption because the surface epithelial barrier was compromised but not lost.

This focal lesion to the surface epithelium was often associated with comparable, low-level disruption of gland epithelia (scored separately).

Scoring rubric for lesion to epithelium per photomicrograph:

- 0 - Focal epithelial lesion not present
- 1 - Focal epithelial lesion present in 1/4 of the lumen width
- 2 - Focal epithelial lesion present in 2/4 of the lumen width
- 3 - Focal epithelial lesion present in 3/4 of the lumen width
- 4 - Focal epithelial lesion present throughout the lumen width

► **Denuded Surface**
(*lamina propria directly exposed to lumen*)



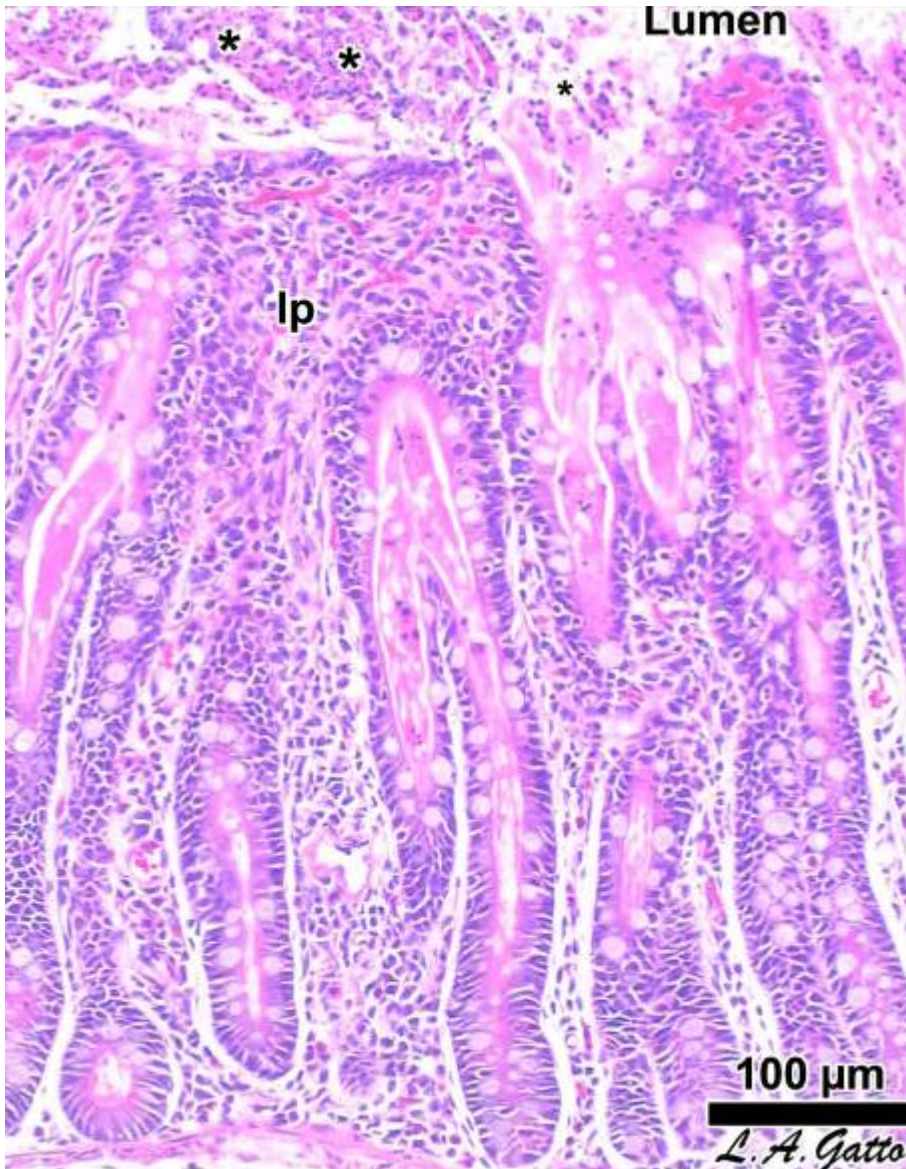
Denudation of the wall surface through loss of the epithelium constituted complete absence of surface epithelial barrier and left the connective tissues and capillaries of the lamina propria (**lp**) directly exposed to the intestinal lumen.

This was deemed a severe histological disruption, which was commonly accompanied by congestion of the end-capillary bed and loss of architecture in glands (scored separately).

Scoring rubric for denuded surface per photomicrograph:

- 0 - Denuded surface not present
- 1 - Denuded surface present in 1/4 of the lumen width
- 2 - Denuded surface present in 2/4 of the lumen width
- 3 - Denuded surface present in 3/4 of the lumen width
- 4 - Denuded surface present throughout the lumen width

► **Sloughing of Lamina Propria**
(connective tissue disintegrating into intestinal lumen)



Sloughing (**asterisks**) of the upper compartment of the Lamina Propria (**lp**) entailed the loss of tissues constituting the base of villi and the openings of glands into the intestinal lumen.

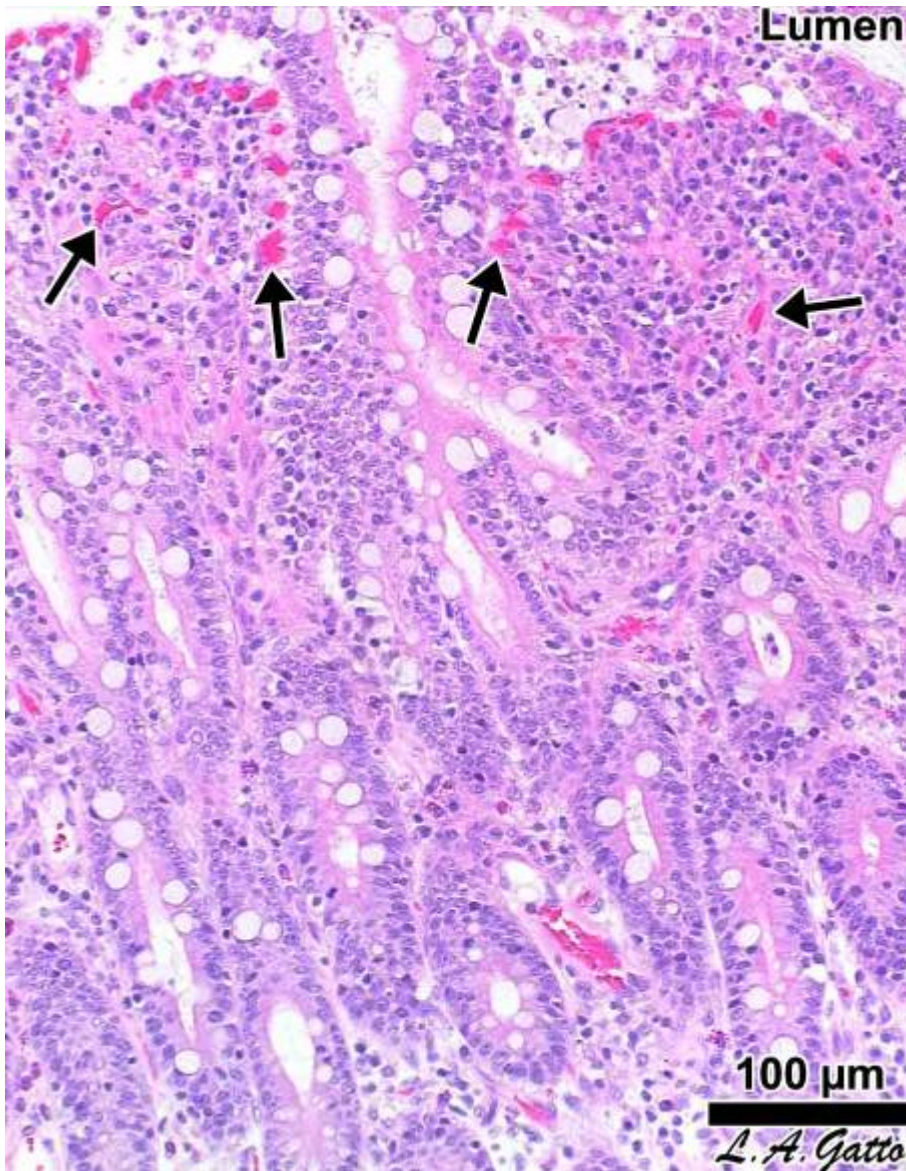
The end-capillary bed was often lost among the more severe occurrences of this lesion.

Scoring rubric for sloughing of Lamina Propria per photomicrograph:

- 0 - Sloughing not present
- 1 - Sloughing present in 1/4 of the lumen width
- 2 - Sloughing present in 2/4 of the lumen width
- 3 - Sloughing present in 3/4 of the lumen width
- 4 - Sloughing present throughout the lumen width

► **Congested Capillaries (Upper Lamina Propria)**

(blood-filled vessels near base of villi)



Congested capillaries (**arrows**) are conspicuous for their blood-filled appearance.

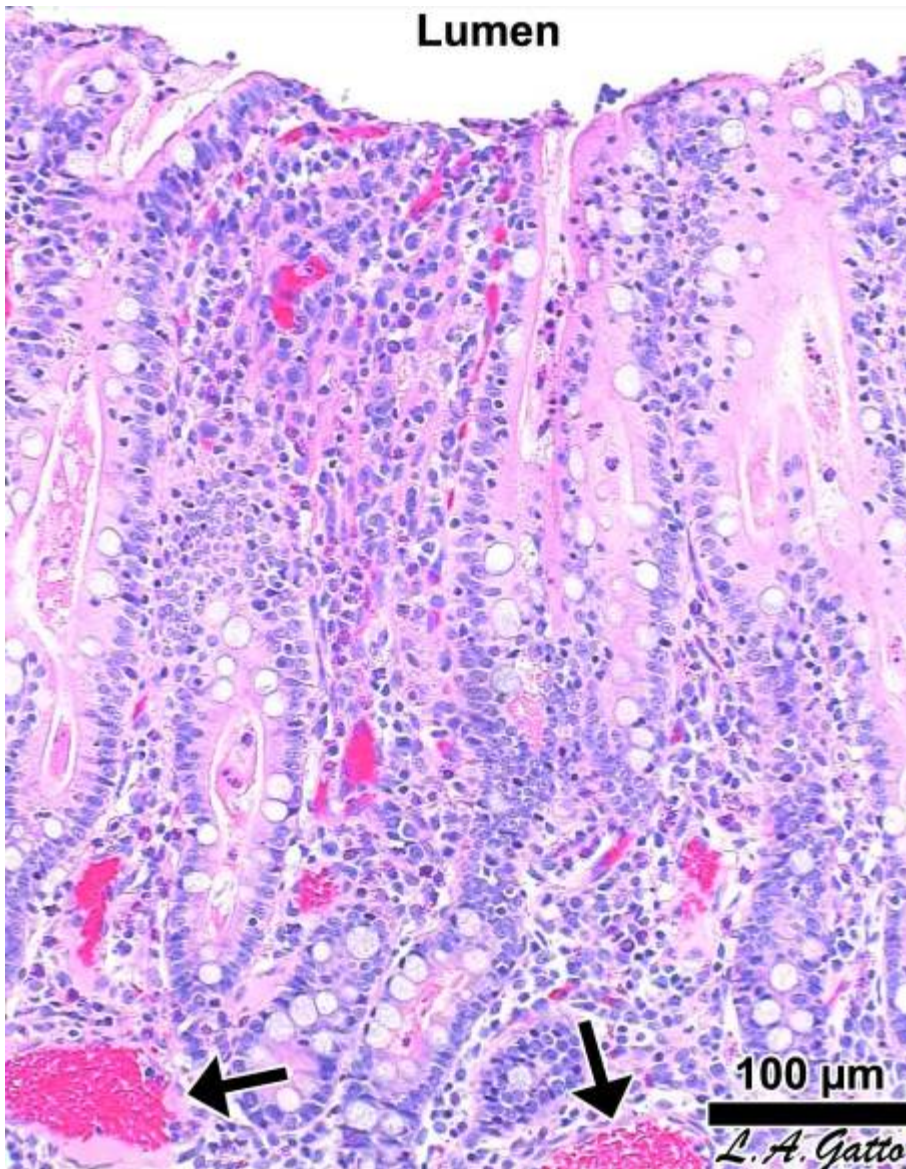
The end-capillary bed consists of small capillaries located in the upper compartment of the tunica mucosa, such as those featured in this photomicrograph.

This is evidence of poor blood drainage within the capillary bed, and pathological significance arises from the resulting hypoxia.

Scoring rubric for congested upper capillaries per photomicrograph:

- 0 - Congested upper capillaries not present
- 1 - Congested upper capillaries present in 1/4 of the lumen width
- 2 - Congested upper capillaries present in 2/4 of the lumen width
- 3 - Congested upper capillaries present in 3/4 of the lumen width
- 4 - Congested upper capillaries present throughout the lumen width

► **Congested Capillaries (Lower Lamina Propria)**
(*blood-filled vessels near base of lamina propria*)



Congested capillaries are conspicuous for their blood-filled appearance.

Large capillaries located in the lower compartment of the tunica mucosa (**arrows**) drain the end-capillary bed located in the upper mucosa.

Congestion of drainage is further evidence of poor blood flow within the capillary bed, which results in hypoxia.

Scoring rubric for congested lower capillaries per photomicrograph:

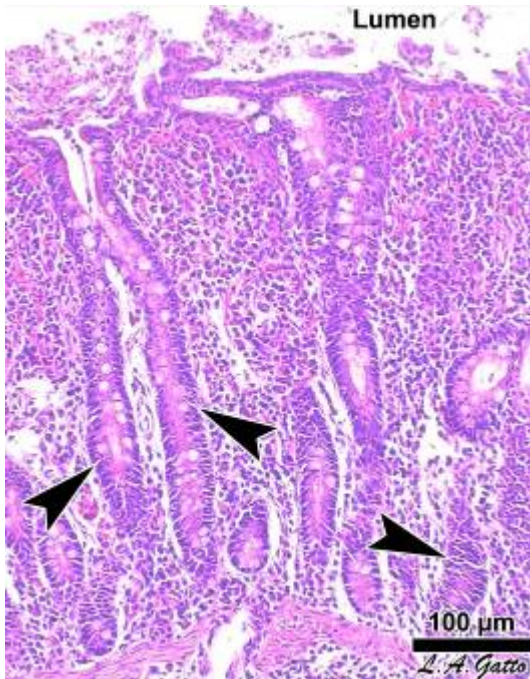
- 0 - Congested lower capillaries not present
- 1 - Congested lower capillaries present in 1/4 of the lumen width
- 2 - Congested lower capillaries present in 2/4 of the lumen width
- 3 - Congested lower capillaries present in 3/4 of the lumen width
- 4 - Congested lower capillaries present throughout the lumen width

► Lesion to Gland

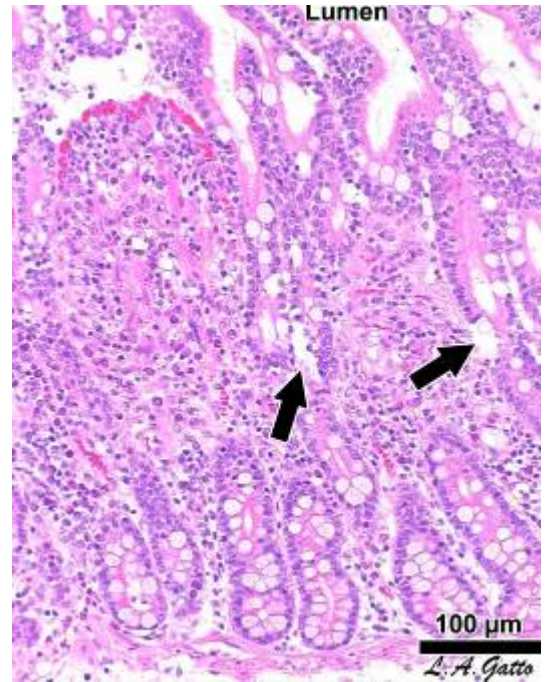
(loss of epithelial barrier or loss of tubule architecture in lower mucosal compartment)

Scoring rubric for lesion to intestinal gland: 0 to 4

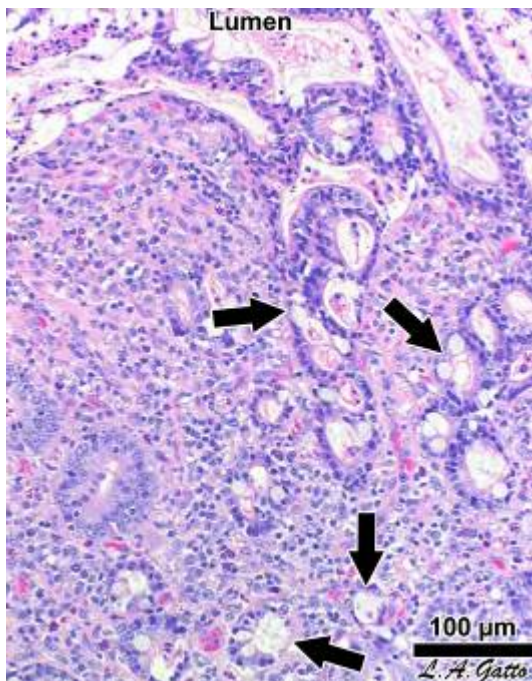
1 - Paracellular spaces in the epithelium



2 - discontinuous gland epithelium (gap in tubule wall)



3 - focal loss of gland tubule architecture



4 - loss of tubule (or segment)

