

OBSTETRICS & GYNECOLOGY



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- Comments from the reviewers and editors (email to author requesting revisions)
- Response from the author (cover letter submitted with revised manuscript)*

**The corresponding author has opted to make this information publicly available.*

Personal or nonessential information may be redacted at the editor's discretion.

Questions about these materials may be directed to the *Obstetrics & Gynecology* editorial office:
obgyn@greenjournal.org.

Date: Apr 15, 2022
To: "Stephen Mitchell Scott" [REDACTED]
From: "The Green Journal" em@greenjournal.org
Subject: Your Submission ONG-22-320

RE: Manuscript Number ONG-22-320

Vulvar Aphthous Ulcers in an Adolescent Receiving COVID Vaccination

Dear Dr. Scott:

Thank you for sending us your work for consideration for publication in Obstetrics & Gynecology. Your manuscript has been reviewed by the Editorial Board and by special expert referees. The Editors would like to invite you to submit a revised version for further consideration.

If you wish to revise your manuscript, please read the following comments submitted by the reviewers and Editors. Each point raised requires a response, by either revising your manuscript or making a clear argument as to why no revision is needed in the cover letter.

To facilitate our review, we prefer that the cover letter you submit with your revised manuscript include each reviewer and Editor comment below, followed by your response. That is, a point-by-point response is required to each of the EDITOR COMMENTS (if applicable), REVIEWER COMMENTS, STATISTICAL EDITOR COMMENTS (if applicable), and EDITORIAL OFFICE COMMENTS below. Your manuscript will be returned to you if a point-by-point response to each of these sections is not included.

The revised manuscript should indicate the position of all changes made. Please use the "track changes" feature in your document (do not use strikethrough or underline formatting).

Your submission will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by May 06, 2022, we will assume you wish to withdraw the manuscript from further consideration.

REVIEWER COMMENTS:

Reviewer #1: This is a case report of an adolescent non sexually active female who developed a genital ulcer after receiving the COVID mRNA vaccine.

- 1- Consider adding arrows for the figures to orient the readers where to look. Especially that this case can be helpful for providers outside of the OBGYN field.
- 2- In the sentence: "A case report of NSGU has been cited in the literature" (line 108). Consider clarifying that the case report was after COVID vaccination not after the virus, for a better transition in the paragraph.
- 3- Line 113, can you specify what previously documented specific side effects support the association, if there is anything other than reference 11.
- 4- Are the authors aware from their literature review if there is an increased risk of genital ulcers for immunocompromised patients after COVID vaccine? Can they make a comment to that?
- 5- Also, regarding immunocompromised patients, consider including a recommendation on what to use instead of steroids for severe lesions -if there is enough knowledge about the subject.

Reviewer #2:

Well written case report.

1. Is there a possibility of undiagnosed underlying history of herpes with a outbreak after COVID vaccine?

2. Did she have any COVID recently prior to COVID vaccination?

3. Any possibility of underlying undiagnosed connective tissue diseases such as Behcet's or undiagnosed autoimmune diseases?

Need more case reports to associate with COVID vaccine.

Reviewer #3:

Overall Comments: The authors present a case report in an adolescent female who develops non-sexually acquired genital ulcers (NSGU, vulvar aphthous ulcers) after receiving COVID vaccination. Mucosal inflammation with viral infections have been previously noted and are managed mainly with supportive care with pain management and sometimes topical/oral steroids. The case is well written and a review of data associated with active viral infection is presented as well as a plausible physiologic basis for reaction to an antiviral vaccination. A review of the literature notes that these associations have been reported (Wojcicki and Flynn, J Ped Adolesc Gyn, Oct, 2021 [response to vaccine]; Christl et al, J Ped Adolesc Gyn, June, 2021, [response to viral infection]).

Specific Comments:

Title: good

Précis: ok

Abstract: Helpful summary of the case

Teaching Points: OK, maybe add that treatment is mainly supportive

Introduction: Provides rationale for case report

Case: Well presented

Discussion: Provides a good review of the literature including the Christl et al citation noted above; but there is Wojcicki and Flynn citation that should be noted. Would like to know if this is applicable to adult women as well.

Tables/Figures: Would place in the back of the case presentation and provide figure legends. Perhaps arrows to highlight lesions, active and with resolution

EDITORIAL OFFICE COMMENTS:

1. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:

- * Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.

- * Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).

- * Name the IRB or Ethics Committee institution in the Methods section (if applicable).

- * Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

3. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

4. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "Patients with obesity" instead of "obese patients," "Women with disabilities" instead of "disabled

women," "women with HIV" instead of "HIV-positive women," "women who are blind" instead of "blind women."

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

6. Make sure your manuscript meets the following word limit. The word limit includes the manuscript body text only (for example, the Introduction through the Discussion in Original Research manuscripts), and excludes the title page, précis, abstract, tables, boxes, and figure legends, reference list, and supplemental digital content. Figures are not included in the word count.

Case Reports: 1,500 words

7. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

- * All financial support of the study must be acknowledged.
- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.
- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.
- * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting or indicate whether the meeting was held virtually).
- * If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."
- * Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

8. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make sure there are no inconsistencies between the abstract and the manuscript, and that the abstract has a clear conclusion statement based on the results found in the manuscript.

In addition, the abstract length should follow journal guidelines. Please provide a word count.

Case Reports: 125 words

9. Teaching Points: The Editors suggest that one of the teaching points should highlight that the adolescent population may be more prone to ulcers. This could be combined with your first point.

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

11. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

12. Please review examples of our current reference style at https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the formal reference list. Please cite them on the line in parentheses.

If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still a current document. In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Please make sure your references are numbered in order of appearance in the text.

13. Figures 1-3: Please upload as figure files on Editorial Manager and provide legends.

14. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at <http://links.lww.com/LWW-ES/A48>. The cost for publishing an article as open access can be found at <https://wkauthorservices.editage.com/open-access/hybrid.html>.

If your article is accepted, you will receive an email from the Editorial Office asking you to choose a publication route (traditional or open access). Please keep an eye out for that future email and be sure to respond to it promptly.

If you choose to revise your manuscript, please submit your revision through Editorial Manager at <http://ong.editorialmanager.com>. Your manuscript should be uploaded as a Microsoft Word document. Your revision's cover letter should include a point-by-point response to each of the received comments in this letter. Do not omit your responses to the EDITOR COMMENTS (if applicable), the REVIEWER COMMENTS, the STATISTICAL EDITOR COMMENTS (if applicable), or the EDITORIAL OFFICE COMMENTS.

If you submit a revision, we will assume that it has been developed in consultation with your coauthors and that each author has given approval to the final form of the revision.


Again, your manuscript will be maintained in active status for 21 days from the date of this letter. If we have not heard from you by May 06, 2022, we will assume you wish to withdraw the manuscript from further consideration.

Sincerely,

Jason D. Wright, MD
Editor-in-Chief

2020 IMPACT FACTOR: 7.661
2020 IMPACT FACTOR RANKING: 3rd out of 83 ob/gyn journals

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Dr. Jason D. Wright, MD
Editor-in-Chief
Obstetrics and Gynecology

May 13, 2022

Dear Dr. Wright

I am pleased to submit revisions to Case Report ONG-22-320 article entitled "Vulvar Aphthous Ulcers in an Adolescent Receiving COVID Vaccination" by Stephen Scott, Veronica Alaniz, Leslie Appiah, Cari Holton, and Patricia Huguelet for reconsideration for publication in Obstetrics and Gynecology. This manuscript describes a previously undescribed side effect following COVID vaccination in an adolescent female. The following edits have been made to address the reviewers' and editor's comments and recommendations.

Reviewer 1

Comment 1: Consider adding arrows for the figures to orient the readers where to look. Especially that this case can be helpful for providers outside of the OBGYN field.

Response: Arrows have been added to each figure.

Comment 2: In the sentence: "A case report of NSGU has been cited in the literature" (line 108). Consider clarifying that the case report was after COVID vaccination not after the virus, for a better transition in the paragraph.

Response: We have distinguished the case reports of COVID infections in line 108-110 versus the case reports of ulcers after COVID vaccine in line 120-122.

Comment 3: Line 113, can you specify what previously documented specific side effects support the association, if there is anything other than reference 11.

Response: The symptoms noted in the case report from the previous reference 11 (now reference 14) are listed in line 121-123.

Comment 4: Are the authors aware from their literature review if there is an increased risk of genital ulcers for immunocompromised patients after COVID vaccine? Can they make a comment to that?

Response: We are not aware of any difference in risk among immunocompetent and immunocompromised patients. We have added this statement in lines 123-126.

Comment 5: Also, regarding immunocompromised patients, consider including a recommendation on what to use instead of steroids for severe lesions -if there is enough knowledge about the subject.

Response: We are not aware of data to alter current steroid treatment and have addressed this in lines 157-158.

Reviewer #2:

Comment 1: Is there a possibility of undiagnosed underlying history of herpes with a outbreak after COVID vaccine?

Response: We believe this to be unlikely from her lack of past or current sexual contact. We allude to this with the addition of common misdiagnosis of HSV in line 73, and with reference to our institutional data noting no HSV outbreaks during early work ups for these ulcerations found in line 94-97.

Comment 2: Did she had any COVID recently prior to COVID vaccination?

Response: She did not and this was clarified in line 82-83.

Comment 3: Any possibility of underlying undiagnosed connective tissue diseases such as Bechet's or undiagnosed autoimmune diseases?

Response: Although NSGU may be the first episode of an eventual diagnosis of Bechet's Disease, we are not able to make that diagnosis in this patient. This is clarified in lines 114-118.

Reviewer #3:

Comments: Teaching Points: OK, maybe add that treatment is mainly supportive.

Response: An additional teaching bullet point was made at lines 49-50, and also added to the discussion in lines 146-147.

Discussion: Provides a good review of the literature including the Christl et al citation noted above; but there is Wojcicki and Flynn citation that should be noted. Would like to know if this is applicable to adult women as well.

Response: The Chrystl article was previously referenced as #9. The Wojcicki article was reviewed and added as reference #15. Case series in the literature regarding NSGU have come from the adolescent gynecology field and the average age of eruption is around 14. However, a small percentage of cases are in older adolescents making it possible but less common among adults. We allude to the propensity of these lesions occurring in adolescents in lines 111-114.

Tables/Figures: Would place in the back of the case presentation and provide figure legends. Perhaps arrows to highlight lesions, active and with resolution.

Response: The figures will be placed in the back of the presentation. Arrows have been added to each photo. A legend has been added to the figures.

Editors Comments:

1. If your article is accepted, the journal will publish a copy of this revision letter and your point-by-point responses as supplemental digital content to the published article online. You may opt out by writing separately to the Editorial Office at em@greenjournal.org, and only the revision letter will be posted.

Response: This letter serves as our point-by-point response to all revision requirements.

2. When you submit your revised manuscript, please make the following edits to ensure your submission contains the required information that was previously omitted for the initial double-blind peer review:

* Funding information (ie, grant numbers or industry support statements) should be disclosed on the title page and at the end of the abstract. For industry-sponsored studies, describe on the title page how the funder was or was not involved in the study.

Response: There is no funding information to report.

* Include clinical trial registration numbers, PROSPERO registration numbers, or URLs at the end of the abstract (if applicable).

Response: There is no clinical trial registration number, PROSPERO registration number, or URL to report.

* Name the IRB or Ethics Committee institution in the Methods section (if applicable).

Response: This case report was IRB exempted.

* Add any information about the specific location of the study (ie, city, state, or country), if necessary for context.

The location of the urgent care center and academic children's hospital was identified as Denver, Colorado in line 81.

3. Obstetrics & Gynecology's Copyright Transfer Agreement (CTA) must be completed by all authors. When you uploaded your manuscript, each coauthor received an email with the subject, "Please verify your authorship for a submission to Obstetrics & Gynecology." Please ask your coauthor(s) to complete this form, and confirm the disclosures listed in their CTA are included on the manuscript's title page. If they did not receive the email, they should check their spam/junk folder. Requests to resend the CTA may be sent to em@greenjournal.org.

Response: The CTA was completed and signed by all authors at the original submission.

4. ACOG uses person-first language. Please review your submission to make sure to center the person before anything else. Examples include: "Patients with obesity" instead of "obese patients," "Women with disabilities" instead of "disabled women," "women with HIV" instead of "HIV-positive women," "women who are blind" instead of "blind women."

Response: first person language was replaced in lines 32, 35, 45, 152, and 161.

5. Standard obstetric and gynecology data definitions have been developed through the reVITALize initiative, which was convened by the American College of Obstetricians and Gynecologists and the

members of the Women's Health Registry Alliance. Obstetrics & Gynecology has adopted the use of the reVITALize definitions. Please access the obstetric data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-obstetrics-data-definitions> and the gynecology data definitions at <https://www.acog.org/practice-management/health-it-and-clinical-informatics/revitalize-gynecology-data-definitions>. If use of the reVITALize definitions is problematic, please discuss this in your point-by-point response to this letter.

Response: The particular disorder of Non-Sexually Acquired Genital Ulcers is not defined in the revitalize definitions as there is not an category list of definitions for adolescent gynecology conditions.

6. Make sure your manuscript meets the following word limit. The word limit includes the manuscript body text only (for example, the Introduction through the Discussion in Original Research manuscripts), and excludes the title page, précis, abstract, tables, boxes, and figure legends, reference list, and supplemental digital content. Figures are not included in the word count.

Response: the manuscript word count is 1318. This is below the 1500 limit.

7. Specific rules govern the use of acknowledgments in the journal. Please review the following guidelines and edit your title page as needed:

- * All financial support of the study must be acknowledged.

Response: No financial support was used for this case report

- * Any and all manuscript preparation assistance, including but not limited to topic development, data collection, analysis, writing, or editorial assistance, must be disclosed in the acknowledgments. Such acknowledgments must identify the entities that provided and paid for this assistance, whether directly or indirectly.

Response: Kendra Hutchens, PhD, was acknowledged for her editorial assistance.

- * All persons who contributed to the work reported in the manuscript, but not sufficiently to be authors, must be acknowledged. Written permission must be obtained from all individuals named in the acknowledgments, as readers may infer their endorsement of the data and conclusions. Please note that your response in the journal's electronic author form verifies that permission has been obtained from all named persons.

Response: Kendra Hutchens, PhD, was acknowledged for her editorial assistance.

- * If all or part of the paper was presented at the Annual Clinical and Scientific Meeting of the American College of Obstetricians and Gynecologists or at any other organizational meeting, that presentation should be noted (include the exact dates and location of the meeting or indicate whether the meeting was held virtually).

Response: This article has not been presented at any meeting

- * If your manuscript was uploaded to a preprint server prior to submitting your manuscript to Obstetrics & Gynecology, add the following statement to your title page: "Before submission to Obstetrics & Gynecology, this article was posted to a preprint server at: [URL]."

Response: the manuscript was NOT uploaded to a preprint server.

* Do not use only authors' initials in the acknowledgement or Financial Disclosure; spell out their names the way they appear in the byline.

Response: All names have been spelled out.

8. Be sure that each statement and any data in the abstract are also stated in the body of your manuscript, tables, or figures. Statements and data that appear in the abstract must also appear in the body text for consistency. Make sure there are no inconsistencies between the abstract and the manuscript, and that the abstract has a clear conclusion statement based on the results found in the manuscript.

Response: The three figures shown in the article are listed in lines 94, 100, and 103

Case Reports: 125 words

Response: The abstract word count is 121

9. Teaching Points: The Editors suggest that one of the teaching points should highlight that the adolescent population may be more prone to ulcers. This could be combined with your first point.

Response: We have amended a teaching point to highlight that adolescents are prone to this condition

10. Only standard abbreviations and acronyms are allowed. A selected list is available online at <http://edmgr.ovid.com/ong/accounts/abbreviations.pdf>. Abbreviations and acronyms cannot be used in the title or précis. Abbreviations and acronyms must be spelled out the first time they are used in the abstract and again in the body of the manuscript.

Response: We have removed the anacronym NSGU from the article.

11. ACOG avoids using "provider." Please replace "provider" throughout your paper with either a specific term that defines the group to which are referring (for example, "physicians," "nurses," etc.), or use "health care professional" if a specific term is not applicable.

Response: We have replaced the instances of the term "provider" with "health care professional" at lines 72, 80, 86, and 168.

12. Please review examples of our current reference style at https://edmgr.ovid.com/ong/accounts/ifa_suppl_refstyle.pdf. Include the digital object identifier (DOI) with any journal article references and an accessed date with website references.

Response: No references have a DOI to list.

Unpublished data, in-press items, personal communications, letters to the editor, theses, package inserts, submissions, meeting presentations, and abstracts may be included in the text but not in the formal reference list. Please cite them on the line in parentheses.

Response: There is no unpublished data referenced in the manuscript.

If you cite ACOG documents in your manuscript, be sure the references you are citing are still current and available. Check the Clinical Guidance page at <https://www.acog.org/clinical> (click on "Clinical Guidance" at the top). If the reference is still available on the site and isn't listed as "Withdrawn," it's still

a current document. In most cases, if an ACOG document has been withdrawn, it should not be referenced in your manuscript.

Response: No ACOG documents were cited in this manuscript.

Please make sure your references are numbered in order of appearance in the text.

Response: References were numbered in order of first appearance in the manuscript.

13. Figures 1-3: Please upload as figure files on Editorial Manager and provide legends.

Response: Legends were added to the uploaded for the Figures 1,2,3.

14. Authors whose manuscripts have been accepted for publication have the option to pay an article processing charge and publish open access. With this choice, articles are made freely available online immediately upon publication. An information sheet is available at <http://links.lww.com/LWW-ES/A48>. The cost for publishing an article as open access can be found at <https://wkauthorservices.edmgr.com/open-access/hybrid.html>.

Response: The authors elect to not submit the article for open access.

The authors hope these changes adequately address every recommendation and will be viewed favorably for publication consideration.

A handwritten signature in black ink, appearing to read 'Stephen Scott, MD, MPH'.

*The manuscript's guarantor.

Stephen Scott, MD, MPH
Associate Professor, Departments of Ob/Gyn & Pediatrics
University of Colorado, School of Medicine