Letters to the Editor

New-Onset Ulcerative Colitis in Patients With COVID-19

Original Article: Ulcerative Colitis: Rapid Evidence Review

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To the Editor: Dr. Adams and colleagues note that certain infections may be predisposed to the development of ulcerative colitis and concisely summarize evidence on the treatment of patients with ulcerative colitis who become infected with SARS-CoV-2. However, it is important to be aware that there is also evidence to suggest that COVID-19 might lead to ulcerative colitis.

Published case reports include ulcerative colitis confirmed by colonoscopy in a 19-year-old woman who presented to the hospital with gastrointestinal COVID-19,[1] a 51-year-old man hospitalized for COVID-19 pneumonia who developed colitis two weeks after discharge,[2] a "young female" who developed new colitis one month after hospitalization for COVID-19,[3] a 55-year-old man who developed new colitis three months after hospitalization for respiratory COVID-19,[4] a 37-year-old man who developed colitis two months after recovery from moderately severe respiratory COVID-19,[5] a 64-year-old man who developed colitis three weeks after recovery from mild respiratory COVID-19,[5] and a 71-year-old woman with no history of inflammatory bowel disease who died from complications of acute ulcerative colitis following admission to the hospital for COVID-19 pneumonia.[6]

The mechanisms by which infection with SARS-CoV-2 might induce new-onset ulcerative colitis in a previously healthy patient are unclear. The presence of angiotensin-converting enzyme 2 receptors in the intestinal epithelium may allow binding of the viral spike protein and cellular entry,[1,2,4] generalized intestinal inflammation in response to infection may play a role,[3] and tumor necrosis factor (part of the cytokine storm characteristic of severe COVID-19 and part of the inflammatory response in ulcerative colitis) may play a role.[5] Physicians should be aware that new-onset diarrhea in patients recovering or recovered from COVID-19 could represent new-onset ulcerative colitis rather than a transient intestinal upset or viral gastroenteritis.

Editor's Note: This letter was sent to the authors of "Ulcerative Colitis: Rapid Evidence Review," who declined to reply.

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Caution Before Antibiotic De-escalation Following Negative MRSA Nares Testing

Original Article: Diabetes-Related Foot Infections: Diagnosis and Treatment

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To the Editor: The authors provide an excellent primer on how to diagnose and manage diabetes mellitus-related foot infections. However, one of their key recommendations for practice is problematic. The authors recommend that antibiotic methicillin-resistant *Staphylococcus aureus* (MRSA) coverage may be discontinued in a patient with a diabetes-related foot infection if

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This series is coordinated by Kenny Lin, MD, MPH, deputy editor.

they have a negative MRSA nares culture due to its high negative predictive value. Although antibiotic stewardship is important, the consequences of untreated MRSA infections can be significant.

Negative MRSA nares cultures have been used to de-escalate MRSA antibiotic therapy in patients with respiratory tract infections; studies validating nares culture use found a relatively low prevalence of MRSA pneumonia (4% to 9%).[1] It is important to remember the role of disease prevalence in calculating negative predictive value. The performance of MRSA nasal screening in predicting clinical MRSA infections correlates with the prevalence of MRSA in that specific infection source. MRSA nares screening has a lower negative predictive value in skin and soft tissue infections than in infectious sources with lower MRSA prevalence because these infections have a high prevalence of MRSA.[2]

Even among skin and soft tissue infections, one study found significant variance in MRSA prevalence, with nonextremity cultures having a prevalence of MRSA at 8.7% compared with ulcers and extremity infections with a prevalence of 27.8%. This study also found that nearly one-third of patients with MRSA skin and soft tissue infections were not nasally colonized, suggesting that colonization may not precede disease and that this negative test would not rule out MRSA when prevalence is moderate to high.[3]

All available research assessing the utility of MRSA nares screening to predict MRSA in skin and soft tissue infections is based on retrospective data. One study found a negative predictive value of 73% using MRSA nares screening, which performed better than using MRSA clinical risk factors.[4] Although this may be the case, a negative predictive value of 73% would still miss a significant number of actual MRSA infections.

Prospective trials are needed to establish the safety and effectiveness of MRSA nares screening to guide antibiotic therapy, especially in diabetes-related foot infections. Evidence is not strong enough to recommend discontinuing MRSA antibiotic coverage in diabetes-related foot infections based solely on a negative MRSA nares test.

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The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the U.S. Air Force, the U.S. Department of Defense, or the U.S. government.

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In Reply: We appreciate the caution raised by Dr. Gaillardetz in response to one of our key practice recommendations. We agree that a negative MRSA nares test should not be the only factor in deciding to discontinue MRSA antibiotic coverage for a diabetes-related foot infection, and prospective studies to validate the clinical utility of a MRSA nares culture to guide empiric antibiotic coverage would be valuable. Many factors, such as a patient's history of foot infections, severity of illness, risk of worsening infection, and community MRSA prevalence, should play a role in de-escalating antibiotic therapy. The key practice recommendation from our article should have stated that stopping MRSA coverage in response to a negative nares swab could be considered rather than universally recommended.

MRSA nares testing to guide antibiotic de-escalation is a promising antimicrobial stewardship strategy.[1,2] Antimicrobial resistance and multidrug-resistant organisms are a growing threat to global public health.[3] Overprescribing antibiotics is a common driver of antimicrobial resistance. New tools are needed to minimize the use of broad antimicrobials, shorten antibiotic courses, and allow for earlier de-escalation of treatment without worsening clinical outcomes.[3]

Thankfully, multiple retrospective studies report high negative predictive values of negative MRSA nares cultures in patients with diabetes-related foot infections.[1,2] An analysis of more than 8,000 patients (7.5% of whom had MRSA foot infections) found an 89.6% negative predictive value.[1] In another study, the negative predictive value was 94% in a population of 200 patients with diabetes-related foot infections.[2]

Mounting evidence supports the value of a negative MRSA nares test to reduce inappropriate antibiotic use and the development of bacterial resistance. We think our original B rating is appropriate based on limited-quality patient-oriented evidence but would note the importance of not relying on a negative MRSA nares culture as the only factor when de-escalating antibiotic coverage in patients with diabetes-related foot infections.

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Cannabis Use During Pregnancy

Original Article: Cannabis Essentials: Tools for Clinical Practice

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To the Editor: We appreciated the thoughtful review by Dr. Sazegar on cannabis use. Rates of cannabis use in pregnancy are increasing because of the lessening of legal restrictions, changes in cultural norms, and the COVID-19 pandemic.[1] The review recommends that physicians advise against cannabis use in pregnancy in concordance with national guidelines.[2] Unfortunately, pregnant patients report receiving mixed messages about cannabis safety from their physicians. A study showed that one-half of physicians do not respond with any recommendations when a pregnant patient discloses cannabis use.[3] Patients with questions about the safety of cannabis use in pregnancy report seeking answers from retail cannabis stores and the internet—sources that often normalize the use of cannabis for common issues during pregnancy, such as nausea and anxiety.[4]

Some patients are not comfortable discussing cannabis use during pregnancy because disclosure to a physician may trigger a referral to Child Protective Services (CPS). Depending on the state, the consequences of testing positive for an illegal substance can be severe, and, at the very least, a referral to CPS can feel like a rebuke of a person's parenting. The burden of test and refer policies is not shared equally across the population; Black parents are more likely to be referred to CPS.[5] The American College of Obstetricians and Gynecologists recommends universal question-based screening for substance use during pregnancy but cautions that biologic drug testing should occur only after completing an informed consent process that includes reviewing the benefits, risks, and alternatives for testing.[6] Although heavy use is almost certainly harmful, the criminalization of cannabis use in pregnancy is not solely based on evidence of harm because many common parenting behaviors that endanger the fetus and newborn do not trigger a CPS referral (e.g., tobacco use, co-sleeping, vaccine refusal).

Patients should be able to openly discuss the health risks of cannabis use with their physicians without fear of legal consequences. We propose using the WEED mnemonic to remember steps to address cannabis use in pregnancy: welcome questions about cannabis use; explore alternatives to cannabis for common pregnancy ailments such as anxiety and nausea; explain potential risks of cannabis use; deliver a harm-reduction message by recommending a decrease in the dose and frequency of use for patients who are not able or willing to stay abstinent during pregnancy.

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In Reply: I would like to thank Drs. Frank and Morrison for furthering the discussion about cannabis use in pregnancy. Cannabis policy is not always aligned with cannabis science; criminalization that disproportionately affects minority populations is heartbreaking. The American Society of Addiction Medicine has officially recommended decriminalizing and rescheduling cannabis from Schedule 1 of the Controlled Substances Act to allow for further research into its medical uses, health risks, and impact on special populations.[1]

Mixed messaging about cannabis use from physicians and lack of disclosure from patients are not unique to pregnancy.[2,3] One survey of Colorado primary care physicians and their patients showed that approximately one-half of physicians were unaware of cannabis use among patients who reported they used cannabis.[2] Population-level interventions to curb cannabis use in pregnancy should ideally involve dispensaries as stakeholders. A 2019 survey of legal dispensaries in Canada found that 93% of respondents advise against cannabis use for nausea and vomiting during pregnancy, whereas a study in Colorado found that 69% of dispensaries recommend cannabis for this use.[4,5] Interventions that encourage dispensaries to refer pregnant patients to their primary care physicians for a discussion about cannabis safety are worthy of consideration. I echo the sentiment that all patients (pregnant or not) need to feel safe discussing cannabis use with their physicians without fear of legal consequences. Conceptualizing cannabis use in the context of other harmful parenting behaviors, as highlighted by Drs. Frank and Morrison, can provide helpful talking points in advocacy work.

Establishing the safety of any drug in pregnancy is complex, and patients often value honesty about this uncertainty. In preconception and prenatal counseling, it can be helpful to frame the discussion in terms of the known adverse effects of cannabis on the developing brain, as discussed in my article. Discussing cannabis use with patients should ideally include a patient-centered, trauma-informed approach with motivational interviewing. I recommend starting the discussion with a nonjudgmental question such as, "Do you sometimes use cannabis (now that it's legal)?" and ending with a discussion about harm reduction. The take-home message for patients should be that cannabis use, in any form, is not recommended in pregnancy because of the absence of safety data, low-strength evidence of potential harm, and expert reviews that consider the known risks of cannabis to the developing brain.

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Correction

Misused eponym. In the article, "Orthostatic Hypotension: A Practical Approach" (January 2022, p. 39), an outdated eponym was used to describe the standing test for measuring blood pressure and heart rate changes under gravitational stress. The term "Schellong test" has been removed from the article in the abstract (page 39), SORT table (page 40), the second paragraph (pages 40-41) and the seventh paragraph (page 42) of the "Clinical Presentation and Evaluation" section, the first item under Indications in Table 6 (page 43), and Figure 2 (page 45). The term "Schellong test" was also removed from Question 7 of the January 2022 CME Quiz. The online versions of this article and the CME Quiz have been corrected. ■