

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

Section Editor: Stephen B. Hanauer, MD

Vaccination of Patients With Inflammatory Bowel Disease



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G&H How does the vaccination rate in patients with inflammatory bowel disease compare with that of the general population?

FF Vaccination rates in patients with inflammatory bowel disease (IBD) have been found to be lower than those of the general population. One reason for the difference is that patients with IBD, who are usually otherwise healthy, often think of their gastroenterologist as their primary provider of care, but the gastroenterology team does not perceive that. Consequently, these patients are expecting recommendations for vaccinations from their gastroenterologist, but the gastroenterologist believes that the primary care doctor is responsible for determining which vaccinations are needed and for administering the vaccinations. This fragmentation of care may result in lower rates of vaccination in this high-risk group of patients.

G&H What other challenges or barriers are associated with vaccination of these patients?

FF There are several barriers encountered in clinical practice. There is a lack of recognition of the importance of vaccination in otherwise healthy people with IBD. Patients are frequently concerned that their IBD may be exacerbated by vaccination. Thus, it is crucial that the gastroenterology team reassures patients that there are no data that vaccination will worsen their disease activity. In addition, there is no evidence to support an association of childhood vaccination with the development of IBD. There is also a lack of access to vaccination, as both the gastroenterologist and the primary care doctor may not

offer this service in their offices. Finally, there may be issues regarding copayments for vaccination.

G&H Why is vaccination important in patients with IBD?

FF Immunomodulators and biologics are being used more frequently and earlier in the course of treatment in a subset of patients with IBD. In addition, there has been a consensus that combination therapy is preferred, especially in high-risk patients with IBD, which increases the degree of immunosuppression. It is accepted that immunosuppressed patients, when exposed to infectious agents, can develop severe and, on rare occasions, life-threatening infections. Thus, it is incumbent on the gastroenterologist to either offer vaccinations to their patients or educate the primary care provider regarding which vaccinations are necessary to prevent these rare but serious infectious complications associated with IBD therapy.

Because managing patients with IBD is becoming increasingly complex and gastroenterologists have limited time with patients, vaccinations may not be high on their list of priorities. However, keeping patients safe on effective medical therapy is important; therefore, vaccination counseling should be considered an essential aspect of care when evaluating and treating patients with IBD.

G&H Which patients with IBD are at greatest risk of vaccine-preventable infections?

FF All patients with IBD, not only immunosuppressed patients, are at risk for developing certain vaccine-preventable infections. A Danish study found that even prior to the

diagnosis of ulcerative colitis or Crohn's disease, patients with IBD have an increased risk of developing pneumococcal pneumonia, suggesting that the presence of IBD alone increases the risk of infection. Therefore, providers should not wait until patients with IBD start immunosuppressive therapy to update their vaccination status.

IBD patients on immunosuppression are at an increased risk of developing vaccine-preventable diseases. The highest risk is in patients on triple immunosuppression including corticosteroids, immunomodulators, and biologics.

G&H Does immunosuppression have an effect on vaccine efficacy in IBD patients?

FF The level of immunosuppression predicts the likelihood of a robust immune response to vaccination. Immunosuppression can be classified as high level (eg, combination therapy with corticosteroids, thiopurines, methotrexate, or biologics) or low level (eg, monotherapy with standard doses of immunomodulators). Patients on monotherapy with thiopurines and/or biologics may have an adequate response to vaccination, but once patients are on combination therapy, their vaccine response decreases.

The level of immunosuppression also plays a role in terms of which types of vaccines (inactive or live) can be used. Patients with IBD can receive all inactive vaccines, regardless of their level of immunosuppression. However, live vaccines—such as the measles, mumps, and rubella vaccine; the varicella zoster (chickenpox) vaccine; and the herpes zoster (shingles) vaccine should be used with caution in patients who are on high-level immunosuppression. This is one of the most controversial issues in the vaccination of patients with IBD and an area of ongoing research. For example, research is currently underway on the safety of using the live herpes zoster vaccine (Zostavax, Merck) in IBD patients on anti-tumor necrosis factor agents (NCT02538341). An inactive vaccine for herpes zoster (Shingrix, GlaxoSmithKline) given as two doses 2 to 6 months apart is expected to become available by the end of 2017 and is indicated for patients 50 years and older; this vaccine could be used in immunocompromised patients.

G&H Can household members of immunosuppressed patients receive live vaccines?

FF Yes, there is no contraindication to using live vaccines in household members of immunosuppressed IBD patients. An example of such a scenario would be whether an infant cared for by an immunosuppressed parent with IBD could receive the chicken pox vaccine.

On rare occasions, a rash can develop in patients receiving live vaccines. If the household member develops a rash after vaccination, the immunocompromised IBD patient should avoid contact with the vaccinated individual until the rash resolves.

G&H Specifically, which vaccinations are recommended for patients with IBD?

FF Patients with IBD should follow all age-appropriate vaccination recommendations made by the Advisory Committee on Immunization Practices (ACIP) published yearly in the *Annals of Internal Medicine*. These include, but are not limited to, hepatitis A, hepatitis B, and pneumococcal pneumonia vaccinations. If patients with IBD are not immune to hepatitis A and/or hepatitis B, they should be offered a booster or a full vaccination series.

It is important to understand the order in which the 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23) should be administered. The ACIP recommends that immunosuppressed IBD patients receive PCV13, followed by PPSV23 2 to 12 months later. If the patient has already received PPSV23, then he or she should receive PCV13 at least 1 year later. A second dose of PPSV23 should be administered 5 years after the first dose and again after the age of 65 years if more than 5 years have elapsed since the previous dose.

In addition, gastroenterologists should recommend the human papilloma virus vaccine to their male and female IBD patients aged 26 years or younger if they have not received it as an adolescent.

Other vaccines listed in the ACIP recommendations include tetanus and diphtheria/tetanus, diphtheria, and acellular pertussis; measles, mumps, and rubella; meningococcus; varicella zoster; and herpes zoster. Providers should refer to the ACIP recommendations for additional details. Tables 1 and 2 include a list of vaccines to consider.

G&H Are additional vaccines needed for patients with IBD who are traveling?

FF Additional vaccines are needed for patients with IBD who are traveling to developing countries. Prior to travel, these patients should be evaluated by an infectious disease expert or at a traveler's clinic. The website for the Centers for Disease Control and Prevention (<https://wwwnc.cdc.gov/travel>) is a useful resource for both patients and clinicians trying to determine which areas of the world require which vaccinations. There are certain live vaccines, for example the yellow-fever vaccine, that need to be considered prior to traveling.

Table 1. Inactivated Vaccines for Patients With IBD

<p>Influenza: All patients with IBD should be vaccinated seasonally with the intramuscular/intradermal inactivated influenza vaccine prior to starting immunosuppressive therapy.</p>
<p>Pneumococcal pneumonia: All patients with IBD should be vaccinated once with the PCV13 followed by the PPSV23 (first dose after 8 weeks if immunocompromised, or after ≥ 1 year if immunocompetent; second PPSV23 dose after 5 years; and third dose after 65 years of age). If previously vaccinated with the PPSV23, then the PCV13 should be administered at least 1 year after the PPSV23 in both immunocompromised and immunocompetent adults.</p>
<p>Hepatitis A: Check hepatitis A immune status at the patient's initial visit. If nonimmune to hepatitis A, vaccinate the patient with a 2-dose series (0 months and 6-12 months).</p>
<p>Hepatitis B: Check hepatitis B immune status at the patient's initial visit. If nonimmune to hepatitis B, vaccinate the patient with a 3-dose series (0 months, and 1 and 6 months after first dose) and recheck titers 1 to 2 months after last vaccination. If the patient remains nonimmune, offer booster with a double dose of hepatitis B vaccine or offer combined hepatitis A/B vaccination.</p>
<p>Human papilloma virus: All male and female IBD patients between the ages of 11 and 26 years should be vaccinated with the human papilloma virus vaccine.</p>
<p>Meningococcus: Patients with IBD should be vaccinated with the meningococcal vaccine according to standard ACIP recommendations for the general population.</p>
<p>Td/TDap: All patients with IBD should be vaccinated with Td every 10 years. TDap should be substituted once for the Td vaccine to provide additional coverage for pertussis.</p>

ACIP, Advisory Committee on Immunization Practices; IBD, inflammatory bowel disease; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent pneumococcal polysaccharide vaccine; Td, tetanus and diphtheria; TDap, tetanus, diphtheria, and acellular pertussis.

Reproduced from Reich J, Wasan SK, Farraye FA. Vaccinating patients with inflammatory bowel disease. *Gastroenterol Hepatol (N Y)*. 2016;12(9):540-546.

Table 2. Live Vaccines for Patients With IBD

<p>MMR: Vaccinate all nonimmune patients with the MMR vaccine as long as they have not been on immunosuppressive therapy within the previous 3 months and there are no plans to start immunosuppressive therapy within the next 6 weeks.</p>
<p>Varicella zoster: Vaccinate all nonimmune patients with the varicella zoster vaccine as long as they have not been on immunosuppressive therapy within the previous 3 months and there are no plans to start immunosuppressive therapy within the next 6 weeks.</p>
<p>Herpes zoster: Vaccinate all patients over the age of 60 years with the herpes zoster vaccine. Vaccination is safe in patients on low-dose immunosuppression but contraindicated in patients on biologic therapy or on corticosteroids. Do not vaccinate patients on high-dose immunosuppressive therapy within the past 3 months or who plan to start high-dose immunosuppressive therapy within the next 6 weeks.</p>

IBD, inflammatory bowel disease; MMR, measles, mumps, and rubella.

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G&H What strategies have been used or examined to increase the vaccination rate of patients with IBD?

FF One strategy has been to educate gastroenterologists as to the importance of vaccination. Over the past several years, there has been an appreciation of the importance of vaccination for IBD patients, with an increase in the published literature on this topic. In a prospective interventional study in which health care professionals received systematic oral and written information about vaccination guidelines 3 times over 6 months, there was a significant increase in adherence to vaccination guidelines. In my referral practice, I am seeing more patients in whom vaccination issues have been addressed. Educating patients as to the importance of vaccination is crucial. In addition to recommendations from the gastroenterology team, gastroenterology societies have posted information on this issue on their websites.

Another strategy for increasing vaccination is for gastroenterologists to offer vaccinations in their own office. This is an easy and effective way for gastroenterologists to bring their patients up to date with their vaccinations whenever patients visit the office for routine care. If a

practice cannot offer vaccination, the gastroenterologist should refer patients to their primary care provider with explicit recommendations for vaccination or provide a prescription for the vaccine and refer patients to their local pharmacy.

Incorporating reminders for vaccination into electronic medical records provides another opportunity to increase vaccination rates.

G&H What specific resources for vaccinations are available to help gastroenterologists?

FF It is helpful for providers to keep a copy of the Crohn's and Colitis Foundation's health maintenance recommendations posted in their office. This 1-page checklist (available at <http://www.crohnscolitisfoundation.org/science-and-professionals/programs-materials/ccfa-health-maintenance.pdf>) includes all recommended vaccines and also comments on other important health maintenance items, such as screening for cervical and skin cancer, depression, and osteoporosis. In addition, Cornerstones Health has a vaccination checklist (available at <http://www.cornerstoneshealth.org/wp-content/uploads/2017/06/Monitoring-and-Prevention-3.10.2017.pdf>) that can be downloaded, printed, and placed in each examination room to reinforce the importance of vaccination. Primary care providers as well as gastroenterologists can use these checklists as reminders in their busy practices.

G&H How aware are patients with IBD of the importance of vaccination?

FF In an online study that my colleagues and I conducted using the Crohn's and Colitis Foundation Partners cohort, a recommendation for vaccination was found to be highly predictive of patients getting a vaccination. Thus, even if gastroenterologists cannot offer vaccination in their office, a recommendation may motivate patients to be vaccinated, either at their primary care provider's office or at a pharmacy. Many patients think that vaccinations are for children and adolescents, and do not realize that certain vaccinations are necessary for all adults. Therefore, it is important that providers educate patients on the importance of vaccination.

G&H Do you have advice for gastroenterologists in terms of vaccination in the setting of IBD?

FF I would advise gastroenterologists to use the first office visit of a newly diagnosed patient with IBD to formulate a series of recommendations for vaccination. In our practice, my colleagues and I obtain a vaccination history when patients are initially seen and then periodically thereafter. Serology for hepatitis A, hepatitis B, and varicella can also be obtained, and serologic testing for measles, mumps, and rubella can be considered. Many patients with IBD will require escalation of medical therapy to include corticosteroids, immunomodulators, and biologics; therefore, when seeing a newly diagnosed, nonimmunosuppressed patient with IBD, gastroenterologists have the ideal window of opportunity to bring the patient's vaccination history up to date.

Dr Farraye has no relevant conflicts of interest to disclose.

Suggested Reading

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