

Immunizations in Children with Inflammatory Bowel Disease Treated with Immunosuppressive Therapy

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Abstract: The vast majority of patients with inflammatory bowel disease (IBD) will receive immunosuppressive therapy at some point for their disease, whether for the short term (such as a course of corticosteroids) or long term (such as maintenance therapy with immunomodulators or biologics). The systemic immunosuppression places patients at increased risk for infections. Therefore, it is important that patients are up-to-date with immunizations to minimize vaccine-preventable infections. However, the literature shows that the rate of immunization in patients with IBD is low. Ideally, the vaccination status is checked at diagnosis, and patients are immunized with the vaccines they need. Drawing titers is helpful in cases in which vaccination history is unclear or to confirm that titers are at an adequate level in cases in which patients have been vaccinated. Current guidelines recommend that patients with IBD follow the same routine immunization schedule as healthy children, but patients should not be administered live vaccines if they are receiving immunosuppressive therapy. Therefore, it is ideal to administer any necessary vaccinations as early as possible, prior to starting immunosuppressive therapy. Patients may receive inactivated vaccines regardless of immunosuppressive status. The IBD literature suggests that inactivated vaccines are safe and do not worsen disease activity. In general, patients with IBD mount an immune response to vaccines, but the response may be lower if patients are receiving immunosuppressive therapy, especially tumor necrosis factor inhibitors.

Inflammatory bowel disease (IBD) is characterized by chronic inflammation of the gastrointestinal tract. The specific pathogenesis of IBD remains unknown, but growing evidence in the literature has identified over 140 genetic variants (such as *NOD2* and interleukin-23R).¹⁻⁴ The genetic alterations, in combination with environmental factors, ultimately lead to altered mucosal immunity, which in turn can lead to intestinal inflammation or fibrosis.⁵ In addition to having a suboptimal innate immunity, the

Keywords

Inflammatory bowel disease, Crohn's disease, ulcerative colitis, vaccine, immunization, immunosuppression

immune system of patients with IBD may be further weakened by medications used to treat their disease.

The vast majority of children and adults who have Crohn's disease and ulcerative colitis will likely be treated with immunosuppressive medications at some point in the course of their disease, either in the short term to induce remission (such as with a course of corticosteroids) or in long-term maintenance therapy (such as with immunomodulators or tumor necrosis factor [TNF]-alpha inhibitors).⁶

Immunosuppressive medications are a double-edged sword. Although these potent medications may help control disease activity, they also put patients at an increased risk for opportunistic infections and associated complications,⁷ such as cytomegalovirus,^{8,9} Epstein-Barr virus,¹⁰ hepatitis B virus (HBV) reactivation in latent infection,¹¹⁻¹⁴ varicella,¹⁵⁻¹⁷ and histoplasmosis.^{18,19} Similarly, a few studies have found that there is a higher prevalence of cervical dysplasia in women with IBD compared with healthy age-matched controls,^{7,20,21} and immunosuppressive therapy is a risk factor for having an abnormal Pap smear.^{7,21,22} Another study revealed that patients with IBD are at an increased risk for bacterial pneumonia compared with the general population. When patients with IBD with pneumonia were compared with patients with IBD without pneumonia, immunosuppressive therapies (including corticosteroids, thiopurines, and biologics) were found to be risk factors for pneumonia.²³

Immunizations Are Underutilized

Fortunately, there are methods to minimize infections. They include proper hand washing or use of alcohol-based hand sanitizers, avoidance of sick contacts, administration of prophylaxis if exposed, adequate nutrition, and maintenance of a healthy lifestyle. Another way to minimize infections (eg, influenza, human papillomavirus [HPV], and varicella) is through vaccination. However, the valuable tool of vaccination is underutilized by both the gastroenterologist and patient.

A survey by Wasan and colleagues of gastroenterologists who treat adult patients revealed that the majority believed the responsibility to ensure that patients with IBD were up-to-date with immunizations should fall on the primary care physician (PCP).²⁴ However, some patients with IBD visit the gastroenterologist more frequently than the PCP and may view the gastroenterologist as their primary medical care provider. Therefore, gastroenterologists should be mindful of patients' immunizations.

It is important for gastroenterologists to educate both patients and PCPs about immunizations by including a reminder in the consult note and to ensure that patients are receiving the appropriate vaccines at the

appropriate time (either at their own office or the PCP's). However, the survey by Wasan and colleagues found that only approximately half of gastroenterologists routinely inquired about patients' vaccination history, and being "too busy/forgot" was the most common reason for not regularly recommending an immunization.²⁴ In addition, only 12% of gastroenterologists could correctly answer which vaccines should or should not be administered when patients are receiving or not receiving immunosuppressive medications. Patients disclosed that the clinician who encouraged them to receive the influenza vaccine was primarily their family physician, followed by family/friends and then their gastroenterologist.²⁵

Patients with IBD have a low rate of immunization for vaccine-preventable diseases. Melmed and colleagues surveyed 169 adults with IBD about their immunization history and exposure risk.²⁶ The study found that only 28% routinely received influenza vaccine, 9% received pneumococcal vaccination, and 45% had a tetanus booster within the past 10 years. However, the rate of routine immunizations in children in certain parts of Australia and Canada is approximately 90%.^{27,28} Interestingly, a study by Crawford and colleagues found that adherence to additional recommended vaccines was poor, with only 5% of children receiving a pneumococcal booster and only 10% receiving influenza vaccine.²⁷

Common reasons patients have for not receiving influenza vaccination include fear of adverse effects or serious complications, belief that the vaccine is not effective, concern that the vaccine will induce an IBD flare, lack of awareness that the vaccine is indicated, belief that the vaccine is unnecessary, and, importantly, the medical care provider either did not offer the vaccine or advised against it.²⁵⁻²⁷ A number of recent reviews and guidelines provide important information on appropriate use of vaccines.

Immunization Guidelines

There are many different published recommendations on vaccinating immunocompromised patients. Such "guidelines" are often limited by a lack of primary data and discrepant recommendations between authorities. In 2013, the Infectious Disease Society of America (IDSA) prepared a comprehensive document of recommendations outlining the controversies.²⁹ This IDSA Guideline is freely available online at <http://www.idsociety.org/Templates/Content.aspx?id=32212256011> and can be used by practitioners in cases of clinical uncertainty.

Current immunization guidelines recommend vaccinating all patients with IBD with inactivated vaccines, regardless of immunosuppression status. Therefore, patients with IBD generally follow the same routine vaccination schedule as the general population. However, live

vaccines—such as measles, mumps, and rubella (MMR), varicella, and intranasal influenza vaccines—should not be given to immunosuppressed patients. A number of studies on the safety and immunogenicity of inactivated vaccines in patients with IBD have been conducted; however, there remains a paucity of data on live vaccines.

When Are Patients Considered to Be Immunosuppressed?

Patients with IBD on aminosallylate monotherapy are not considered immunosuppressed and should follow the same routine vaccination schedule as the general population. Patients considered to be immunosuppressed are those receiving 6-mercaptopurine (6-MP), azathioprine, methotrexate, biologics, tacrolimus, cyclosporine, or high-dose corticosteroids (defined as ≥ 20 mg/day, or ≥ 2 mg/kg/day if < 10 kg, of prednisone or its equivalent if used for at least 14 days).

It is recommended that immunosuppressive therapy be discontinued for at least 3 months prior to administering live vaccines, with the exception of corticosteroids, which should be discontinued for at least 1 month. If live vaccines are to be administered prior to starting immunosuppressive medications, then it is optimal to wait at least 4 weeks after varicella vaccination and at least 6 weeks after MMR vaccination before initiating immunosuppressive therapy. Patients who are severely malnourished are also considered immunosuppressed.³⁰⁻³²

When to Immunize

The ideal time to check a patient's immunization status and administer "catch-up" vaccines is at the diagnosis of IBD. This is especially important for live vaccines, which should be administered prior to initiating immunosuppressive therapy. Fortunately, because live vaccines (eg, MMR and varicella) are routinely recommended and administered to young children, most children with IBD would have already received live vaccines by the time of diagnosis because it is less common for children to present at younger than age 5 years. However, in cases in which patients are "behind" on vaccines and will be placed on aminosallylates as maintenance therapy but need to start corticosteroids for induction of IBD, it may be better to wait until after corticosteroids are weaned before administering live vaccines.

In cases in which patients will be started on immunosuppressive agents as maintenance therapy (with or without corticosteroids), it is important to obtain immunization records to ascertain which vaccines have not been administered and discuss the risks and benefits of immunizing (and withholding therapy) vs starting immunosuppressive therapy first with patients and their families.

In general, checking serology is helpful in cases in which the immunization status is unclear. Even in patients who have a history of vaccination, obtaining titers is useful in assessing whether antibodies are at an adequate level because titers may diminish over time.^{26,33} Titers commonly available in laboratories include those for hepatitis A virus, HBV, MMR, and varicella.

Assessing Vaccine Efficacy

Vaccines contain live attenuated or killed inactivated microorganisms or synthesized particles that act as antigens to trigger a cascade of immune reactions in the body, ultimately leading to formation of antibodies and memory cells that will be activated should there be an exposure to the wild-type organism in the future. Typically, investigators obtain a blood sample before and at a certain time interval after administration of a vaccine to measure antibody titer levels. The extent of immune response is made by comparing the antibody titer levels at the 2 time points.

Various terms may be used to describe vaccine immunogenicity. Seroconversion is the development of antibodies after vaccination in a person who did not previously have a detectable titer. A person is considered seroprotected if the antibody level has reached or exceeded the minimum threshold considered necessary to be protective against wild-type infection. Geometric mean titer (GMT) is defined as the average titer in a group of patients who have been vaccinated.

Routine Vaccines

The following section is a summary of the 2013 routine vaccine recommendations for children and adolescents by the Centers for Disease Control and Prevention and Advisory Committee on Immunization Practices³⁴ (Table). Data available on the immunogenicity and safety of each vaccine in patients with IBD are also reviewed.

Inactivated (Killed) Vaccines

Hepatitis A Virus The hepatitis A virus vaccine is a 2-dose regimen administered 6 to 18 months apart. The first dose is generally given at age 12 to 23 months. Two pediatric studies suggest that children with IBD have excellent immunogenicity (seroconversion rates of 97% to 100%) and are similar to healthy controls (100%) after completing the 2-dose series.^{35,36} However, 1 of these studies found that the seroconversion rate was lower after the first vaccine dose in patients with IBD (39%) compared with controls (64%; $P = .00001$). This emphasizes the importance of completing the vaccine series as recommended.³⁵ The vaccine was well tolerated without worsening of disease activity.^{35,36}

Table. Routine Immunizations for Children

Age Range	Inactivated Vaccines	Live Vaccines
Infancy and toddlerhood (birth to 3 years old)	Hepatitis A virus Hepatitis B virus DTaP ¹ Hib ² Pneumococcal (PCV13) IPV ³	Rotavirus MMR ⁶ Varicella
Early childhood (4-6 years old)	DTaP ¹ IPV ³	MMR Varicella
School-age and adolescence (7-18 years old)	Tdap ⁴ HPV ⁵ Meningococcal	
Annually	Influenza (intramuscular)	Influenza (intranasal)

DTaP, diphtheria and tetanus toxoids and acellular pertussis; Hib, *Haemophilus influenzae* type b; HPV, human papillomavirus; IPV, inactivated poliovirus; MMR, measles, mumps, and rubella; PCV13, pneumococcal conjugate vaccine; Tdap, tetanus and diphtheria toxoids and acellular pertussis.

A high seroconversion rate of 97.6% was also found in a study of 419 adult patients with IBD after completing the 2-dose series. However, the seroconversion rate was lower in patients receiving TNF inhibitor therapy compared with patients who were not on such therapy (92.4% vs 99.1%; $P=.001$) as well as in patients treated with 2 or more immunosuppressive agents compared with patients on fewer than 2 immunosuppressive agents (92.6% vs 98.4%; $P=.03$). Response rates were similar between patients on TNF inhibitor monotherapy and patients on a TNF inhibitor combined with another immunosuppressant.³⁷

Hepatitis B Virus The HBV vaccine is a 3-dose series typically given in infancy and early toddlerhood. It is important to check that patients are negative for HBV infection, especially prior to starting immunosuppressive therapy, including biologics, as cases of viral reactivation have occurred in patients with latent HBV infection treated with TNF inhibitors, resulting in severe viral hepatitis and/or liver failure.¹¹⁻¹⁴ If patients are seronegative for HBV, they should be given the vaccine series (at Months 0, 1, and 4-6) and have titers rechecked 1 month after completing the series. If patients do not mount an adequate response, they should be revaccinated using a double dose following the standard HBV vaccine regimen or an accelerated schedule (Months 0, 1, and 2).^{31,34,38}

A study by Gisbert and colleagues³⁸ in 148 adult patients with IBD suggests that seroconversion (defined as anti-HBV surface antigen [HBs] >10 IU/L) is higher for those who followed the accelerated double-dose schedule

compared with the standard dose (75% vs 41%; $P<.001$). In another study by Gisbert and colleagues³⁹ involving 241 adult patients with IBD who were immunized with the double-dose accelerated HBV vaccine schedule, seroconversion occurred in 59%, and complete response (anti-HBs >100 IU/L) occurred in 39%. Older age and use of anti-TNF therapy were associated with poorer immunogenicity. Treatment with thiopurines or methotrexate did not influence immune response. Patients with anti-HBs less than 100 IU/L were revaccinated using the same double-dose accelerated schedule. Of the 95 patients who received the second set of vaccinations, 42% had a complete response.

In one pediatric study, children who had not been immunized against HBV were given the vaccine series. Seroconversion (anti-HBs ≥ 10 mIU/mL) occurred in 70% of patients with IBD and 90% of healthy controls ($P=.02$). A booster dose was administered to children who did not seroconvert. Response then occurred in 50% (7/14) of patients with IBD and 60% (3/5; $P=NS$) of controls.³⁶ In the adult IBD literature, an adequate immune response to HBV vaccination occurred in 48% to 76% of patients.^{40,41} There were no vaccine-associated serious adverse events.^{36,38,40}

In a prospective study of 100 children and young adults treated with infliximab (Remicade, Janssen) for IBD, patients were asked about their history of HBV vaccination, and serology for HBV was drawn.⁴² Thirteen percent of the patients had never been immunized against HBV. Of the 87 children who had been immunized (mean time of 13 years prior to drawing titers), 49 (56%) had immunity (defined as anti-HBs ≥ 10 mIU/mL). Older age, lower albumin levels, and presence of pancolitis were associated with lack of a protective antibody level. Concurrent use of immunomodulators with infliximab was not associated with lack of immunity.

A booster dose was administered to patients who had received the vaccine series prior to the study but were found to lack immunity. Of the 34 patients who received a booster vaccine, 26 (76%) mounted an anamnestic response. Children who did not mount a response to the booster dose tended to receive infliximab more frequently compared with those who responded (every 5.9 ± 1.2 weeks vs every 7.1 ± 1.8 weeks; $P=.01$).

Another study by Gisbert and colleagues of 100 adult patients with IBD found that the cumulative loss of anti-HBs titers (<10 IU/L) was 2% at 6 months and 15% at 12 months postvaccination.⁴³ TNF inhibitor therapy was associated with a 3-fold increased risk of loss of response. Other studies found that suboptimal immunogenicity was associated with IBD duration of 110 months or more, albumin levels greater than 3.6 mg/mL, active IBD, and immunosuppressive therapy.^{38,40,41}

Diphtheria, Tetanus, and Pertussis The diphtheria and tetanus toxoids and acellular pertussis vaccine is a 5-dose series typically administered at ages 2, 4, 6, and 15 to 18 months and 4 to 6 years. The tetanus and diphtheria toxoids and acellular pertussis vaccine is recommended at age 11 to 12 years followed by a tetanus and diphtheria booster every 10 years. Data on the tetanus booster currently exist only in adult patients, and findings are conflicting. Some studies demonstrate a defective formation of B cells after vaccination,^{44,45} whereas other studies suggest an appropriate immune response in patients with IBD.^{46,47}

Haemophilus Influenzae Type B The *Haemophilus influenzae* type b (Hib) conjugate vaccine is administered as a primary 3-dose series in infancy (at ages 2, 4, and 6 months) and a booster at age 12 to 15 months. Data on the Hib vaccine and IBD are limited to one adult study consisting of 31 patients with Crohn's disease and 12 patients with ulcerative colitis who were immunized 24 weeks after starting 6-MP.⁴⁶ Thiopurine use did not suppress cellular or humoral immune response. In addition, patients tolerated the vaccine without worsened disease severity of IBD.

Pneumococcal The pneumococcal conjugate vaccine is given as a primary series in infancy (at ages 2, 4, and 6 months) and a booster at age 12 to 15 months. To date, there are no studies on this specific vaccine in children with IBD. However, the adult IBD literature is consistent in finding that immunogenicity to the 23-valent pneumococcal polysaccharide vaccine is poorer in patients receiving TNF inhibitor therapy (either as monotherapy or in combination with immunomodulators, 45% to 63%) compared with patients not receiving immunosuppressive therapy (78% to 89%) and healthy controls (85%).⁴⁸⁻⁵⁰ Immunomodulator monotherapy was not associated with a hindered immune response (79%). The vaccine was well tolerated without serious adverse events.^{49,50}

Poliovirus The inactivated poliovirus (IPV) vaccine has replaced the live attenuated oral poliovirus vaccine in the United States due to concern for vaccine-associated paralytic poliomyelitis. IPV is routinely given as a primary series at ages 2, 4, and 6 to 18 months and as a booster at age 4 to 6 years. There are currently no studies on poliovirus vaccine in patients with IBD.

Human Papillomavirus HPV vaccine is available as either a bivalent (HPV2; Cervarix, GlaxoSmithKline) or quadrivalent (HPV4; Gardasil, Merck & Co) vaccine. Both HPV2 and HPV4 immunize against HPV types 16 and 18, which are responsible for approximately 75% of cervical cancers. The advantage of HPV4 is that it also immunizes against HPV types 6 and 11, which cause approximately 90% of

genital warts. Both vaccines are licensed for girls age 9 to 26 years. However, only the HPV4 vaccine is licensed for boys (also for ages 9 to 26 years), who often tend to be asymptomatic carriers and distributors of the virus. The HPV vaccine is generally recommended at age 11 to 12 years and is given as a 3-dose series at Months 0, 1 to 2, and 6.

Jacobson and colleagues administered 3 doses of the HPV4 vaccine to 37 girls and young women age 9 to 26 years receiving immunomodulator or TNF inhibitor therapy for IBD (prospective group).⁵¹ Antibody levels to each serotype were obtained immediately prior to the first dose and 1 month after the final dose. The investigators also drew titers in 15 girls and young women with IBD on immunomodulator or TNF inhibitor therapy who had previously completed the 3-dose HPV vaccine series at their pediatrician's office (range, 0.5 to 27 months prior to enrollment, retrospective group). All patients in the prospective and retrospective groups mounted an excellent immune response, with 100% seropositivity to HPV types 6, 11, and 16. Seropositivity was lower for type 18 (96% in the prospective group and 40% in the retrospective group). GMTs for each serotype in the prospective group were similar to those of healthy historical female controls from Merck studies. There were no serious adverse events or worsened disease activity related to the vaccine.

Meningococcal The quadrivalent meningococcal conjugate vaccine is generally recommended at age 11 to 12 years, with a booster at 16 years. If the first dose is given at age 13 to 15 years, then a booster is recommended at age 16 to 18 years, with a minimum of 8 weeks between doses. A booster is not indicated if the first dose is given after age 16 years. Dorming college freshmen and graduating high school seniors who expect to dorm should be given 1 dose if they have not been immunized. No data currently exist on the meningococcal vaccine in patients with IBD.

Influenza The influenza vaccine is available as an inactivated form, administered intramuscularly for children age 6 months and older, and as a live attenuated form, administered intranasally for children age 2 years and older. Children age 8 years and younger who have not been previously immunized with influenza should receive 2 doses at least 4 weeks apart. It is recommended that patients with IBD receive the intramuscular form of the influenza vaccine and, when available, the influenza/swine combination vaccine each year. For patients with known or suspected influenza infection, physicians should consider withholding immunosuppressive therapy until the patient clinically improves and his or her infection resolves. Antiviral medications, such as oseltamivir, should be given if clinically indicated, regardless of the patient's immunosuppression status.

The pediatric IBD data demonstrate that the inactivated trivalent influenza vaccine is safe and without serious adverse events.^{52,53} In addition, the vaccine does not appear to worsen IBD activity. Disease activity scores pre- and postvaccination (as measured by the Pediatric Crohn's Disease Activity Index for Crohn's disease and the Modified Harvey-Bradshaw score or Lichtiger Colitis Activity Index for ulcerative colitis or indeterminate colitis) were not statistically significant.^{52,53} The vaccine is generally immunogenic, especially to the two A strains. However, patients on immunosuppressive therapy, especially TNF inhibitors, have a poorer response to strain B compared with patients not receiving immunosuppressive therapy and healthy controls.⁵²⁻⁵⁴

Vaccine studies in adult patients with IBD that evaluated the 2009 H1N1 influenza vaccine agree that the vaccine is generally well tolerated.^{55,56} Immunogenicity is lower in patients on TNF inhibitor therapy compared with patients on nonimmunosuppressive therapy and healthy controls. Moreover, immune response is poorer for patients on combination therapy (TNF inhibitor combined with a thiopurine or corticosteroids) compared with patients on TNF inhibitor monotherapy.

Live Attenuated Vaccines

Measles, Mumps, and Rubella The first dose of the MMR vaccine is typically administered at age 12 to 15 months. The second dose is administered at age 4 to 6 years; however, the second dose may be given earlier than age 4 years as long as there is a minimum of 4 weeks between the 2 doses.

If the vaccination history is unclear, titers to individual components of the vaccine should be obtained, and patients should be vaccinated if they lack immunity. However, because the MMR vaccine is a live vaccine, it is currently not recommended in patients with IBD who are receiving immunosuppressive therapy.³⁰ If there is anticipation to start immunosuppressive medications, it is advised to wait at least 6 weeks after vaccination.³¹

The data currently available on adult patients with IBD suggest that approximately 30% to 37% are seronegative to measles, mumps, and/or rubella, even if they had a history of wild-type infection.^{57,58} Fifty-four percent of patients receiving immunosuppressive therapy were found to be seronegative to 1 or more viral components of the MMR vaccine.⁵⁸ To date, there are no data on the immunogenicity of the MMR vaccine in pediatric patients with IBD.

Varicella The varicella vaccine is a 2-dose regimen. The first dose is typically administered at age 12 to 15 months and the second dose at age 4 to 6 years. The second dose can be given before age 4 years; however, it is preferred that

there is a minimum of 3 months between doses (although a minimum of 4 weeks is also acceptable). For children age 7 to 12 years who need to "catch up," the 2 doses should be at least 3 months apart (although a minimum of 4 weeks is also acceptable). For children age 13 years and older who need to be immunized, the 2 doses should be at least 4 weeks apart.

Guidelines currently recommend that the varicella vaccine, which is live, not be given to patients with IBD who are receiving immunosuppressive therapy.³⁰ It is even more important, however, to protect this vulnerable subpopulation against wild-type infection because these patients are at an increased risk for complications of varicella virus infection, some of which can be severe.¹⁵⁻¹⁷

Interestingly, although the zoster vaccine has at least 10 times more varicella zoster virus than the varicella (chickenpox) vaccine, the zoster vaccine is recommended for adult patients on low-dose corticosteroids (<20 mg/day prednisone or equivalent), a short course of corticosteroids (<14 days), 6-MP at up to 1.5 mg/kg/day, azathioprine at up to 3 mg/kg/day, or methotrexate at up to 0.4 mg/kg/week.^{31,59}

If patients are not on immunosuppressive medications, they should be vaccinated if there is no history of chickenpox infection or varicella vaccination. If the history is unclear, titers should be drawn and patients should be vaccinated if they lack adequate protection. Although a history of wild-type infection or vaccination is generally a good predictor of a good antibody level,^{26,33} obtaining titers would still be helpful because antibody levels may wane over time.^{32,33}

In the difficult scenario in which a child is expected to start immunosuppressive therapy but needs to be vaccinated, there should be at least a 4-week interval between vaccination and onset of immunosuppressive therapy.^{31,32} Therefore, the medical care provider should weigh the benefits and risks. Factors contributing to the decision-making process include the child's disease activity (because therapy should be withheld for at least 4 weeks), risk of vaccine-associated adverse events, potential for exposure to wild-type varicella, and possible complications of chickenpox while on immunosuppressive therapy if not immunized. If the medical care provider decides to immunize a child while receiving immunosuppressive therapy, consulting an infectious disease specialist would be helpful.

If a child on immunosuppressive therapy is not immune to varicella and has significant exposure to active varicella, varicella zoster immune globulin (VariZIG, Cangene Corporation) or acyclovir should be given. Varicella zoster immune globulin should be administered as soon as possible and within 96 hours of exposure. If the exposure has exceeded 96 hours, or if varicella zoster immune globulin is not available, some recommend giving acyclovir within 7 to 10 days of exposure.³² If an

immunocompromised child acquires wild-type varicella infection, intravenous acyclovir should be administered.³²

A case series consisting of 6 children with IBD who were administered varicella vaccine while on treatment with either 6-MP or infliximab found that an immune response developed in 5 of the 6 children. All 6 children tolerated the vaccine without adverse events.⁶⁰ Therefore, in the situation in which there is a high incidence of wild-type varicella, it is important to have a discussion with the patient's family about weighing the benefits of protection from wild-type varicella against the risks of vaccine-associated adverse events.

A retrospective study conducted by Ansari and colleagues evaluated the vaccination history and varicella titers of 163 pediatric patients with IBD.⁶¹ The investigators found that two-thirds of patients had either a history of chickenpox or received at least 1 vaccine dose. At the diagnosis of IBD, 77% of patients had a documented positive titer, 11% had a negative titer, and the remaining 12% did not have an antibody level available. Ten patients with a negative or unknown titer were immunized prior to starting immunosuppressive therapy. Postvaccination antibody levels were obtained in 8 of these 10 patients, and all 8 responded.

Household Contacts of Patients with Inflammatory Bowel Disease

It is important that household members of children with IBD who are receiving immunosuppressive therapy are up-to-date with routine immunizations to minimize infections in patients. It is recommended that household contacts receive the necessary inactivated vaccinations, including the intramuscular influenza vaccine (not intranasal influenza vaccine, which is a live vaccine). Household members also can receive the MMR vaccine without being concerned of harm or viral spread to the patient.^{31,62} Household members can receive the varicella vaccine; however, if a vaccine-related rash develops in contacts, they should avoid close contact with the pediatric patient if the patient has no immunity to varicella. In this situation, varicella zoster immune globulin is not indicated because secondary infection from the vaccine is expected to be mild.^{31,63}

Summary

Although advances in medicine have produced medications to help control IBD and improve quality of life, patients are at an increased risk for infection due to these medications. Therefore, it is important to minimize infections and their associated complications by simply vaccinating patients to avoid the morbidity and mortality of a vaccine-preventable infection.

Unfortunately, the immunization rate is low in young patients with IBD, partly due to the lack of appropriate counseling and attention on the part of the gastroenterologist and also concern about vaccine-associated complications or low efficacy on the part of the gastroenterologist and patient. As gastroenterologists, we sometimes play the role of PCPs because patients have regular contact/visits with us and turn to us first for medical advice even if the topic is not directly related to our field. Therefore, we have the potential to play a critical role in helping patients remain up-to-date with immunizations and should be more proactive in helping them stay healthy with this simple yet valuable tool.

Current guidelines recommend that patients with IBD follow the same routine immunization schedule as healthy children but should avoid live vaccines if receiving immunosuppressive therapy. Children can be given inactivated vaccines regardless of immunosuppression status.³⁰ It is preferable for physicians to check the immunization status of their patients at the time of diagnosis and immunize patients with any necessary vaccines prior to starting immunosuppressive therapy, especially in the case of live vaccines. Obtaining antibody levels (to hepatitis A virus, HBV, MMR, and varicella) may be helpful in cases in which the history of vaccination or wild-type infection is unclear or to confirm that titers are at an adequate level. However, vaccination does not necessarily translate into adequate immunization. The data in both adult and pediatric IBD literature reveal that inactivated vaccines are generally safe and effective and do not exacerbate IBD. However, immunogenicity may be lower in patients on immunosuppressive therapy, especially TNF inhibitors. Despite this, having a suboptimal immunogenicity is still better than a complete lack of titers because having at least some immunogenicity offers a degree of protection.

Future studies are much needed to evaluate the safety and immunogenicity of individual vaccines using different doses and schedules in patients with IBD receiving various therapies, especially immunosuppressive medications. It is also important to evaluate the sustainability of titers, as antibody levels may wane over time, leaving patients and medical care providers falsely assuming that patients are adequately protected when they are actually susceptible.

Dr Lu has received research support from Merck & Co, Inc. Dr Bousvaros has received research support from Merck & Co, Inc and Prometheus Laboratories and has received consulting fees from Takeda, Cubist, Dyax, Millennium, and Nutricia.

The authors thank the Wolfman, MacInnes, Rasmussen, Ward, and Clark families for their financial support to the IBD center at Boston Children's Hospital to fund research and writing of manuscripts.

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