Vaccination Issues in Patients with Inflammatory Bowel Disease Receiving Immunosuppression

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Abstract: Treatment regimens for Crohn's disease and ulcerative colitis increase susceptibility to infections, many of which can be prevented by vaccinations. Increased awareness concerning vaccine-preventable diseases has led to several studies investigating the immunologic responses to vaccines in immunosuppressed patients with inflammatory bowel disease. This review provides an overview of the evidence-based rationale for currently accepted recommendations regarding the use of both inactivated and live vaccines in this unique population.

Treatment regimens for patients with inflammatory bowel disease (IBD) have evolved dramatically over the past 10 years and continue to change with the advent of new medications. Treatment for IBD generally involves induction therapy followed by maintenance therapy, with the primary goal of achieving sustained clinical remission. Maintenance therapy for IBD, especially Crohn's disease (CD), usually requires immunosuppressive therapy, including immunomodulators (eg, 6-mercaptopurine, azathioprine, or methotrexate), biologic therapy (eg, infliximab [Remicade, Janssen Biotech], adalimumab [Humira, Abbott], certolizumab pegol [Cimzia, UCB], or natalizumab [Tysabri, Biogen Idec]), or the combination of immunomodulators and biologic agents.

Clinicians have become increasingly aware of the risk of infection associated with these therapies, including disseminated zoster, pneumococcal sepsis, and acute hepatitis B virus infection in the setting of immunosuppressive therapy.[1-10] Preventative vaccinations are available to protect against several of these infections. Numerous papers recommend routine vaccination; in fact, the Advisory Committee on Immunization Practices (ACIP) has set forth guidelines on vaccinations in patients with altered immunocompetence, including those on immunosuppression.[11,12] Furthermore, guidelines based on expert opinion were published in 2004 by Sands and colleagues.[13] In general, adults with IBD should be

Table 1. Available Vaccines and Associated Recommendations in Inflammatory Bowel Disease Patients on Immunosuppression

Vaccines recommended per routine guidelines, regardless of immunosuppression
Inactivated influenza (trivalent inactivated vaccine)
Tetanus (as part of Td, Tdap, or DTaP)
HPV (quadrivalent vaccine against types 6, 11, 16, and 18)
Meningococcus (MCV4 or MPSV-4)
Hepatitis A (single-antigen vaccine or as part of hepatitis A and B combination vaccine)
Hepatitis B vaccine
Vaccines recommended per routine guidelines, ideally before initiation of immunosuppression
Pneumococcus (PCV13 or PPSV23)
Pertussis (as part of Tdap or DTaP)
Contraindicated vaccines
Live, attenuated influenza (intranasal vaccine)
Varicella zoster vaccine
Herpes zoster (live zoster vaccine)
Yellow fever vaccine
Measles-mumps-rubella vaccine
Typhoid live oral vaccine
Smallpox vaccine
Tuberculosis Bacillus Calmette-Guérin vaccine
Polio live oral vaccine
Anthrax vaccine

DTaP=pediatric combination vaccination against diphtheria, tetanus, and acellular pertussis; HPV=human papillomavirus; MCV4=quadrivalent meningococcal vaccine; MPSV-4=quadrivalent meningococcal polysaccharide vaccine; PCV13=13-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine; Td=combined tetanus and diptheria toxoid; Tdap=adult combination vaccination against tetanus, diptheria, and acellular pertussis.

advised to adhere to standard recommended immunization schedules, but they should avoid live vaccines while on immunosuppressive therapy (Table 1).[13,14]

As awareness increases regarding the risk of vaccine-preventable infections in IBD patients who are on immunosuppressive therapy, an increasing number of studies have sought to evaluate the safety profiles and immunologic responses to various vaccines in this special population. The aim of this article is to review current evidence and provide a general approach to vaccination of patients with IBD who are on immunosuppressive medication.

Inactivated Vaccines

Influenza

Influenza infection occurs as an annual epidemic. Due to frequent antigenic drift, a new vaccine is produced annually. In 2009, the World Health Organization declared a new strain of influenza A (H1N1) to be a pandemic strain. Thus, as of the 2010 season, the annual influenza vaccine also contains the H1N1 component. Both a trivalent inactivated vaccine (TIV) and an intranasal, live, attenuated vaccine are available for prevention of influenza.

Morbidity and mortality from influenza infection are increased in individuals who are immunocompromised. In the United States, approximately 36,000 deaths were associated with influenza annually between 1990 and 1999.[15] Although all adults and children over the age of 6 months should receive an influenza vaccination, current vaccination guidelines specifically target individuals who are immunosuppressed due to medications.[16] Currently, no efficacy studies have evaluated clinical protection from influenza after administration of the vaccine in the IBD population. However, several studies in patients with IBD and other immune-mediated conditions have used vaccine response titers as a surrogate for efficacy.[17]

In a prospective cohort study, deBruyn and colleagues compared immunogenicity of the TIV in 61 children with IBD versus 55 healthy sibling controls.[18] Response was defined as a 4-fold or greater increase between preimmunization and postimmunization antibody titers against the 3 antigens in the TIV. Serologic protection was defined as a postimmunization titer greater than or equal to 1:40. Compared to controls, there was no difference in the proportion of children with IBD who achieved an immunogenic response or serologic protection against the 2 influenza A components of the vaccine (A/Brisbane/10/2007 and A/Brisbane/59/2007). Moreover, there were no differences in immunogenic response between the immunosuppressed and nonimmunosuppressed IBD groups. However, a significantly lower proportion of the IBD group achieved an immunogenic response toward the influenza B component of the vaccine (B/Florida/4/2006; P=.002). In addition, impaired serologic protection against the influenza B component was demonstrated among immunosuppressed children with IBD compared to nonimmunosuppressed children (P=.02).

Another study also demonstrated significantly lower serologic protection against strain B in children with IBD who were receiving biologic therapy compared to historical controls (P=.03).[19] As with the previous study, the proportion of patients who were seroprotected against the 2 influenza A components was similar between children with IBD and historical controls.

Cullen and coauthors conducted an observational, prospective study evaluating the serologic response to the H1N1 influenza vaccine in a cohort of 105 patients with IBD.[20] Prevaccination and postvaccination hemagglutinin inhibition titers and geometric mean titers (GMTs) were measured. The overall rate of seroprotection was 50%. Seroconversion was significantly blunted in patients who were on combined immunosuppression compared to those who were not on immunosuppression. Furthermore, patients on combined immunosuppression did not respond as well compared to those on monotherapy immunosuppression. The authors concluded that patients with IBD, particularly those on immunosuppressive therapy, have a low immunogenic response to the H1N1 vaccine.

There are limited data assessing the safety of the influenza vaccine in patients with IBD, particularly those on immunosuppressive medications. One multicenter, prospective, cohort study evaluated local and systemic symptoms 4 weeks after vaccination against influenza H1N1 in 575 patients with IBD who were receiving immunosuppressive therapy.[21] The vaccine was generally well tolerated, with 34.6% and 15.5% of patients reporting local and systemic symptoms, respectively; all symptoms disappeared within 72 hours. Fewer than 5% of patients experienced a flare of disease, defined as an increase of 3 or more points in a clinical activity score. The authors concluded that the H1N1 vaccine is well tolerated by patients with IBD, regardless of therapy, and that the risk of flare appears to be low.

In summary, the TIV appears to be safe and well tolerated in patients with IBD, and it induces acceptable rates of seroprotection against strain A, regardless of immunosuppression status. However, immunogenic response may be impaired toward the B strain and H1N1 components of the vaccine. Given this evidence, we recommend administration of TIV to all adults and children with IBD, regardless of immunosuppressive status. However, the live, attenuated influenza vaccine should not be administered to those receiving immunosuppressive therapy or their household contacts.

Tetanus

Tetanus is a rare neuromuscular condition caused by the neurotoxin produced by *Clostridium tetani*. It is often contracted through wound contamination. Current guidelines recommend routine booster vaccination with Td (combined tetanus and diphtheria toxoid) every 10 years.[22] One study revealed that postvaccination antitetanus antibody levels were equally increased in 10 patients with clinically inactive CD (these patients were off all medications) compared to 12 healthy controls.[23] The authors concluded that immunization resulted in "normal antibody synthesis," but they did not comment on whether seroprotective levels were achieved. In another study, Dotan and coworkers evaluated the serologic response to Td in 37 patients with IBD who initiated thiopurine therapy at the time of enrollment.[24] They found that a majority of patients (73%) achieved seroconversion. However, results were not compared to healthy controls.

Another study evaluated booster response rates and GMTs following administration of tetanus boosters in 59 IBD patients who were categorized by their level of immunosuppression (ie, no therapy, immunomodulator monotherapy, biologic monotherapy, or combined immunomodulator and biologic therapy). Serum antibody levels and GMTs were measured at baseline and approximately 4 weeks after vaccination. All patients with IBD who were not on immunosuppression achieved protective tetanus titers, in contrast to only 78% of those on combined therapy (P=.01).[25]

Although data are limited with regard to the immunogenic response of the tetanus vaccine in IBD patients on immunosuppression, current evidence suggests that good responses can be achieved in this population of patients. All patients should receive the Td booster every 10 years per current guidelines, regardless of immunosuppression status.

Pertussis

Bordetella pertussis causes a highly contagious upper respiratory infection known as whooping cough. Rare but serious complications can include pneumonia, encephalopathy, and seizures. Most healthy adults and older children suffer a mild, subacute course of chronic cough; however, children younger than 2 years (ie, those too young for vaccination) are vulnerable to serious, often fatal, complications.

In 2010, California experienced its worst pertussis epidemic in over 50 years, with over 9,000 cases and 10 infant deaths reported.[26] A public health campaign targeted all adults for booster vaccination with Tdap (a combination vaccine against tetanus, diphtheria, and acellular pertussis). Current guidelines recommend giving a booster vaccination with Tdap at age 11–12 years and replacing 1 scheduled Td booster with Tdap after the age of 18 years.[22]

Only 1 study has assessed the safety and immunogenicity of the pertussis booster in patients with IBD.[25] Fifty-nine patients with IBD stratified by therapeutic regimen were vaccinated with Tdap. Serum antibody titers against pertussis toxoid (PT) and pertussis filamentous hemagglutinin (FHA) were measured at baseline and 4 weeks after vaccination. Both antigens showed no differences in response rates between patients off medications and those on biologic monotherapy. However, responses to PT were lower in patients on immunomodulator monotherapy, and postvaccination protective titers to FHA were lowest in those on combined immunomodulator and biologic therapy (P=.01). No adverse reactions

were noted following vaccination. In summary, patients with IBD should receive the Tdap vaccine per current guideline schedules, ideally before initiation of immunomodulator therapy.

Pneumococcal Infection

Per the ACIP, an estimated 3,000 cases of meningitis and 500,000 cases of pneumonia are attributed to *Streptococcus pneumoniae* each year in the United States.[27-30] Furthermore, pneumococcal infection causes an estimated 40,000 deaths annually in the United States.[27,28,31] Pneumoccoccal infection therefore accounts for more deaths than any other vaccine-preventable bacterial disease.[32]

Risk factors for pneumococcal infection include age greater than 64 years, chronic illness, and chronic immunosuppressive therapy—all of which can apply to patients with IBD. Currently available vaccines include the 23-valent polysaccharide vaccine (PPSV23) and the 13-valent conjugate vaccine that represent common and/or virulent serotypes that cause invasive pneumococcal infections among children and adults in the United States.[33-35] Current guidelines recommend vaccinating patients with chronic conditions and those on medications that increase the risk of infection.[36] Due to potential antibody decline, revaccination 5 years after the initial vaccination is recommended for immunocompromised patients, those with functional asplenia, and those with chronic medical conditions (ie, patients with IBD).[36]

We assessed the response to PPSV23 in 21 IBD patients on combined immunomodulator and biologic therapy and compared it to the response of 25 nonimmunosuppressed patients.[37] Patients on combined therapy had a significantly lower response rate compared to nonimmunosuppressed patients. Serologic response rates were similar between nonimmunosuppressed patients and 19 healthy controls. GMTs were also lower for 4 out of 5 serotypes when compared to nonimmunosuppressed patients and for all serotypes when compared to healthy controls. These results suggest that the combined use of immunomodulators and biologic therapy impairs patients' immunogenic response to the pneumococcal vaccine. Patients on monotherapy were not included in this study; thus, it is difficult to differentiate the impact of immunomodulators versus that of biologic therapy.

In a prospective cohort study, Dotan and coauthors evaluated the effects of thiopurines on immune response in 28 IBD patients vaccinated with PPSV23.[24] All patients initiated thiopurine therapy at or near the time of vaccination. Antibody levels against 14 pneumococcal serotypes were measured at baseline and 3 weeks postvaccination. Seventy-five percent of patients demonstrated a serologic response to at least 4 serotypes. The vaccine was well tolerated, without any flares during the entire follow-up period. The authors concluded that thiopurines, at doses commonly used in IBD patients, do not diminish immune response to the pneumococcal vaccine. However, healthy controls did not participate in this study. Another study evaluated antibody responses to the pneumococcal vaccine in 96 patients with IBD.[38] This study demonstrated a significantly blunted response in patients receiving a biologic agent alone or in combination with azathioprine compared to patients receiving only 5-aminosalicylic acid.

Available data for pneumococcal vaccination in IBD patients suggest that combination therapy with an immunomodulator and a biologic agent may significantly blunt vaccine responses.[17] Therefore, while all adults who are immunosuppressed can safely receive the vaccine, it should ideally be administered prior to initiation of immunosuppression.

Human Papillomavirus

Multiple sources have demonstrated the causative link between human papillomavirus (HPV) and genital warts, cervical cancer, and other anogenital cancers.[39-46] High-risk types of HPV (eg, types 16 and 18) are associated with 70% of all cervical and anogenital cancers.[40-42] In 2006, the ACIP recommended the use of a quadrivalent vaccine targeted against HPV types 6, 11, 16, and 18 (HPV4; Gardasil, Merck) in females aged 9–26 years.[47] Recently, the ACIP expanded its guidelines and recommendations to include males aged 9–26 years.[48]

Only 1 study has assessed the immunologic response to the HPV4 vaccine in patients with IBD. In this study, 30 girls and women with IBD who were on immunomodulator or biologic therapy received the vaccine. More than 90% of the patients became seropositive to each of the 4 serotypes, and postvaccination GMTs were comparable to those of historical controls.[49] The vaccine was well tolerated, without any incidence of flares. The researchers concluded that the HPV4 vaccine is safe and immunogenic in most women with IBD who are on immunosuppressive therapy.

A prospective cohort study aimed to assess the incidence of cutaneous HPV lesions in 230 IBD patients on and off azathioprine therapy.[50] Through comprehensive skin examinations and self-report questionnaires covering a period of 207 patient-years, the authors determined that 17.2% of patients on azathioprine had an increased number of skin warts. In comparison, only 3.3% of patients off azathioprine had an increased number of skin warts (P=.006). However, it is unclear whether viral cultures were performed to confirm the presence of HPV in the reported skin warts. Nonetheless, the study authors recommended temporary reduction or discontinuation of azathioprine in those with disabling warts. The HPV vaccine was not approved for use at the time of this study.

Bhatia and colleagues demonstrated that women with IBD have a higher risk of abnormal Pap smears, and 2 other retrospective studies also reported similar results.[51-53] However, other studies have not found an association between IBD and cervical dysplasia unless patients are receiving immunosuppressive therapy or they smoke.[54,55]

Based on the increased risk of HPV-associated dysplasia in women with IBD and the availability of the inactivated HPV4 vaccine, we recommend HPV vaccination of all women and men (particularly men who have sex with men) with IBD up to the age of 26 years, per the ACIP guidelines.[47]

Meningococcal Infection

The ACIP recommends vaccination against *Neisseria meningitides* in all persons aged 11–12 years, with a follow-up booster at age 16 years. Those with terminal complement deficiencies and asplenia should receive a 2-dose primary series of vaccines separated by 2 months with a repeat booster every 5 years thereafter. Other at-risk individuals—such as college freshmen, military recruits, microbiologists who are routinely exposed to the bacterium, and individuals who travel or reside in areas where the bacterium is endemic—should receive a 1-time vaccination, regardless of age.[56] No studies have evaluated the immunogenic profile of the meningococcal vaccine in the IBD population. However, as the vaccine is noninfectious, it is safe and recommended for at-risk individuals with IBD, regardless of their immunosuppression status.

Hepatitis A Virus

Vaccination against hepatitis A virus is currently recommended for all children and at-risk adults.[57] Risk factors for hepatitis A virus infection among individuals with IBD are the same as for those without IBD, including travel to endemic areas, men who have sex with men, and the use of illicit drugs. Vaccination is offered through a single-antigen vaccine or in combination with the hepatitis B antigen. All available vaccines are inactivated.

One prospective study assessed the immunogenic response to the single-antigen vaccine in 66 children and adolescents with IBD.[58] Seroconversion rates were similar among patients with IBD compared to healthy controls. Immunosuppressive therapy did not affect seroconversion after patients had completed the entire vaccination course. No adverse effects were reported. Thus, the hepatitis A vaccine is a noninfectious vaccine that is safe and well tolerated. Patients with IBD who are at risk for hepatitis A virus infection should be vaccinated.

Hepatitis B Virus

Fulminant hepatitis B in IBD patients on immunosuppressive therapy has been reported in the literature, with some cases resulting in death.[59-61] Vaccination is available and is recommended as a series of 3 injections given to children or unvaccinated, at-risk adults. One study of 129 patients with IBD demonstrated inadequate antibody responses in more than half of the study population.[62] Thus, prevaccination and postvaccination serology is recommended to assess for response in all IBD patients.

Patients with persistent seronegativity following the initial series should be revaccinated using the combined hepatitis A and B vaccine at twice the standard dose. The effectiveness of increased-dose combined vaccination was demonstrated by Nyström and coworkers.[63] Forty-four patients who failed to mount an appropriate response after vaccination with a standard hepatitis B vaccination schedule were revaccinated with double-dose combined hepatitis A and B vaccine. Ninety-five percent of previous nonresponders demonstrated an adequate rise in hepatitis B surface antibody titers.

Patients with IBD, particularly those on immunosuppression, are at risk for the development of viral hepatitis and should be vaccinated per current guidelines. For those patients with an inadequate response, revaccination with double-dose hepatitis A and B bivalent vaccine is recommended.

Live Vaccines

Varicella and Herpes Zoster

Varicella zoster virus (VZV) commonly causes chickenpox in children, but it may also be seen in adults, in whom it generally has a more severe presentation. Reactivation can occur after a period of latency, resulting in herpes zoster, more commonly referred to as shingles. The most common complication of shingles is postherpetic neuralgia. Other less common complications include meningoencephalitis, cerebellitis, herpes zoster ophthalmicus, and Ramsay Hunt syndrome. The incidence of disseminated disease in immunocompromised adults with VZV has been reported to be approximately 30%.[64] Mortality rates are reported at 25.2 deaths per 100,000 cases among adults 30–49 years of age.[64] In fact, 2 cohort studies reported that the herpes virus infections were the most common immunosuppression-related viral infections in IBD patients.[65,66]

Primary prevention with the varicella vaccine is routinely recommended for immunocompetent children aged 12–15 months, with a booster at 4–6 years of age and for those 13 years or older without evidence of varicella immunity.[67] The live zoster vaccine (Zostavax, Merck) is recommended as a 1-time vaccination in individuals aged 60 years or older. In 2011, the US Food and Drug Administration approved the zoster vaccine for individuals aged 50 years and older. However, due to supply shortages, the vaccine is recommended for those aged 60 years and older. On this basis, it is our opinion that the zoster vaccine can be offered to IBD

patients aged 50 years and older, in light of their increased risk of infection and associated morbidity.

Both the varicella and zoster vaccines are live, attenuated vaccines, which poses a dilemma when they are indicated in patients on immunosuppressive medications, as these individuals should generally avoid live vaccines.[6,13,14,17,68-71] One large, nested, case-control study demonstrated that a higher incidence of herpes zoster was associated with a prescription for corticosteroids (odds ratio [OR], 1.5; 95% confidence interval [CI], 1.1–2.2) and immunomodulators (OR, 3.1; 95% CI, 1.7–5.6).[9] A review of the literature identified 20 reported cases of primary VZV infection and 32 cases of herpes zoster in the IBD population.[72] All patients were on some form of immunosuppression, with a large number of patients on combined immunomodulator and biologic therapy. Of the 20 cases of primary VZV infection, 5 resulted in death, all of which occurred in patients who were on immunosuppression at the time of diagnosis.

It is clear that immunosuppression increases the risk of VZV infection and herpes zoster in patients with IBD and that this infection carries significant morbidity. However, there is a paucity of studies aimed at understanding the benefits and risks of administering these vaccines in this special population. Lu and Bousvaros described a series of 6 children with IBD who received the varicella vaccine booster while on immunosuppressive medications.[73] Five of these children met the criteria for seropositivity; none developed complications or primary infections. The authors concluded that the benefits of immunization may outweigh the risks among at-risk, vaccine-naïve children on immunosuppression.

Clinical consensus acknowledges the inherent risk of administering a live vaccine to patients with immunodeficiency due to medications. However, the current ACIP recommendations report that patients receiving short-term (ie, <14 days) or low-to-moderate–dose (ie, <20 mg/day) corticosteroid therapy are not considered to be sufficiently immunosuppressed to justify avoiding the live zoster vaccine. Their position also applies to patients on low-dose methotrexate (ie, ≤0.4 mg/kg/week), azathioprine (≤3.0 mg/kg/day), or 6-mercaptopurine (≤1.5 mg/kg/day).[69] This recommendation represents the opinion of the guideline authors, although it is unclear whether this opinion extends to other live vaccines, including the varicella vaccine. The benefits of vaccine administration should be weighed against the risks of infection on an individual basis. Expert consensus recommends vaccinating IBD patients who do not have a reliable history of disease or vaccination and who have not initiated therapy with immunosuppressive medications.[13] Serologic testing is recommended to help guide vaccination practices in those without clear chickenpox or vaccination history. If possible, patients with recent varicella exposure (passive exposure or vaccination) who plan on starting immunosuppressive therapy should wait 4 weeks before initiating therapy.[68]

Yellow Fever

Yellow fever is a viral disease primarily transmitted by mosquitoes in endemic areas. Yellow fever vaccine is a live, attenuated vaccine indicated in individuals traveling to these areas. Serious adverse effects have been reported in association with the vaccine, such as encephalitis (known as neurotropic disease) and multiorgan system failure (known as viscerotropic disease), with some cases occurring in immunocompromised individuals. Per ACIP guidelines, vaccination is contraindicated in patients with altered immune status due to immunosuppressive therapy, excluding those on low-dose steroid therapy (ie, 20 mg prednisone or equivalent per day) or short-term steroid therapy (ie, <2 weeks).[74] If travel to endemic areas is absolutely necessary, patients should be strongly advised of the risks and educated about the prevention of mosquito bites. Additionally, clinicians should give these patients a vaccination waiver.[74]

Measles, Mumps, and Rubella

The measles-mumps-rubella (MMR) vaccine is recommended for several groups: children; unvaccinated adults born after 1957; and certain at-risk, unvaccinated populations.[75] The vaccine is only available as a live, attenuated vaccine. As such, it is generally contraindicated in patients with IBD who are on immunosuppressive therapy. Susceptible close contacts of these patients should be vaccinated. Although there are no studies investigating use of this vaccine in nonimmunosuppressed patients with IBD, whether to vaccinate patients prior to initiating therapy can be considered on a case-by-case basis.[76]

Considerations Regarding Other Live Vaccines

As a corollary to the general rule that live vaccines should be avoided among patients who are immunosuppressed, additional considerations apply with respect to household contacts. These risks are largely theoretical; however, certain precautions are advised. Household contacts of immunosuppressed individuals are encouraged not to receive the live intransasal influenza vaccination, due to the risk of transmission; instead, they should receive the inactivated injectable vaccine. While rotovirus vaccination is not contraindicated among immunosuppressed household contacts, stringent handwashing should be practiced after changing the diaper of a recently vaccinated infant. For household recipients of the varicella vaccine, contact precautions should be observed if a rash develops following vaccine administration; these precautions should be continued until resolution of the rash. The MMR vaccine is not contraindicated in this setting. Finally, infants

born to mothers who received anti–tumor necrosis factor therapy during the third trimester of pregnancy should not receive live virus vaccines during the first 6 months of life, as evidenced by a fatal case of disseminated Bacillus Calmette-Guérin (BCG) after vaccination of an infant exposed to infliximab in utero.[77]

Travel Considerations

Patients travelling to areas where vaccine-preventable infections are endemic should be advised to seek appropriate counseling from a travel medicine specialist, and they should receive appropriate prophylaxis in anticipation of potential exposure to endemic infections. Inactivated vaccines can be safely administered to patients on immunosuppression. These vaccines include those against hepatitis A, Japanese encephalitis, and rabies, as well as the inactivated form of the typhoid and polio vaccines. However, special considerations may be warranted for live vaccines (eg, yellow fever and BCG) in the setting of immunosuppression, as described above, with appropriate counseling by a travel medicine specialist when vaccines are contraindicated and the risk of endemic infection is high.[78]

Summary

Many therapeutic regimens for IBD include immunosuppressive therapy or combinations thereof. Because of the increasing use of these medications, risks of infection have increased. Many of these infections can be prevented by vaccinations.

First, a detailed history should be obtained during the initial consultation. This history should include a thorough medical and travel history to identify factors that may increase a patient's risk of infection, as well as a vaccination history. Serologic testing to assess baseline immunity against varicella is recommended to allow for timely administration of this live vaccine among those without a clear history of prior varicella infection or vaccination.

Patients with IBD who are on immunosuppression have shown good response rates against most influenza strains and should receive the TIV annually. Pneumococcal vaccination is recommended as a single-dose vaccine between ages 19 years and 64 years, with a booster at age 65 years in patients with chronic inflammatory conditions such as IBD and booster revaccination after 5 years. As immunogenic responses may be blunted in those on immunosuppression, vaccination should ideally be given before initiation of therapy. Tetanus and pertussis vaccinations are safe and should be given per routine guidelines. However, patients on immunomodulators, either as monotherapy or part of combined therapy with biologic agents, may not respond as well to vaccination; thus, vaccination should ideally be administered before initiating immunomodulator therapy. High-risk HPV serotypes correlate with cervical, penile, and anal cancer risk. Women and men up to the age of 26 years with IBD can be offered the HPV vaccine.

The hepatitis A vaccine is safe and well tolerated, and it should be offered to all at-risk patients. Accelerated viral replication and fulminant failure can occur in those with chronic hepatitis B infection who are on immunosuppression. Patients should undergo vaccination, with postvaccination confirmation of serologic response. We recommend that nonresponders receive double-dose bivalent hepatitis A and B vaccination. Other inactivated vaccinations should be administered based on recommended schedules. Finally, live vaccines should generally be avoided among patients who are immunosuppressed, with the caveats delineated above in cases where the benefits of vaccination outweigh the risks and with appropriate input from infectious disease or travel medicine specialists.

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