Crohn's Disease: The Subsequent Visit

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Abstract: The diagnosis and subsequent management of Crohn's disease are challenging for both the patient and the gastroenterologist. After the initial assessment, subsequent visits should assess the patient's readiness to begin therapy, monitor progress if therapy has been initiated, assess for complications of the disease or therapy, and ensure that all appropriate health maintenance measures are current. This article is intended to be a companion to our earlier paper "Crohn's Disease: The First Visit," which was published in *Gastroenterology & Hepatology* in March 2011. This article will offer a methodologic and sequential approach to subsequent office visits, as well as provide a checklist for the assessment of Crohn's disease.

Subsequent office visits and initiation of therapy for Crohn's disease often prove as challenging to gastroenterologists and patients as the initial evaluation and diagnostic process. Many primary care providers do not feel comfortable providing care for patients with inflammatory bowel disease (IBD).[1] This hesitance poses a particular problem in that either the gastroenterologist must assume a primary care role or treatment must be delayed until the patient establishes a relationship with another primary care provider who feels comfortable managing his or her IBD therapy. To ensure that gastroenterologists deliver the highest quality of care, we must clarify the limits of our responsibility with the patient while confirming that all appropriate health maintenance indices, such as vaccinations, are up-to-date. It falls to the gastroenterologist to discuss these issues with the primary care provider and to make certain that the patient is current on all general health maintenance issues, as the mainstay of treatment for IBD utilizes agents that affect the immune system (eg, steroids, antimetabolites, and biologic agents).[2] This paper will offer recommendations to optimize subsequent office visits, provide a checklist to improve efficacy, and give guidance regarding the health maintenance needs of Crohn's disease patients who are receiving immunomodulator and/or biologic therapies.

Step One: Clinical Status Assessment

After the diagnosis of Crohn's disease is made, the initial office visit is the time to optimize care by confirming the diagnosis, assessing disease severity, and preparing for the initiation of therapy or assessing the need to alter therapy.[2] Subsequent office visits should

determine if the goals of therapy, which are to induce and maintain remission and to improve the patient's quality of life, are being attained.

The initial step to achieving these treatment goals is to assess the patient's status. Such an assessment should include gathering information about important historical factors, such as weight loss, complications of disease or treatment, extraintestinal manifestations of IBD, and symptoms including diarrhea and pain. Inquiries should be made about hospitalizations, surgeries, work history, and quality-of-life issues.

Quality of life is an important outcome to assess in all patients. Several objective indices have been developed to evaluate disease activity, severity, and response to treatment. These indices include the Crohn's Disease Activity Index (CDAI), the Inflammatory Bowel Disease Questionnaire, and the Harvey-Bradshaw Index (HBI). The CDAI and HBI have both been used in studies to define response and remission.[2-6] Both indices include an evaluation of specific complications and extraintestinal manifestations of IBD, such as arthralgias, skin issues, and perianal disease. The CDAI addresses the percent deviation from standard weight, which should be noted at all follow-up visits, whereas a strength of the HBI is its simplicity and reproducibility. However, the use of multiple indices may prove tedious. If clinicians use indices, we advocate the use of 1 index for all patients at all visits.

Step Two: Vaccinations

Patients with chronic diseases, including IBD, are at an increased risk for infections, particularly when they are receiving immunomodulator therapy; however, some of these infections are preventable by vaccination.[7-10] The current definition of "immunosuppressed" includes treatment with glucocorticoids (prednisone >20 mg/day for 14 days), 6-mercaptopurine or azathioprine, methotrexate, or tumor necrosis factor α (TNFα) inhibitors, either currently or within the past 3 months. Many, if not most, Crohn's disease patients fall under this category at some time during the course of their illness. A main tenet of limiting infectious complications is patient compliance with appropriate vaccination schedules.

Many gastroenterologists feel that the onus of vaccination falls on the primary care provider.[9] Gastroenterologists often fail to gather an adequate vaccination history and lack knowledge of appropriate immunization guidelines. Furthermore, there is a pervasive fear that Crohn's disease patients will not mount an adequate response to vaccination or that vaccinations will increase disease activity.[11-13] Fortunately, several studies have concluded that IBD patients can mount an appropriate response to vaccination and that the disease course is not altered by vaccination.[14,15]

Table 1. Recommended Immunization Schedule

Vaccine	Dosing schedule
Td/Tdap	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years. For patients >65 years of age, administer Td booster every 10 years.
HPV	3 doses in females 9–26 years of age and in males 11–26 years of age
Varicella	2 doses
Herpes zoster	1 dose in patients ≥60 years of age
MMR	1 or 2 doses in patients 19–49 years of age. 1 dose after 50 years of age if a risk factor (medical, occupational, or lifestyle) is present.
Influenza	1 dose annually
Pneumococcal (polysaccharide)	1 or 2 doses in patients 19–49 years of age if a risk factor (medical, occupational, or lifestyle) is present. 1 dose in all patients >65 years of age.
Hepatitis A virus	2 doses (6 months apart) in patients with a risk factor (medical, occupational, or lifestyle)
Hepatitis B virus	3 doses (at 0, 1, and 6 months) in patients with a risk factor (medical, occupational, or lifestyle)
Meningococcal	1 or more doses in patients with a risk factor (medical, occupational, or lifestyle)

HPV=human papillomavirus; MMR=measles, mumps, and rubella; Td=tetanus and diphtheria; Tdap=tetanus, diphtheria, and pertussis.

Modified from Advisory Committee on Immunization Practices.[15]

Table 1 includes general considerations regarding immunization of IBD patients, which vaccines to administer, and issues regarding the immunization schedule.[14,15] Live vaccines are contraindicated for patients who are receiving steroids, immunomodulators, or biologic therapy. However, according to current recommendations from the Centers for Disease Control and Prevention (CDC), patients on methotrexate, azathioprine, and/or low-dose steroids may receive the herpes zoster vaccine.[14] Patients on anti-TNFα agents should not receive live vaccines. Current recommendations for inactivated vaccines are listed in Table 2. Additionally, all age-appropriate vaccinations are recommended for close contacts and household members of individuals receiving steroids, immunomodulators, or biologic agents. If a household member or close contact develops a rash after receiving the varicella or herpes zoster vaccine, personal contact with the immunosuppressed individual should be avoided.[14]

The human papillomavirus (HPV) vaccine is an inactive vaccine and should be administered to all immu-

Table 2. Inactivated Vaccine Recommendations

Vaccine	Check titer before vaccination?	Action
Td/Tdap	No	Administer the vaccine if it has not been given over the past 10 years, or give Tdap if Td was administered ≥2 years ago.
HPV	No	3 doses at 0, 2, and 6 months in females 9–26 years of age and in males 11–26 years of age
Influenza	No	Administer annually. Use trivalent inactivated influenza vaccine. Avoid live attenuated influenza vaccine.
Pneumococcal	No	Vaccinate if no vaccine has been given previously. 1-time revaccination after 5 years if the patient is immunosuppressed.
Hepatitis A virus	Yes	2 doses at 0 and 6–12 months or 0 and 6–18 months. Booster given >10 years.
Hepatitis B virus	Yes	3 doses at 1, 1–2, and 4–6 months. Check postvaccination titers 1 month after finishing last dose. If there is no response, revaccinate with a double dose.
Combination hepatitis A/B virus	Yes	May be given instead of individual hepatitis A virus vaccine and hepatitis B virus vaccine, particularly in individuals who do not respond to hepatitis B virus vaccination.
Meningococcal	No	Vaccinate at-risk patients if no vaccine has been given previously.

HPV=human papillomavirus; Td=tetanus and diphtheria; Tdap=tetanus, diphtheria, and pertussis.

Modified from Wasan SK, et al[14] and Advisory Committee on Immunization Practices.[15]

nosuppressed males and females in accordance with age specifications. The current guidelines recommend that all females aged 9–26 years receive the 3-step vaccination.[15] Guidelines also now recommend that males with IBD aged 11–26 years should receive the HPV vaccine.[2,15] Studies are underway regarding the vaccination of females over the age of 26 years.[14]

Given the potential need for immunosuppressive medications, immunization is advised for hepatitis A virus (HAV); hepatitis B virus; pneumococcus; influenza; HPV; tetanus and diphtheria, and, if needed, pertussis (either the Td or Tdap vaccine); varicella; and, in appropriate circumstances, herpes zoster and meningococcal disease.[2] If a vaccine history was not already obtained at the first visit, it should be obtained at the subsequent visit, and appropriate vaccines should be administered. The gastroenterologist should check that the ordered vaccines and all doses have been completed. Revaccination is advised for influenza (annually), pneumococcus (1-time revaccination after 5 years if the patient is immunosuppressed), Td/Tdap (every 10 years), and HAV (booster after 10 years).

Step Three: General Health Maintenance

Gastroenterologists treating Crohn's disease patients need to be cognizant of all aspects of general health maintenance. Bone health, smoking history, depression, and infectious disease exposures are not only important factors to acknowledge but also play important roles in triggering manifestations of disease and moderating disease activity.

Studies have shown that women with IBD who are receiving immunomodulator therapy have an increased risk of abnormal Papanicolaou (Pap) smears.[16,17] Women with Crohn's disease therefore need to remain current on cervical cancer screenings, and providers must document an up-to-date Pap smear when initiating immunosuppressive therapy.[16,17] Annual gynecologic visits are recommended by the American College of Obstetrics and Gynecology for women who are receiving immunosuppressive drugs.[18]

The myriad of detrimental side effects of cigarette smoking is magnified in patients with Crohn's disease. The prevalence of Crohn's disease is increased among smokers. Additionally, smokers with Crohn's disease have an increased severity of disease, increased frequency of flares, and increased dependence on steroids and/or immunomodulator therapy.[19,20] Smoking cessation has been shown to decrease these risks.[19] Gastroenterologists should discuss smoking cessation with active smokers at every office visit.

Additional aspects for the gastroenterologist to consider under the category of general health maintenance include infectious disease exposures, bone health, and depression. Crohn's disease patients are at an increased risk for developing infections—both opportunistic infec-

Table 3. Crohn's Disease Subsequent Visit Checklist

1. Clinical status assessment
• Indices (CDAI* or HBI; IBDQ) or thorough review of systems
• Weight loss
• Complications (hospitalizations, surgeries, work history, quality of life)
• Extraintestinal manifestations (eye, skin, joint)
2. Vaccinations
• Initial visit vaccinations, with all doses completed (HAV: 2 doses; HBV, HPV: 3 doses**)
• Subsequent vaccinations (including influenza: annual; Td/Tdap: every 10 years; pneumococcal: 1-time revaccination in immunosuppressed patients; HAV: booster after 10 years)
3. General health maintenance
• Gynecologic examination (annual)†
• Assessment of smoking status
• PPD/chest radiograph (annual)**
• Metabolic bone disease screening (including vitamin D levels, bone density testing**)
• Depression screening
4. Surveillance
• Dermatologic examination†
• Ophthalmologic examination (annual)
• Colonic dysplasia screening

*A CDAI calculator is available at http://www.ibdjohn.com/cdai/.
**See text for details. †In patients on immunomodulator therapy.

CDAI=Crohn's Disease Activity Index; HAV=hepatitis A virus; HBI=Harvey-Bradshaw Index; HBV=hepatitis B virus; HPV=human papillomavirus; IBDQ=Inflammatory Bowel Disease Questionnaire; PPD=purified protein derivative; Td/Tdap=tetanus, diphtheria, and pertussis.

tions and reactivation of latent disease—due to their use of immunomodulator therapy. Anti-TNFα biologic therapy carries an increased risk for activation of latent tuberculosis. Prior to initiating biologic therapy, the provider should screen for tuberculosis via the purified protein derivative (PPD) test or a chest radiograph, when appropriate.[21] Although the false-negative rate of the PPD test may be as high as 25% with active disease from anergy and other factors, a better diagnostic method is not currently available.[22] Baseline chest radiographs and tuberculin skin testing can reduce tuberculosis rates by as much as 90%.[21] T-cell–based assays—such as QuantiFERON (Cellestis), T-Spot.TB (Oxford Immunotec), and ELISpot (Mabtech)—can be helpful in patients with prior exposure to tuberculosis or the Bacillus Calmette-Guérin vaccine.[23] The role of annual tuberculosis surveillance remains unclear but should be considered in high-risk patients, such as individuals who travel to endemic areas or who are exposed to tuberculosis as a consequence of their occupation (eg, healthcare workers).

No consensus currently exists regarding hepatitis C virus (HCV) and HIV screening prior to initiating immunomodulator therapy. The prevalence of HCV infection in patients with IBD seems to be similar to its prevalence in the general population, and IBD patients do not appear to be at additional risk for HCV infection.[24] The risk of HCV reactivation due to immunomodulator therapy appears to be low, and there is no consensus to support HCV screening prior to initiation of immunosuppressive therapies. Screening for these infections should be considered on a case-by-case basis in conjunction with current CDC recommendations. Hepatitis B virus (HBV) screening is necessary before initiating biologic therapy. Fatal fulminant HBV has been reported and can be prevented by vaccination or treatment of individuals with chronic HBV disease or carriers.[2]

Patients with IBD, including Crohn's disease patients, are at risk for developing the metabolic bone diseases osteopenia and osteoporosis.[25] Risk factors for these conditions include malabsorption and steroid use. Crohn's disease patients should have their 25-hydroxyvitamin D levels measured, and bone density scans should be obtained in patients who have additional risk factors.[25] Calcium and vitamin D supplementation must be provided for all patients who are receiving steroids, and referral to an endocrinology specialist for consideration of bisphosphonates is recommended for higher-risk individuals and those with abnormal bone density scan results.[25]

Finally, gastroenterologists must be aware that depression is common in individuals with Crohn's disease. Estimates suggest that the risk of depression may be as high as 35%, with various factors, including frequent relapses and use of steroids, conferring an increased risk.[26] A variety of well-tolerated treatments for depression are available for Crohn's disease patients.[26] A multidisciplinary approach and multitiered treatment plan may provide optimum care.

Step Four: Surveillance

Specialized annual surveillance protocols must be implemented when caring for Crohn's disease patients. Particular attention must be paid to the skin, eyes, and gastrointestinal tract, and coordination of care between dermatology, ophthalmology, and gastroenterology is required. Recently, clinicians have begun to appreciate that immunosuppressed IBD patients have an increased risk for developing nonmelanoma and melanoma skin cancers.[27] Also, estimates suggest that approximately

10% of IBD patients develop eye problems.[28] These ophthalmologic issues may be harbingers of disease or may be related to disease treatment, such as steroid-induced glaucoma or cataracts. Crohn's disease patients, particularly those receiving immunosuppressive therapy, should participate in specialized routine surveillance programs and should be counseled to present to their physician's office when eye or skin changes are noted. Early detection of eye or skin disease results in prompt treatment, which increases the likelihood of preserving vision and limits morbidity due to skin cancer.

IBD patients must undergo surveillance for colorectal neoplasia. Patients with Crohn's disease should have a screening colonoscopy 8 years after the onset of symptoms.[29] The colonoscopy should optimally be performed when the patient's disease is in remission; however, surveillance should not be delayed while waiting for remission.[30] Optimal surveillance intervals for patients with extensive and long-standing Crohn's colitis have not been strictly defined, but surveillance should occur every 1–5 years, according to risk factors.[31] Risk factors include primary sclerosing cholangitis, a family history of colon cancer, and duration and extent of disease. Chromoendoscopy with targeted biopsies has demonstrated increased sensitivity for detecting dysplasia.[29] However, if this option is unavailable or the endoscopist lacks experience in this technique, a total of 32 biopsies taken throughout the colon, with additional biopsies taken from the rectum and sigmoid, are recommended for patients with extensive Crohn's colitis.[29,30]

Conclusion

Subsequent office visits by a Crohn's disease patient are an opportunity for both the patient and the gastroenterologist to prepare for or undertake various IBD therapies.[31] A checklist like the one shown in Table 3 can be a tool to remind providers to consider several important factors, which can allow for an efficient assessment of Crohn's disease patients and facilitate initiation or continuation of appropriate therapy.

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