Crohn’s Disease: The First Visit

Jack A. Di Palma, MD, and Francis A. Farraye, MD, MSc

Abstract: A Crohn’s disease patient’s first visit to a new practice is the optimal time to collect important clinical data and identify appropriate therapies. A methodologic approach to this visit is crucial. The focus of this visit should be on preparing the patient for the initiation of treatment, with particular attention to the necessary steps prior to the use of immunosuppressive and biologic agents. This paper is intended to provide recommendations and a checklist for the initial assessment and evaluation of patients with Crohn’s disease.

Step One: Obtain Historical Information

The chronology and manifestations of a patient’s Crohn’s disease may yield insight on future disease course. For example, young age at disease onset (<40 years) may be a predictor of poor prognosis or aggressive disease course, and it may be a factor in determining the need for biologic therapy (Table 2). Other historical predictors of poor prognosis include cigarette smoking, steroid use, disabling symptoms lasting more than 12 months, hospitalizations, weight loss, and the need for surgical resection. It is also important to know a patient’s history of extraintestinal manifestations associated with chronic inflammatory bowel disease (IBD)—such as sacroiliitis, ankylosing spondylitis, pyoderma gangrenosum, or uveitis—in order to understand the disease course and choose optimal therapy. Knowing a patient’s social and work histories, as well as the disease’s
Discuss the characteristics and intensity of abdominal pain, as well as the presence of chronic or nocturnal diarrhea, fever, weight loss, and rectal bleeding, may reflect consideration of biologics is also important for patients with extensive small-bowel disease, fistulizing disease, and deep ulcerations on endoscopy. A family history of IBD should be obtained, and the disease course and severity should be noted in all affected relatives. A patient’s initial history should also include any prior interventions, whether successful or unsuccessful. A meticulous review of these historical data, in addition to imaging and pathology results, may help to confirm a diagnosis of Crohn’s disease and enable better understanding of the disease course.

**Step Two: Evaluate Disease Activity**

If a patient’s history and previous evaluation suggest Crohn’s disease, a treatment plan should be determined based on objective evidence of disease activity as well as the severity and extent of disease. For example, a patient with a 20-year history of short-segment ileal disease should be managed differently from a patient with newly diagnosed, extensive, colonic Crohn’s disease with perianal fistula. Symptoms, laboratory tests (including measurement of inflammatory markers), serologies, and imaging studies can all help to assess disease activity; however, no single gold-standard indicator has been established.

**Symptoms**

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It is crucial to use objective measurements to assess inflammation, as patients with irritable bowel syndrome may also have severe pain and diarrhea. Clinical signs include cachexia, abdominal masses, fistulas, or abscesses. Patients should be questioned regarding signs and symptoms of extraintestinal manifestations of IBD, including arthralgias, cutaneous involvement, and ocular problems. In children, anemia, fever, and growth failure with delayed attainment of developmental milestones may be seen. Clinical patterns may imply disease location and type (fibrostenotic, inflammatory, or fistulizing) and may predict outcomes.

**Indices**

The Crohn’s Disease Activity Index (CDAI; Table 3), Harvey-Bradshaw Index (HBI; Table 4), and various endoscopic mucosal assessment scores (Table 5) have been used in clinical studies to determine disease activity and severity as well as response to therapy. The short-form Inflammatory Bowel Disease Questionnaire (IBDQ; Table 6) is composed of 10 questions (compared to 32 questions in the original IBDQ), is easily administered, and can be used to follow the disease’s impact on quality of life. Both the HBI and short-form IBDQ are well suited for use in clinical practice.

The CDAI and HBI have been used in studies to define response and remission. However, the CDAI is cumbersome and requires logarithmic regression analysis for calculation. An online CDAI calculator (available at http://www.ibdjohn.com/cdai/) allows for rapid calculation of the index and, thus, is practical for obtaining objective assessments of disease activity over multiple visits. Because the CDAI requires a hemoglobin test, the patient’s CDAI score is often unavailable when the patient is being seen in the physician’s office. In clinical practice, the HBI score utilizes readily available clinical data and is helpful for defining active disease. Endoscopic indices can be used to quantify ileocolonic lesions and confirm mucosal healing.

**Biochemical Markers**

C-reactive protein (CRP) appears to be an accurate marker of Crohn’s disease activity. CRP is an acute-phase protein that is sensitive for detecting inflammation, infection, and tissue injury. In Crohn’s disease, CRP level is increased in most patients with active disease and may correlate with CDAI score. A low CRP level may be useful to predict inactive Crohn’s disease, whereas a very high CRP level may predict progression to fibrostenotic disease. It should be noted, however, that up to 50% of patients with Crohn’s disease will not have an elevated CRP level, despite documented active inflammation.

Fecal calprotectin and lactoferrin are markers of inflammation that correlate with endoscopic disease activity. Schoepfer and colleagues showed that calprotectin correlated most closely with an endoscopic score.
Step Three: Consider Assessing Inflammatory Bowel Disease Serology in Select Patients

A variety of markers and antimicrobial peptides and antibodies have been associated with IBD. They can be used to help distinguish ulcerative colitis from Crohn’s disease and to predict prognosis.\(^\text{12,13}\) None of these markers are sensitive enough to establish a diagnosis of IBD by themselves. Antibodies against *Saccharomyces cerevisiae* (ASCA) are the most thoroughly studied markers and have a sensitivity of 60% for Crohn’s disease. Perinuclear antineutrophil cytoplasmic antibodies (pANCA) have a sensitivity of 40–60% for ulcerative colitis. Outer membrane porin protein C (OmpC) to *Escherichia coli* has a sensitivity of 20–40% for Crohn’s disease. These antibodies, as well as a number of other antibodies directed against bacteria, yeasts, or sugars, may have prognostic implications. The nucleotide-binding oligomerization domain 2 (*NOD2*) gene has been associated with fibrostenosing Crohn’s disease. Oligomannan (ASCA) has been associated with aggressive disease and the need for surgery. Anti-OmpC has been associated with fibrostenosis, perforating disease, and the need for small-bowel surgery. Crohn’s disease–related bacterial sequence (I2) is associated with small-bowel disease, fibrostenosis, need for surgery, and pouchitis. CBir1 flagellin (anti-CBir 1) is associated with penetrating disease, fibrostenosis, and pouchitis. Multiple positive serologic markers may predict a poor prognosis, prompting the consideration of early aggressive therapeutic interventions.\(^\text{13,14}\)

Step Four: Obtain the Patient’s Vaccination History, and Administer Appropriate Vaccinations

Treatment of IBD currently involves mesalamine; antibiotics; steroids; immunosuppressive agents, such as 6-mercaptopurine (6-MP), azathioprine (AZA), and methotrexate; and biologic agents, such as infliximab (Remicade,
Table 7. Recommended Adult Immunization Schedule

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Dosing schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Td/Tdap</td>
<td>Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years. For patients &gt;65 years of age, administer Td booster every 10 years.</td>
</tr>
<tr>
<td>HPV</td>
<td>3 doses in females 12–26 years of age</td>
</tr>
<tr>
<td>Varicella</td>
<td>2 doses</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1 dose in patients &gt;60 years of age</td>
</tr>
<tr>
<td>MMR</td>
<td>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.</td>
</tr>
<tr>
<td>Influenza</td>
<td>1 dose annually</td>
</tr>
<tr>
<td>Pneumococcal (polysaccharide)</td>
<td>1 or 2 doses in patients 19–49 years of age. 1 dose in all patients &gt;65 years of age.</td>
</tr>
<tr>
<td>Hepatitis A virus</td>
<td>2 doses (6 months apart) in patients with a risk factor (medical, occupational, or lifestyle)</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>3 doses (at 0, 1, and 6 months) in patients with a risk factor (medical, occupational, or lifestyle)</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>1 or more doses in patients with a risk factor (medical, occupational, or lifestyle)</td>
</tr>
</tbody>
</table>

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

Modified from Advisory Committee on Immunization Practices.17

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CROHN'S DISEASE: THE FIRST VISIT

There are several issues in the management of immunosuppressives and immunosuppressive treatment. Biologic agents should not be given when an abscess or serious infection is present. Multiple sclerosis and optic neuritis are also contraindications to treatment with biologic medications. In patients with moderate-to-severe heart failure (New York Heart Association Classes 3 and 4 congestive heart failure), infliximab is contraindicated in doses over 5 mg/kg. The annual incidence of tuberculosis in the United States is approximately 5 per 100,000 patients per year. With anti–tumor necrosis factor agents, there is a 4–90-fold increased risk of tuberculosis reactivation, usually occurring shortly after initiation of therapy.15 Infections are often atypical, and anergy influences the sensitivity of testing. Baseline chest radiographs and tuberculin skin testing can reduce tuberculosis rates by

**Step Five: Prepare for Therapy**

The mainstay of IBD therapy is anti-inflammatory and immunosuppressive treatment directed at the immune response that causes tissue damage.13 AZA and 6-MP are widely used in IBD patients, as are biologic agents. For AZA and 6-MP therapy, pretreatment measurement of thiopurine methyltransferase (TPMT) enzyme activity or genetic testing is advised. Full doses are recommended (AZA 2.0–2.5 mg/kg or 6-MP 1–1.5 mg/kg) in patients with normal enzyme activity. Measurement of TPMT levels does not eliminate the need for routine monitoring of complete blood cell counts and liver function tests.

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up to 90%. In patients with known prior exposure to tuberculosis or the bacille Calmette-Guerin vaccine, the use of quantiFERON gold assay (Cellestis Limited) has been suggested.

A standard series of blood tests should be obtained at the first visit of patients with Crohn’s disease, and these tests should be repeated periodically thereafter. These tests should include measurements of iron, vitamin B12, and vitamin D levels. Patients with previous steroid exposure or extensive disease should also undergo a bone density study.

Other recommendations include screening for skin cancer and human papillomavirus-associated cervical dysplasia, as well as annual skin and gynecologic examinations.

**Optional Patient Resources**

A number of online resources are available if patients request additional information to better understand their disease. The Crohn’s and Colitis Foundation of America’s website (www.ccfa.org) contains easy-to-read information on diagnosis and disease management. Other useful resources include websites from the National Institutes of Health (http://www.nlm.nih.gov/medlineplus/crohns-disease.html), The Foundation for Clinical Research in Inflammatory Bowel Disease (http://www.myibd.org/PatientEducation/DiseaseBasics/index.html), and various universities and medical centers (eg, http://www.mayo-clinic.com/health/crohns-disease/DS00104).

**Summary**

The first visit of a patient with Crohn’s disease is an opportunity for both the patient and gastroenterologist to prepare for various therapeutic options that may be needed.

**Table 8. Inactivated Vaccine Recommendations**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Check titer before vaccination?</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Td/Tdap</td>
<td>No</td>
<td>Administer the vaccine if it has not been given over the past 10 years, or give Tdap if Td was administered ≥2 years ago.</td>
</tr>
<tr>
<td>HPV</td>
<td>No</td>
<td>3 doses at 0, 2, and 6 months in females 12–26 years of age</td>
</tr>
<tr>
<td>Influenza</td>
<td>No</td>
<td>Administer annually. Use trivalent inactivated influenza vaccine. Avoid live attenuated influenza vaccine.</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>No</td>
<td>Vaccinate if no vaccine had been given previously. 1-time revaccination after 5 years if the patient is immunosuppressed.</td>
</tr>
<tr>
<td>Hepatitis A virus</td>
<td>Yes</td>
<td>2 doses at 0 and 6–12 months or 0 and 6–18 months. Booster given &gt;10 years.</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Yes</td>
<td>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.</td>
</tr>
<tr>
<td>Combination hepatitis A/B virus</td>
<td>Yes</td>
<td>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.</td>
</tr>
<tr>
<td>Meningococcal</td>
<td>No</td>
<td>Vaccinate at-risk patients if no vaccine had been given previously.</td>
</tr>
</tbody>
</table>

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

Modified from Wasan SK, et al.¹⁵

**Table 9. Expert Consensus Definition of Immunosuppression**

- **T**reatment with glucocorticoids (> prednisone 20 mg/day equivalent or 2 mg/kg/day if <10 kg, for ≥2 weeks and within 3 months of stopping)
- **O**ngoing treatment with effective doses of 6-MP/AZA or discontinuation within the previous 3 months
- **T**reatment with methotrexate or discontinuation within the previous 3 months
- **T**reatment with tumor necrosis factor inhibitors or discontinuation within the previous 3 months
- **S**ignificant protein-calorie malnutrition

6-MP=6-mercaptopurine; AZA=azathioprine.

Modified from Sands BE, et al.¹⁸
A checklist, such as the one provided in Table 1, can help remind gastroenterologists to consider factors that enable efficient assessment of patients with Crohn’s disease and facilitate initiation of appropriate therapy. The use of immunosuppressive and biologic agents requires certain assessments and testing for safe and effective treatment.

References