EVIDENCE-BASED
CARE SHEET

Crohn's Disease: Inducing/Maintaining Remission with Medications

What We Know

- Crohn's disease (CD) is an incurable inflammatory condition that can affect any part of the gastrointestinal (GI) system, impairs intestinal absorption of nutrients, and causes growth impairment and delayed puberty in pediatric patients. Although its course is often relapsing/remitting and patient response to treatment varies widely, most patients with CD lead normal lives but have a slightly shorter life expectancy.[1, 2, 3, 4, 7, 9, 10] (For more information, see *Quick Lesson About…Crohn's Disease*)
  - Treatment goals focus on achieving and maintaining remission to alleviate symptomatic discomfort, halt disease progression, and decrease the risk of complications; individual pharmacologic agents target different steps of the inflammatory cascade and immune system response in CD, but multiple drugs are usually necessary to achieve and maintain remission[1, 3, 4, 7, 9, 10]
    - CD is staged according to disease location, activity, and severity. Treatment, which usually begins with medication and lifestyle changes, frequently involves surgery for resolution of sequelae[7, 9]
- Medical treatment of CD involves lifetime surveillance and medication regimens that are periodically changed; pharmacologic regimens are prescribed according to the location and stage of the disease activity. CD stages are categorized as[3, 7]
  - mild to moderate disease in patients who are ambulatory, eating, and have achieved control of signs and symptoms[3, 7]
  - moderate to severe disease in patients who are unresponsive to treatment for mild disease and who have more pronounced manifestations of fever, weight loss > 10% of total body weight, dehydration, anemia, abdominal pain, or intermittent vomiting[3, 7]
  - severe to fulminant disease in patients with persistent CD manifestations despite corticosteroid therapy and who have a high fever, persistent vomiting, malnourishment, intestinal obstruction, abscess, rebound tenderness, or cachexia[3, 7]
  - in remission in patients who have no clinical manifestations or inflammatory sequelae, and have laboratory and endoscopic evidence of disease abatement and intestinal mucosal healing[3, 7]
    - Patients who respond to medical or surgical treatment and have no evidence of residual disease have achieved remission; corticosteroid-dependent patients are not considered to be in remission[3, 7]
- Thorough patient assessment is critical to the formulation of an individualized drug regimen because medications routinely used for treatment of CD (e.g., corticosteroids, immune system suppressants [e.g., azathioprine, 6 MP, infliximab], monoclonal antibodies) have the potential to cause life-threatening complications and comorbid disease conditions[1, 7, 9] (for more information, see the *Quick Lesson* referenced above)
  - Laboratory and other diagnostic studies completed before and after initiation of pharmacologic treatment, thorough clinician knowledge of the manufacturer's profile for each drug, and intensive patient monitoring are essential[4, 7, 9]
  - Each patient—and family members of pediatric patients—should be educated on the individualized drug regimen and how to monitor treatment efficacy and for adverse effects, complications, and new or worsening disease manifestations (e.g., distention, fever, bleeding, pain, fatigue, weight loss, diarrhea)[7, 10]
- Clinicians differ on what is the appropriate first-line therapy; first-line drug choices for inducing remission most commonly include single or combination treatment with[1, 3, 7, 9]
  - corticosteroids (e.g., prednisone, prednisolone, methylprednisolone, budesonide, betamethasone sodium phosphate), which are short-term anti-inflammatory immunosuppressants used for treatment of acute manifestations in all disease stages. They have not proven effective in maintaining remission[1, 3, 4, 7, 8, 9]
    - Some adults and most children experience symptomatic relief due to clinical remission of inflammation without concurrent intestinal mucosal healing[7]
  - antibiotics (usually metronidazole [Flagyl] or ciprofloxacin [Cipro]) are used in all stages of disease activity for resolving inflammation, abscesses, fistulas, and perianal CD[1, 9]

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Authors
Darlene A Strayer, RN, MBA
Carita Caple, RN, BSN, MSHS

Reviewers
Gilberto Cabrera, MD
Cinahl Information Systems
Glendale, California

Nursing Practice Council
Glendale Adventist Medical Center
Glendale, California

Editor
Diane Pravikoff, RN, PhD, FAAN
Cinahl Information Systems

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  - In severe CD, metronidazole and ciprofloxacin are often given concurrently[7, 9]
- aminosalicylate (5-ASA) anti-inflammatory agents; sulfasalazine, which primarily targets the colon; and mesalazine, for which multiple formulations are available that target different sites in the GI tract[3, 7]
- azathioprine or methotrexate, which are immunomodulator agents that interrupt the immune response and reduce inflammation[1, 3, 5, 6, 7, 9]
  - Maximum treatment efficacy requires 3–6 months of receiving azathioprine or methotrexate, so continued corticosteroid or other treatment is usual[6]

- Patients whose CD does not respond to first-line treatment or who are unable to discontinue corticosteroid therapy are evaluated for individualized second-line treatment, which may include single or combination therapy with[1, 3, 7, 9]
  - sulfasalazine, mesalazine, azathioprine, or methotrexate for patients who did not receive these options as first-line treatment[1, 5, 6, 7, 9]
  - anti-tumor necrosis factor (anti-TNF) drugs (e.g., infliximab, adalimumab, certolizumab, natalizumab), which are biologic treatments that can induce remission in patients who are refractory to other drugs[1, 2, 3, 7, 9]
    - Anti-TNF drugs are often given concurrently with an immunomodulator, which increases the effectiveness of both drugs[2, 7]
      - In a study of patients with moderate to severe CD, the combination of infliximab and azathioprine induced remission in 57% of patients at week 26, compared with remission rates of 44% and 30% in patients on infliximab monotherapy and azathioprine monotherapy, respectively[2]
    - Anti-TNF drugs increase the risk of infections and lymphoma[2, 6]
- Continuing pharmacologic therapy is essential to maintain remission in CD; drugs commonly used as monotherapy or combined with other drugs for maintenance therapy include[1, 3, 7, 9]
  - the immunomodulator agents azathioprine, 6-mercaptopurine, or methotrexate[6]
  - anti-TNF drugs in patients who respond to induction doses. These patients are more likely to exhibit long-lasting remission while receiving maintenance doses at regular intervals; giving episodic doses when symptoms recur has not proven to be effective[7]
- Genetic research suggests that the disease process of CD is initiated by inborn or acquired immune system dysfunction, which ignites early inflammatory activity; a cure for CD is believed possible only by development of a pharmacologic or other agent that restores long-term T cell tolerance or repairs the basic immune system dysfunction[9]

What We Can Do

- Learn about medication use to induce and maintain in patients with CD so you can accurately assess your patients' personal characteristics and health education needs; share this information with your colleagues
- Educate your patients with CD about the[1, 3, 6, 7, 9, 10]
  - importance of lifetime medical surveillance, maintaining a healthy lifestyle, strict treatment regimen adherence, and seeking immediate medical attention for new or worsening signs and symptoms
  - inevitability of periodic alteration in disease activity in spite of strict treatment regimen adherence, which necessitates intermittent drug regimen changes and usually, surgical intervention for complications (e.g., abscess, fistula, intestinal perforation, hemorrhage, perianal disease)
  - risks (e.g., cardiac events and reactivation of tuberculosis or other infections with anti-TNF drugs) and benefits of pharmacologic therapy for CD
  - specific actions patients should take to counteract potential adverse effects of medications (e.g., folic acid supplementation for patients receiving methotrexate)
    - Consult a drug information resource for a complete listing of adverse effects
  - importance of continuing additional treatment-specific laboratory and diagnostic testing while receiving treatment

Note

Recent review of the literature has found no updated research evidence on this topic since previous publication on August 27, 2010.

Coding Matrix

References are rated in order of strength:

M Published meta-analysis
SR Published systematic or integrative literature review
RCT Published research (randomized controlled trial)
R Published research (**not** randomized controlled trial)
C Case histories, case studies
G Published guidelines
RV Published review of the literature
RU Published research utilization report
QI Published quality improvement report
L Legislation
PGR Published government report
PFR Published funded report
PP Policies, procedures, protocols
X Practice exemplars, stories, opinions
GI General or background information/texts/reports
U Unpublished research, reviews, poster presentations or other such materials
CP Conference proceedings, abstracts, presentations

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