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Crohn Disease

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EB CME

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Crohn disease is a chronic condition of the gastrointestinal tract.

- It is characterized by transmural, granulomatous inflammation that occurs in a discontinuous pattern, with a tendency to form fistulae.
- The cause is unknown, but may depend on interactions among genetic predisposition, environmental triggers, and mucosal immunity.

Corticosteroids are first-line treatments to induce remission of acute disease.

- Budesonide is generally recommended in mild to moderate ileocaecal disease because it is only slightly less effective in inducing remission than prednisolone and has a superior adverse effect profile.
- Prednisolone or methylprednisolone is generally recommended for severe or more extensive disease because of their superior effectiveness.

Azathioprine and mercaptopurine are effective in inducing remission and healing fistulae in Crohn disease, provided that at least 17 weeks of treatment are given. Monitoring for myelosuppression is obligatory.

- Aminosalicylates (mesalazine, sulfasalazine) may reduce disease activity, but we do not know which regimen is best to induce remission.
- Methotrexate at a dosage of 25 mg weekly increases remission rates and has a corticosteroid-sparing effect. There is consensus that it is also effective for maintenance.
- Infliximab (a cytokine inhibitor) is effective in inducing and maintaining remission in Crohn disease, but the long-term adverse effect profile is unclear; infliximab is therefore generally reserved for treatment of disease that is refractory to corticosteroids or other immunomodulators.
- Antibiotics and cyclosporine are unlikely to be beneficial in inducing remission.

Bowel-sparing surgery to induce remission may be preferable to extensive resection, to avoid short bowel syndrome. Segmental and subtotal colectomy have similar remission rates.

Laparoscopic resection may reduce postoperative hospital stay, but we do not know whether strictureplasty is effective.

Azathioprine has been shown to be beneficial in maintaining remission in Crohn disease, either alone or after surgery, and has a corticosteroid-sparing effect, but it is associated with important adverse effects.

- Cyclosporine or oral corticosteroids alone are unlikely to be beneficial in maintaining remission after medical treatment.
- Methotrexate and infliximab may also maintain remission compared with placebo.
- Smoking cessation reduces the risk of relapse, and enteral nutrition may be effective.
- Fish oil and probiotics have not been shown to be effective.

Mesalazine seems effective in maintaining medically induced remission, but we do not know how effective other aminosalicylates are in maintaining remission.

Definition

Crohn disease is a chronic inflammatory condition of the gastrointestinal tract, characterized by transmural granulomatous inflammation, a discontinuous pattern of distribution, and fistulae. Although any part of the digestive tract from mouth to anus

Clinical Questions

What are the effects of medical interventions to induce remission in adults with Crohn disease?	
Beneficial	Corticosteroids (oral)
	Infliximab
Likely to be beneficial	Aminosalicylates (improved Crohn Disease Activity Index compared with placebo)
	Methotrexate
Trade-off between benefits and harms	Azathioprine or mercaptopurine
Unlikely to be beneficial	Antibiotics
Likely to be ineffective or harmful	Cyclosporine
What are the effects of surgical interventions to induce and maintain remission in adults with small bowel Crohn disease?	
Likely to be beneficial	Laparoscopic vs. open ileocecal resection (reduced postoperative hospital stay)
	Limited vs. extended resection
Unknown effectiveness	Strictureplasty
What are the effects of surgical interventions to induce remission in adults with colonic Crohn disease?	
Likely to be beneficial	Segmental colectomy
What are the effects of medical interventions to maintain remission in adults with Crohn disease?	
Likely to be beneficial	Aminosalicylates (mesalazine seems more effective than placebo at maintaining medically induced remission; insufficient evidence to assess other aminosalicylates)
	Infliximab
	Methotrexate
Trade-off between benefits and harms	Azathioprine
Likely to be ineffective or harmful	Cyclosporine
	Corticosteroids (oral)
What are the effects of medical interventions to maintain remission after surgery in adults with Crohn disease?	
Likely to be beneficial	Aminosalicylates
	Azathioprine/mercaptopurine
What are the effects of lifestyle interventions to maintain remission in adults with Crohn disease?	
Beneficial	Smoking cessation
Likely to be beneficial	Enteral nutrition (compared with unrestricted diet)
Unknown effectiveness	Fish oil
	Probiotics

may be affected, Crohn disease most often occurs in the terminal ileum, ileocecal region, colon, and perianal region. The disease may be further classified into inflammatory, fistulating, and stricturing disease. The symptoms vary but commonly include diarrhea, abdominal pain, weight loss, blood or mucus in the stool, perineal pain, discharge, and irritation resulting from perianal fistulae. Extraintestinal manifestations of the disease include arthritis, uveitis, and skin rash.

Diagnosis. There is no single method for the diagnosis of Crohn disease. Diagnosis is made by clinical evaluation and a combination of endoscopic, histologic, radiologic, and biochemical investigations.

Internationally accepted criteria for the diagnosis of Crohn disease have been defined by Lennard-Jones. After exclusion of infection, ischemia, irradiation, and malignancy as causes for intestinal inflammation, a combination of at least three of the following findings on clinical examination, radiologic investigation, endoscopy, and histologic examination of endoscopic biopsies or excised specimens is considered diagnostic: chronic inflammatory lesions of the oral cavity, pylorus or duodenum, small bowel, or anus; a discontinuous disease distribution (areas of abnormal mucosa separated by normal mucosa); transmural inflammation (fissuring ulcer, abscess, or fistula); fibrosis (stricture); lymphoid aggregates or aphthoid ulcers; retention of colonic mucin on biopsy in the presence of active inflammation; and granulomata (of the noncaseating type and not caused by foreign bodies).

Further macroscopic findings that are not included in the Lennard-Jones classification but are considered diagnostic for Crohn disease include fat wrapping, cobblestoning, and thickening of the intestinal wall. Laboratory findings consistent with Crohn disease include anemia, thrombocytosis, raised C-reactive protein levels, and a raised erythrocyte sedimentation rate. It may be difficult to distinguish Crohn disease from ulcerative colitis, particularly when only the colon is affected. In 10 to 15 percent of patients originally diagnosed as having Crohn disease, the diagnosis changes to ulcerative colitis during the first year.

Incidence and Prevalence

Estimates of the incidence of Crohn disease worldwide vary considerably. In Europe, incidence rates range from 0.7 (Croatia) to 9.8 (Scotland) new cases per 100,000 persons per year, whereas in North America the rates range from 3.6 (California) to 15.6 (Manitoba, Canada). The incidence of Crohn disease is increasing, with incidence rates in the United Kingdom, Italy, Iceland, Finland, and the United States doubling between 1955 and 1995. Crohn disease is most commonly diagnosed in late adolescence and early adulthood, but the mean age at diagnosis in North American studies ranges from 33.4 to 45 years. Crohn disease appears to affect women more commonly than men. In a systematic review of North American cohort studies of Crohn disease, the percentage of women affected by the disease varied from 48 to 66 percent, and was more than 50 percent in nine out of 11 studies.

Etiology

The true etiology of Crohn disease remains unknown. Current etiologic theories suggest that the disease results from a genetic predisposition, regulatory defects in the gut mucosal immune system, and environmental triggers. Defects in the gut mucosal immune system are mainly related to disordered activity of T cells (a type of white blood cell). Environmental triggers that have been linked with Crohn disease include smoking, diet (high sugar intake), and the balance of beneficial and harmful bacteria in the gut. Finally, there have been debates since *Mycobacterium avium paratuberculosis* was cultured from intestinal tissue of persons with Crohn disease, with little agreement on whether this bacterium is an infective cause of Crohn disease.

Prognosis

Crohn disease is a lifelong condition, with periods of active disease alternating with periods of remission. It causes significant disability, with only 75 percent of persons with Crohn disease being fully capable of work in the year of diagnosis, and 15 percent of persons unable to work after five to 10 years of disease. At least 50 percent of persons with Crohn disease require surgical treatment during the first 10 years of disease, and approximately 70 to 80 percent will require surgery during their lifetime. Persons with Crohn disease are at higher risk of developing colorectal and small bowel cancer than those without the disease.

Mortality. Mortality rates among persons with Crohn disease are slightly higher than in those without it. A systematic review of seven population-based cohort studies found that in six of the seven studies, estimates of standardized mortality ratios were more than 1, with estimates ranging from 0.72 (95% confidence interval, 0.49 to 1.01) to 2.16 (95% confidence interval, 1.54 to 2.94). The review also found that mortality rates in Crohn disease have not changed during the past 40 years.

EDITOR'S NOTE: Mesalazine is called mesalamine in the United States.

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