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Key Inforbits

- Overview of Crohn's and Colitis
- Risk Factors for Crohn's and Colitis
- Pharmacological Treatment
- Non-Pharmacological Treatment



What is Crohn's/Colitis?

Crohn's disease and ulcerative colitis are two distinct conditions that fall under the collective term of inflammatory bowel disease. Inflammatory bowel disease incidence is increasing worldwide with the majority of cases in Western countries.¹ The incidence of Crohn's disease is 6 to 15.5 cases per 100,000 persons per year while ulcerative colitis ranges from 1.2 to 20 cases per 100,000 persons per year.^{1,2} The exact cause of these conditions is unknown, but prevailing theories are that they are caused by a combination of environmental, immunological, and infectious factors.

Individuals with inflammatory bowel disease have an increased amount of intestinal bacteria when compared to patients without the disorder. One etiologic theory of infectious pathogenesis of Crohn's/colitis is that the body loses tolerance to the normal GI bacteria.¹ Immunological causes are thought to be from autoimmune and non-autoimmune mechanisms with patients displaying increased inflammatory cytokines. Environmental causes can be lifestyle, dietary or drug-related.

There are many risk factors for developing a type of irritable bowel disease (IBD). Crohn's disease risk factors are age, ethnicity, family history, and smoking.^{3,4} Crohn's disease and ulcerative colitis may develop at any age but most occur before 30. Ulcerative colitis can develop until after age 60.^{3,4} Caucasian and Ashkenazi Jewish descendants are more likely to develop IBD.^{3,4} The incidence of IBD is increasing worldwide with the highest rates occurring in North America, Northern Europe, and Great Britain.⁴ Having a first second and third degree relative diagnosed with IBD can increase a patient's risk especially those with first degree relatives who have been diagnosed.^{3,4}

Patients with ulcerative colitis may experience rectal bleeding, abdominal pain and/or abdominal tenderness. Patients with Crohn's may experience similar symptoms with the addition of fever, malaise, and abdominal fistulas.¹

Crohn's Disease	Ulcerative Colitis
<ul style="list-style-type: none"> ● Inflammation may develop anywhere in the GI tract from the mouth to the anus ● Most commonly occurs at the end of the small intestine ● May appear in patches ● May extend through entire thickness of bowel wall ● About 67% of people in remission will have at least 1 relapse over the next 5 years 	<ul style="list-style-type: none"> ● Localized to the large intestine (colon and rectum) ● Involves a section or the entire colon ● Appears in a continuous pattern ● Inflammation occurs in innermost lining of the intestines ● About 30% of people in remission will experience a relapse in the next year

Adapted from DiPiro JT, et al, eds. Pharmacotherapy: A Pathophysiologic Approach, 10e. 2017

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Non-Pharmacological Treatment Options

In trying to manage inflammatory bowel conditions without the aid of pharmaceutical intervention, the options for patients are quite limited. One potential option is diet; however, this option is controversial. While many sources agree that the refined “Western” diet is contributing to the incidence of both ulcerative colitis and Crohn's disease, researchers have not been able to identify a group that would be considered “high risk” and could then be studied over an extended period of time to see if dietary changes could, in fact, reduce the incidence of inflammatory conditions. As far as managing the condition with diet alone, there is no guideline recommended diet for this patient population. Rather, patients should avoid foods that they know cause them problems while making sure to eat sufficient amounts of healthy food to provide them with the nutrients they need to maintain proper body function.^{1,2}

Some sources recommend the use of probiotics, although this is also a somewhat controversial topic. A meta-analysis of studies conducted on patients with ulcerative colitis did show some benefit of probiotics (defined as remission or lack of relapse) in both active and inactive disease, but analysis of a few studies in patients with Crohn's disease did not demonstrate any real benefit. Add that to the fact that many of the trials analyzed were not placebo controlled and did not have uniformity in regards to the bacterial strains used, and it becomes even more difficult to confidently recommend the use of probiotics at this time. More uniform and controlled research is needed, but hopefully this may become a valid and effective treatment option for patients with inflammatory bowel conditions.^{1,3}

Surgery is the final non-pharm option available, but it is also usually the last resort for patients with inflammatory bowel disease. In patients with ulcerative colitis, colectomy is indicated after failure of maximal pharmaceutical therapy or in the case of complications like toxic megacolon or bowel perforation. It may also be necessary in patients with a high risk of conversion to cancer. In ulcerative colitis, total colectomy is usually curative, and patients can

either have an ileostomy or an ileal pouch. In these cases, quality of life is reported to be good with very few complications. In the case of Crohn's Disease, which can include the small as well as large bowel, surgical criteria are not as clear, and recurrence is fairly common. Generally, surgery is indicated more for complications than for curative effect. Some of these complications include strictures/obstructions, cancer, and fistulas. A potential concern in Crohn's patients who undergo resection of small bowel is malnutrition, so these patients should be evaluated frequently.¹

References

1. Hemstreet BA. Chapter 34. Inflammatory Bowel Disease. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. *Pharmacotherapy: A Pathophysiologic Approach*, 10e. New York, NY: McGraw-Hill; 2017. Accessed 2017 Nov 28. Available from: <http://accesspharmacy.mhmedical.com/content.aspx?bookid=1861§ionid=146059124>
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Pharmacological Treatment Options

The most commonly used treatment method is pharmacological treatment. In inflammatory bowel disease, the most commonly used agents are the aminosalicylates (ASA's), corticosteroids, immunosuppressants, and biologicals.¹ The chart below outlines these options and their role in treatment, but a small discussion of these options is still warranted.

The ASA's are the most commonly used drugs in IBD patients. Sulfasalazine is the most commonly used agent, but in patients with sulfa allergies the mesalamine component is effective as well. Mesalamine can be administered by mouth, by suppository, or by enema depending on the location of disease. Various delayed release oral formulations of mesalamine also offer the option of targeted therapy in either the small bowel or the colon, as well as allowing for once daily dosing.¹

Corticosteroids are effective in treating IBD due to their anti-inflammatory effects. They also have immune modulating properties, which adds to their efficacy. While guidelines recommend standard corticosteroid therapy as effective, budesonide is an attractive option since it is delayed release and therefore allows for more targeted therapy in the small bowel and colon.^{1,2}

Immunomodulators can be effective due to their ability to inhibit the production of inflammatory cytokines as well as reduce the number of immune cells. They are usually used after failure of ASA treatment, but can be used in conjunction with mesalamine and its derivatives in refractory patients. They can also be used alongside corticosteroids and tumor necrosis factor alpha (TNF- α) antagonists as well.^{1,2}

Biological agents work by inhibiting TNF- α as well as the α_4 subunit of the integrin molecule responsible for leukocyte adhesion. These agents can be used as induction as well as maintenance therapy, and can be used to induce remission as well as prevent relapse.¹

Antibiotics have been shown to help induce remission as well as prevent relapse, but they are not currently recommended due to the fact that no determination of the best class of antibiotics to use has been made.²



Image from:

<https://www.healthline.com/health/crohns-disease/quotes>

	Products	Effective at Inducing Remission in UC?	Effective at Preventing Relapse in UC?	Effective at Inducing Remission in CD?	Effective at Preventing Relapse in CD?
ASA's	Sulfasalazine Mesalamine Olsalazine Balsalazide	Yes	Yes	No	No
Corticosteroids	Budesonide	Yes	---	Yes*	No
Immunosuppressants	Cyclosporine Azathioprine Mercaptopurine Methotrexate	Azathioprine, mercaptopurine, methotrexate: No IV Cyclosporine: Yes**	Azathioprine, mercaptopurine: Yes Methotrexate: No	Azathioprine, mercaptopurine, cyclosporine: No IM Methotrexate: Yes	Azathioprine, mercaptopurine, methotrexate: Yes Cyclosporine: No
Biologicals	Adalimumab Certolizumab Infliximab Natalizumab Vedolizumab Golimumab	Yes	***	Yes	Yes

Adapted from An Evidence-Based Systematic Review on Medical Therapies in Inflammatory Bowel Disease.²

* Guidelines state that standard steroid therapy is more effective than budesonide

** Study cited did not have clear definitions of relapse, only stated that 9/11 patients responded to treatment

*** There are currently no RCTs in regard to biologics and relapse prevention in patients with ulcerative colitis

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The Last "dose" ... "Happiness is largely a matter of digestion."
- Lin Yutang (writer and inventor) (1895-1976)

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