28. IBD: Medical Management

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Introduction

- The cause of inflammatory bowel disease (IBD) is unknown, but it is believed to be an uncontrolled immune response within the intestinal mucosa leading to inflammation in genetically predisposed individuals.
- Multifactorial evidence suggests a defect of innate immune response to microbial agents and abnormalities in adaptive immunity and epithelial barrier function.
- The goals of therapy include controlling symptoms, improving quality of life, and minimizing short-term and long-term complications of disease and treatment.
- There are two phases of treatment: (1) inducing remission in active disease and (2) maintaining remission.
- Surgery is usually reserved for treating medically refractory disease or for specific complications.

Crohn's Disease: Medical Management

- CD is a chronic inflammatory condition that can affect any area of the gastrointestinal tract from the mouth to the anus.
- The disease most commonly affects the ileum and colon.

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Mild-to-Moderate Crohn's Disease

- Individuals with mild-to-moderate disease have fewer than four stools daily and are ambulatory and able to tolerate solid foods and liquids.
- Aminosalicylates and antibiotics are often used to treat mild-to-moderate Crohn's disease.
- The topically acting steroid, budesonide, is increasingly used as a drug of choice for mild-to-moderate disease of the terminal ileum or proximal colon.

Sulfasalazine and 5-Aminosalicylates

- Sulfasalazine (SSZ) and 5-aminosalicylates (5-ASA) are often used as first-line therapy.
- The National Cooperative Crohn's Disease Study demonstrated the benefits of SSZ 6 g/day over placebo for up to 16 weeks in patients with active ileocolonic and colonic CD.
- In contrast, SSZ did not induce remission at 3 g/day as monotherapy but was shown to be beneficial in combination with methylprednisolone.
- SSZ is not consistently effective for patients with active disease limited to the small intestine.
- Delayed-release formulations of mesalamine include Eudragit-S-coated mesalamine (Asacol®) that releases 5-ASA in the terminal ileum and cecum at pH 7 and Eudragit-L-coated mesalamine formulations (Salofalk®, Mesasal®, and Claversal®) that release in the mid-ileum at pH 6.
- Pentasa® (a sustained-release formulation of mesalamine microgranules enclosed within a semipermeable membrane of ethylcellulose) is designed for controlled release throughout the small and large intestine, beginning in the duodenum.
- Newer azo-bonded formulations designed for release in the colon include the 5-ASA dimers, olsalazine (Dipentum®) and balsalazide (Colazal®), which are composed of 5-ASA molecules azo-bonded to the inert carrier molecule 4-aminobenzoyl-β alanine.
- Lialda® is a delayed-release tablet containing mesalamine that allows for once-daily dosing and releases at pH 7 or above, normally in the terminal ileum.
- Apriso®, also a mesalamine compound, is an extended-release capsule that is taken once daily and dissolves at pH 6 starting in the small intestine and continuing throughout the colon.
- 5-ASA has not consistently demonstrated efficacy in controlled clinical trials.
- Table 28.1 describes dosing guidelines for SSZ and 5-ASA. Response to therapy should be evaluated after 6–12 weeks.
- Topically delivered preparations of 5-ASA (suppositories, enemas) have not been evaluated in controlled trials in patients with distal colonic CD.
- SSZ and 5-ASA are not recommended for maintenance of remission.

Table 28.1 Sulfasalazine and 5-aminosalicylates

Generic	Brand	Daily dose	Site of action
Sulfasalazine	Azulfidine	4–6 g daily in divided doses	Colon
	Azulfidine EN-Tabs	4–6 g daily in divided doses	Colon
Mesalamine	Canasa (suppositories)	500–1,000 mg daily QHS	Rectum
	Rowasa (enemas)	1–4 g daily QHS	Rectum/distal colon
	Asacol	2.4–4.8 g daily in divided doses	Terminal ileum/colon
	Pentasa	2–4 g daily in divided doses	Distal small bowel/colon
	Lialda	2.4–4.8 g daily in a single dose	Colon
	Apriso	1.5 g daily in a single dose QAM	Colon
Olsalazine	Dipentum	1.5–3 g daily	Colon
Balsalazide	Colazal	6.75 g daily	Colon

- Headache and gastrointestinal upset are common dose-dependent side effects of SSZ.
- SSZ depletes folate and should therefore be given with a folate supplement.
- SSZ may cause reversible sperm abnormalities, leading to relative infertility that reverses within 3 months of stopping the drug.

Antibiotics

- Antibiotics are valuable in treating perianal or perforating complications of CD.
- Side effects occur in up to 50 % of patients who take metronidazole short term and include gastrointestinal intolerance, metallic taste, and reaction to alcohol.
- Peripheral neuropathy, possibly irreversible, may occur with long-term use.
- Ciprofloxacin was shown in one study to be as effective as 5-ASA for achieving remission in mild-to-moderate active disease.
- Combination treatment with metronidazole and ciprofloxacin may be an alternative to steroid treatment in mild-to-moderate active CD.
- Side effects include gastrointestinal upset, skin reactions, and an increase in transaminase levels.
- Ciprofloxacin has been associated with rare cases of tendonitis and Achilles tendon rupture.

Budesonide

- Multiple randomized controlled trials have demonstrated the efficacy of budesonide over placebo for the induction of remission in patients with mild-to-moderately active ileal or ileo-right colonic disease.

- Budesonide has also been shown to be a more effective treatment than 5-ASA.
- Several studies have compared budesonide with prednisone and found that rates of clinical remission were similar in each group and the occurrence of corticosteroid-related side effects was considerably less.

Moderate-to-Severe Crohn's Disease

- The treatment options for these patients include corticosteroids, biologic agents, and the early addition of immunomodulator therapy with azathioprine (AZA), 6-mercaptopurine (6-MP), or methotrexate (MTX) as an adjunct or a bridge to maintenance therapy.

Oral Corticosteroids

- Oral corticosteroids are effective for the induction of remission in patients with moderate-to-severe CD.
- Prednisone doses of 40–60 mg daily are often prescribed for 2–6 weeks to induce remission.
- 50–70 % of patients will achieve remission at these doses. Higher doses of prednisone (1 mg/kg) or methylprednisolone (1 mg/kg) have had somewhat higher response rates of 80–90 %; however, there is an increased incidence of side effects.
- Prednisone doses are tapered by 5–10 mg/week until 20 mg and then by 2.5–5 mg weekly from 15 or 20 mg until discontinuation of therapy.
- Corticosteroids are not recommended as maintenance agents.
- 50 % of patients treated for active symptoms with a corticosteroid will become "steroid dependent" or "steroid resistant."
- Studies suggest that younger patients, smokers, and/or those with colonic disease have the highest risk of becoming corticosteroid dependent.
- Common findings include insomnia, fluid retention, acne, moon face, abdominal striae, weight gain, hypertension, hyperglycemia, glaucoma, cataracts, and mood disturbances. Musculoskeletal complications, such as osteoporosis, osteonecrosis, and myopathy, are important side effects.

Immunomodulators

- AZA and 6-MP are effective for maintaining a corticosteroid-induced remission and are beneficial as steroid-sparing agents.
- In clinical practice, AZA 2.0–2.5 mg/kg and 6-MP 1.01.5 mg/kg are used for maintenance therapy.
- Clinical benefit may not be evident for 3–4 months after initiation but may be durable.
- Adverse events include leukopenia, liver function abnormalities, pancreatitis (3–7 %), and lymphoma.

- Monitoring of complete blood counts, initially every 1–2 weeks, then, at least every 3 months, is recommended.
- Nonmelanoma skin cancers and cervical cancer may also occur more frequently. There is a slightly increased risk of lymphoma.
- Genetic polymorphisms of thiopurine methyltransferase (TPMT), the primary enzyme metabolizing 6-MP, have been identified, and drug metabolite levels may be measured.
- Prior to starting AZA or 6-MP, TPMT enzyme activity or genotype should be determined.
- AZA and 6-MP should be avoided in patients deficient in TPMT.
- Patients with heterozygous genotype of intermediate activity should initiate therapy at reduced doses, generally, AZA 1.0–1.25 mg/kg or 6-MP 0.5–0.75 mg/kg daily.

Methotrexate (MTX)

- MTX may be used to induce remission and as a steroid-sparing agent in patients with corticosteroid-refractory or corticosteroid-dependent CD.
- Folic acid 1 mg daily is routinely given.
- MTX is an alternative agent to AZA and 6-MP for maintenance of remission.
- MTX is contraindicated in pregnancy as it is teratogenic and abortifacient.

Biologic Therapy

- Biologic therapies (primarily anti-tumor necrosis factor antibodies) have been considered when CD is moderately to severely active despite therapy with aminosalicylates, corticosteroids, and/or immunomodulators or if corticosteroids or immunomodulators are contraindicated, not tolerated, or ineffective.
- Biologic therapy may also be indicated if patients are corticosteroid dependent or refractory.
- Patients with complications such as draining fistulas or extraintestinal manifestations may derive particular benefit from biologic therapy.
- Infliximab (chimeric monoclonal antibody) has been shown to effectively induce remission in patients with moderate-to-severe CD and to maintain remission in those patients.
- Infliximab is also useful for treating patients with corticosteroid-dependent and fistulizing disease.
- Patients treated with infliximab experience fewer hospitalizations and surgeries related to CD.
- The occurrence of extraintestinal manifestations, such as spondyloarthropathy, arthralgias, and pyoderma gangrenosum, may be reduced with infliximab.
- Approximately 30 % of patients have no response to infliximab, and not all responders have a complete response.

- Elevated C-reactive protein (CRP), nonstricturing and pure colonic disease subtypes, and concomitant use of immunomodulators have been described as positive predictors for response to infliximab. AZA and 6-MP are most commonly used as concomitant suppression. Methotrexate (MTX) may also be used.
- Initial response rates to adalimumab and certolizumab pegol were 58 % (the Netherlands randomized patients).
- Initiation of more intensive treatment early in the course of disease may result in better outcomes.
- Significantly more patients treated with infliximab alone or the combination of infliximab and azathioprine had relief of symptoms than patients treated with azathioprine alone.
- Patients with CD who are naive to immunomodulators and biologic agents are more likely to have enhanced mucosal healing when they are treated with infliximab and AZA and attain a corticosteroid-free clinical remission.
- Response to anti-TNF agents decreases with longer duration of disease.
- Natalizumab is a humanized monoclonal antibody that targets human α_4 integrin, thereby interfering with trafficking of leukocytes into the mucosa.
- Natalizumab is indicated for the induction and maintenance of response or remission in patients with moderate to severely active CD.
- Natalizumab should only be used in patients who are refractory or intolerant to immunomodulators and anti-TNF therapy and for whom surgery is not an acceptable option. See Table 28.2 for specific indications and Table 28.3 for dosing guidelines for biologic therapies.
- Anti-TNF agents and natalizumab have been shown in randomized placebo-controlled trials to be effective for maintenance of remission in patients with moderate-to-severe CD

Loss of Response to Anti-TNF Agents

- One-third of patients who initially respond to an anti-TNF agent will subsequently lose response over the course of 6–12 months.
- Therefore, a reasonable approach to loss of response to infliximab is to test for HACA and levels of infliximab. Patients with detectable HACA (normal <1.69 mcg/ml, levels ≥8 mcg/ml associated with loss of response) should be changed to an alternative anti-TNF agent, or less desirably, the dose could be increased.
- Concomitant immune suppression with AZA, 6-MP, or MTX reduces the development of antibodies.

Adverse Events Associated with Biologics

- Infusion or injection site reactions, autoimmunity (positive ANA, anti-double-stranded DNA antibodies; rare lupus-like reactions), activation of latent tuberculosis, and development of opportunistic infections.
- Fungal infections caused by *Histoplasma capsulatum*.

Table 28.2 Indications for biologic therapies

	Crohn's disease				Ulcerative colitis
Indication	Infliximab	Adalimumab	Certolizumab	Natalizumab	Infliximab
Induction of response and remission	X	X	X	X[1]	X
Maintenance of response and remission	X	X	X	X	X
Mucosal healing	X	X	X		X
Induction of response in adults with draining perianal fistulas	X	X			
Induction of response in adults with draining abdominal or rectovaginal fistulas	X				
Steroid-sparing agent	X	X		X	X
Treatment of spondyloarthropathy, arthritis/arthralgia, pyoderma gangrenosum and erythema nodosum, uveitis, and other ocular manifestations of Crohn's disease	X	X			X
Loss of response or intolerance to infliximab		X	X	X	

X[1] Must have also failed anti-TNF therapy and have evidence of inflammation

- All patients should be screened for tuberculosis with tuberculin skin testing (and chest X-ray if skin testing is positive) prior to initiating therapy with infliximab.
- Leukopenia, neutropenia, thrombocytopenia, or pancytopenia.
- Rarely, liver toxicity may occur and present as acute liver failure, jaundice, hepatitis, and cholestasis.
- Neurologic disorders including optic neuritis, seizures, and new onset or exacerbation of central nervous system demyelinating disorders, including multiple sclerosis.
- Hepatosplenic T-cell lymphoma, a lethal form of non-Hodgkin's lymphoma. Natalizumab may cause headache or rare infusion reactions.

Contraindications to Biologic Therapies

- Contraindications to anti-TNF agents are consistent across the class and include the following:
  1. Known hypersensitivity to agent, if severe.
  2. Active infection.

Table 28.3 Dosing guidelines for biologic therapy

Biologic agent	Induction regimen	Maintenance dose	Attenuated response	Discontinue therapy
Infliximab	5 mg/kg IV at weeks 0, 2, and 6	5 mg/kg IV every 8 weeks beginning at week 14	10 mg/kg at 8-week intervals, or 5 mg/kg every 4 weeks	No response after two doses or infusions are required more frequently than every 4 weeks
Adalimumab	160 mg SC on day 1 of week 0, then 80 mg SC on day 1 of week 2	40 mg SC every other week	40 mg SC weekly or 80 mg every other week	No response to induction therapy or duration of response decreases to less than 1 week
Certolizumab	400 mg SC at weeks 0, 2, and 4	400 mg SC every 4 weeks	Extra dose of 400 mg SC 2 weeks after last dose	No response to induction therapy or when the duration of response decreases to 2 weeks
Natalizumab	300 mg IV at weeks 0, 4, and 8	300 mg IV every 4 weeks	Other dosing regimens have not been adequately evaluated	Lack of response or inability to discontinue steroids by week 12

3. Untreated latent tuberculosis.
4. Preexisting demyelinating disorder.
5. Moderate-to-severe congestive heart failure.
6. Current or recent malignancy, without advice from an oncologist.
7. Further treatment with infliximab is contraindicated when the patient presents with uncontrolled infusion reactions.

Contraindications to Natalizumab

1. Known hypersensitivity to agent, if severe
2. Active infection
3. Current or past PML
4. Liver disease
5. Continued treatment with an immune modulator or anti-TNF antibody

Tacrolimus

- Various small studies have shown a trend toward clinical benefit especially in fistulizing disease.
- Oral therapy is usually started with 0.1–0.2 mg/kg/day as a twice-daily divided dose.
- Adverse effects: renal insufficiency, liver function abnormalities, infection, hyperglycemia, hypertension, and myelosuppression.

- Drug levels, blood counts, liver enzymes, renal function, glucose level, and blood pressure need to be monitored.

Severe Crohn's Disease

- Symptoms include high fever, frequent vomiting, evidence of intestinal obstruction, rebound tenderness, cachexia, or evidence of an abscess.
- Severe disease may be treated with high-dose intravenous corticosteroids.
- AZA or 6-MP should be initiated in patients who respond to IV corticosteroids.
- A patient who does not respond after 5–7 days of therapy may benefit from infliximab or intravenous (IV) cyclosporine (CSA).
- Failure to respond to medical therapy or worsening symptoms are indications for surgery.

Indications for Surgery in Crohn's Disease

- Approximately two-thirds of patients with CD will require surgery.
- The disease predictably recurs at the anastomotic site, and stricturoplasty is a reasonable surgical alternative if previous small-bowel resections place the patient at risk of short bowel syndrome.
- Any patient who fails to respond to 7–10 days of intensive inpatient management should be strongly considered for surgery.
- The indications for emergency surgery include primary free perforation or secondary rupture of an abscess into the peritoneal cavity and massive, uncontrollable hemorrhage.
- Urgent surgical procedures are required for fulminant Crohn's colitis with or without toxic megacolon and severe perianal sepsis.
- Elective procedures are an option for definitive treatment of intra-abdominal abscesses, complete or incomplete obstruction of the bowel, or an intractable course of disease (including steroid dependence or steroid resistance) and neoplastic or preneoplastic lesions.

Crohn's Disease: Maintenance Therapy After Medical Induction of Remission

- Randomized controlled trials investigating the use of SSZ or 5-ASA have not demonstrated significant maintenance benefits in CD.
- 5-ASA (at a dose of 4 g daily) has not been efficacious in preventing relapse after corticosteroid-induced remissions.
- Immunomodulators, including AZA, 6-MP, and MTX, as well as anti-TNF agents and natalizumab may be effective maintenance agents.

Postoperative Reoccurrence of Crohn's Disease and Prophylaxis

- Factors associated with an increased risk of early postoperative recurrence include smoking, absence of prophylactic postoperative therapy, and extent of disease greater than 100 cm.
- SSZ has not been statistically superior to placebo in preventing postoperative relapse. 5-ASA is associated with a modest pooled risk reduction of 13 % for those patients with surgically induced remissions with isolated small-bowel disease.
- Data supporting the use of AZA and 6-MP for prevention of postoperative recurrence are limited; however, the data suggest possible efficacy.
- Infliximab may be used as a postoperative prophylactic agent. It has been shown to prevent postoperative clinical and endoscopic recurrence after ileocecal resection.
- Imidazole antibiotics, including metronidazole, decrease short-term, but not long-term, endoscopic recurrence and are limited by side effects. Corticosteroids do not prevent postoperative relapse.
- There is insufficient evidence to support the use of probiotics in preventing postoperative recurrence of CD.
- Overall, there are no consistent recommendations regarding medical therapy after surgical resection for Crohn's disease.

Perianal Crohn's Disease

- Medications commonly used for the treatment of perianal fistulas include antibiotics, immunomodulators, and anti-TNF agents.
- There is no role for the use of 5-ASA or corticosteroids in the treatment of perianal fistulas.
- Perianal fistulas typically respond to metronidazole alone or in combination with ciprofloxacin; however, continuous therapy may be necessary.
- Simple, superficial fistulas may respond completely to fistulotomy and antibiotics. Complex fistulas may respond best to combined medical/surgical approaches.
- Infliximab is effective at acutely closing fistula and maintaining closure with maintenance dosing.

Ulcerative Colitis: Medical Management

Proctitis

- Treated with topical therapies such as enemas or suppositories or oral agents.
- Topical formulations of 5-ASA are considered first-line therapy for the treatment of proctitis. These agents are considered more effective than

rectal steroids and have been shown to be more effective than oral 5-ASA.
- Suppositories are preferred over enemas.
- Response is usually seen within 2–3 weeks with increased response rates (63–79 %) at 4–6 weeks.
- For patients not responding to rectal 5-ASA alone, combination treatment with topical corticosteroids (foam or enema) is better than either therapy alone.

Distal Ulcerative Colitis

- Patients with distal colitis can be treated with topical 5-ASA (suppositories, enemas), topical corticosteroids (suppositories, enemas), oral 5-ASA, or a combination of these agents.
- Rectal therapies may have a more rapid effect than oral therapies. Rectal 5-ASA is considered superior to rectal corticosteroids for inducing remission; however, combination therapy with a topical corticosteroid may be more effective than monotherapy.
- Therapy with a combination of oral and rectal 5-ASA achieves higher remission rates than either therapy alone.

Mild-to-Moderate Extensive Ulcerative Colitis

Sulfasalazine and 5-Aminosalicylates

- SSZ and oral 5-ASA are considered first-line agents for induction of remission in mild-to-moderate UC. SSZ achieves remission in 64–80 % of patients at doses of 2–6 g daily.
- Clinical response can be achieved in up to 84 % of patients taking a 5-ASA.
- Combining oral 5-ASA with topical 5-ASA preparations has been shown to be well tolerated and more efficacious in patients with extensive UC.

Corticosteroids

- Oral corticosteroids successfully induce remission in the majority of patients.
- Doses of prednisone 20–60 mg/day are often used, but doses greater than 60 mg/day have no additional benefit.
- Prednisone is tapered by 5–10 mg weekly until 15–20 mg, then tapered by 2.5–5 mg weekly.

Severe and Fulminant Extensive Ulcerative Colitis

Intravenous Corticosteroids

- Approximately 60 % of patients with severe/fulminant colitis treated with IV corticosteroids respond fully.
- Doses of hydrocortisone 100 mg IV three times daily or methylprednisolone 60 mg IV daily are used to induce remission.
- Continuous infusion of corticosteroids is not more efficacious than bolus dosing. Patients who fail to improve within 3–7 days (depending on severity of illness) should be considered for colectomy or rescue therapy with CSA or infliximab.

Azathioprine/6-Mercaptopurine

- In patients with persistently active, steroid-dependent, or steroid-refractory UC, immunomodulators (AZA or 6-MP) should be considered.
- AZA or 6-MP can induce a clinical remission or response in 30–50 % of patients, improve overall symptoms, and allow the dose of steroids to be reduced or discontinued.
- Infliximab is an alternative agent for refractory disease.

Cyclosporine

- Intravenous CSA is used as rescue therapy for severe corticosteroid-refractory UC.
- Studies report response rates between 70 and 80 % in patients with this type of UC.
- CSA is initiated as a continuous infusion while continuing IV corticosteroids.
- General improvement is seen within 4–5 days of initiating treatment.
- If no improvement is noted within 7 days or the condition deteriorates during treatment with CSA, surgery should be considered.
- Symptoms of CSA toxicity include infection, paresthesia, nausea, tremors, headache hypertension, and permanent or temporary renal toxicity.
- Patients who are noncompliant, have a history of uncontrolled seizures, or active infection should not receive CSA.

Tacrolimus

- Tacrolimus is a steroid-sparing agent.
- The most common affect is mild finger tremor.

Infliximab

- Infliximab is the only anti-TNF agent approved for use in UC.
- It has been shown to successfully induce and maintain remission in patients with moderate-to-severe and corticosteroid-dependent UC.

- Infliximab is used as a steroid-sparing agent in patients with corticosteroid-dependent or corticosteroid-refractory UC.
- Infliximab appears to decrease the rate of colectomy at 3 months and 1 year.

Ulcerative Colitis: Maintenance Therapy After Medical Induction of Remission

- Rectal and oral 5-ASA are effective for maintaining remission of distal UC and proctitis even when used on an intermittent basis. Up to 90 % of patients with extensive colitis can be maintained in remission using oral once-daily 5-ASA therapy.
- AZA and 6-MP are useful as corticosteroid-sparing agents, for maintaining remission in patients not adequately controlled by 5-ASA alone and for maintaining CSA-induced remission.
- Infliximab is able to maintain remission in patients with UC for up to 54 weeks.

Indications for Surgery in Ulcerative Colitis

- Between 20 and 30 % of UC patients will eventually require surgery.
- Indications for emergency surgery include massive hemorrhage, toxic megacolon, perforation, and severe colitis unresponsive to medical therapy.
- Elective surgery may be performed for cancer/dysplasia, failure of therapy, adverse events resulting from medial therapy, malnutrition, growth retardation in children, and control of certain extraintestinal manifestations.

Preoperative Treatment Effect on Postsurgical Complications

- Studies have shown that corticosteroid use prior to surgery increases the risk of postoperative infectious complications.
- Patients taking corticosteroids preoperatively may have doubled the risk of infectious complications.
- Patients taking >40 mg had a considerably higher risk of developing postoperative complications.
- Treatment with AZA or 6-MP prior to surgery is not a risk factor for postoperative complications.
- Effect of preoperative infliximab on postsurgical complications is controversial.
- Two retrospective studies in patients with CD suggest that infliximab infused within 8–12 weeks before abdominal surgery is not associated with an increased rate of postoperative complications.

- Analysis of a third retrospective series found that infliximab use within 3 months prior to surgery is associated with increased rates of postoperative sepsis, abscess, and hospital readmission in patients with CD. The data regarding postsurgical complications in UC patients receiving infliximab prior to surgery are limited. Infliximab use prior to surgery may be associated with an increased risk of pouch failure and infectious complications related to the pouch.

Pouchitis

- Pouchitis is the most common long-term complication of ileal pouch anal anastomosis (IPAA).
- Patients respond to 2 weeks of ciprofloxacin at 500 mg twice daily or metronidazole 750–1,200 mg/day.
- 60 % will go on to develop a second episode, and approximately 20 % of patients will have refractory or relapsing symptoms.
- If patients relapse at least three times within 1 year, chronic maintenance therapy with lower doses of antibiotics is recommended.
- Approximately 20 % of patients develop chronic refractory pouchitis.
- Combination antibiotic therapy may be the most effective.
- Rifaximin alone or in combination with ciprofloxacin is an effective treatment. Budesonide and infliximab may be used as alternative treatments.
- Maintenance with VSL #3, a probiotic, is an option.

Crohn's Disease of the Pouch

- CD of the pouch may be treated with topical and oral 5-ASA, oral or topical corticosteroids, antibiotics, and immunomodulators.

Conclusion

- Aminosalicylates are first-line agents for the treatment of mild-to-moderate disease and for maintaining remission; however, in the case of CD, evidence of efficacy is sparse.
- Antibiotics are somewhat effective in colonic CD but are not considered useful as treatment for UC, although efficacious for the treatment of pouchitis.
- Corticosteroids are effective for inducing remission in more severe disease but are associated with multiple side effects.
- Corticosteroids are not recommended as maintenance therapy.
- Immunomodulators, AZA, 6-MP, and MTX, are best employed as maintenance agents and, in the case of AZA and 6-MP, require approximately 3–4 months to be effective.
- Infliximab is the only anti-TNF agent currently approved for use in UC.