INFLAMMATORY BOWEL DISEASE

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INTRODUCTION

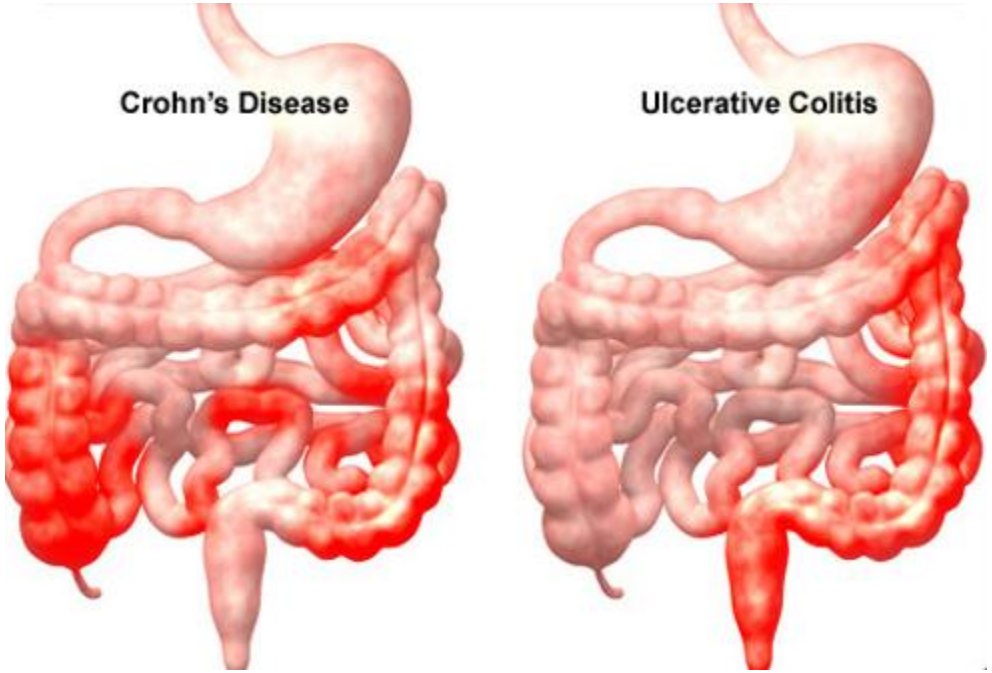
Inflammatory bowel disease (IBD) can be divided into two chronic inflammatory disorders of the gastro-intestinal tract

- **Crohn's disease**
- **Ulcerative colitis**

INTRODUCTION

Crohn's disease affects any part of the gastro-intestinal tract

Ulcerative colitis affects the colon and rectum only.

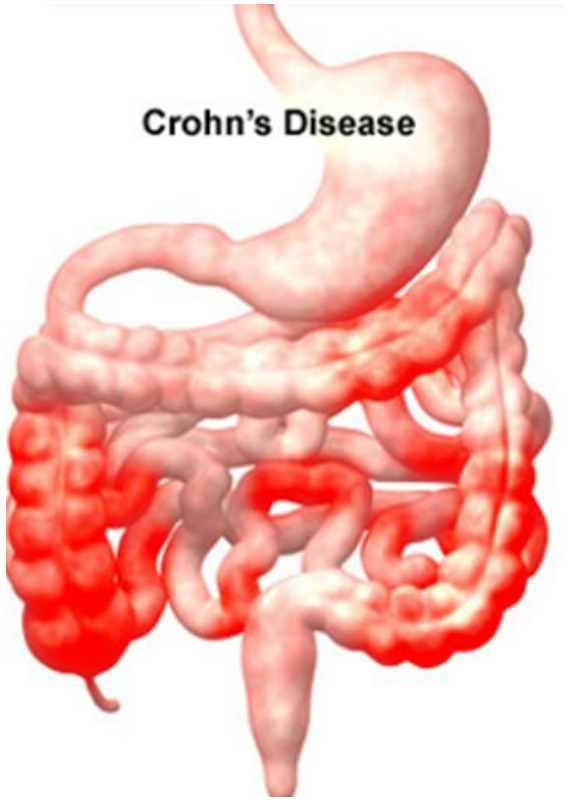


CROHN'S DISEASE

Crohn's disease affects any part of the gastro-intestinal tract.

Crohn's disease can involve one area of the gut or multiple areas, with unaffected areas in between being known as '**skip lesions**'.

The areas of the **small bowel** affected are typically **thickened** and **narrow**.

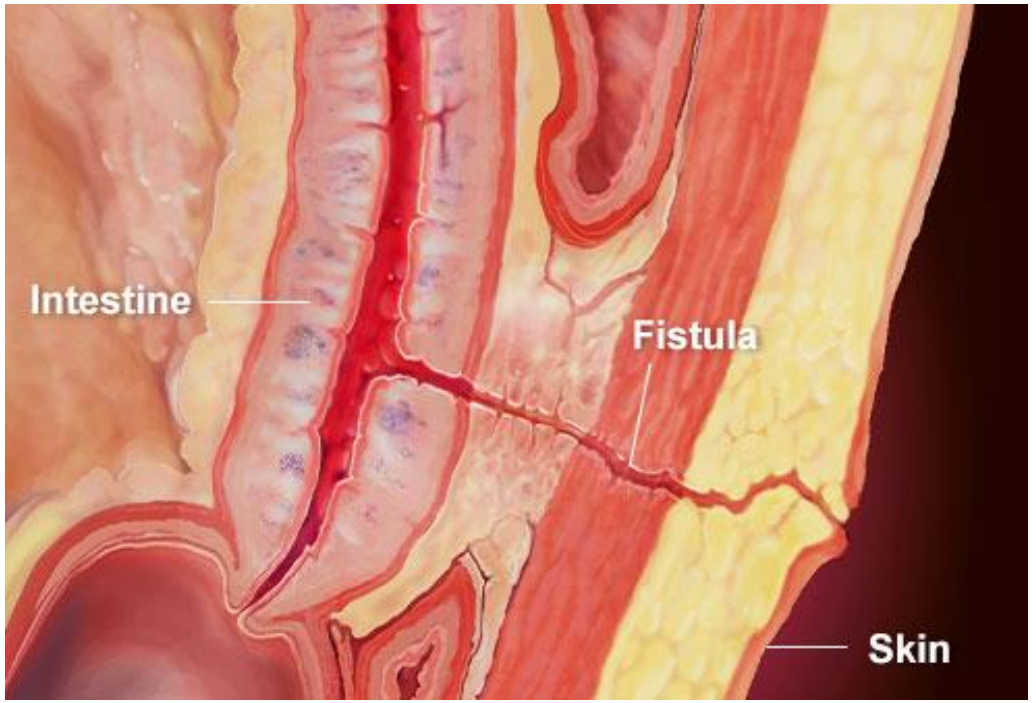


CROHN'S DISEASE

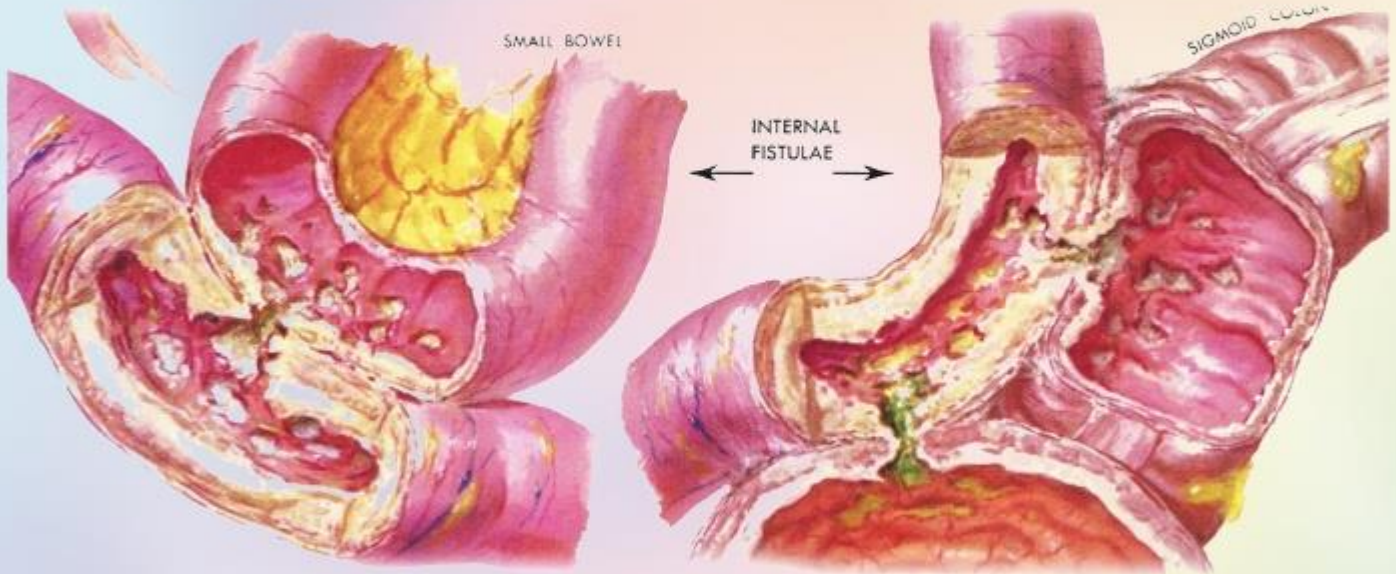
A **red ring** is often the **1st visible abnormality** seen on **colonoscopy**.

Intestinal strictures arise from chronic inflammation and fibrosis which eventually may lead to **bowel obstruction**.

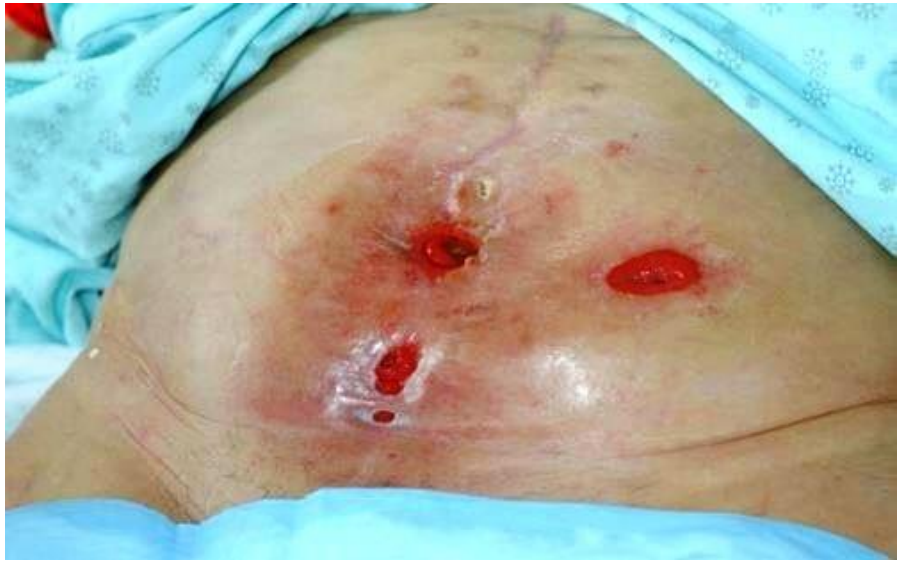
Local gut perforation may cause **abscesses** which may also lead to **fistulae**.



Crohn's Disease: Clinical Features



Internal Fistulae

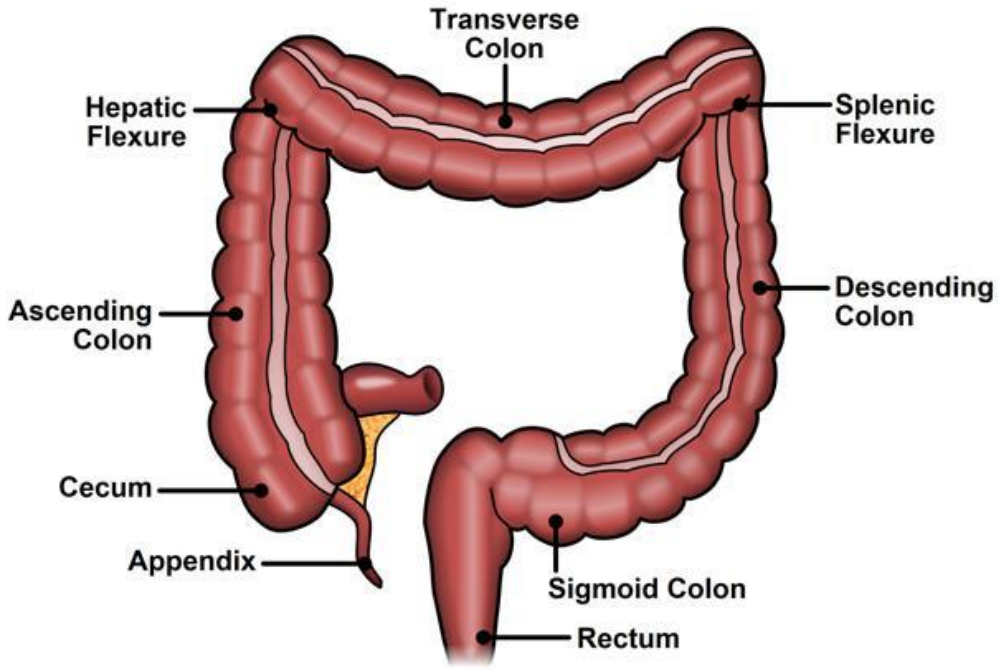


ULCERATIVE COLITIS

At first presentation, ulcerative colitis is

- 40% of cases to the rectum
- 40% of cases to sigmoid and descending colon
- 20% of cases to whole colon

The reason why some patients have **extensive** disease and some have **limited** disease is **unknown**.

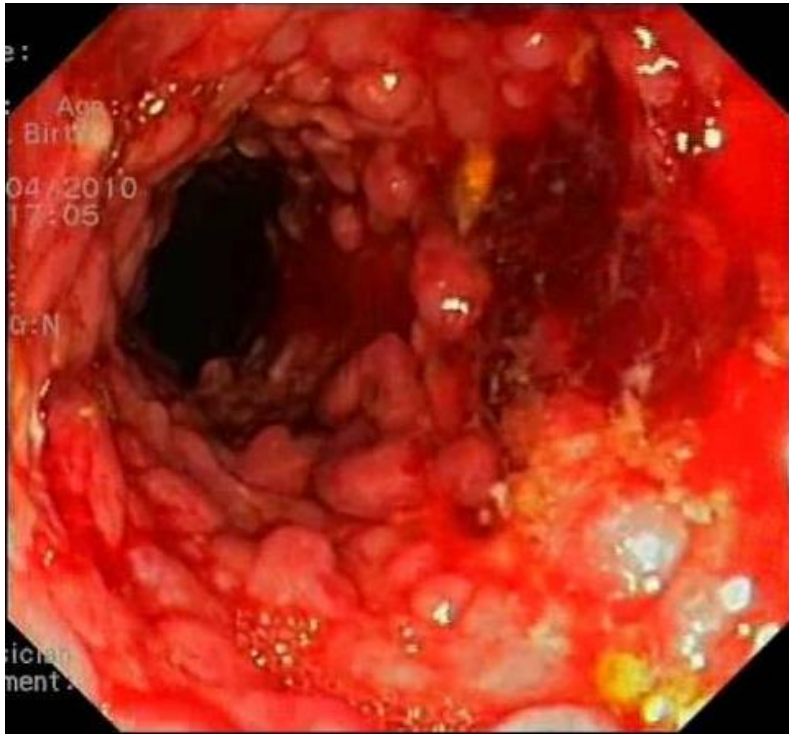


ULCERATIVE COLITIS

The colon appears

- **mucopurulent** (containing both mucus and pus)
- **erythematous**
- **granular**
- **superficial ulceration** that in severe cases leads to **ulceration**

As the colon heals by granulation, **post-inflammatory polyps** may form.



THE CHALLENGE….

Current available treatment for IBD is **not curative**.

IBD follows a **relapsing** and **remitting** course that is **unpredictable** and causes disruption to a patient's lifestyle.

The management of IBD patients poses a challenge to the multidisciplinary team both **clinically** and **economically**.

EPIDEMIOLOGY

The peak incidence of **IBD** occurs between **10** and **40 years**, although it can occur at any age, with 15% of cases diagnosed in individuals over the age of 60 years.

The incidence appears **equal** between **males** and **females**, although some studies in **Crohn's disease** show a slight female predominance.

ETIOLOGY

The causative agents of IBD are **largely unknown**, although a number of factors are thought to play a role.

ETIOLOGY - DIET

Evidence that dietary intake is involved in the etiology of IBD is **inconclusive**, although several dietary factors have been associated with IBD, including

- **fat intake**
- **fast food ingestion**
- **milk and fiber consumption**
- **protein intake**
- **spicy foods**

ETIOLOGY - DIET

During the course of the disease, patients are able to identify foods which **aggravate their symptoms**, for example, milk or spicy foods.

Up to 5% of patients with **ulcerative colitis** improve by **avoiding cow's milk**.

Those that are **breastfed as infants** have a reduced risk of developing IBD

ETIOLOGY - SMOKING

Smoking

- worsens the clinical course of the disease
- increases the risk of relapse
- increases the need for surgery

ETIOLOGY - INFECTION

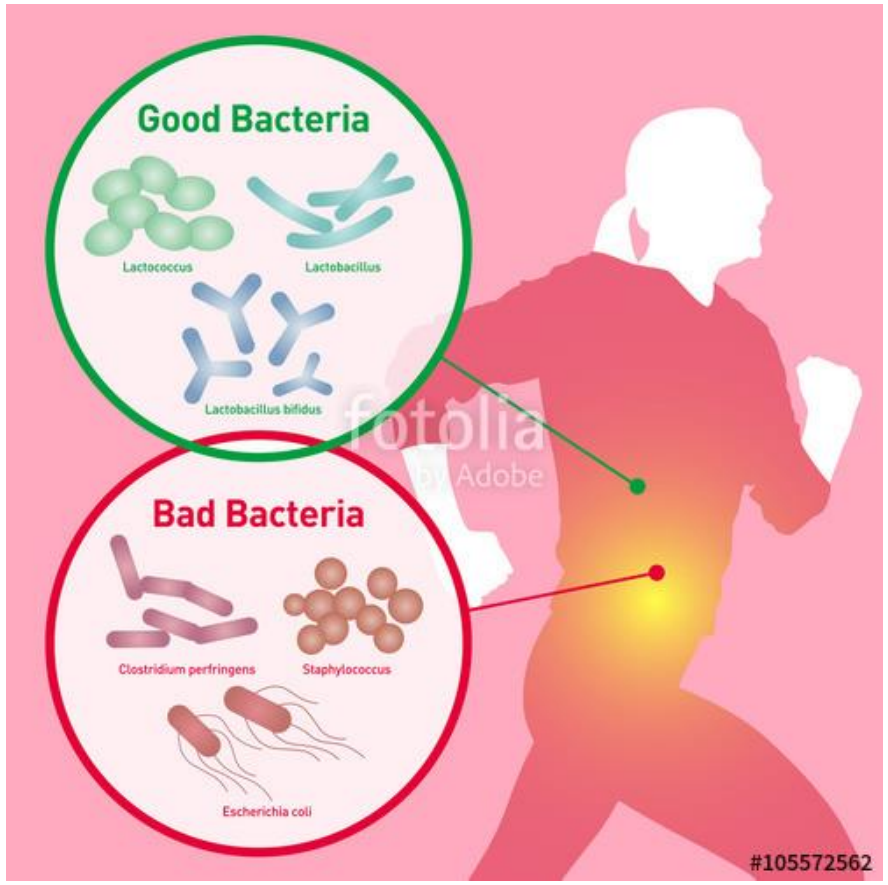
Exposure to ***Mycobacterium paratuberculosis*** has been considered a causative agent of **Crohn's disease**, although current evidence indicates it is not an aetiological factor.

Ulcerative colitis may present after an episode of **infective diarrhoea**, but overall there is little evidence to support the role of a single infective agent.

ETIOLOGY - ENTERIC MICROFLORA

Enteric microflora plays an important role in the pathogenesis of IBD because the gut acts as a sensitizing organ that contributes to the systemic immune response.

Patients with IBD show a **loss of immunological tolerance to intestinal microflora** and consequently **antibiotics** often play a role in the treatment of IBD.



ETIOLOGY - ENTERIC MICROFLORA

More recently, manipulating the intestinal flora using probiotics, prebiotics and synbiotic has proven to be an effective therapeutic strategy.

Probiotics such as **Bifidobacteria** and **Lactobacilli** alter the intestinal microflora balance favorably.

Prebiotics are a non-digestible food ingredient stimulate the growth of beneficial microorganisms in the colon.

Synbiotics are a combination of both prebiotics and probiotics, have been successfully used.

ETIOLOGY - DRUGS

Non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac have been reported to exacerbate IBD.

It is thought this may result from direct inhibition of the synthesis of cytoprotective prostaglandins.

Antibiotics may also precipitate a relapse in disease due to a change in the enteric microflora.

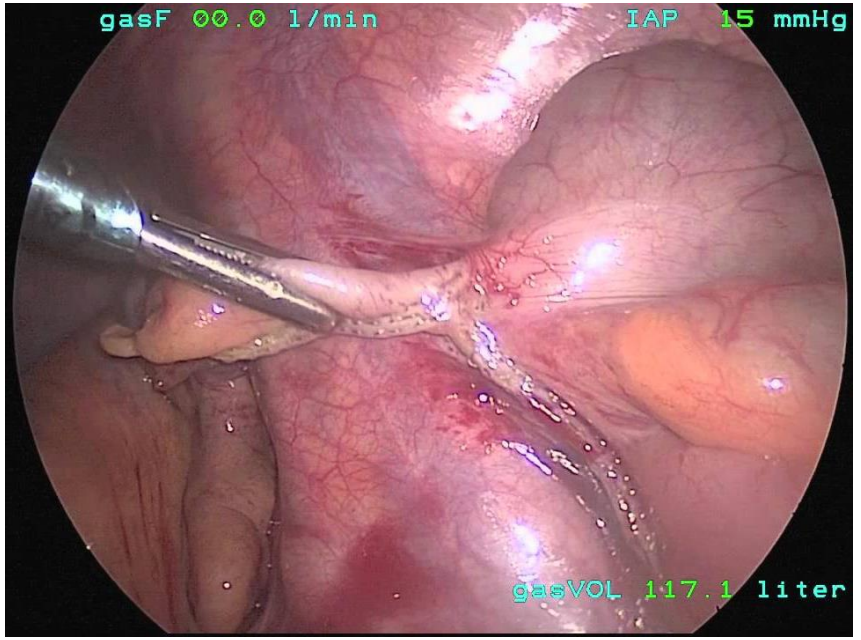
ETIOLOGY - DRUGS

The risk of developing **Crohn's disease** is thought to be increased in women taking the **oral contraceptive pill**, possibly caused by **vascular changes.**

There has been much debate about the link between bowel disease and **measles**, **measles vaccine**, **mumps** and **rubella immunization**. However, current evidence has indicated no proven correlation.

ETIOLOGY - APPENDECTOMY

Appendectomy has a protective effect in both **Crohn's disease** and **Ulcerative colitis.**



Appendectomy before diagnosis of IBD

- delays disease onset in ulcerative colitis and Crohn's disease
- lead to a milder disease phenotype in ulcerative colitis

ETIOLOGY - STRESS

It is thought that **stress** activates inflammatory mediators at enteric nerve endings in the gut wall.

In addition to **stress** as a trigger factor, living with IBD can also be stressful.

ETIOLOGY - STRESS

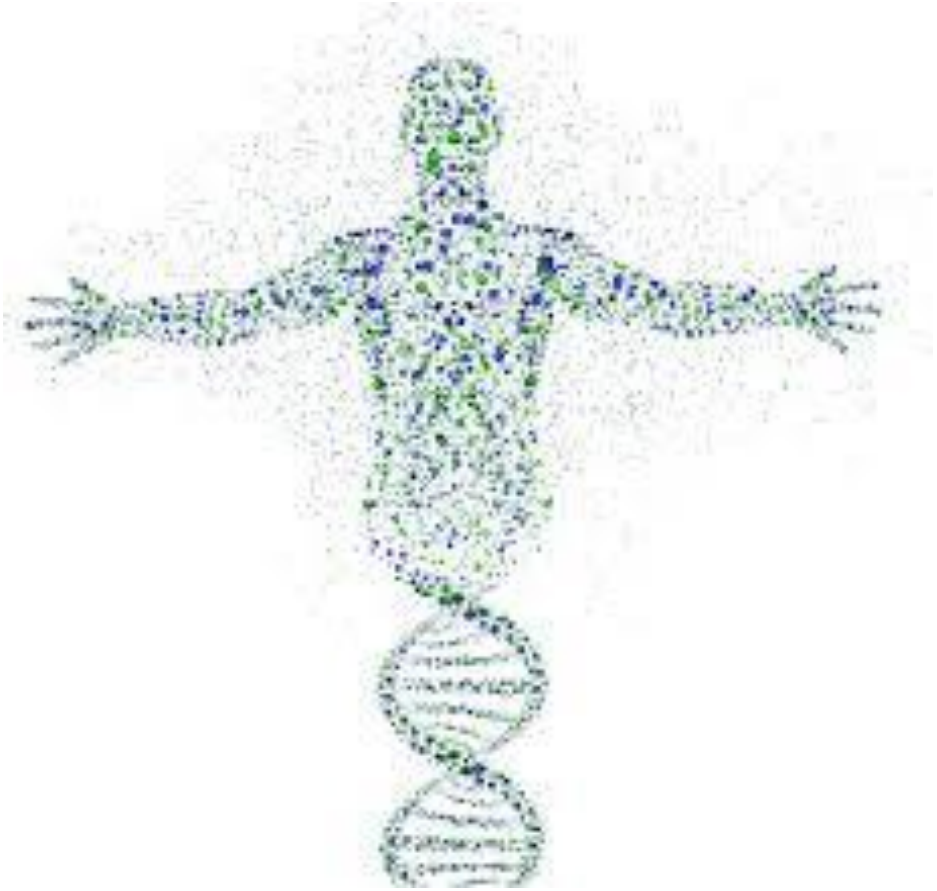
Its chronic nature, it difficult for patients to cope because of the

- **lack of curative treatment**
- **distressing symptoms**
- **impact on lifestyle**

ETIOLOGY - GENETIC

Fifteen percent of **first degree relatives** have IBD.

There is mounting evidence that **Crohn's disease** and **ulcerative colitis** result from an inappropriate response of the immune system in the mucosa of the gastro-intestinal tract to normal **enteric flora**.



ETIOLOGY - ETHNIC & FAMILIAL

Jews are more prone to IBD than non-Jews.

In **North America**, IBD is more common in **whites** than **blacks**.

First degree relatives of those with IBD have a **10-fold increase** in risk of developing the disease.

PATHOPHYSIOLOGY

In individuals with **IBD**, trigger factors typically cause a **severe**, **prolonged** and **inappropriate inflammatory response** in the gastro-intestinal tract.

The ongoing inflammatory reaction leads to an **alteration in the normal architecture of the digestive tract**.

It is thought that **chronic inflammation** is characterized by increased activity of effector lymphocytes and pro-inflammatory cytokines that override normal control mechanisms.

COLITIS

In some cases, the pathology of the disease has not been identified as either Crohn's disease or ulcerative colitis.

In **microscopic colitis**, the main feature is

- **watery diarrhoea** in the presence of a **normal colonoscopy**
- **chronic inflammation** in the **absence of crypt architectural distortion on mucosal biopsies**

COLITIS

NSAIDs and **proton pump inhibitors (PPIs)** are implicated as the cause in up to **50%** of cases of **microscopic colitis**.

Pseudomembraneous colitis is caused by *Clostridium difficile*, usually after prolonged or multiple **antibiotics**.

The use of **PPIs** predisposes patients to **infection**. It is diagnosed by sigmoidoscopy and detection of C. *difficile* toxin in the stool.

CLINICAL MANIFESTATION - CROHN'S DISEASE

The clinical features of **Crohn's disease** depend largely on

- the site of the bowel affected
- the extent and the severity of the pathological process

CLINICAL MANIFESTATION - CROHN'S DISEASE

Crohn's disease tends to be **more disabling** than **ulcerative colitis** with 25% of patients unable to work 1 year after diagnosis.

The predominant symptoms in Crohn's disease are

- **diarrhoea**
- **abdominal pain**
- **weight loss**

CLINICAL MANIFESTATION - CROHN'S DISEASE

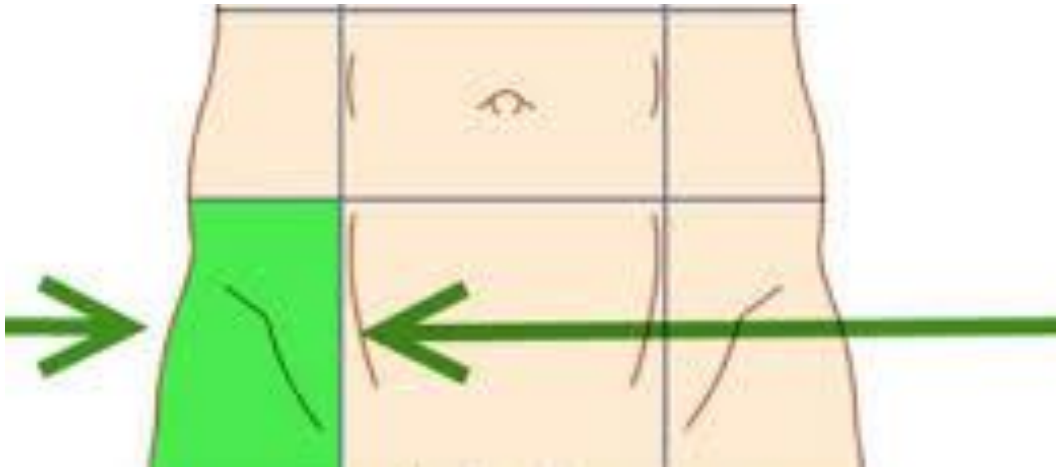
Weight loss occurs in most patients, irrespective of disease location.

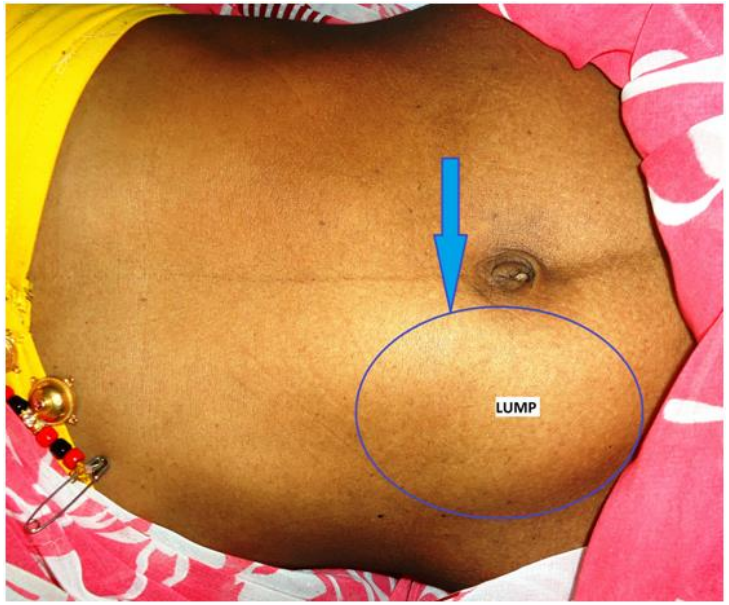
The main cause is decreased **oral intake**, although **malnutrition** is also **common**.

There is a slight increase in mortality in patients with extensive Crohn's disease.

CLINICAL MANIFESTATION - CROHN'S DISEASE

Patients may present with pain and/or a **tender palpable mass** in the **right iliac fossa**.





CLINICAL MANIFESTATION - CROHN'S DISEASE

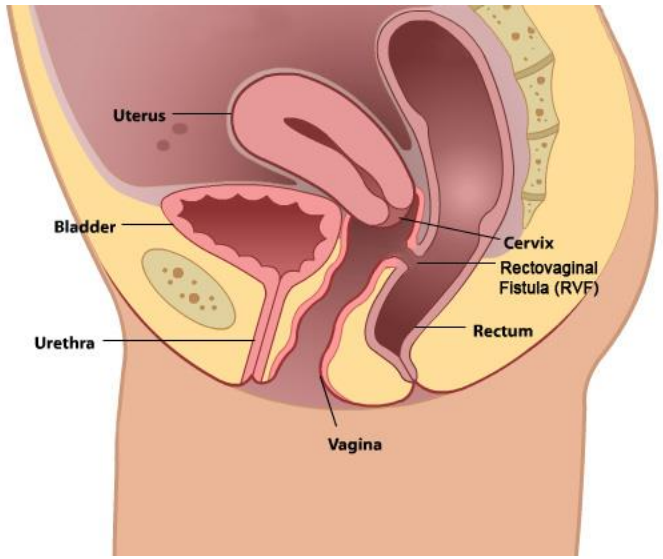
Small bowel obstruction may also occur as a consequence of **inflammation**, **fibrosis** and **stricture formation**.

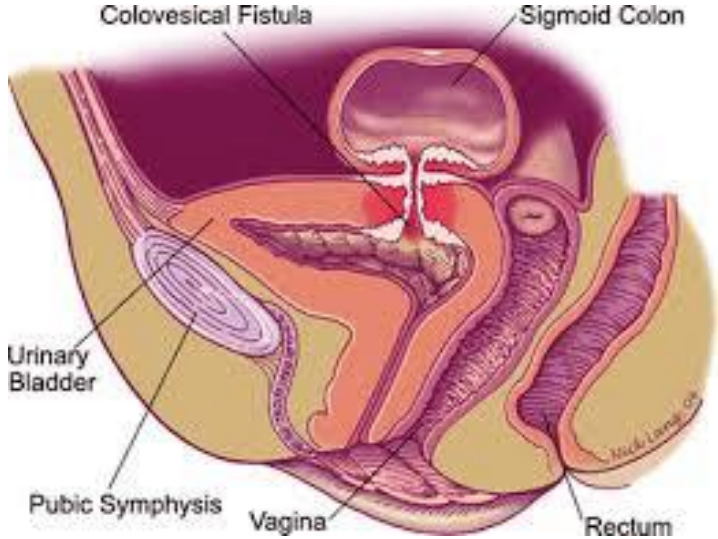
Patients often describe a more generalized **intermittent pain** which is **colicky** with **abdominal distension, vomiting** and **constipation**.

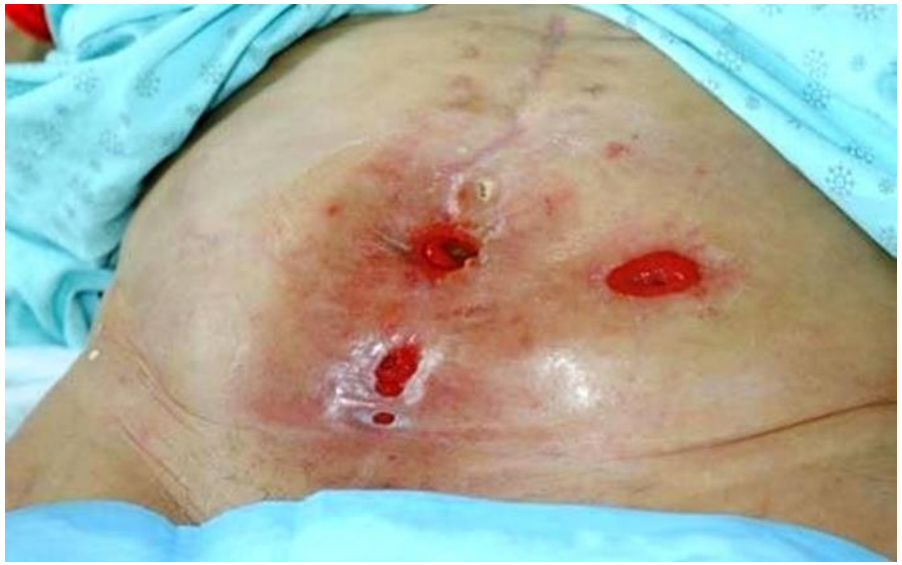
When inflammation or **abscesses** are the predominant pathology, many patients present with **constant pain** and **fever**.

CLINICAL MANIFESTATION - CROHN'S DISEASE

Enteric fistulae occur and may involve the **skin**, **bladder** or **vagina**.







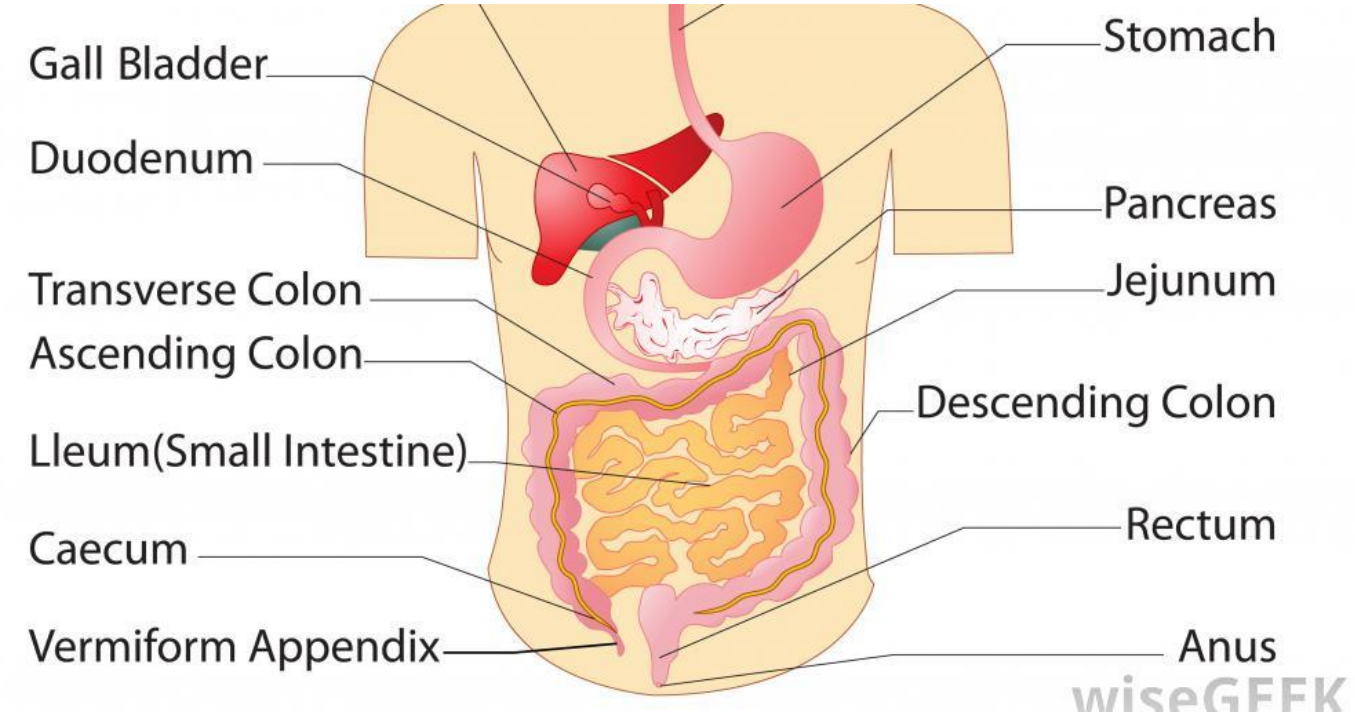
CLINICAL MANIFESTATION - CROHN'S DISEASE

Vitamin B12 and **folic acid** deficiencies predispose to macrocytic anemia.

Bile acid malabsorption also occurs in such patients predisposes them to **cholesterol gallstones** and **oxalate renal stones**.

CLINICAL MANIFESTATION - CROHN'S DISEASE

Patients with severe involvement of the **colon** or the **terminal ileum** often have **electrolyte abnormalities**, **hypoalbuminaemia** and **iron-deficiency anemia**.



CLINICAL MANIFESTATION - ULCERATIVE COLITIS

Typical symptoms of **ulcerative colitis** include **bloody diarrhoea** (the most predominant symptom) with mucus, abdominal pain with fever, and weight loss in severe cases.

Blood loss is more common in **ulcerative colitis** than **Crohn's disease**. The symptoms of ulcerative colitis are similar to Crohn's colitis with patients being **tachycardic**, **anemic**, **febrile**, **fatigued**, **dehydrated** and **thin.**

Approximately **50% of patients** with **ulcerative colitis** have some form of relapse each year, and severe attacks can be life-threatening.

CLINICAL MANIFESTATION - ULCERATIVE COLITIS

In addition to the typical symptoms of ulcerative colitis, patients with **acute severe disease** may present

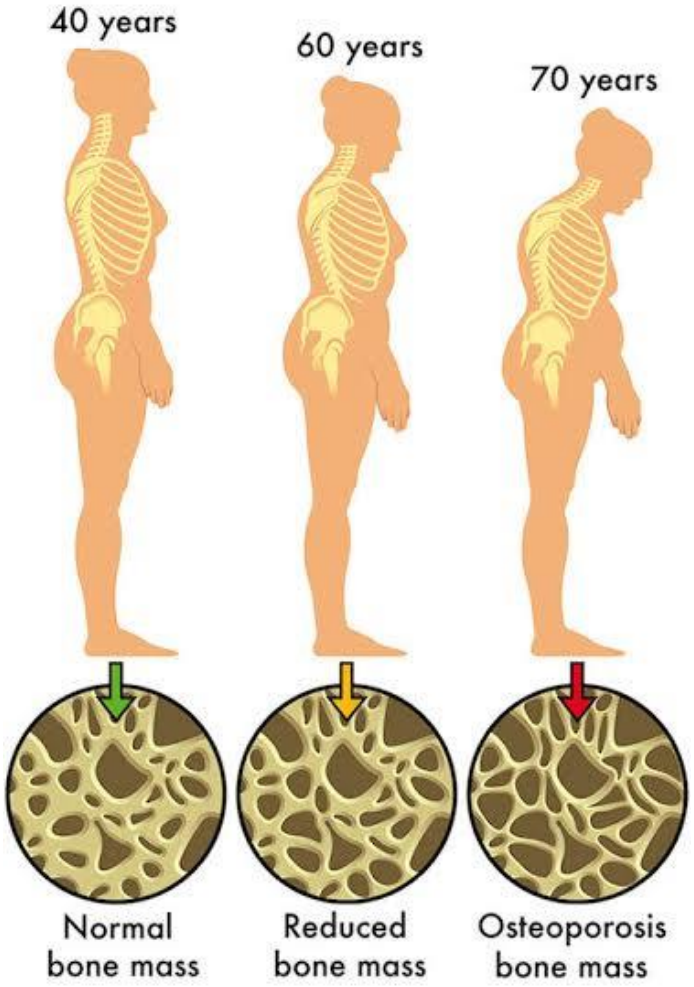
- **with >six bloody stools per day**
- **with a fever (>37.8 °C)**
- **tachycardia (>90 bpm)**
- **anemia (Hb < 10.5 g/dL)**
- **elevated inflammatory markers (ESR > 30 mm/h; C-reactive protein > 8)**

EXTRA-INTESTINAL COMPLICATIONS OF IBD

Around **20–30%** of patients with IBD will present with extraintestinal manifestations.

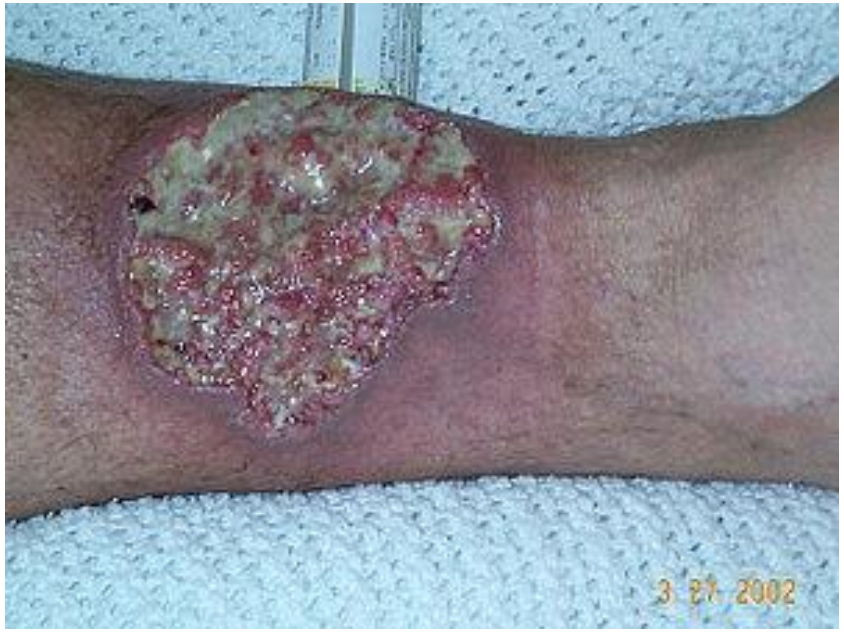
Complications include

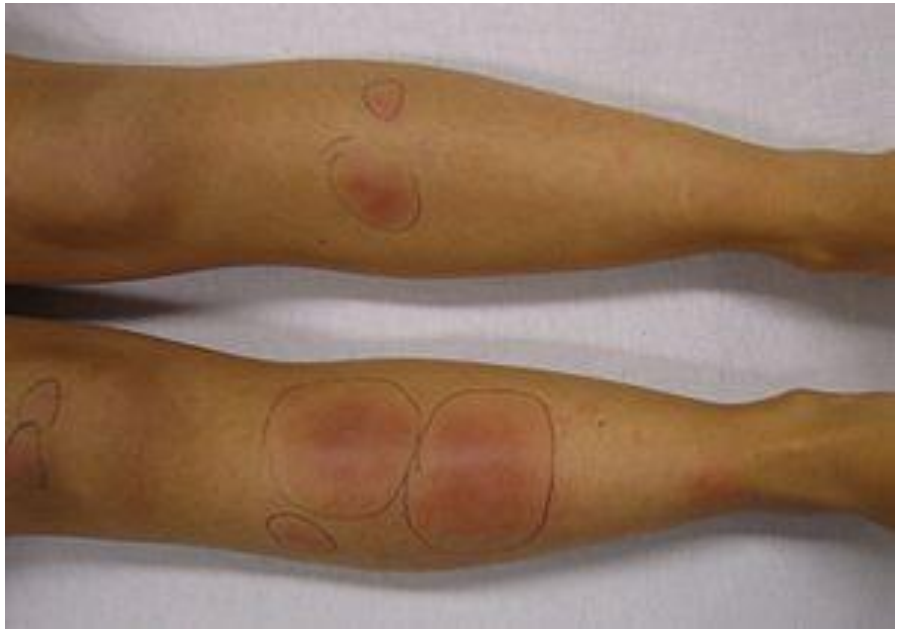
- **Joints** (arthropathies)
- **Bone** (Osteopenia, potentially leading to osteoporosis)



EXTRA-INTESTINAL COMPLICATIONS OF IBD

- **Skin**
  - **Erythema nodosum** is an inflammation of the fat cells under the skin.
  - **Pyoderma gangrenosum** is a condition that causes tissue to become necrotic, causing deep ulcers that usually occur on the legs.



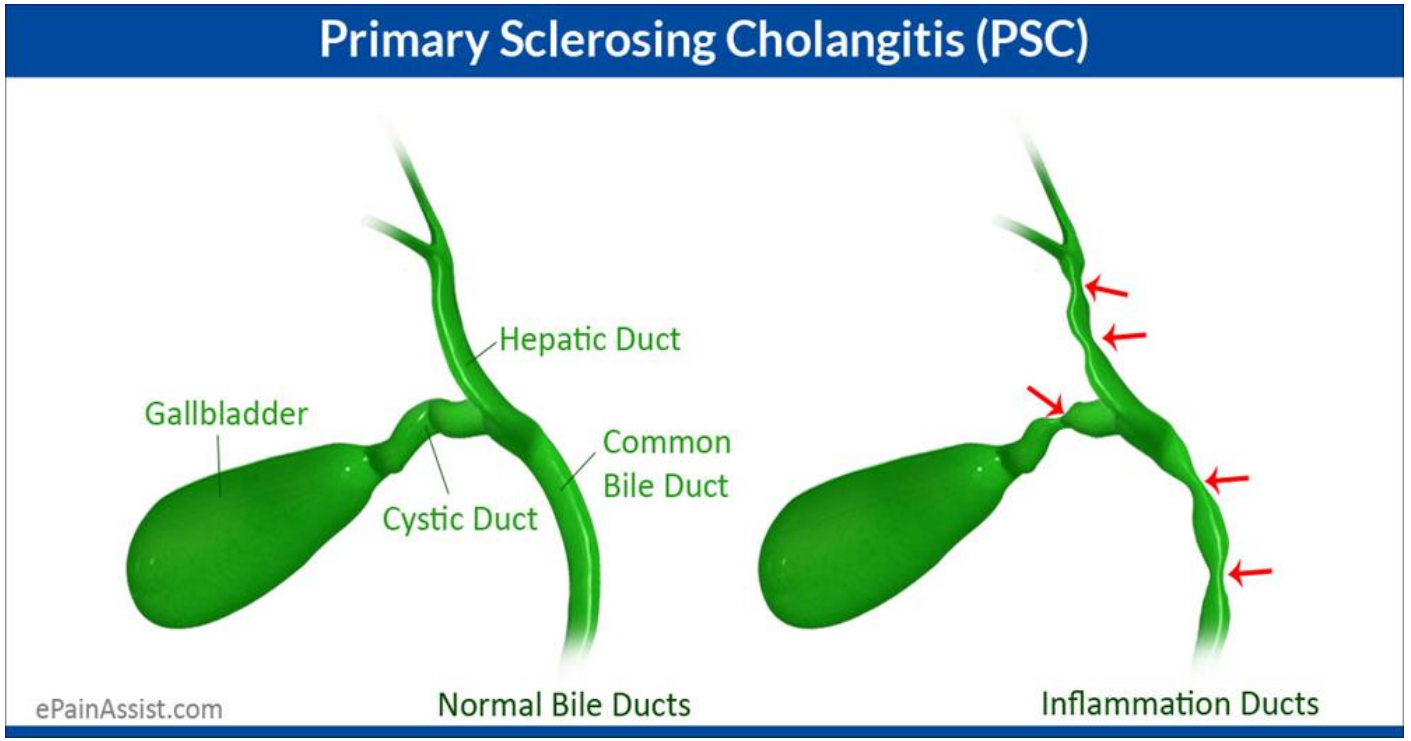


EXTRA-INTESTINAL COMPLICATIONS OF IBD

- **Eyes**
  - **Episcleritis** (intense burning and itching with localized area of blood vessels)
  - **Uveitis** (headache, burning red eye, blurred vision) is often associated with joint and skin manifestations of IBD.

EXTRA-INTESTINAL COMPLICATIONS OF IBD

- **Liver**: biliary complications of IBD are **gallstones** and **sclerosing cholangitis** which occurs in **5%** of patients with **ulcerative colitis** but less frequently in those with Crohn's disease.



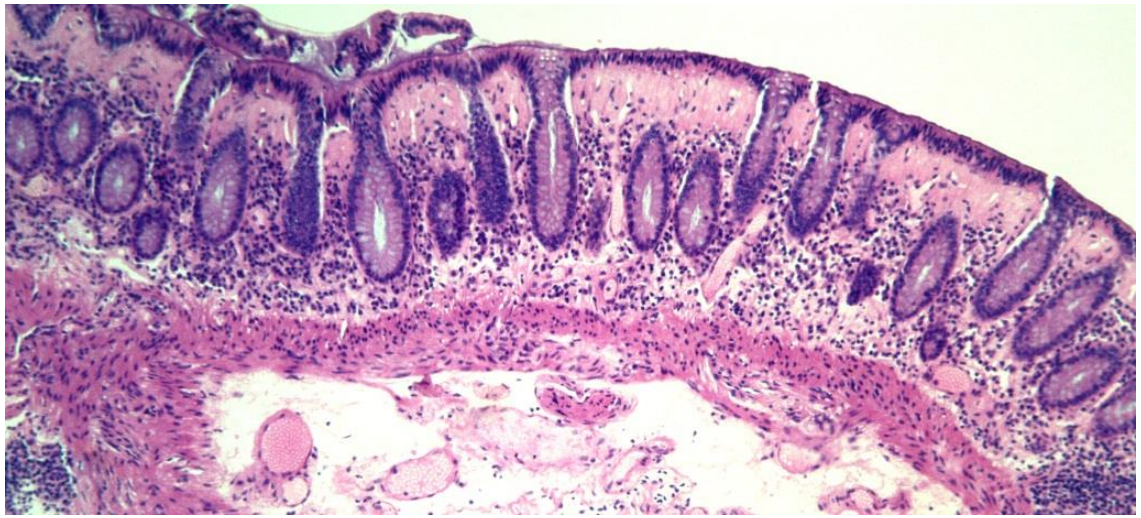
EXTRA-INTESTINAL COMPLICATIONS OF IBD

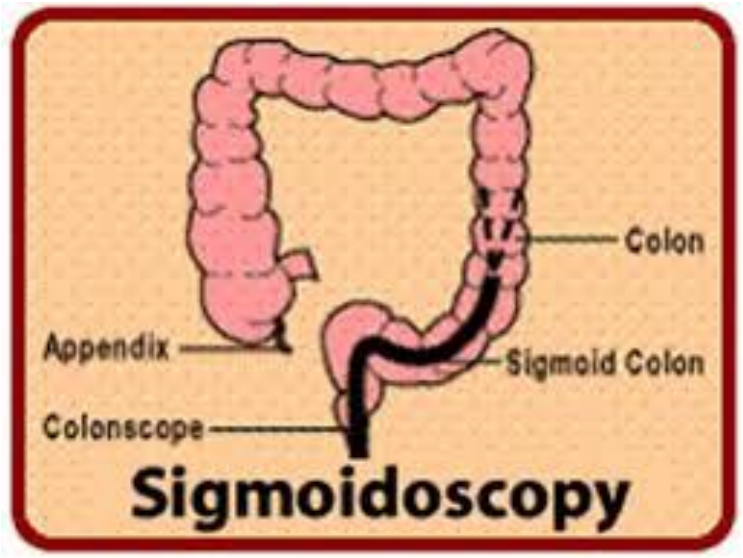
- **Thromboembolic complications** occur in around 1–2% of IBD patients.
- **Anemia:** around **one-third** of patients have **haemoglobin levels below 12 g/dL**.
- The main causes are
  - **chronic intestinal bleeding with iron loss** causes a **microcytic anemia**
  - **chronic inflammatory disease** causes **normocytic anemia**
  - **Folate, iron, vitamin B12 malabsorption** are also common
  - The side effects of commonly used drugs in IBD, for example, **methotrexate and azathioprine** can give rise to symptoms of anemia

INVESTIGATIONS - ENDOSCOPY

The key diagnostic investigation in IBD is lower gastro-intestinal tract endoscopy (**sigmoidoscopy** and **colonoscopy**), which allows

- **direct visualization of the large bowel**
- **histopathological assessment from biopsies**





INVESTIGATIONS - ENDOSCOPY

The risk of developing **colorectal cancer is 7–10%** after 20 years in patients with colonic disease.

Therefore, **routine colonoscopy** is essential in the early detection of **colorectal cancer**.

Treatment response to biologics, for example infliximab, can be assessed via mucosal healing seen at colonoscopy.

INVESTIGATIONS - ENDOSCOPY

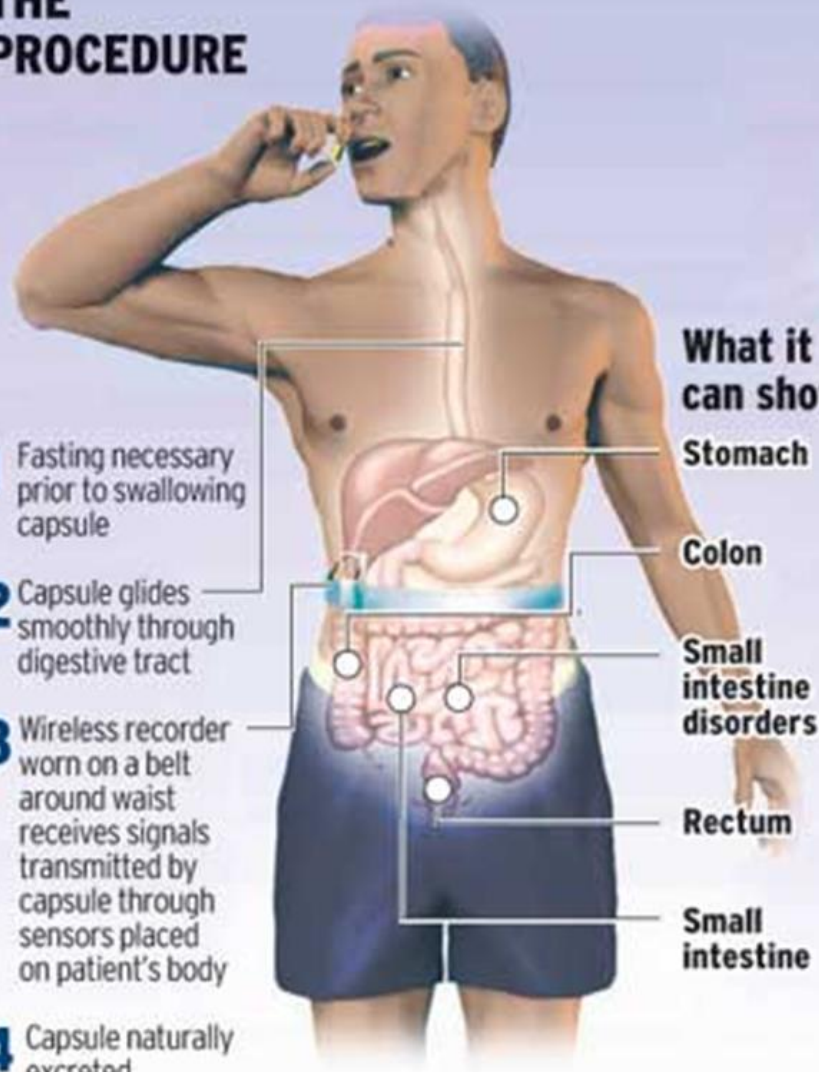
In patients with **severe symptoms**, it is sometimes necessary to delay the colonoscopy because of the **increased risk of perforation**.

Wireless capsule endoscopy is a relatively new procedure where the small bowel can be viewed and can be useful in patients with non-stricturing Crohn's disease.

Capsule endoscopy

A capsule fitted with a disposable mini video camera can examine parts of the small intestine that standard scopes can't reach for diagnosing unexplained bleeding or other abnormalities. The video data is transmitted and stored in a recorder worn on a belt, and is later downloaded to a computer that the doctor can study.

THE PROCEDURE

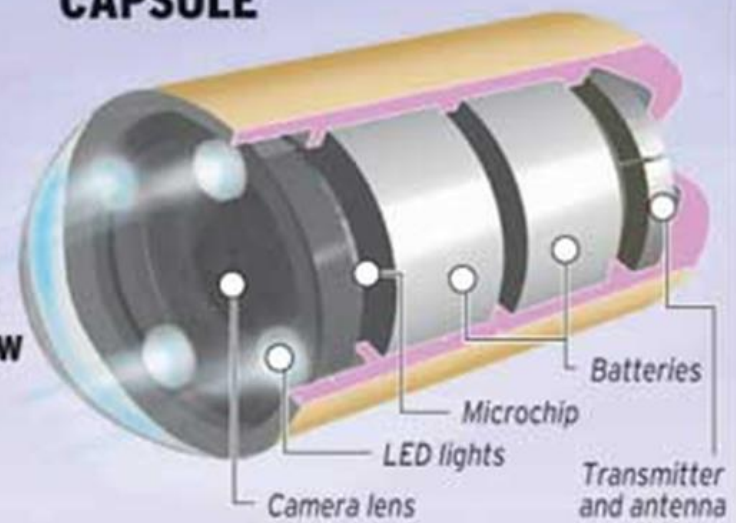


1. Fasting necessary prior to swallowing capsule
2. Capsule glides smoothly through digestive tract
3. Wireless recorder worn on a belt around waist receives signals transmitted by capsule through sensors placed on patient's body
4. Capsule naturally excreted

What it can show

- Stomach
- Colon
- Small intestine disorders
- Rectum
- Small intestine

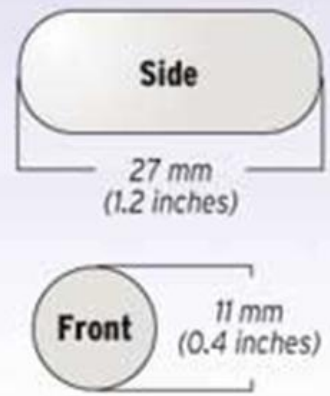
THE CAPSULE



Advantages:

- Painless
- No sedation
- Provides 3-D, color images of small intestines without surgery
- Allows doctors to make early, accurate diagnosis of problems so they can recommend most appropriate treatment

Size:



SOURCE: GIVEN IMAGING

KNIGHT RIDDER/TRIBUNE

INVESTIGATIONS - RADIOLOGY

Radiological imaging is **complementary** to clinical and endoscopic assessment.

Radiological examination still plays a key role in IBD affecting the **small bowel**, although **endoscopy** has generally replaced conventional X-ray examinations of the colon.

Computed tomography (CT scan) and **magnetic resonance imagery (MRI)** are the best radiological methods for locating and defining **fistulae** and **abscesses** in active **Crohn's disease**.

LABORATORY FINDINGS

Although not diagnostic, active disease is suggested in patients

- **raised C-reactive protein (CRP)**
- **raised erythrocyte sedimentation rate (ESR)**
- **low haemoglobin**
- **raised platelet count**
- **low Vitamin B12 may be in patients with chronic terminal ileal disease.**
- **Low folate, serum albumin, magnesium, calcium, zinc and essential fatty acids also indicate chronic inflammation and malabsorption**

LABORATORY FINDINGS - STOOL TESTS

Red and **white blood cells** can be seen on microscopic examination of fresh stools.

Microscopic identification of infective cells such as **amoeba** may also be visualized.

Stool tests **do not diagnose IBD** but contribute to excluding alternative diagnoses.

TREATMENT OF INFLAMMATORY BOWEL DISEASE

At present there is **no cure for IBD** since the exact cause of the condition is unknown.

A wide range of drugs and nutritional supplements are available to maintain the patient in **long periods of remission** in both Crohn's disease and ulcerative colitis.

However, **surgical intervention** will eventually become necessary when the patient relapses and fails to respond to drug therapy.

NUTRITIONAL THERAPY

Nutritional therapy can be considered as an **adjunctive** or **primary** treatment.

Although a potential problem for all patients with IBD, patients with **Crohn's disease** are at particular **risk of becoming malnourished** and developing a variety of nutritional deficiencies.

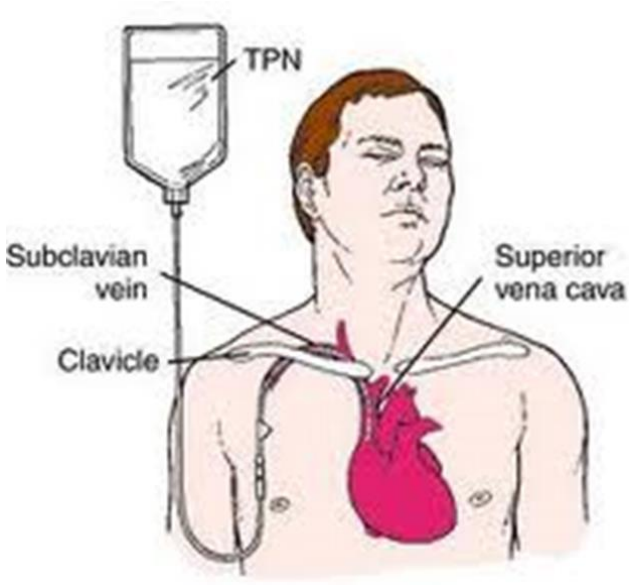
NUTRITIONAL THERAPY

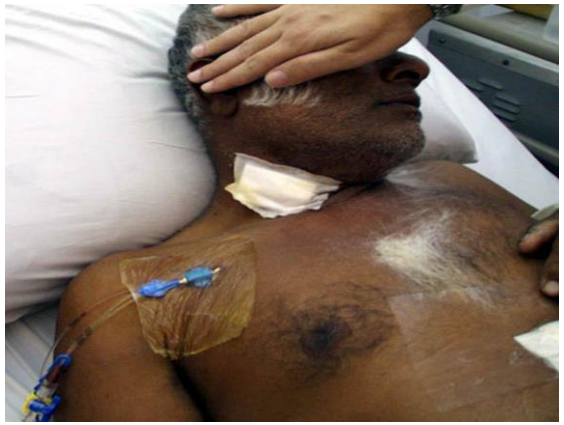
Patients who have **functional** and **structural damage** or **extensive small bowel resection** may experience many nutritional deficiencies because of malabsorption. They may suffer from:

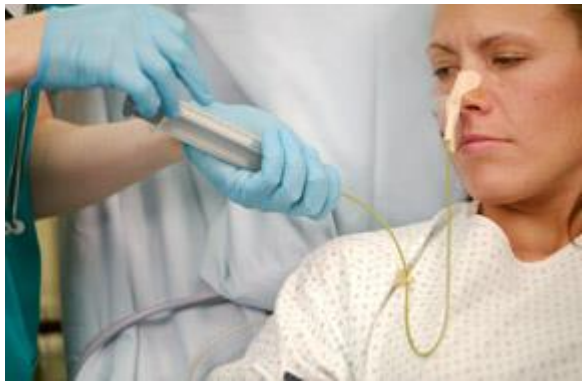
- Iron depletion
- hypoproteinaemia
- deficiencies in water- and fat-soluble vitamins
- deficiencies trace elements
- deficiencies electrolytes

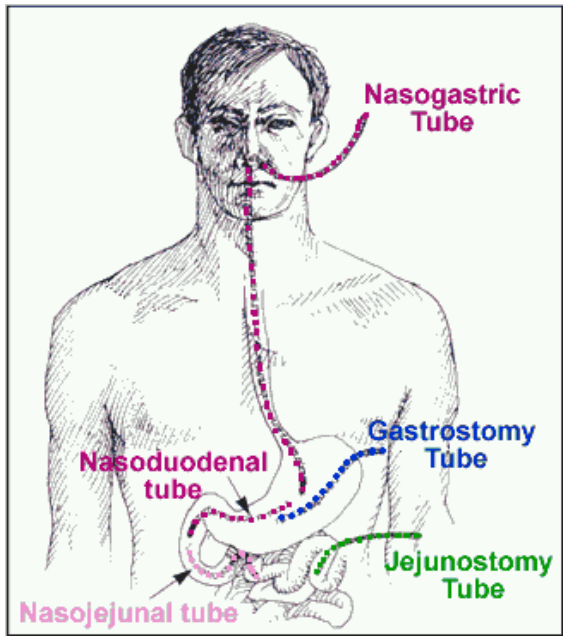
NUTRITIONAL THERAPY

Enteral nutrition could be the first choice. However, sometimes enteral nutrition is not indicated or adequate, a **Total Parenteral Nutrition (TPN)** regimen may be prescribed. Some patients receive concurrent enteral and parenteral feeding.









DRUG TREATMENT

The main goals of drug treatment are to

- **treat acute attacks effectively**
- **induce and maintain remission**
- **limit drug toxicity**
- **modify the pattern of disease**
- **avoid and/or manage complications**
- **select patients who will benefit from surgery**

DRUG TREATMENT

The choice of drug and route of administration depends

- **on the site** and **severity of the disease**
- **treatment history**
- **patient preference** (patients will continue on medication for years)
- **acceptability**
- **possible side effects** (not only affect choice but will impact on medication adherence)

CORTICOSTEROIDS

Hydrocortisone and **prednisolone** are the mainstay of treatment in **active** ulcerative colitis and Crohn's disease.

Prednisolone administered **orally** or **rectally** is the steroid of choice, although in emergency situations **hydrocortisone** or **methylprednisolone** is used when the **parenteral** route is required.

CORTICOSTEROIDS

Corticosteroids have direct anti-inflammatory and immunosuppressive actions which rapidly control symptoms.

They can be used either alone or in combination, with a suitable **mesalazine** (aminosalicylates) formulation or **immunosuppressant**, to induce remission.

CORTICOSTEROIDS

Oral corticosteroids should not be used for maintenance treatment because of **serious long-term side effects**, and **abrupt withdrawal should be avoided**.

Patients should be maintained on **aminosalicylates** or **immunosuppressants**, as appropriate, or referred for **surgery**.

CORTICOSTEROIDS - FORMULATIONS

Oral prednisolone will control mild and moderate IBD and 70% of patients improve after **2 - 4 weeks of 40 mg/day.**

This is gradually reduced over the next 4–6 weeks to prevent **acute adrenal insufficiency** and **early relapse**.

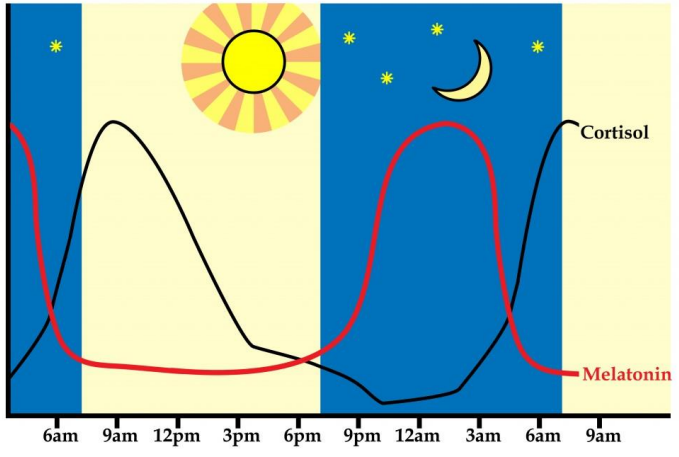
An example of a reducing regimen for oral steroids

40 mg/day for 1 week
30 mg/day for 1 week
20 mg/day for 4 weeks
15 mg/day for 1 week
10 mg/day for 1 week
5 mg/day for 1 week then stop

CORTICOSTEROIDS - FORMULATIONS

Oral corticosteroids should be taken in the morning to mimic the **diurnal rhythm** of the body's **cortisol secretion** and prevent **sleep disturbance**.

Uncoated steroid tablets are suitable for most patients while **enteric-coated** preparations do not offer any proven advantage and should **be avoided in patients with short bowel inflammation** or **strictures** because of poor absorption and bolus release at stricture sites.



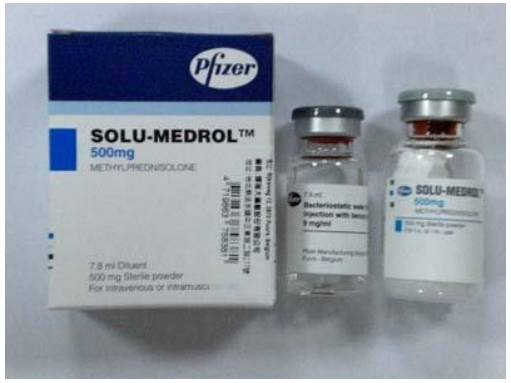
CORTICOSTEROIDS - FORMULATIONS

Severe extensive disease requires hospitalization. Patients are given one of the followings

- **IM/IV hydrocortisone** sodium succinate 100 mg three or four times a day for 5 days.

or

- **IM/IV methylprednisolone** 15–20 mg three or four times a day, for 5 days.



CORTICOSTEROIDS - FORMULATIONS

Rectal corticosteroid preparations are available as suppositories, and liquid enemas.

Hydrocortisone is readily absorbed from the rectal mucosa with high peak concentrations compared to **prednisolone enema**.

Topical preparations may play a role either **alone** or in **combination** with **oral steroids**.

CORTICOSTEROIDS - FORMULATIONS

Budesonide, available orally and rectally, is currently licensed for **Crohn's disease** affecting the ileum and descending colon.

It is **less effective** than **conventional corticosteroids** in inducing remission in active Crohn's disease, but has fewer side effects than **prednisolone**.

AMINOSALICYLATES

The aminosalicylates currently licensed for the treatment of IBD include **sulphasalazine**, **mesalazine**, **olsalazine** and **balsalazide**. Their mode of action is unclear.

AMINOSALICYLATES

Available as **oral** or **rectal preparations**, aminosalicylates can be used in **combination with steroids** to induce and maintain remission, in mild to moderate ulcerative colitis.

The use of **aminosalicylates** in **Crohn's disease** is less well established.

There is evidence of patient benefit with **high-dose mesalazine (over 2 g/day)** in **reducing relapse post-small bowel resection (Crohn's disease)**.

AMINOSALICYLATES

The **optimal dose** of **sulfasalazine** to achieve and **maintain remission** is usually in the range of 2–4 g per day in 2–4 divided doses.

Acute attacks require 4–8 g per day in divided doses until remission occurs, but at these doses associated side effects are often observed.

Mesalazine is tolerated by **80%** of patients who are **intolerant** of **sulphasalazine**.

AMINOSALICYLATES

Mesalazine enemas (1 g in 100 mL), **foam enemas** (1 g per application) or **suppositories** (250 mg, 500 mg and 1 g) are effective alternatives for treating distal ulcerative colitis and proctitis (an inflammation of the lining of the rectum).

Rectal administrations of Aminosalicylates formulations are significantly better than **rectal corticosteroids** in inducing remission in ulcerative colitis but steroids are considerably cheaper.

In **severe ulcerative colitis**, oral and topical formulations should be combined to give prompt symptom relief. Topical and oral Aminosalicylates is better than either alone.

IMMUNOSUPPRESSANTS

Azathioprine, 6-mercaptopurine, methotrexate, cyclosporine and mycophenolate are immunosuppressants used

- in patients unresponsive to steroids and aminosalicylates
- in patients who relapse when steroids are withdrawn.

They are used to induce and maintain remission. **All are unlicensed for use in IBD but are routinely used**.

Treatment may be for up to **5 years** because earlier withdrawal increases the rate of relapse. They can take several weeks to work and require regular monitoring.

IMMUNOSUPPRESSANTS - THIOGUANINES

Thioguanines (azathioprine and mercaptopurine)

Oral maintenance doses for **azathioprine** are usually 2–2.5 mg/kg/day and for **mercaptopurine**, 1–1.5 mg/kg/day.

Doses are adjusted to **patient response**, **tolerance**, **white cell** and **platelet counts**.

Patients are usually prescribed a reducing dose of corticosteroid in addition because mercaptopurine and azathioprine can take several weeks to show a therapeutic benefit.

IMMUNOSUPPRESSANTS - THIOGUANINES

The most common side effects azathioprine and mercaptopurine occur within 2–3 weeks of starting treatment and rapidly stop on withdrawal.

These include **flulike symptoms** (myalgia, headache), **nausea** and **diarrhoea**.

One of the most significant drug interactions is with **allopurinol** which **inhibits the metabolism** of azathioprine and mercaptopurine. Patients receiving these drugs concomitantly should have their dose of azathioprine reduced to approximately one-third to a quarter of the usual dose.

IMMUNOSUPPRESSANTS - METHOTREXATE

A **low-dose** regimen of **methotrexate** is effective in inducing and maintaining remission in patients with chronically active **Crohn's disease**.

Patients receive **once weekly** doses of methotrexate ranging from **15** to **25 mg** on the same day each week.

IMMUNOSUPPRESSANTS - METHOTREXATE

These can be given orally or by subcutaneous or intramuscular injection.

Oral medication is more practical, although parenteral administration may be more effective and better tolerated.

Methotrexate is reserved for patients **intolerant** or **unresponsive** to **Thioguanines**.

IMMUNOSUPPRESSANTS - METHOTREXATE

Adverse effects associated with **methotrexate** are essentially **gastro-intestinal** (nausea, vomiting, diarrhoea and stomatitis).

These may also be **reduced** by prescribing weekly doses of **folic acid 5 mg**.

Monitoring is undertaken because of the serious side effects of **hepatotoxicity**, **bone marrow suppression** and **pneumonitis**.

IMMUNOSUPPRESSANTS - CYCLOSPORINE

Studies suggest that cyclosporine is effective rescue therapy for severe **ulcerative colitis** failing to respond to intravenous steroids. Its use in Crohn's disease is unproven.

When patients with severe colitis fail to show a response to treatment with parenteral steroids, then cyclosporine at an intravenous dose of 2 mg/kg/day should be considered.

If patients **respond** to **parenteral cyclosporine** they can subsequently be maintained on an **oral** dose **for 3–6 months**.

IMMUNOSUPPRESSANTS - CYCLOSPORINE

Major complications include **nephrotoxicity**, **neurotoxicity**, **hepatotoxicity** and **hypertension**.

Cyclosporine blood levels should be **monitored** and **maintained** within the range of **100–200 ng/mL**.

Grapefruit juice, macrolide antibiotics (mainly erythromycin and clarithromycin), ketoconazole, fluconazole, itraconazole, diltiazem, verapamil, and oral contraceptives are just some of the drugs that **increase cyclosporine levels** and **toxicity**.

BIOLOGIC AGENTS

Tumor Necrosis Factor alpha (TNF-α) are

- efficacious in treating signs and symptoms of Crohn's disease and ulcerative colitis
- reducing corticosteroid requirements
- reducing draining fistulae
- achieving mucosal healing
- reducing the need for major abdominal surgery or hospitalization

BIOLOGIC AGENTS

They are indicated for patients who have failed or are intolerant or who have contraindications to conventional therapy including

- **corticosteroids**
- **immunomodulators**

Not all patients will require biological therapy which is **expensive** and is a significant **cost** to the Health Service or to the patient.

Some patients may get **greater benefit** from early use of these agents such as patients who are **steroid dependent** or who have **complex fistulising disease**.

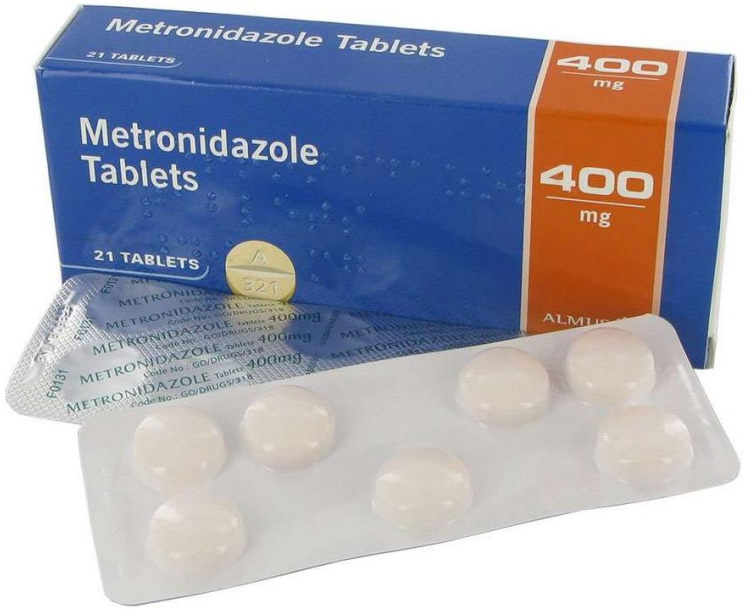
BIOLOGIC AGENTS

Biologic agents that are licensed for use in IBD are **Infliximab** and **adalimumab**.

ANTIBIOTICS

Metronidazole has been used in **Crohn's disease**

- **associated with perianal disease**
- **sepsis associated with fistulae**
- **perforation and bacterial overgrowth in the small bowel**



Doses of 0.6–1.5 g/day are typically used and well tolerated.

Metronidazole appears to be ineffective in **ulcerative colitis**.

ANTIBIOTICS

The associated paresthesia appears to be **dose related**, occurring frequently with treatment of **greater than 3 months duration**.

In such patients, doses should be gradually reduced or the drug alternated with another antibiotic, for example, **ciprofloxacin**, **tetracycline**, which have shown some limited benefit.

Other treatments

THALIDOMIDE

The use of **thalidomide** is restricted to **refractory** cases of **Crohn's disease**.

Daily doses in the range of 50–400 mg have proved beneficial when used for periods of 1 week to several months.

Side effects during treatment include **sedation**, **dry skin** and **reduced libido**.

Thalidomide is teratogenic and should never be used in women of child-bearing age.

ANTIDIARRHEALS

Codeine, **diphenoxylate**, and **loperamide** should be used with caution to treat diarrhoea and abdominal cramping in IBD.

Their use may mask

- **Inflammation**
- **Infection**
- **Bowel obstruction**

COLESTYRAMINE

Colestyramine has been used in **Crohn's disease** following ileal resection to reduce diarrhoea associated with bile acid malabsorption.

Doses of up to 4 g three times a day inhibit the secretion of water and electrolytes stimulated by bile acids.

FISH OILS (OMEGA-3 FATTY ACIDS)

Fish liver oils have been used with some success in treatment of both ulcerative colitis and Crohn's disease.

MISCELLANEOUS TREATMENTS

There are many limited trials, studies and case series in the literature evaluating other therapies for ulcerative colitis and Crohn's disease.

These include probiotics, sodium cromoglicate, bismuth and arsenic salts, sucralfate, nicotine, somatostatin analogues, lidocaine, chloroquine, d-penicillamine, antituberculous agents, heparin, aloe vera, and worm therapy (helminths).

SURGICAL TREATMENT

Fifty to **eighty** percent of **Crohn's disease** patients will require surgery within **5–10 years** of diagnosis.

In contrast, **20–30%** of **ulcerative colitis** patients will usually undergo **colectomy** with **5 years**.

ARE YOU FEELING BORED????