Inflammatory bowel disease

Objectives:

- What is the disease?
- Epidemiology of IBDs
- Pathophysiology of IBDs
- Ulcerative colitis
- Crohn's disease

Resources:

- Davidson's.
- Slides
- Surgical recall.
- Raslan's notes.
- Team 434

Done by: Raghda AlQassim & Sara AlKhalifa
Leaders: Abdulrahman Alsayyari & Monerah Alsalouli
Reviewed by: Ahmad Alyahya
Thanks to Afnan Almalki

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We highly advise you to study IBD medicine lecture first

Once you stop learning
you start dying.

Inflammatory Bowel Disease

Introduction:

- Inflammatory bowel disease (IBD) is a term generally used to denote two diseases of unknown etiology with similar general characteristics:
    - Ulcerative Colitis (**UC**)
    - Crohn's Disease (**CD**)
- The distinction between the two entities can usually be established based on clinical history and examination and pathologic criteria, including:
    - Hx and Ex.
    - Radiologic and Endoscopic studies,
    - Gross appearance.
    - Histology.
- About 10% to 15% of patients with inflammatory disease confined to the colon, a clear distinction cannot be made, and the disease is labeled **indeterminate colitis** (it means they only have isolated colon disease and we can't determine whether it's crohn's or ulcerative colitis. If stomach, small intestine, mouth are involved this is crohns طول على but if it's isolated colon here is the problem we don't know if its UC or CD so we call it indeterminate colitis.
- The medical and surgical management of ulcerative colitis and Crohn's disease often differ significantly.
- In 20% of cases, grossly it looks like UC while microscopic features say it is CD
- Also, sometimes the biopsy looks like UC but the clinical features suggests CD.
- In medicine it's not very important to distinguish the two diseases because they have the same treatment. However, in surgery we have to distinguish the two diseases because ulcerative colitis could be treated completely with surgery. But if crohns is treated with surgery, it is very likely that the patient will relapse.

Pathophysiology:

The etiology is not completely understood, but several factors play a role:

1. Host factors: Genetics (Twins, Relatives, & children) Family history is the most important and greatest risk factor!
2. Environmental factors:
    a. **Smoking** the only difference between UC and CD regarding risk factors (causes Crohn's, protective against UC).
        i. Smoking is known to exacerbate existing Crohn's disease and can accelerate its recurrence after resection.
        ii. Smoking appears to confer protective effect against the development of ulcerative colitis as well as providing a therapeutic influence; nicotine has been reported to induce remission in some cases.
    b. Infection (measles and mycobacterium avium paratuberculosis)
    c. immunologic.
    d. migration to endemic area (e.g. Canada)
3. Appendectomy appear to be **protective** in developing ulcerative colitis.

Current theory: There is a genetic defect that affects the immune system, so that it attacks the bowel wall in response to stimulation by an offending antigen, like a bacteria, a virus, or a protein in the food.

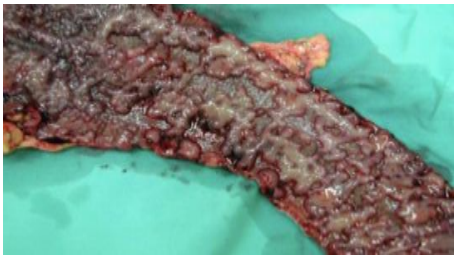
Ulcerative Colitis

Definition:

- A chronic disease that affects the mucosa and submucosa, with sparing of the muscularis of the rectum and colon.
- Surgery is curative.
- In the majority of cases, the disease is contiguous, affecting the rectum and extending proximally. In 5% of cases, it is segmental and the rectum is occasionally spared. “Proctitis is the most common”

Epidemiology:

- There appears to be a seasonal variation in the activity of the disease, with onset as well as relapse occurring statistically more often between August and January.
- Commonly affects patients younger than 30 years.
- A small secondary peak in the incidence occurs in the sixth decade. It has 2 peaks.



Macroscopic appearance:

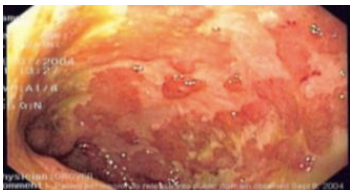
- Despite the disease's name, ulceration of the mucosa is not invariably present. MCQ!! In UC the earliest manifestation is not ulcers unlike **CD**

In CD the earliest gross appearance is ULCERS! But in UC the earliest appearance is INFLAMMATION of the mucosa! (يقول كتب سؤال عنه (كاتبين ١٠ أسئلة من المحاضرة وهم يختارون)

- The typical gross appearance of ulcerative colitis is hyperemic mucosa. لا يلعب عليكم السؤال UC doesn’t have ulcers it has hyperemic edematous mucosa, ulceration might happen but late on with complications.
- Friable and granular mucosa is common in more severe cases, and ulceration may not be readily evident, especially early in the course of the disease.
- Ulceration may appear and vary widely, from small superficial erosions to patchy ulceration of the full thickness of the mucosa.
- **Rectum** is almost always involved with the inflammatory process.

  In fact, rectal involvement (proctitis) is the sine qua non يعني حتمي لازم يكون موجود means 99% of times the rectal is involved of the disease, and the diagnosis should be seriously questioned if the rectal mucosa is not affected.

- The mucosal inflammation extends in a continuous (no skip lesions) fashion for a variable distance into the more proximal colon. “Begins distally at rectum then extends proximally to a variable distance”.
- Erythematous mucosa, has a granular surface that looks like sandpaper (enlarged ulcer⇒ sandpaper)
- Loss of haustrations. Colon becomes thick and rigid.
- Pseudopolyps, or inflammatory polyps, represent regeneration of inflamed mucosa and are composed of a variable mixture of non-neoplastic colonic mucosa and inflamed lamina propria we have neoplastic polyps and non-neoplastic polyps.
  Non neoplastic polyps have pseudopolyp and inflammatory polyps.
  When you hear pseudopolyp think of IBD (pseudopolyps happen in small intestine, colon, crohn's or ulcerative colitis)



‘Backwash ileitis’ may produce a dilated and featureless terminal ileum, in which the mucosa appears granular. In contrast to Crohn's disease, ulcerative colitis does not involve the terminal ileum except in cases of backwash ileitis we know that small bowel is only affected in crohn's, so how do you differentiate if this terminal ileum inflammation is in CD or UC? In CD severe narrowing, scarring or fistula develops, but this never happens in UC (so you will see dilation in ulcerative colitis).

Microscopic appearance:

The inflammation is restricted to the mucosa and the submucosa **of the large bowel.** In **severe episodes**, there may be **full-thickness involvement with inflammatory infiltrate**.

- The most characteristic lesion is crypt abscesses (Collections of neutrophils fill and expand the lumen of individual crypts of Lieberkühn, not specific happens in crohn's disease and infectious colitis also but happens mostly in UC, If you see stool culture negative and the crypt abscess not in small bowel think of UC.

Major presentation:

- Diarrhea with passage of mucus/blood (4 to more than 10), 1st DDx in bloody diarrhea
- Fecal urgency. Patients with ulcerative colitis tend to have more urgency than those with Crohn's disease
    - likely because ulcerative colitis is invariably associated with distal proctitis. Severe inflammation in the rectum makes it lose the elasticity and extensibility يصير كأنه ماصورة causes tenesmus and more frequent of passing stool.
- Rectal bleeding bloody diarrhea because of rectal involvement and watery diarrhea in crohn's disease.
- Tenesmus (feeling of painful incomplete defecation)
- Patients with the acute onset of ulcerative colitis often complain of abdominal discomfort, but the pain is seldom as severe as that found in patients with Crohn's disease. Why? Because the small bowel in not involved.

So 3 features in UC different than crohn's;

1. tenesmus
2. more frequent in passing stools
3. bloody diarrhea because the rectal in involved

Extraintestinal manifestations:

- arthritis, ankylosing spondylitis, erythema nodosum, pyoderma gangrenosum, and primary sclerosing cholangitis.
- Arthritis, particularly of the knees, ankles, hips, and shoulders, occurs in about 20% of patients, typically in association with increased activity of the intestinal disease.
- Ankylosing spondylitis occurs in 3% to 5% & Primary sclerosing cholangitis (PSC) occurs in 5% to 8% of patients with ulcerative colitis.
- Colectomy has no effect on the course of these 2 conditions.

Two extra-intestinal manifestations if they develop they cannot be cured by surgery, what are they? AN MCQ QUESTION!

1-PSC (primary sclerosing cholangitis).

2-Ankylosing spondylitis.

Colectomy has no effect in the course of these 2 conditions!

Indications for surgery: (5 months, heartburn, endoscopy, for 13 hours fasting, H pylori)

- Fulminant colitis with toxic megacolon
- Massive bleeding
- Intractable disease
- Dysplasia or carcinoma
- Malnutrition and growth retardation may necessitate resection in pediatric and adolescent patients.

Crohn's disease

Definition:

- A **chronic**, **transmural** inflammatory disease usually gradual of the GI tract of **unknown** cause. Idiopathic, transmural, chronic inflammation, affects the whole GI from mouth to the anus! عادها ٤ مرات
- Crohn's disease can involve any part of the alimentary tract **from the mouth to the anus** but most commonly affects the small intestine, colon, rectum & anus.
- Crohn's disease can also involve the mouth, esophagus, stomach, duodenum, and appendix. Involvement of these sites can accompany disease in the small or large intestine, but in only rare cases have these locations been the only apparent sites of involvement.
- The involvement of both large and small intestine has been noted in about 55% of patients.
- 30% of patients present with small bowel disease alone.
- 15%, the disease appears limited to the large intestine.
- About 80% have small bowel involvement, mostly the terminal ileum.
- The single strongest risk factor for developing disease is having a relative with Crohn's disease. "Not in the slides but the doctor mentioned it".

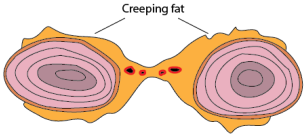
Epidemiology:

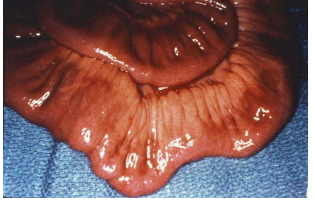
- Crohn's disease primarily attacks young adults in the second and third decades of life, However, a bimodal distribution is apparent with a second, smaller peak occurring in the sixth decade of life. It has 2 peaks: 1-second and third decades. 2-sixth decade.
- The risk for developing Crohn's disease is about two times higher in smokers than in nonsmokers. The patients once they smoke after the surgery they will go back to do another surgery!

Macroscopic appearance:

- The disease process is discontinuous and segmental. Imp الحمدلله ما يأخذ القولون كله يأخذ أماكن ويخلي أماكن عشان كذا نشوف skipped areas grossly
- In patients with colonic disease, rectal sparing is characteristic of **Crohn's disease** and helps to distinguish it from **ulcerative colitis**. When a patient comes with a whole colon affected but the rectum is spared > its most likely CD (don't say CD yet)
- Perirectal and perianal involvement occurs in about 1/3 of patients with Crohn's disease, particularly those with colonic involvement. Perianal disease (fissure, fistula stricture, or abscess) is common and may be the sole presenting, perianal fistula or disease might be the only presentation, feature in 5% of patients and may precede the onset of intestinal disease by months or even years. Crohn's disease should be suspected in any patient with multiple, chronic perianal fistulas.

At exploration: how do we see the GI grossly in Crohn's? laparoscopy فتحة صغيرة بالبطن للمنظار not endoscopy.



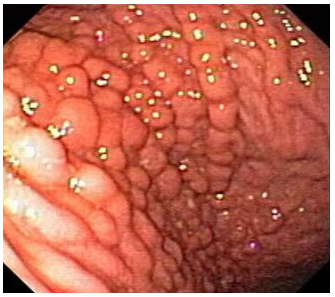


- Thickened grayish-pink or dull purple-red loops of bowel, thick gray-white exudate or fibrosis of the serosa.
- Skip areas areas of diseased bowel separated by areas of grossly appearing normal bowel.
- Extensive fat wrapping "creeping fat"remember the name! fat in the mesentery يجي كأنه لاف على السمول باول caused by the circumferential growth of the mesenteric fat around the bowel wall. (PIC)
- With early acute intestinal inflammation, the bowel wall is hyperemic and boggy.
- As the inflammation becomes chronic, fibrotic scarring develops and the bowel wall becomes thickened and leathery in texture.
- Involved segments often are adherent to adjacent intestinal loops or other viscera, with internal fistulas common in these areas. (Inflammation >> scarring and healing >> fistula formation)
- The mesentery of the involved segment is usually thickened, with enlarged lymph nodes.

On opening the specimen:

- The **earliest** gross manifestation of Crohn's disease is the development of small mucosal ulcerations called **aphthous ulcers**. what's the earliest manifestation in crohn's? Ulcers. Very imp.
- Aphthous ulcers appear as red spots or focal mucosal depressions.
- As the inflammation progresses, the aphthous ulcers enlarge and become stellate.
- Abscess, fistula, fissures, and edematous skin tags. In early stages we have inflammation then this patient will either have 1-a scar (healing by fibrosis) or 2-fistula or perforation (rare)
- Fistula (either small bowel with small bowel, small bowel with vagina, small bowel with bladder) مو كل الفيستويولا نعالجهم
- The ulcers are characteristically linear and may coalesce to produce transverse sinuses with islands of normal appearing mucosa in between, thus giving the characteristic **cobblestone appearance** (pic) اول شي تطلع التقرحات وكل ما يزيد الالتهاب هذي التقرحات تتوزع علي الميوكوزا فبيصير عندي أكثر من تقرح واحد. الجسم بيحاول يطيب ويعالج هذي التقرحات فيبني طبقات طبيعية فوق التقرحات والطبقات المريضة فيصير شي اسمه كوبل ستونز زي الشوارع الي في بريطانيا

- Stricturing
- Mucosal ulcerations may penetrate through the submucosa to form intramural channels that can bore deeply into the bowel wall and create sinuses, abscesses, or fistulas.



Microscopic appearance:

- Mucosal and submucosal edema may be noted microscopically before any gross changes.
- A chronic inflammatory infiltrate appears in the mucosa and submucosa and extends transmurally.
- This inflammatory reaction is characterized by extensive edema, hyperemia, lymphangiectasia, an intense infiltration of mononuclear cells, and lymphoid hyperplasia.
- Well-formed lymphoid aggregates in an edematous fibrotic submucosa is a classic histological feature of the disease.
- Focal ulceration (deep fissuring ulcers).
- Non-caseating Granuloma with Langerhans' giant cells. Granulomas appear later in the course and are found in the wall of the bowel or in regional lymph nodes in 60% to 70% of patients.

19 y/o male patient with failure to thrive (he looked like a 10 years old boy) came with IBD "CD or UC. Unknown!" He showed resistant to all medications so we did total colectomy and end ileostomy and we found granuloma in the submucosa > when you see non-caseating granuloma it's Crohn's!

Major presentation:

- The **most common** symptom is intermittent **colicky** abdominal pain, most commonly in the **lower right abdomen**. The pain may be more severe and localized and may mimic the signs and symptoms of acute appendicitis.
- Watery Diarrhea is the next most common symptom and is present, at least intermittently (interspersed with asymptomatic periods of varying lengths) in about 85% of patients.
- In contrast to ulcerative colitis, patients with Crohn's disease typically have fewer bowel movements, and the stools rarely contain mucus, pus, or blood non-bloody diarrhea (it's watery) and they don't have **tenesmus** why? Because the rectal is spared!

Systemic nonspecific symptoms:

- Low grade fever (present in about ⅓)
- Malabsorption and weight loss
- Loss of strength.
- Malaise.

Complications:

- Obstruction due to scarring and fibrosis
- Perforation very rare.
- Fistulas occur between the sites of perforation and adjacent organs, such as loops of small and large intestine, the urinary bladder, the vagina, the stomach, and sometimes the skin, usually we don't operate on fistula unless there's complications. In case of a fistula between 2 parts of Small bowel, you don't need to do anything.
- Localized abscesses.
- Toxic megacolon in patients with Crohn's colitis.
- Cancer the same percentage as in UC and some Chinese researchers say it's even higher in crohn's

Extraintestinal manifestations: Present in 30% of patients.

- The most common symptoms are skin lesions, which include erythema nodosum and pyoderma gangrenosum,
- Arthritis and arthralgias,
- Uveitis and iritis,
- Hepatitis and Pericholangitis, and
- Aphthous stomatitis
- Amyloidosis,
- Pancreatitis, and
- Nephrotic syndrome
- These symptoms may precede, accompany, or appear independent of the underlying bowel disease.

Treatment:

Both medical and surgical treatments are **palliative not curative** (surgery is curative in UC) IMPORTANT

Surgical treatment (Limited to complications or failure of medical treatment 3 to 6 months! You don't need to know the medications)

- Intestinal obstruction
- Intestinal perforation with fistula formation or abscess
- Free perforation
- GI bleeding
- Urologic complications
- Cancer
- **Perianal disease.**

Elective surgery:

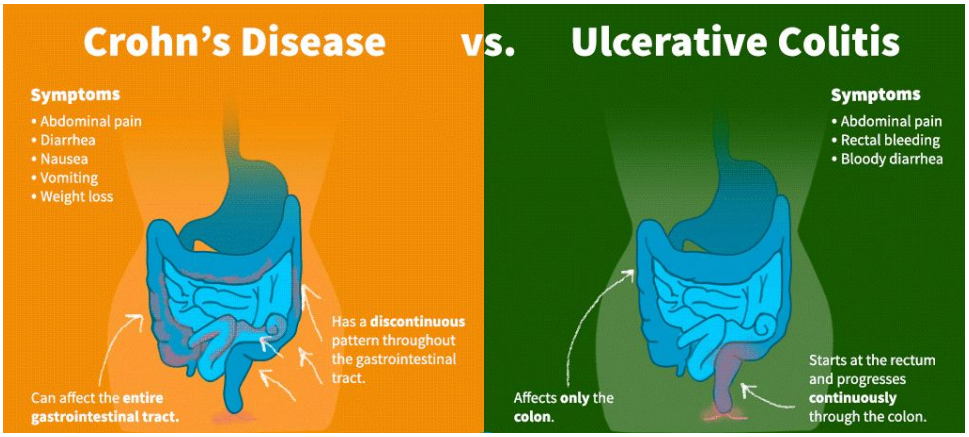
- Chronic subacute obstruction due to fibrotic stricture, adhesions or refractory disease
- Symptomatic disease unresponsive to or poorly controlled by medical management
- Chronic relapsing disease on discontinuation of medical management and steroid dependency
- Complications of medical management (e.g. osteoporosis)
- Concerns about long term immunosuppression, risk of malignancy and viral/atypical infections
- Perianal sepsis and fistula
- Onset of malignancy, including colorectal carcinoma and small bowel lymphoma
- Rarely, control of debilitating extracolonic manifestations such as iritis and sacroiliitis

Emergency:

- Fulminant colitis or acute small bowel relapse unresponsive to medical management
- Acute bowel obstruction
- Life-threatening hemorrhage
- Abscess
- free perforation (uncommon because inflamed segments usually adhere to surrounding structures)
- Perianal abscess

Differential diagnosis:

- Acute appendicitis
- Mesenteric Lymphadenitis
- Ovarian pathology
- Salmonella and Shigella
- Intestinal TB
- Acute distal ileitis may be a manifestation of early Crohn's disease, but it also may be unrelated, such as when it is caused by a bacteriologic agent (e.g., Campylobacter or Yersinia).
- UC
- protozoan infections, such as amebiasis, may present as an ileitis.
- In the immunocompromised host, rare infections, particularly mycobacterial & CMV.



Recall:

What is the cause of IBDs?
No one knows, but probably an autoimmune process with environmental factors contributing.
What is the differential diagnosis?
Crohn's vs Ulcerative colitis, infectious colitis (e.g. C. difficile, amebiasis, shigellosis), ischemic colitis, irritable bowel syndrome, diverticulitis, Zollinger-Ellison syndrome (ZES), colon cancer, carcinoid, ischemic bowel
What are the extra-intestinal manifestations seen in both types of IBDs? "A PIE SACK"

- **A**phthous ulcers
- **P**yoderma gangrenosum
- **I**ritis
- **E**rythema nodosum
- **S**clerosing cholangitis
- **A**rthritis, **A**nkylosing spondylitis
- **C**lubbing
- **K**idney (amyloid deposits, nephrotic syndrome)

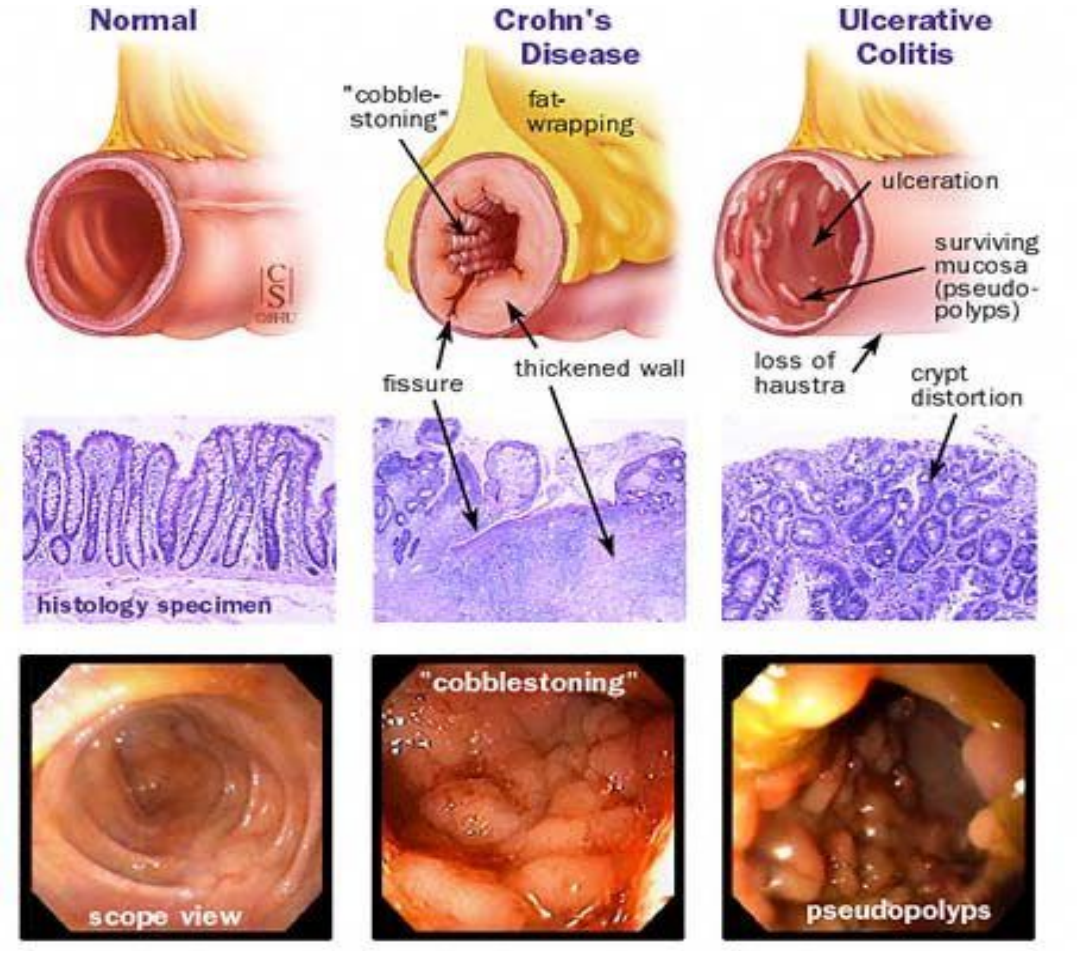
UC at risk population:

- High in jewish population.
- Low in african americans.
- Positive family history

What is toxic megacolon?
Toxic: sepsis febrile, abdominal pain. Megacolon: acutely and massively distended colon
Which disease has cobblestoning more often in endoscopic exam?
Crohn's disease (Think Crohn's = Cobblestoning)
Which disease has pseudopolyps on colonoscopic exam?
Ulcerative colitis; pseudopolyps are polyps of hypertrophic mucosa surrounded by mucosal atrophy
Which disease has a "lead pipe" appearance on barium enema?
Chronic ulcerative colitis
Rectal bleeding/bloody diarrhea is a hallmark of which disease?
Ulcerative colitis (rare in crohn's)
What is the most common indication for surgery in patients with Crohn's disease?
Small bowel obstruction (SBO)
Why do fistulas and abscesses with Crohn's and not UC?
Crohn's is transmural
What is it called when the entire colon is involved?
Pancolitis

Crohn's VS Ulcerative Colitis

	Crohn's disease	Ulcerative colitis
Diarrhea	Common	Common
Rectal bleeding	Less common	Almost always
Abdominal pain (cramps)	Moderate to severe	Mild to moderate
Palpable mass	At times	No (unless large cancer)
Anal complaints	Frequent (>50%)	Infrequent (<20%)
Anal fissure, fistula, abscess	common	Rare
Rectal sparing	Common (50%)	Rare (5%)
Ulceration	Linear, deep, scattered	Superficial, universal
Distribution	Skip areas	Rectum extending proximally



Summery:

	Crohn's disease	Ulcerative colitis
Sex	Female > male	Male > female
age	1st peak: 25-40 years of age 2nd peak: 50-65 years of age	1st peak: 20-35 2nd peak: 50-65 years
Blood in stool	Occasionally	**Yes** (bloody diarrhea "hallmark", fever, weight loss.
Mucus	Occasionally	**Yes**
Systemic symptoms	Frequently	Occasionally
Pain	Frequently (abdominal pain)	Occasionally
Abdominal mass	Yes	rarely
Perineal disease	Frequently	No
Fistula	**Yes**	No
Small intestine obstruction	frequently	No
Colonic obstruction	frequently	Rerely
Response to antibiotics	yes	No
Recurrence after surgery	**yes**	No
Rectal sparing	Frequently (fistula, abscesses, ulcer)	Rarely (always affects the rectum)
Continuous disease	Occasionally (skip areas, regional enteritis)	Yes
Cobblestoning	Yes	No
Granuloma on biopsy	Occasionally	No
Mucosal finding	1. Aphthoid ulcers 2. Granulomas 3. Linear ulcers 4. Transverse ssure 5. Swollen mucosa **6. Full thickness**	1. Granular, flat mucosa 2. Ulcers **3. Crypt abscess** 4. Dilated mucosal vessels **5. pseudopolyps**
Diagnostic tests	Colonoscopy with biopsy, barium enema, UGI with small bowel follow-through, stool cultures	
complications	**Anal** fistula/abscess, **fistula**, stricture, perforation, **abscesses**, toxic megacolon, colovesical fistula, enterovaginal fistula, hemorrhage, **obstruction**, cancer.	**Cancer, toxic megacolon, colonic perforation, hemorrhage**, strictures, obstruction, complications of surgery.
Indications of surgery	Obstruction, massive bleeding, fistula, perforation, suspicion of cancer, abscess (refractory to medical treatment), toxic megacolon (refractory to medical treatment), stricture, dysplasia.	Toxic megacolon (refractory to medical treatment), cancer prophylaxis, massive bleeding, failure of child to mature because of disease and steroids, perforation, suspicion of or documented cancer, acute severe symptoms refractory to medical treatment, inability to wean off of chronic steroids, obstruction, dysplasia and stricture.