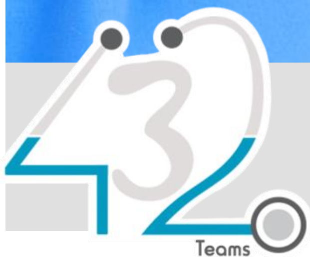
MEDICINE

432 Team

22 Inflammatory Bowel Disease



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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

1- Describe & Distinguish the Inflammatory bowel disease (IBD) is comprised of two major disorders: — Ulcerative colitis (UC), Crohn's disease (CD).

2-Know the disorders have both distinct and overlapping pathologic and clinical characteristics.

3- Know the Genetic factors: NOD2/CARD15

4- Know the ENVIRONMENTAL FACTORS: Smoking, Appendectomy: protect UC, Diet

What is inflammatory bowel disease?

Inflammatory bowel disease (IBD) is comprised of two major disorders:

1) Ulcerative colitis (UC) " Ulcerative = only ulceration, colitis= only involve the colon"

2) Crohn's disease (CD) "inflammation “transmural” involve the whole thickness of the wall of GI tract + could affect any part of GI Tract"

- These disorders have both distinct and overlapping pathologic and clinical characteristics.

Epidemiology:

IBD is more common in the West, but the incidence is increasing in the developing countries including Saudi Arabia "Due to the westernization of lifestyle and diet".

IBD can present at any age:

- The first peak: 15 - 30 years. "Only this peak in KSA"
- A second peak: 50 years

Host Factors:

- **Genetic factors:**

NOD2/CARD15 "It was thought this genetic mutation was only found in Ashkenazi Jews, however this has been proven wrong. Even patients in KSA have the same genetic mutation"

- **Environmental factors:**

1) Smoking: "Smoking a risk factor for Crohn’s Disease, and it is also proven that it worsens the prognosis if the patient persists on smoking after being diagnosed. However, smoking is protective in Ulcerative Colitis, it decreases the symptoms"

2) Appendectomy: “in young age it is protective for Ulcerative Colitis"

3) Diet: “Diet in the first 10 years of life is a major factor for developing IBD. (Western diet)"

Etiologic hypotheses:

1- Persistent infection "mycobacteria" **2- Dysbiosis** "imbalance of microbial colonies in GIT"

3- Defective mucosal integrity "e.g.: increased permeability"

4- Deregulated immune response "in which the immunity in the GIT is decreased when triggered by certain allergies"

A) Ulcerative colitis

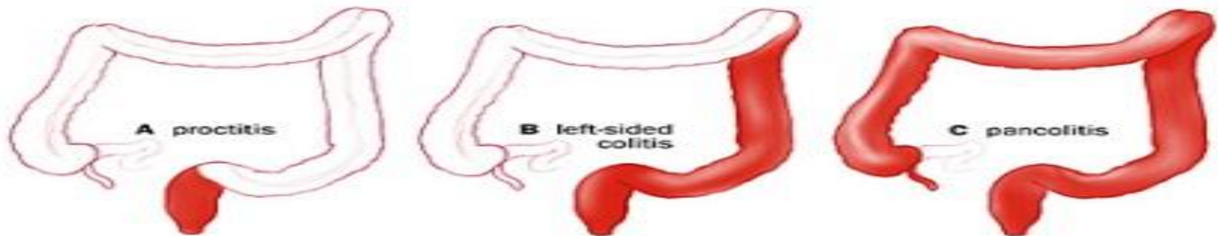
Ulcerative colitis is characterized by recurring episodes of inflammation" Continuous inflammation" limited to the mucosal layer of the colon" No area with normal mucusal layer"

"The only type present without continues inflammation is cecal patch (which is here the rectum affected then there is a normal mucousa then there is affected base of the cecum near the appendix)"

Usually starts in the rectum (distally) then extends proximally "goes up"

Site of the inflammation:

1. **Ulcerative proctitis**: rectum.
2. **Ulcerative proctosigmoiditis**: rectum and sigmoid colon.
3. **Left-sided colitis**: disease that extends beyond the rectum and as far proximally as the splenic flexure.
4. **Extensive colitis**: beyond the splenic flexure.
5. **Pancolitis**: whole colon



- 40-50% of patients have disease limited to the rectum and rectosigmoid
- 30-40% of patients have disease extending beyond the sigmoid " Left-sided colitis"
- 20% of patients have pancolitis

❖ Symptoms:

The major symptoms of UC are:

1. **Diarrhea** "Small volume"
2. **Rectal bleeding**
3. **Tenesmus** (a feeling of incomplete defecation) "usually occurs in the Ulcerative proctitis"
4. **urgency** "1st sign, occur because the inflammed rectum cannot hold the stool"
5. **Passage of mucus**
6. **Crampy abdominal pain**

- Patients with UC develop symptoms much earlier than patients with Crohn's disease because the disease starts in the rectum.
- Systematic symptoms usually appear when the disease extends to the colon.
- Patients with proctitis usually pass fresh blood or blood-stained mucus either mixed with stool or streaked onto the surface of normal or hard stool
- When the disease extends beyond the rectum, blood is usually mixed with stool or grossly bloody diarrhea may be noted
- When the disease is severe, patients pass liquid stool containing blood, pus & fecal matter
- Other symptoms in moderate to severe disease "systemic" include: anorexia, nausea, vomiting, fever, weight loss

❖DIAGNOSIS:

- No single modality is enough for diagnosis of IBD
- Combination of Clinical picture (Hx & P/E), radiographic imaging, laboratory, Endoscopy, histopathology.

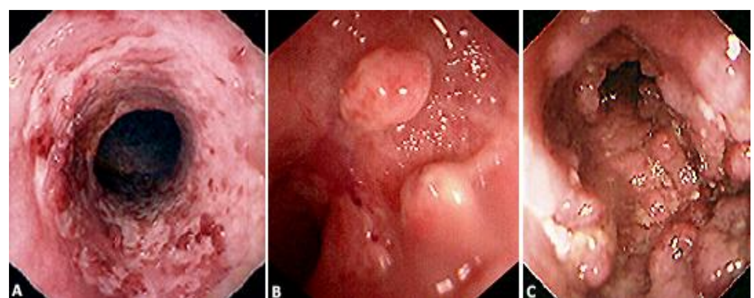
❖ **Colonoscopy:**

The vascular markings are lost, petechiae, exudates, touch friability, and frank hemorrhage may be present.

Colonic involvement is continuous in ulcerative colitis, in contrast to the patchy nature of Crohn's disease.

- Colonoscopy is essential to diagnose UC.
- In colonoscopy it is important to appreciate that there are **No skipped lesions**

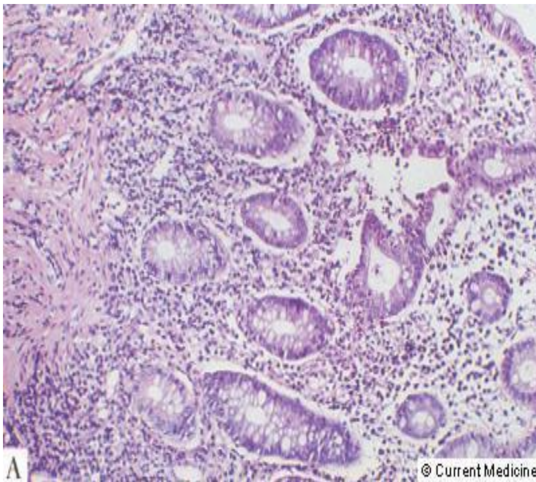
Normal colonoscopy

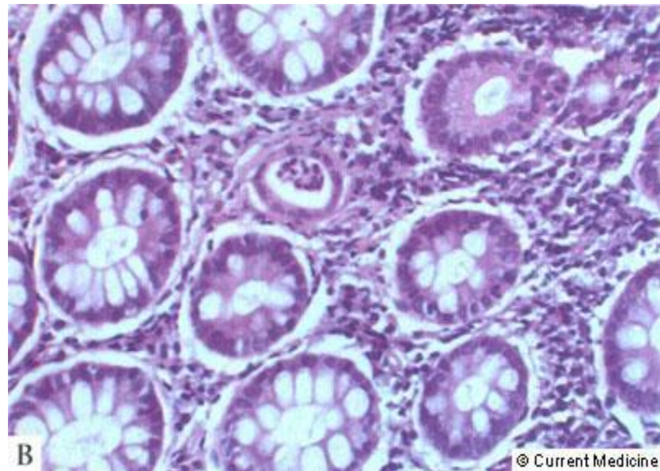


Ulcerative Colitis showing Loss of blood vessels, colonic pseudopolyps, more ulceration, diffuse inflammation

❖ Pathology:

1. Crypt abscesses
2. chronic changes including branching of crypts, atrophy of glands, and loss of mucin in goblet cells





Ulcerative colitis shows: crypt abscesses, chronic changes including branching of crypts, atrophy of glands, and loss of mucin in goblet cells

Normal

❖ Complication:

- **Hemorrhage**
- **Perforation**
- **Toxic megacolon:** transverse colon with a diameter of more than 5,0 cm to 6,0 cm with loss of haustration

"It is characterized by a very dilated colon (megacolon) accompanied by abdominal distension (bloating) It is a very serious complication and needs immediate surgery to remove the colon. Symptoms include: sepsis, fever, tachycardia & abdominal pain"

- **Colon cancer more common in Ulcerative Colitis than Crohn's disease**

Management:

❖ Goals of therapy:

1) Induce then maintain remission.
2) Manage & reduce symptoms
3) Improve quality of life
4) Adequate nutrition
5) Prevent complication of both the disease and medications

❖ Treatment:

- **Rule out infection** " The most important point in management is to rule out infection every time the patient presents with symptoms, because some of the medications decrease their immunity"

- **5 ASA therapy** " 5-aminosalicylic acid" :
  - Only used in ulcerative colitis
  - E.g.: Sulfasalazine, Mesalamine " more common used now due to its less side effects than Sulfasalazine (containing "sulfa" which cause n/v)
  - Oral with Rectal formulations are used in Left-sided colitis and Pancolitis
  - Rectal formulations are used in ulcerative proctitis and proctosigmoiditis
- **Corticosteroids:**
  - Systemic: Prednisolone, cortisone " Try to avoid Corticosteroids as much as you can because of its long term side effects"
  - Local acting: enema. "e.g.: Hydrocortisone enema or suppository"

- **Immunomodulators :**
  - Azithyoprine
  - Methotrexate
- **Anti TNF therapy**

Infliximab, Adalimumab (Humira), Certolizumab pegol (Cimzia)

- **Surgery:** "indicated in four cases (remove the whole colon in UC)"
  1) Severe attacks that fail to respond to medical therapy.
  2) Complications of a severe attack (e.g., perforation, acute dilatation, toxic megacolon).
  3) Chronic continuous disease with an impaired quality of life.
  4) Dysplasia or carcinoma.

B) Crohn's disease (CD)

Crohn's disease is a disorder of uncertain etiology that is characterized by transmural "the whole thickness" inflammation of the gastrointestinal tract.
CD may involve the entire gastrointestinal tract "Affect all the layers of GI tract" from mouth to the perianal area "Anus".

Site of the inflammation:

- 80% Small bowel (50 % "of it of it in the ileocecal" ileocolitis)
- **Majority of the patients will have ileocecal involvement**
- 50% Ileocolic , 30%Ileal, 20% Colic
- 20 % colon.
- 30% perianal disease.
- UGI < 5 %

CLINICAL MANIFESTATIONS:

1) Fatigue 2) Diarrhea 3) Abdominal pain
4) Weight loss 5) Fever 6) Anemia

Patients with Crohn's disease usually present late, because the disease is much more proximal than UC.

- **Because of the transmural involvement (all the layers not just the superficial layer like in UC) patients with Crohn's disease have a great risk of developing:**

1) Phlegmon/abscess:
Walled off inflammatory mass without bacterial infection

2) Fistulas: "More common in CD"
Fistulas are tracts or communications that connect two epithelial-lined organs.

A. Enterovesical "between small bowel and bladder"
B. Enterocutaneous "between small bowel and skin"
C. Enteroenteric "between small bowel and small bowel"
D. Enterovaginal "between small bowel and vagina"

3) Perianal disease

4) Severe oral involvement: aphthous ulcers.

5) Esophageal involvement: odynophagia and dysphagia.

6) Gastroduodenal CD: upper abdominal pain and symptoms of gastric outlet obstruction.

7) High risk of Gallstones "due to the malabsorption of bile in the ileum"

○ Extraintestinal manifestations

CD and ulcerative colitis share a number of extraintestinal manifestations

1) Arthritis:

Type 1: affects large joints, associated with the disease activity

Type 2: affects small joints of the hand. Not associated with the disease activity

Primarily involving large joints in approximately 20 percent of patients without synovial destruction, arthritis is the most common extraintestinal manifestation. Central or axial arthritis, such as sacroiliitis, or ankylosing spondylitis, may also occur. An undifferentiated spondyloarthropathy or ankylosing spondylitis may be the presenting manifestation of CD

2) Eye involvement: uveitis, iritis, and episcleritis

3) Skin disorders:

- Erythema nodosum: large and painful nodules, affect the extensor surface of the limb
- Pyoderma gangrenosum: painless ulceration

4) Primary sclerosing cholangitis: in UC

This typically presents in approximately 5 percent of patients with an elevation in the serum alkaline phosphatase or gamma glutamyl transpeptidase (GGT) concentration.

5) Venous and arterial thromboembolism resulting from hypercoagulability

6) Renal stones:

Calcium oxalate and uric acid kidney stones can result from steatorrhea and diarrhea. Uric acid stones can result from dehydration and metabolic acidosis

7) Bone loss and osteoporosis:

May result related to glucocorticoid use and impaired vitamin D and calcium absorption

8) Vitamin B12 deficiency:

A clinical picture of pernicious anemia can result from severe ileal disease since vitamin B12 is absorbed in the distal 50 to 60 cm of ileum

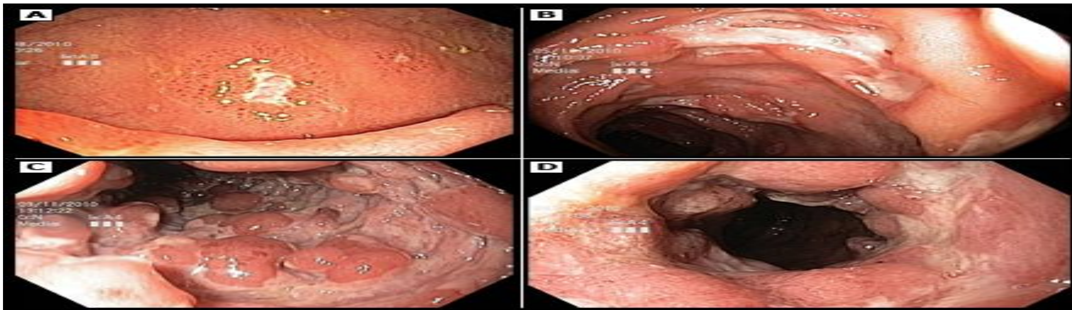
9) Secondary amyloidosis:

It is very rare but may lead to renal failure and other organ system involvement

DIAGNOSIS

- The diagnosis of CD is usually established with endoscopic findings or imaging studies in a patient with a compatible clinical history.
- **Colonoscopy:**

Endoscopic features include focal ulcerations adjacent to areas of normal appearing mucosa along with polypoid mucosal changes that give a cobblestone



- **Colonoscopy: Transmural inflammation with skipped lesions (ulceration adjacent to normal mucosa) with polypoid mucosal changes that give cobblestone appearance. Creeping mesenteric fat can be seen in cases of extensive transmural involvement.**

- **Wireless capsule endoscopy**:

A new method of endoscopy, which is noninvasive. The patient swallows a pill which has two cameras and will take an image every second for 8 hours of the GIT. Eventually, it will pass with the stool

- **Imaging studies**
  - small bowel follow through (SBFT)
  - computed tomography: CTS or CT enterography
  - Magnetic resonance imaging (MRI) or MR enterography

  Imaging studies more important in CD than UC

- **Serologic markers**
  - **Inflammatory markers** : ERS, CRP used to distinguish between IBD and IBS high in IBD but not in IBS
  - **Antibody tests** :
    - Antineutrophil cytoplasmic antibodies (pANCA) "more common in UC"
    - Anti-Saccharomyces cerevisiae antibodies (ASCA) "more common in CD"
  - **Stool markers**: fecal calprotectin high in IBD but not in IBS

Management:

❖ Goals of therapy:

1) Induce then maintain remission.
2) Ameliorate symptoms
3) Improve quality of life
4) Adequate nutrition
5) Prevent complication of both the disease and medications

6) Treatment:

- 5-ASA is not a part of CD treatment
- **Rule out infection** " The most important point in management is to rule out infection every time the patient presents with symptoms, because some of the medications decrease their immunity"

- **Corticosteroids:**
  - Systemic: Prednisolone " Try to avoid Corticosteroids as much as you can because of its long term side effects"
  - Local acting: Budosonide "Local is better than systemic because it will be absorbed then it will goes immediately to the cecal area + less side effect than systemic"

- **Immunomodulators :** "good only for maintaining remission"

  - Azithyoprine
  - Methotrexate
- **Anti TNF therapy** "work better in CD than UC"
- **Surgery** indicated in these cases:

1) Obstruction
2) Severe perianal disease unresponsive to medical therapy
3) Difficult fistulas
4) Major bleeding
5) Severe disability
6) Abscess formation

Summary

Feature	Crohn's disease	Ulcerative colitis
Distinguishing characteristics		
Location	SB or colon	colon
Anatomic distribution	Skip lesions	Continuous
Rectal involvement	Rectal spare	Involved in >90%
Gross bleeding	Only 25%	Universal
Peri-anal disease	1/3	Rare
Fistulization	Yes	No
Granulomas	30%	No
Endoscopic features		
Mucosal involvement	Discontinuous	Continuous
Aphthous ulcers	Common	Rare
Surrounding mucosa	Relatively normal	Abnormal
Longitudinal ulcer	Common	Rare
Cobble stoning	In severe cases	No
Mucosal friability	Uncommon	Common
Vascular pattern	Normal	distorted
Creeping fat	Yes	No
Pathologic features		
Transmural inflammation	Yes	Uncommon
Granulomas	30%	No
Fissures	Common	Rare
Fibrosis	Common	No
Submucosal inflammation	Common	Uncommon
Crypt abscesses	No	Yes

SUMMARY

- IBD consists of two diseases, which are similar, Ulcerative colitis and Crohn's disease.
- Probably autoimmune disorders, but they are no fully understood
- Ulcerative colitis usually affects the rectum and extends proximally; it can affect the entire colon.
- Crohn's disease can affect any area of the GIT, but most commonly the ileum and cecum.
- Ulcerative colitis is characterized by a superficial inflammation that has NO skipped lesions.
- Crohn's disease is characterized by transmural inflammation with skipped lesions "cobblestone appearance".
- Mutations NOD2/CARD15 are associated with IBD.
- Diet in the first 10 years of life is important in developing IBD.
- Smoking is a risk factor for developing Crohn's but is protective from Ulcerative colitis.
- Patients with UC present much earlier than Crohn's because the disease is distal in the GI tract.
- Always use multiple modalities when diagnosing IBD; colonoscopy, imaging, histopathology.
- Imaging is more important in Crohn's disease.
- pANCA is positive in Ulcerative Colitis
- ASCA is positive in Crohn's disease.
- ESR & CRP are used to distinguish between IBD and IBS.
- Colon cancer is more common in Ulcerative Colitis than Crohn's disease.
- Toxic megacolon is a severe complication that accompanies UC more than Crohn's.
- Abscesses, fistulas and Phlegmons are common in Crohn's because of the transmural involvement.
- It is important to rule out infection each time the patient presents with symptoms of IBD.
- Budesonide is used more in Crohn's disease.
- Surgery is indicated in severe disease in IBD, however; in UC the entire colon is usually removed while in Crohn's only the effected are is removed.

Questions

Q1: A 23 years old women have been seen by her family doctor complaining from crampy abdominal pain and constant diarrhea, which is occasionally bloody. She says that the pain is mostly in her right lower quadrant. She's lost about 9kg over the past year. Upon reviewing her labs in follow up visit, the doctor noticed that her ESR and CRP are elevated. **What would be your top diagnosis?**

A. ulcerative colitis.
B. Ischemic colitis.
C. Crohn's disease.
D. Celiac disease.

Q2: A 25 years old female presented with 4 weeks of bloody diarrhea associated with lower crampy abdominal pain, weight loss, urgency and tenesmus. She also gave a history of arthralgia affecting the hand and back. **What is the most likely diagnosis?**

A. Ulcerative colitis.
B. Viral gastroenteritis.
C. Colon cancer.
D. Crohn’s disease.

Q3: Which of the following findings can be seen in ulcerative colitis:

A. Creeping fat
B. fistulas
C. Crypt abscesses
D. Cobblestone appearance

432 Medicine Team Leaders

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Answers:

1st Questions: C

2nd Questions: A

3rd Questions: C