

INFLAMMATORY BOWEL DISEASE

- Refers to two chronic diseases of unknown etiology that cause inflammation of the intestine with extra intestinal manifestations
- Ulcerative colitis and Crohn's disease.
- Although the diseases have some features in common, there are some important differences.

Definition

➤ Ulcerative Colitis (UC) is a chronic inflammatory condition of the colon that is marked by remission and relapses.

➤ - It is a form of inflammatory bowel disease (IBD).

Epidemiology

- Incidence: 8–15 per 100,000 persons .
- Prevalence: 170–230 per 100,000 .
- An increased incidence and prevalence is found in developed nations, northern locale and urban environments; among Caucasians; and among persons of Jewish ethnicity.

Introduction

- Ulcerative colitis (UC) is a chronic disease of unknown etiology characterized by inflammation of the mucosa and submucosa of the large intestine.
- The inflammation usually involves the rectum down to the anal margin and extends proximally in the colon for a variable distance.
- There is no difference between men and women.
- The worldwide incidence is 0.5~24 new cases per 100 000 individuals, and prevalence is 100~200 cases per 100 000.

Ulcerative Colitis: Epidemiology

- High incidence areas: US, UK, northern Europe
- Young adults, commoner in females

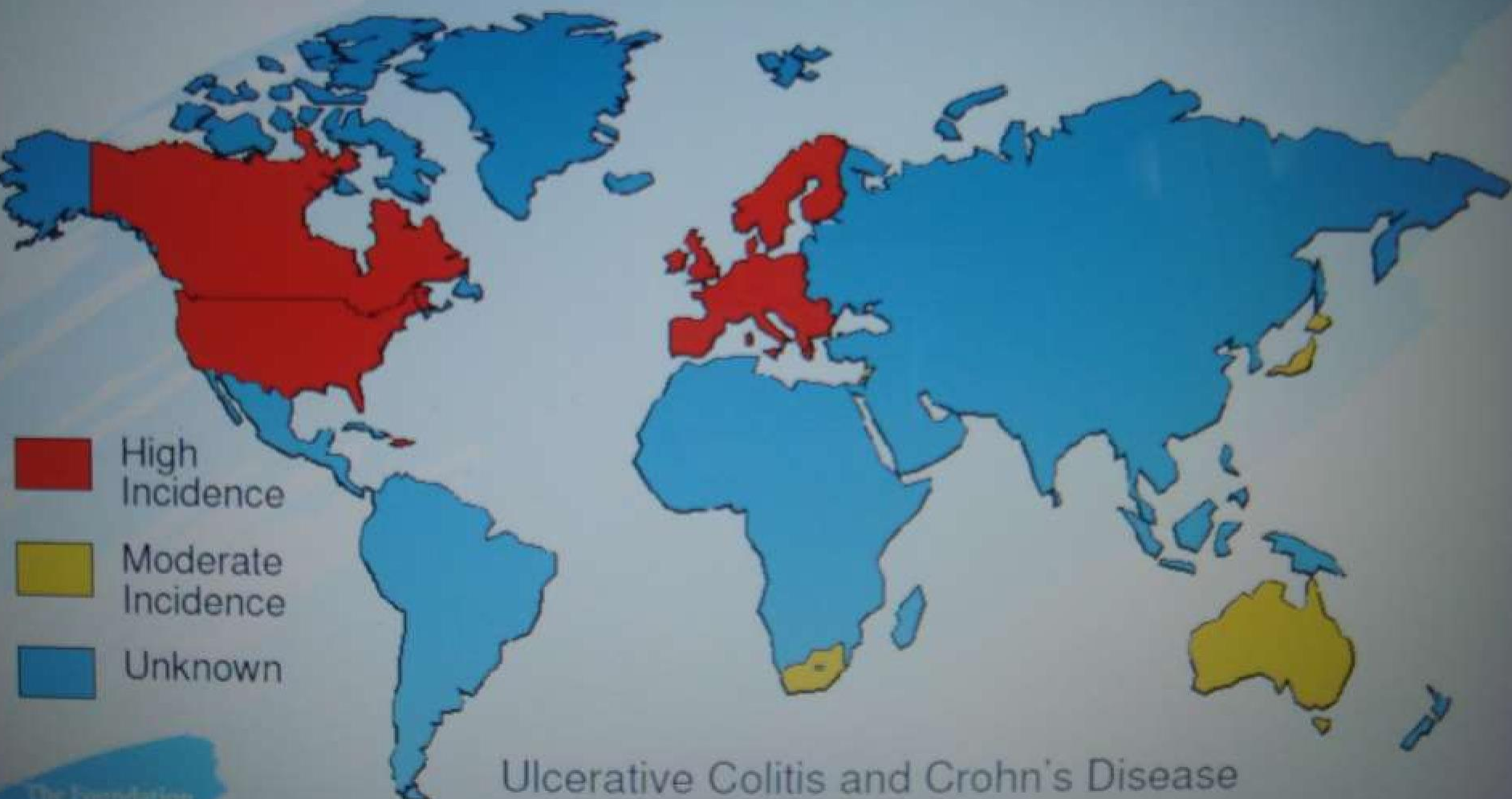
INCIDENCE IS ON THE RISE IN ASIAN (INDIA)
POPULATION

Rise of Incidence in IBD in India

- Familial aggregation
- Nicotine Consumption
- Oral Contraceptives
- Dietary Habits- Refined sugars, Fast food, cereals, bakers yeast etc
- Physical inactivity
- Early weaning
- Hygiene
- Infectious diseases- TB, Measles

Inflammatory Bowel Disease

Geographic Distribution

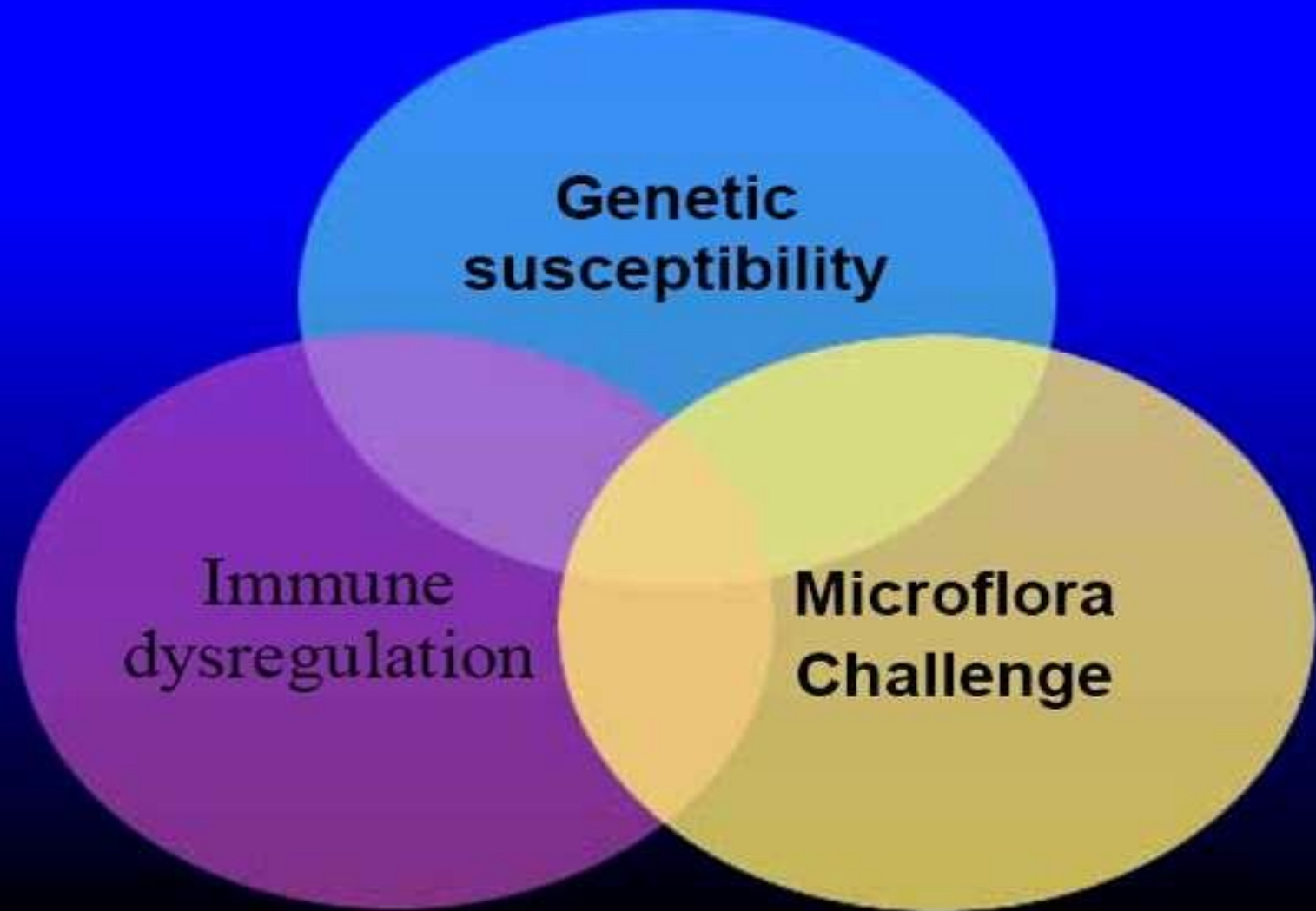


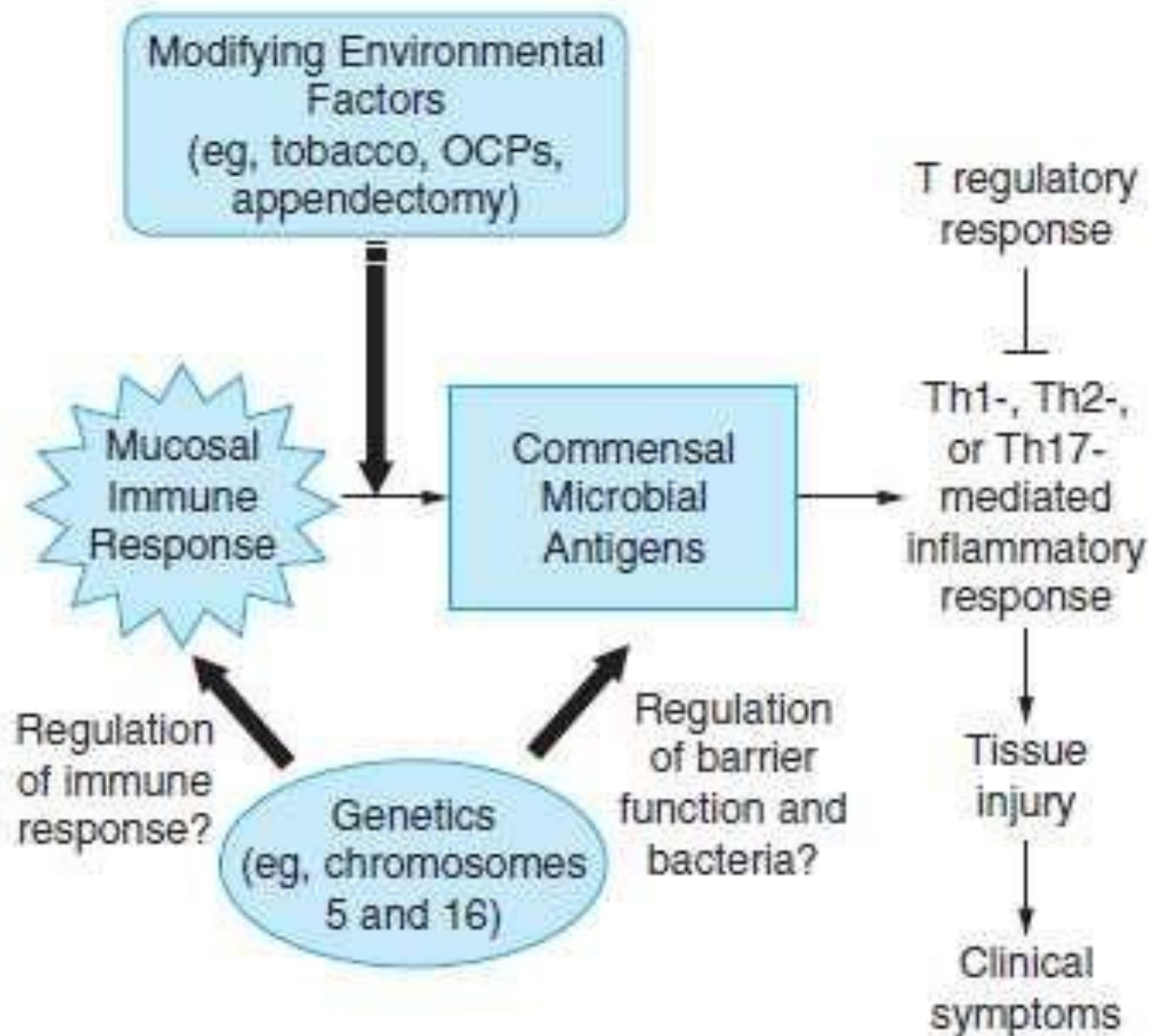
Ulcerative Colitis and Crohn's Disease
Same Distribution

Etiology

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Etiologic Factors in IBD



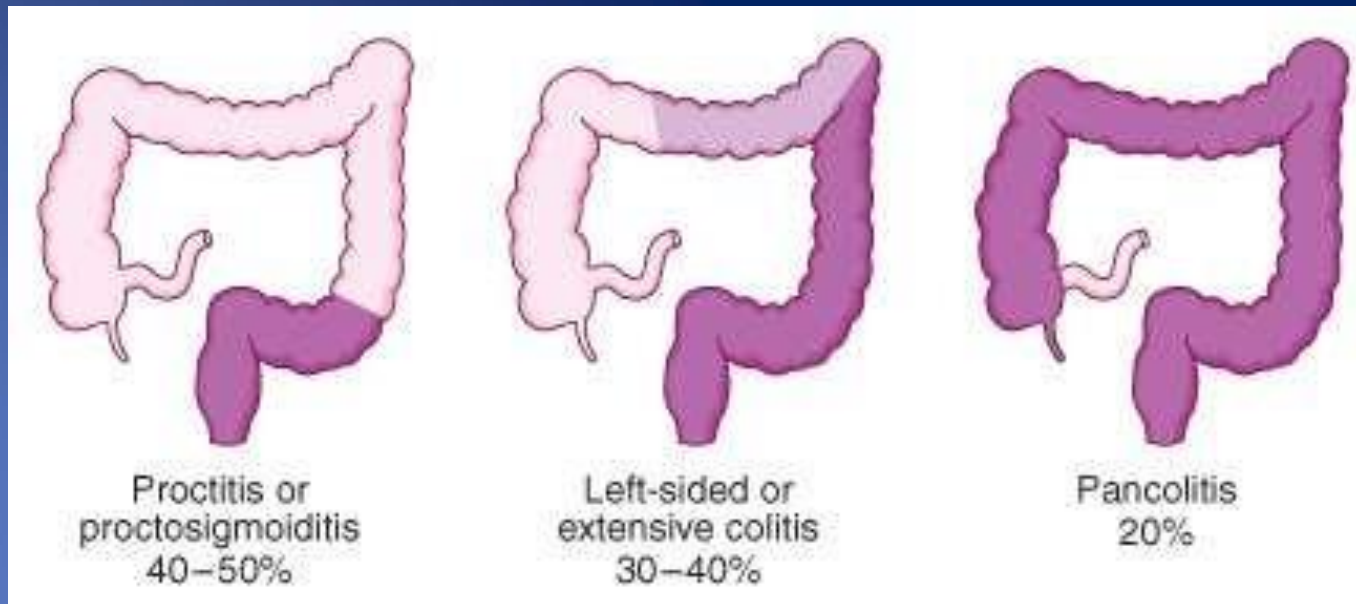


Pathology

The inflammation is limited to the mucosal layer of the colon.

- The rectum is always involved, with inflammation extending proximally in a confluent fashion.
- The disease is classified by the extent of proximal involvement into:
 - **Proctitis:** Involvement limited to the rectum.
 - **Proctosigmoiditis:** Involvement of the rectosigmoid.

- Left-sided colitis:** Involvement of the descending colon up to the splenic flexure.
- Extensive colitis:** Involvement extending proximal to the splenic flexure.
- **Pancolitis (universal colitis):** Involvement of the entire colon. It may be associated with inflammation of the terminal ileum (**backwash ileitis**).

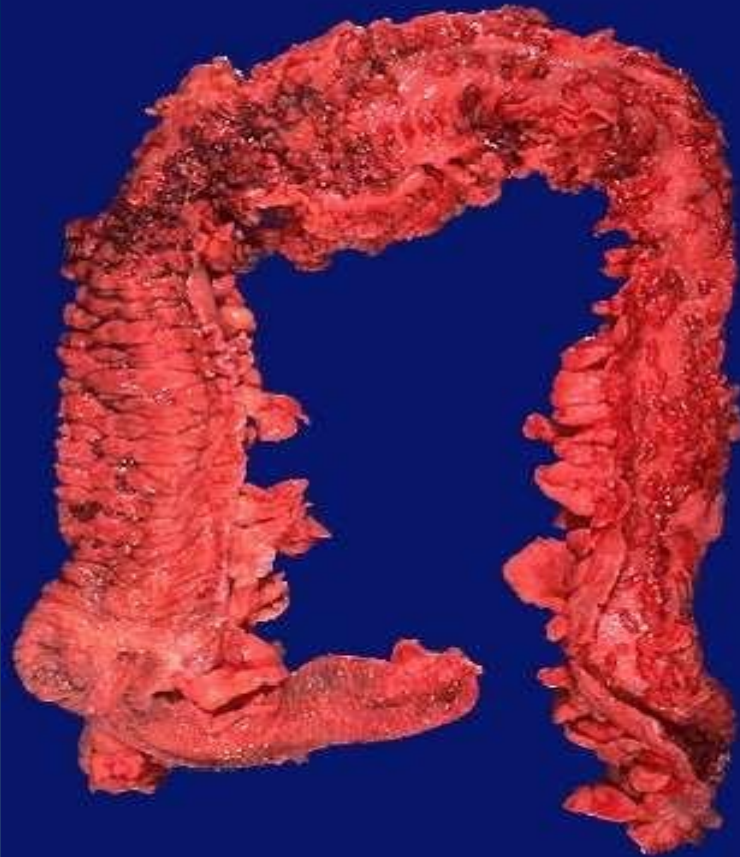
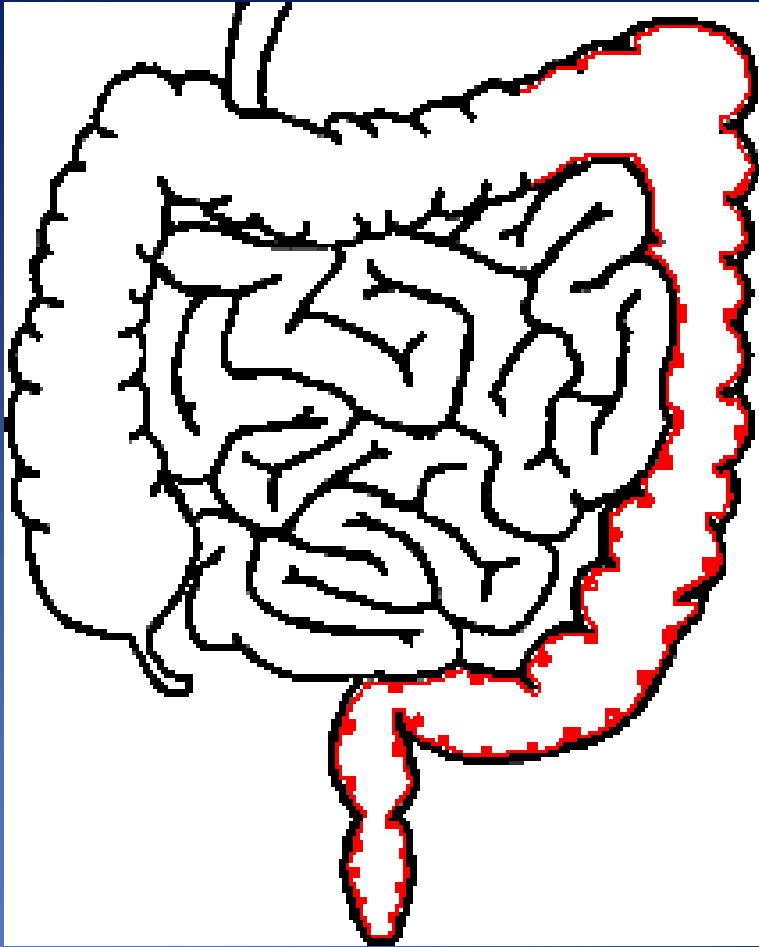


Pathology

Gross Description

- **Ulceroinflammatory disease**, usually limited to colon, diffuse continuous disease from rectum proximally (pancolitis in some cases), see exceptions above; ileitis and involvement of appendix also occurs in continuity with severe colitis;
- Usually no deep fissuring ulceration, no strictures or fistulas, no sinus tract formation, no small intestinal involvement, no serositis, no bowel wall thickening, no fat wrapping
- **Early:** mucosa is hemorrhagic, granular, friable; changes usually diffuse (similar intensity throughout)
- **Late: extensive ulceration** along bowel axis; have pseudopolyps (isolated islands of regenerating mucosa) and flat mucosa; usually normal wall thickness and normal serosa;
- **severe cases** may have megacolon or fibrotic, narrow or shortened colon

Pathology



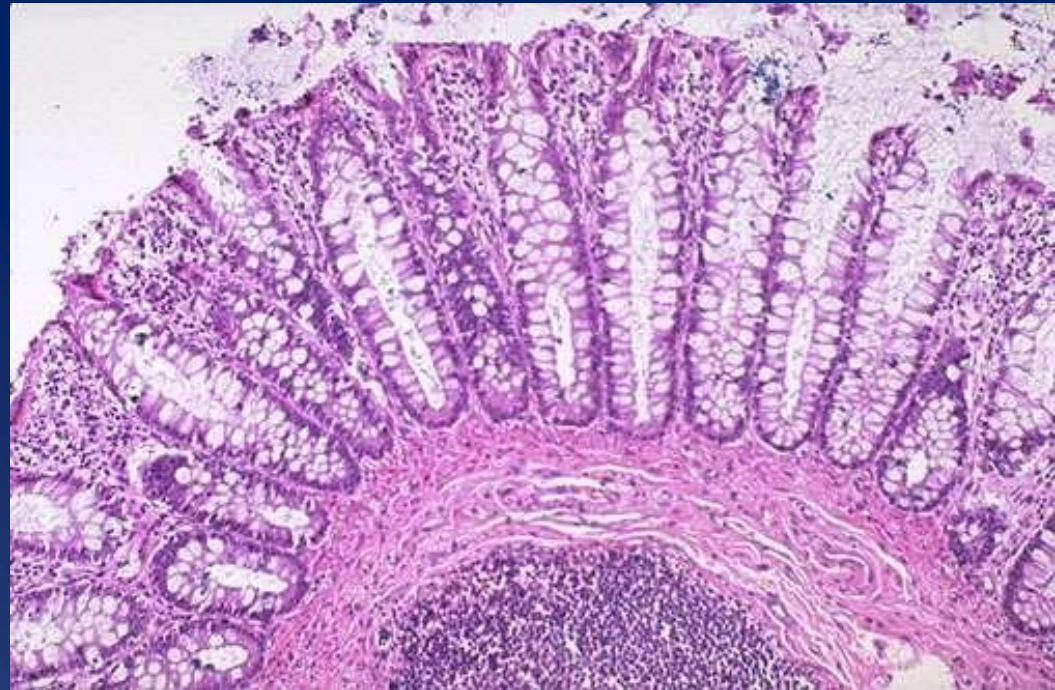
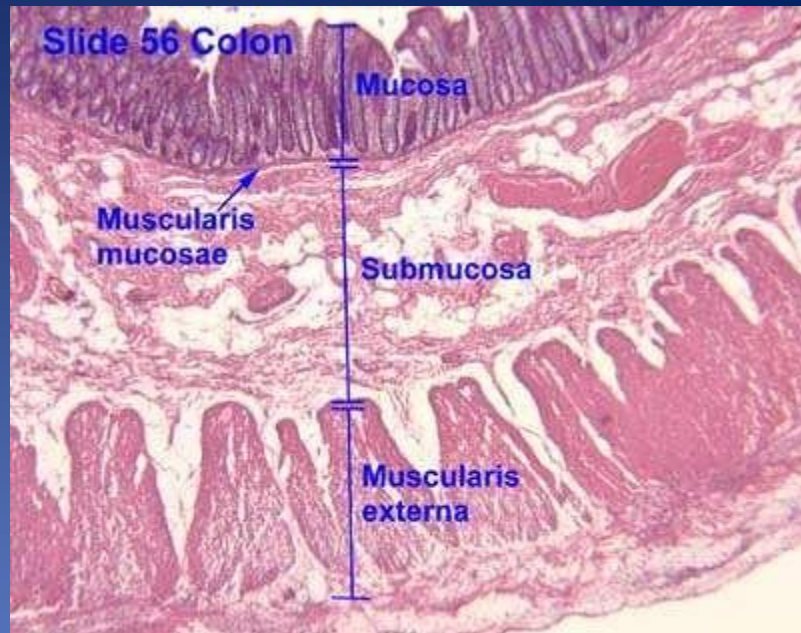
Pathology





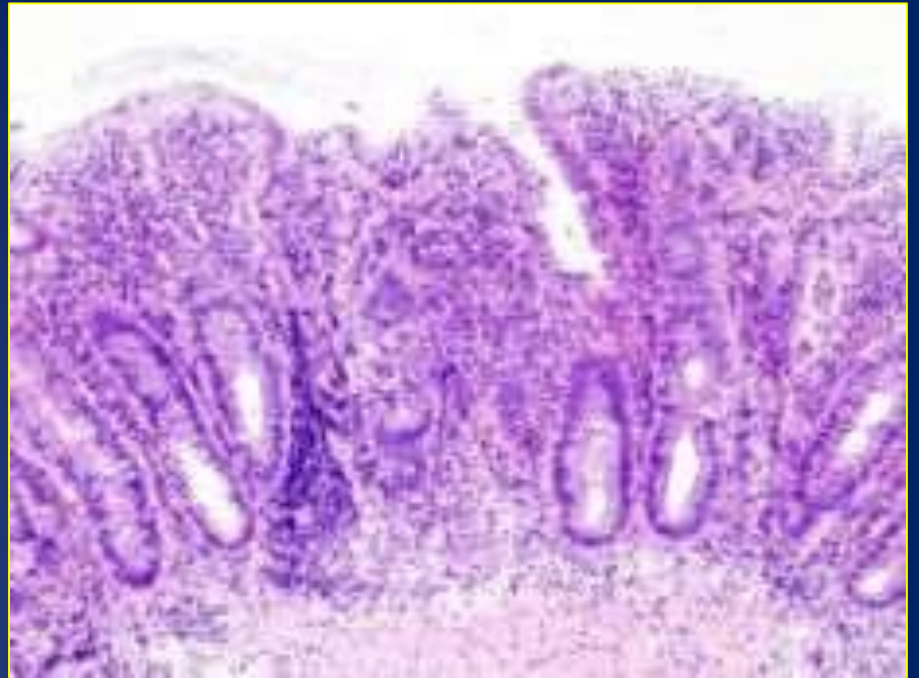
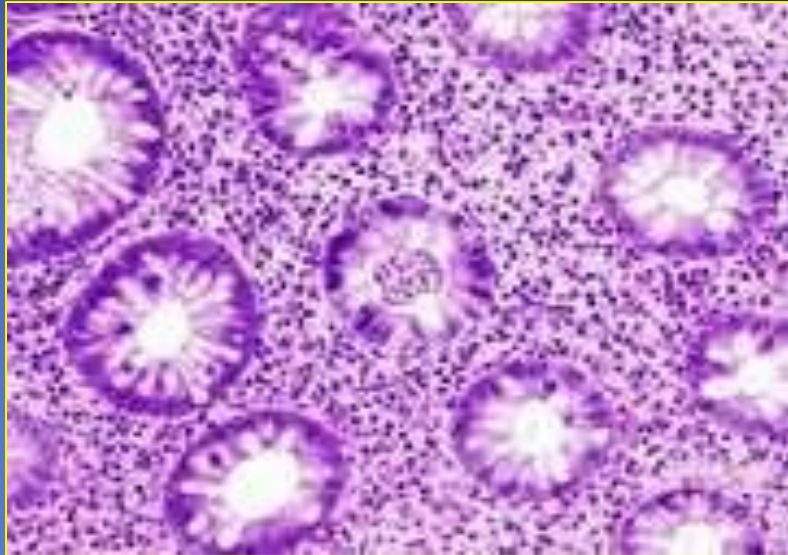
Colonic pseudopolyps of a patient with intractable ulcerative colitis. Colectomy specimen.

This is normal colonic mucosa. Note the crypts that are lined by numerous goblet cells. In the submucosa is a lymphoid nodule.



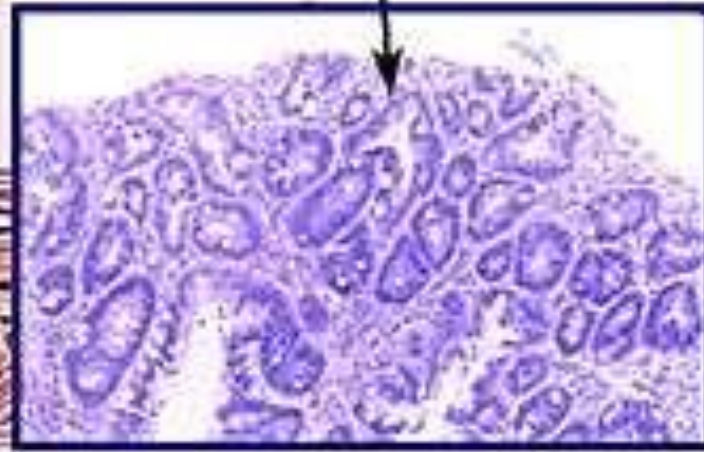
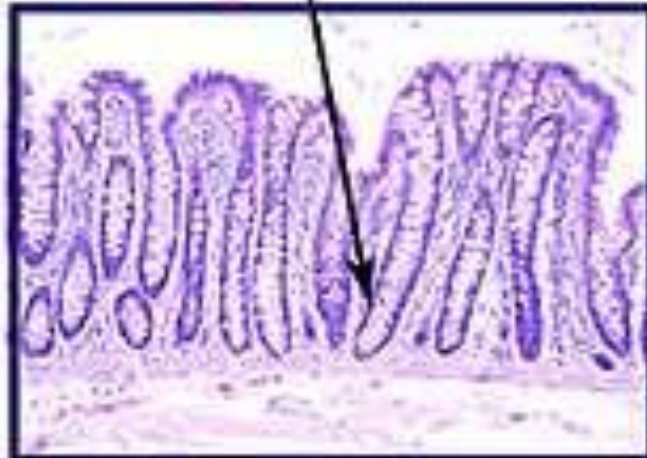
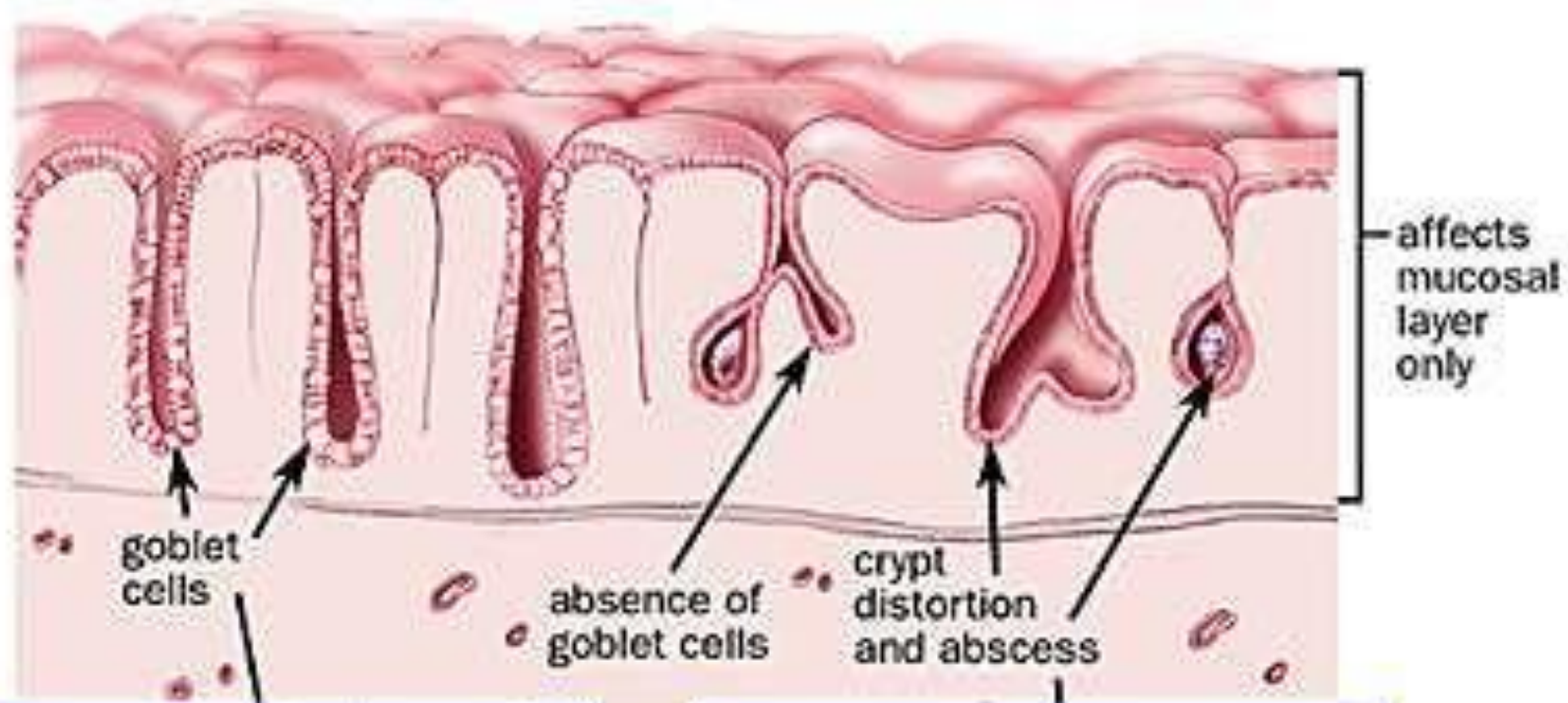
Histopathology

- Distortion of crypt architecture.
- Inflammation of crypts (cryptitis).
- Frank crypt abscesses.
- Inflammatory cells in the lamina propria.
- Pseudopolyps formation.



Normal colon

Ulcerative colitis



Symptoms

- Rectal bleeding and tenesmus are universally present.
- Diarrhea and abdominal pain are more frequent with proximal colon involvement.
- Nausea and weight loss in severe cases.
- Severe abdominal pain or fever suggests fulminant colitis or toxic megacolon.

Clinical Picture

- **Age:** Ulcerative colitis presents at a young age, often in adolescence. The median age of diagnosis is the fourth decade of life.
- **Onset:** acute or subacute.
- **Course:** - Most patients experience intermittent exacerbations with nearly complete remissions between attacks.
- About 5-10% of patients have one attack without subsequent symptoms for decades.

Signs

- Pallor may be evident.
- Mild abdominal tenderness most localized in the hypogastrium or left lower quadrant.
- PR examination may disclose visible red blood.
- Signs of malnutrition.
- Severe tenderness, fever, or tachycardia suggests fulminant disease.

Severity of the disease

Mild disease:

- Stool frequency is less than 4 times/day with or without blood.
- No systemic signs of toxicity.
- There may be mild abdominal pain or cramping.
- Normal ESR.

Moderate disease:

- Stool frequency is more than 4 times/day.
- Minimal signs of toxicity.
- Moderate abdominal pain.

Severe disease:

- Stool frequency > 6 times/day with blood +++.
- Fever > 37.5°C.
- Tachycardia > 90 per minute.
- ESR > 30 mm per hour.
- Anaemia < 10 g/dL haemoglobin.
- Albumin < 30 g/L.

Differential Diagnosis

1 Crohn colitis.

2 Infectious colitis.

3 Ischemic colitis. Acute, painful, self limited, localized, after meals.

4 Radiation colitis. Can cause proctitis, colitis or enteritis.

5- Diversion colitis.

6 Segmental colitis. Idiopathic focal colitis surrounding diverticulae.

7 GIT malignancies. Rectal bleeding, altered bowel habits, pain & anemia.

7- Irritable bowel syndrome (IBS). Abdominal pain & diarrhea.

Comparison between Ulcerative colitis and Crohn disease

	Ulcerative Colitis	Crohn Disease
Onset	Acute or subacute	Insidious
Extension	Affects only the colon	Can affect any part of the GIT from the mouth to the anus
Rectal involvement	Always	Rare
Distribution of disease	Continuous area of inflammation	Patchy areas of inflammation
Skip lesions	Absent	Present
Cobblestone appearance	Absent	Present
Depth of inflammation	Shallow, mucosal	May be transmural, deep into tissues

	Ulcerative Colitis	Crohn Disease
Diarrhea	Bloody	Usually not bloody
Abdominal mass	Absent	May be present
Fistula formation	Rare	Common
Bile duct involvement	Higher rates of PSC	Lower rates of PSC
Cancer risk	Higher than Crohn	Lower than UC
Smoking	Lower risk for smokers	Higher risk for smokers

Complications of Ulcerative Colitis

Complications

- 1 Severe hemorrhage.
- 2 Toxic megacolon.
- 3 Colorectal cancer (CRC).
- 4 Extraintestinal complications.
- 5 Pouchitis.

- Toxic megacolon (transverse colon with a diameter of more than 5.0 cm to 6.0 cm with loss of haustration)

Colorectal Cancer

Risk Factors:

- Duration, severity and extent of the disease.
- Positive family history.
- Concomitant PSC.

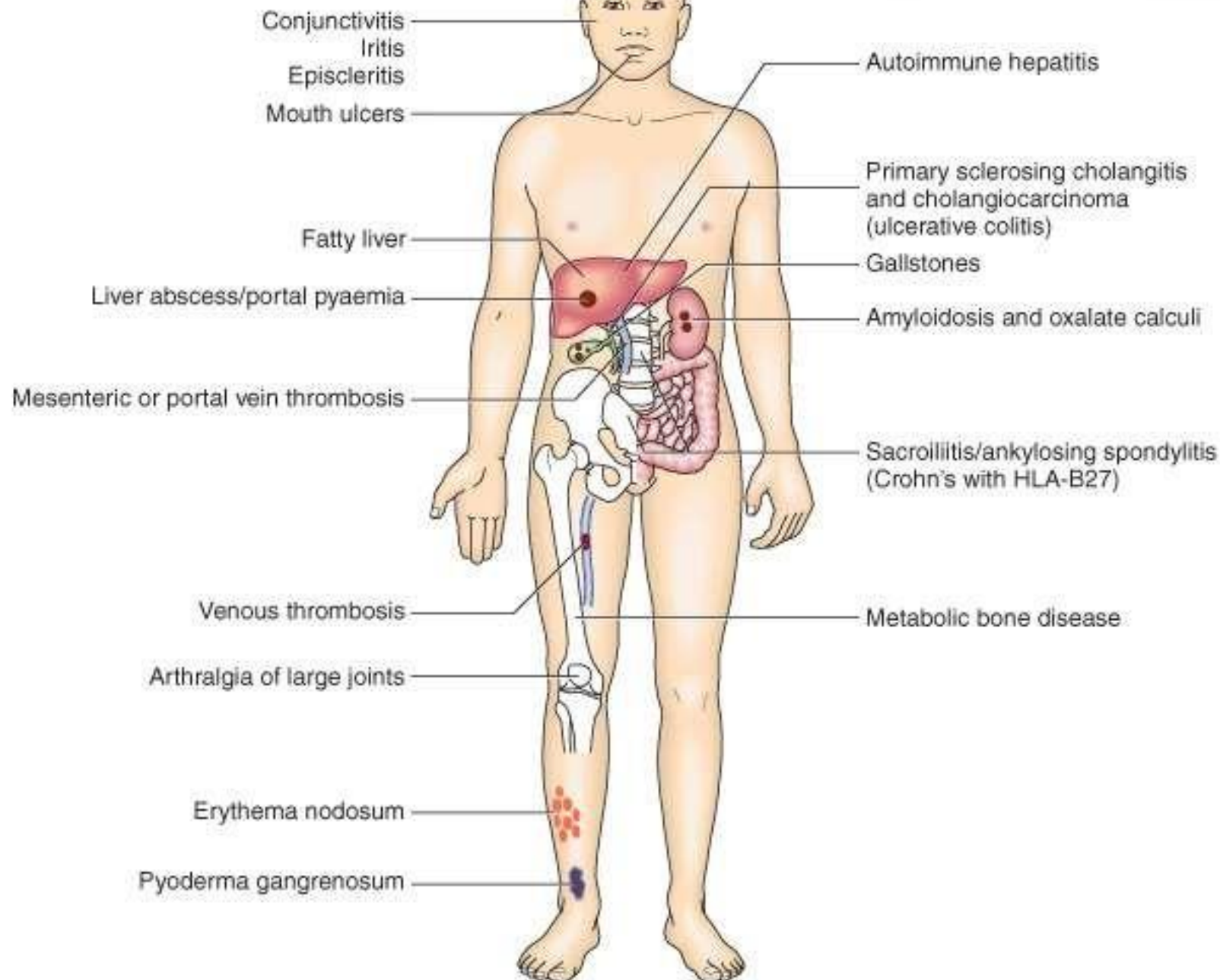
CRC appears after 8-10 years of disease. So, screening colonoscopy is recommended with surveillance examination every 1-2 years with 4 quadrant biopsies every 10 cm throughout the colon.

Extra-intestinal Complications of UC

System or Site	Manifestation
Hepatobiliary	Primary sclerosing cholangitis Cholangiocarcinoma Gallstones
Dermatologic	Erythema nodosum Pyoderma gangrenosum Sweet syndrome
Oral	Aphthous ulceration
Ocular	Episcleritis Uveitis/iritis
Musculoskeletal	Enteropathic arthropathy Sacroiliitis Ankylosing spondylitis Osteopenia/osteoporosis
Hematologic	Thromboembolic disease

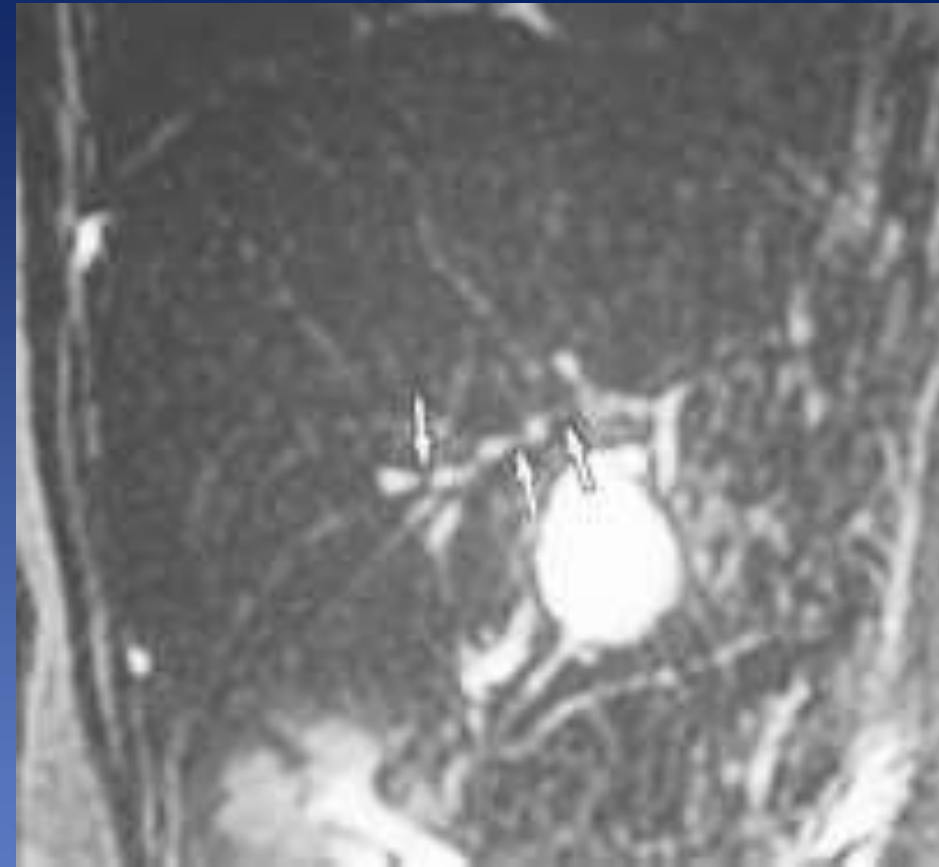
Occur during the active phase of inflammatory bowel disease

Unrelated to inflammatory bowel disease activity



Extra-intestinal Complications of UC

Primary sclerosing cholangitis (PSC)



MRCP



ERCP

Extra-intestinal Complications of UC

Dermatologic manifestations



Erythema nodosum



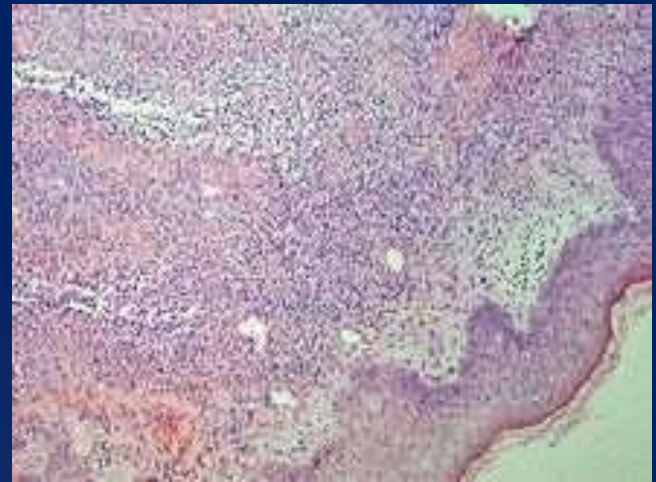
Pyoderma gangrenosum

Extra-intestinal Complications of UC

Sweet's Syndrome (acute febrile neutrophilic dermatosis)

It is a skin disease characterized by sudden onset of fever, leucocytosis, and tender, erythematous, well-demarcated papules and plaques which show dense infiltrates by neutrophil granulocytes on histologic examination.

- It is named for Robert Douglas Sweet.



Punch biopsy of a skin lesion showing neutrophilic infiltration in the dermis with no evidence of vasculitis

Extra-intestinal Complications of UC

Sweet's Syndrome



Pustular lesions with central necrosis on the left leg of a patient with Sweet's syndrome

Extra-intestinal Complications of UC



Aphthous
ulceration

Extra-intestinal Complications of UC

Musculoskeletal Manifestations



Sacroiliitis



Ankylosing Spondilitis

Pouchitis

- Occurs in patients who have undergone an IPAA.
- The etiology is unknown bacterial flora may play a role.
- Symptoms include diarrhea, bleeding, urgency, incontinence, fever, and general malaise.
- Treatment:
 - Antibiotics (metronidazole and ciprofloxacin).
 - Budesonide.
 - Probiotics.

Investigations

A) Laboratory Findings

- Blood picture may show **leucocytosis, anaemia, thrombocytosis.**
- **Hypoalbuminaemia** (in extensive disease).
- **Elevated ESR and CRP.**
- **Stool analysis:** leucocytes and fecal lactoferrin.
Infectious pathogens should be excluded.
- P-ANCA—associated ulcerative colitis is more likely to be medically refractory

B) Imaging Studies

1- Plain Abdominal X-ray:

- Useful predominantly in patients with symptoms of severe or fulminant colitis. So-called thumbprinting appearance, which is due to thickening of the colonic wall + bowel wall edema.
- In toxic megacolon, the bowel is dilated with loss of haustral markings.

Radiograph reveals Thumbprinting



Toxic Megacolon



2- Barium Enema:

- It can be useful for detecting active ulcerative disease, polyps, or masses.
- The colon typically appears granular and shortened.

Double-contrast barium enema. The entire colon is haustral, with a diffuse granular-appearing mucosa. The air-filled terminal ileum is dilated.



Double-contrast barium enema.
Coarsely granular mucosal
ulcerations are visible.



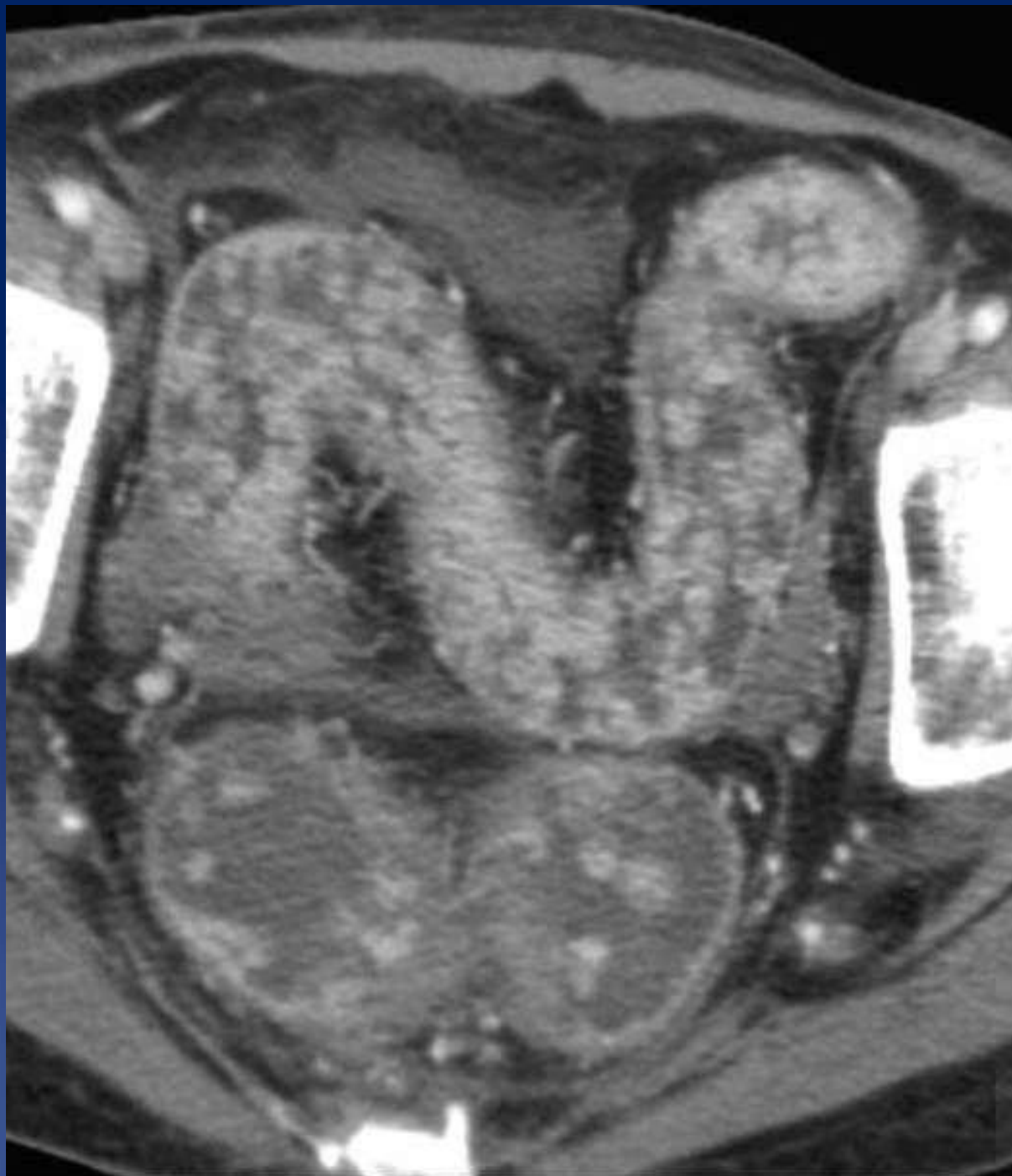
Double-contrast barium enema.
The colon is affected with a
coarsely granular mucosal
pattern. Numerous polypoid
filling defects also are present.



3- CT scan:

- Typically reveals colonic wall thickening.

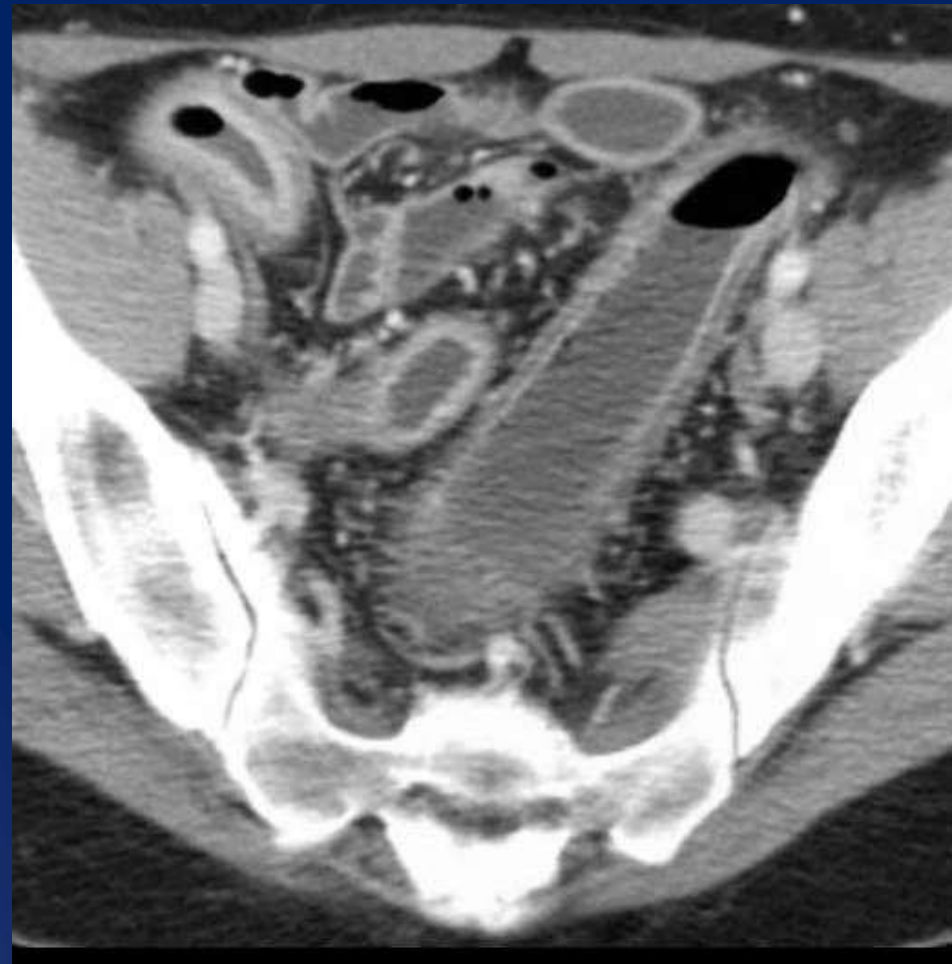
Contrast-enhanced CT. Innumerable enhancing polypoid filling defects are present throughout the rectosigmoid colon. The wall of the colon is hyperenhancing and slightly irregular in contour.



Ulcerative colitis with backwash ileitis



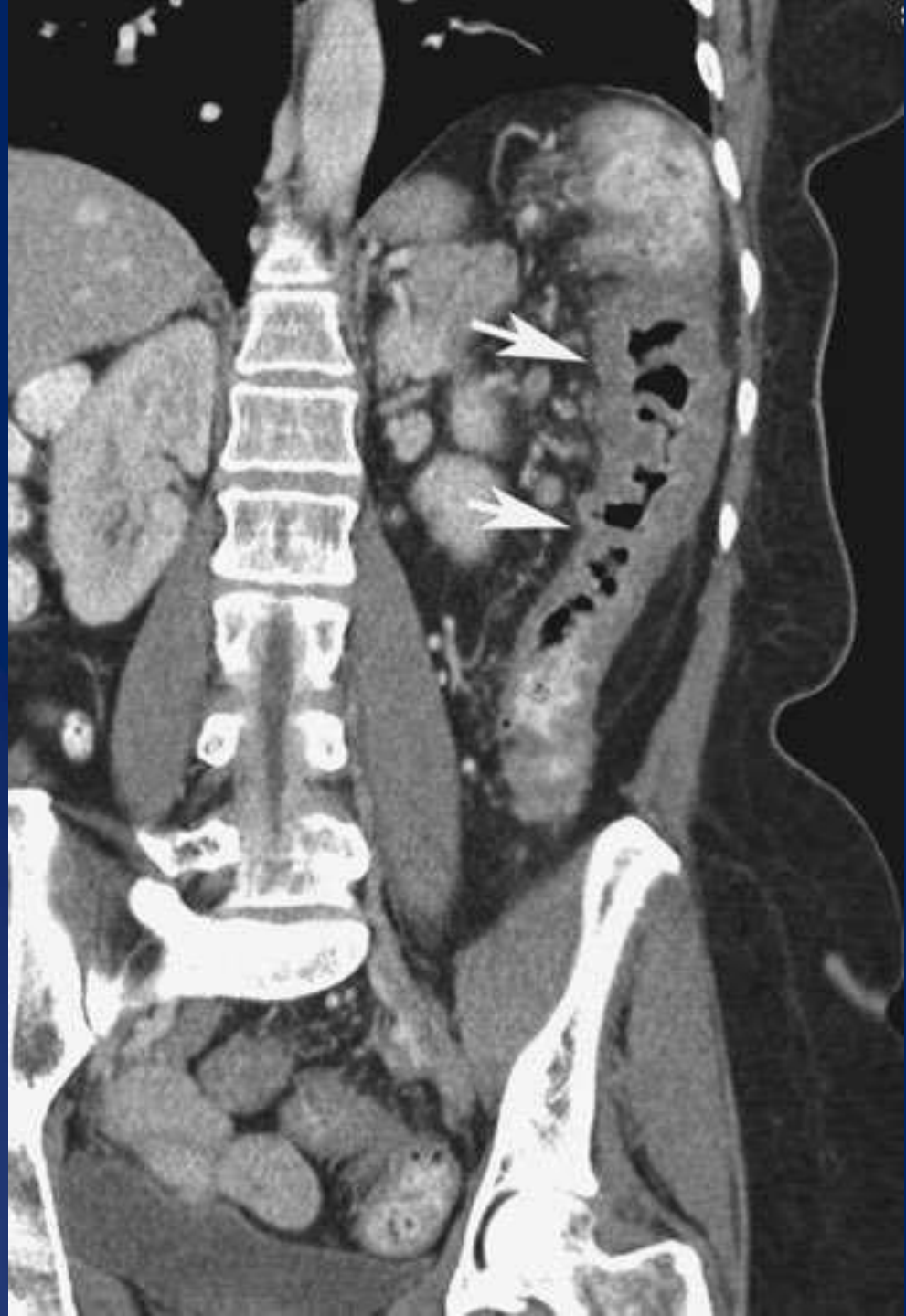
A



B

Contrast-enhanced CT. A and B. Diffuse thickening and hyperenhancement of the wall of the colon and terminal ileum. Engorgement of the vasa recti.

Coronal MDCT image shows mild symmetric wall thickening (arrows) of the left colon with associated lymphadenopathy in the mesocolon.



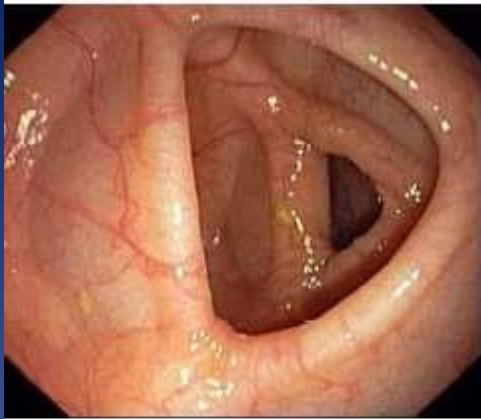
C) Colonoscopy

- Allows assessment of the extent and severity of the disease. Multiple biopsies could be taken.
- It helps to exclude alternative diagnoses, such as infectious or ischemic colitis.

Findings include:

- Mucosal erythema, edema, and granularity and loss of normal vasculature.
- Hemorrhages, ulcerations and a purulent exudate occurs with severe disease.
- Pseudopolyps in patients with long-standing disease.

COLONOSCOPY : UC



- mucosal inflammation
- loss of vascular pattern
- contact bleeding
- congestion
- superficial ulceration
- inflammatory pseudopolyps

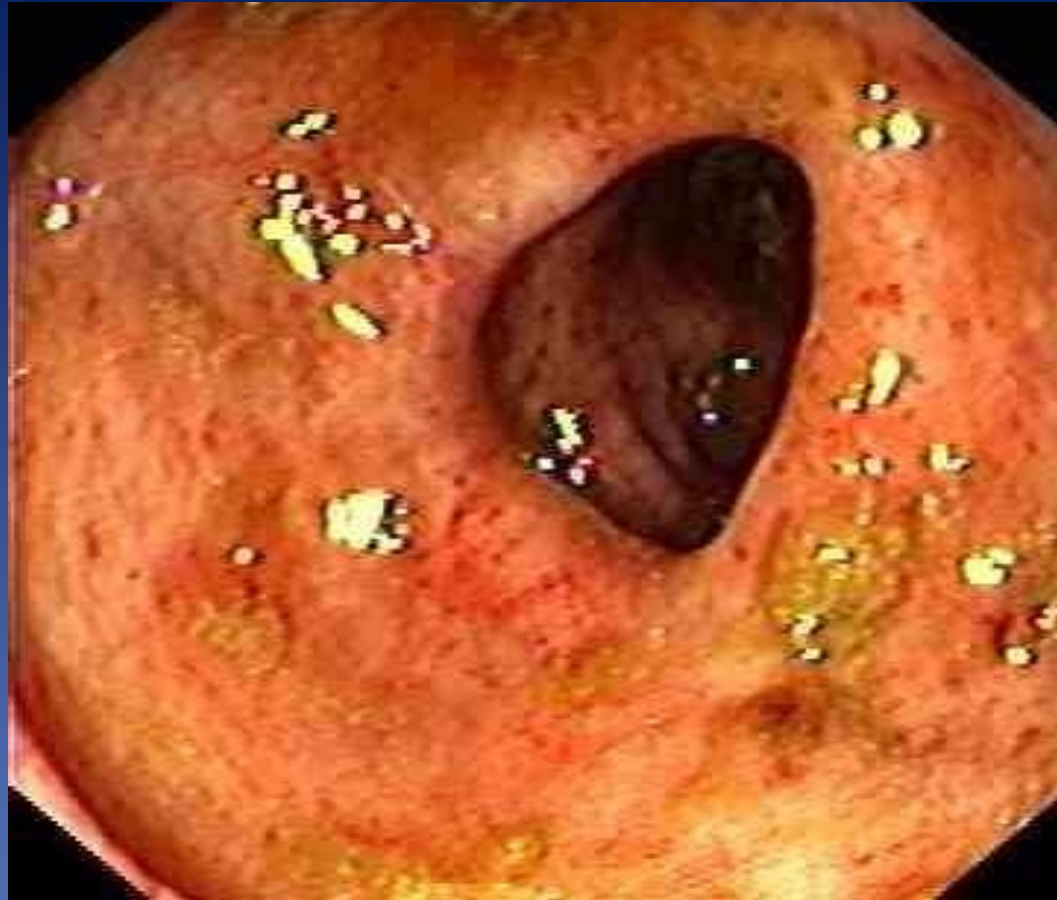
Normal

UC



superficial ulceration and loss of mucosal architecture





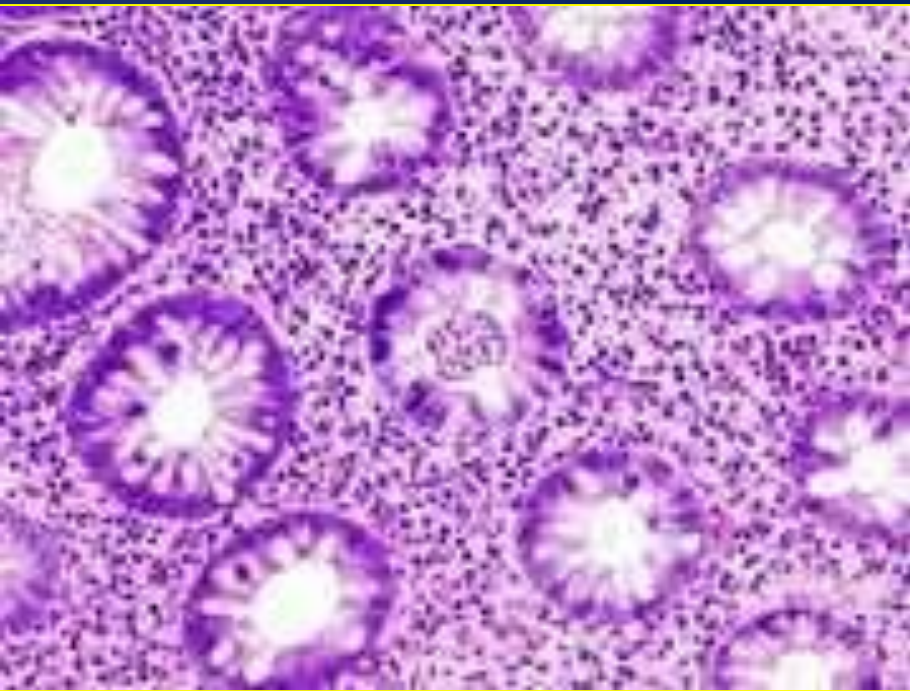


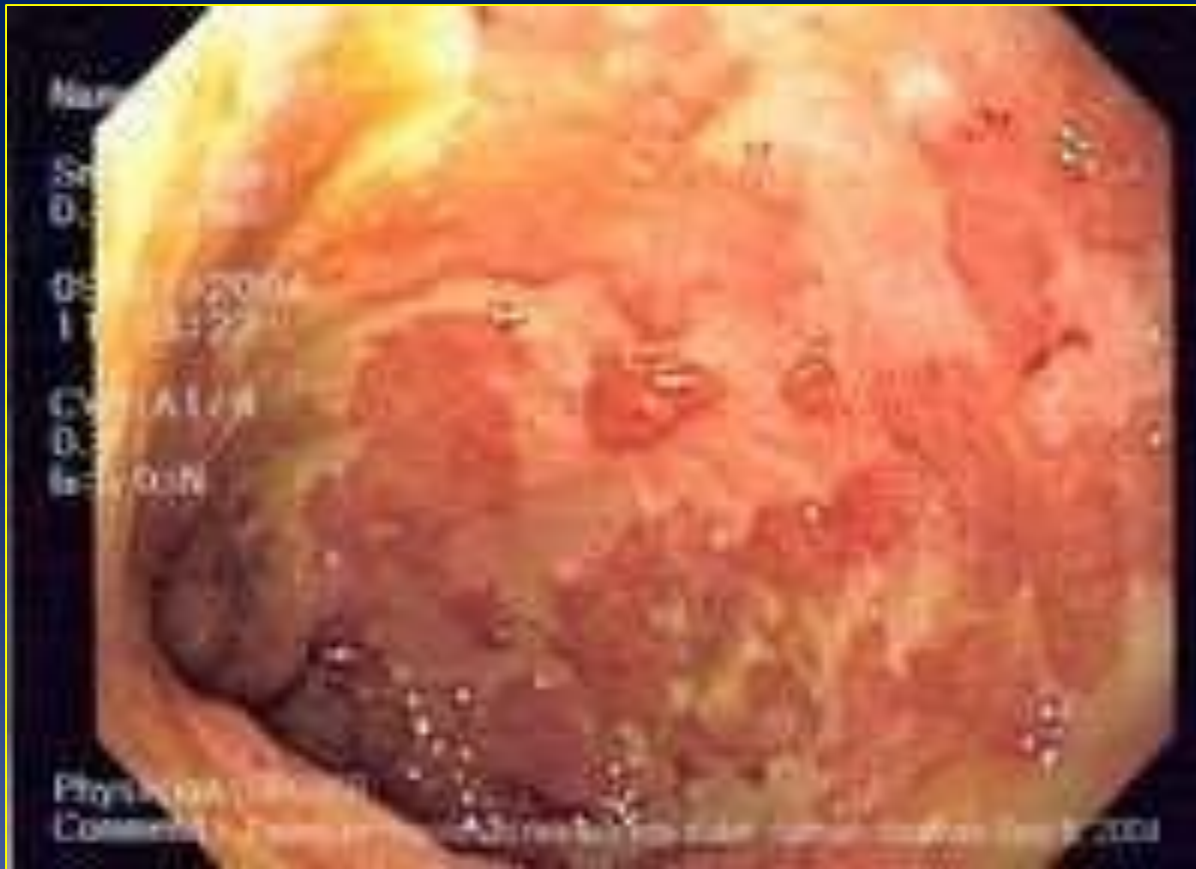


Colonic pseudopolyps

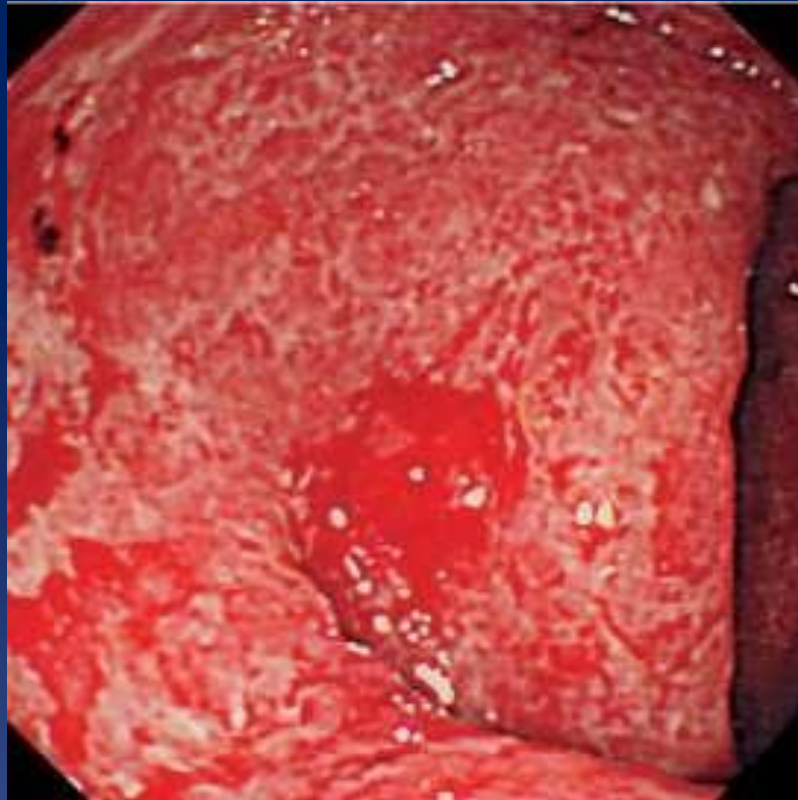
The term 'polyp' is a clinical description of any protrusion of the mucosa.

Microscopic Findings in UC

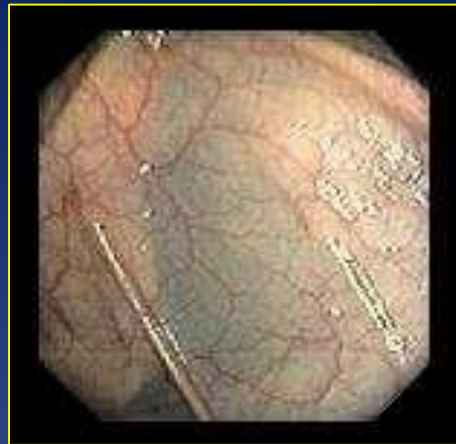
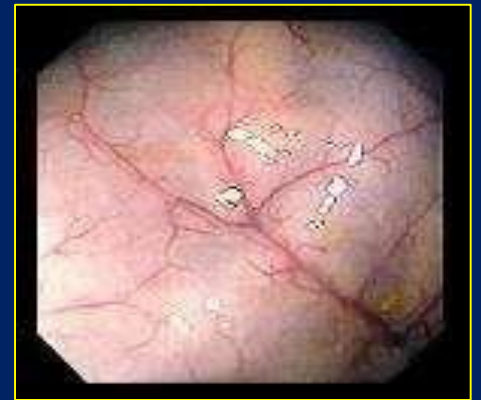




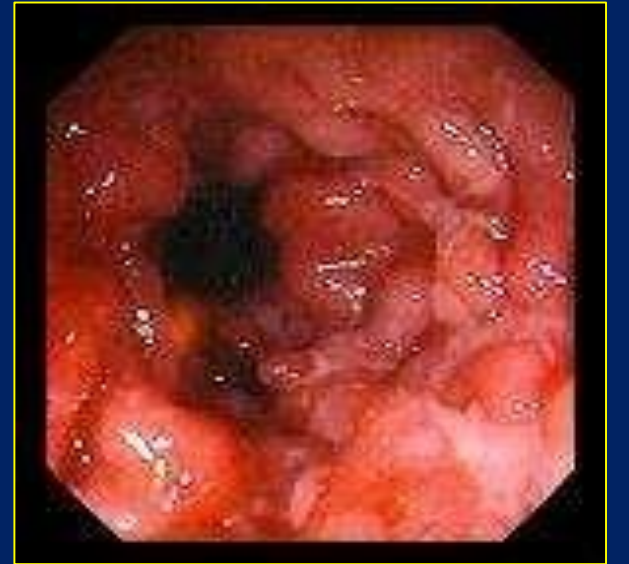
Endoscopic image of ulcerative colitis affecting the left side of the colon. The image shows confluent superficial ulceration and loss of mucosal architecture.



Sigmoidoscopic view of moderately active ulcerative colitis. Mucosa is erythematous and friable with contact bleeding. Submucosal blood vessels are no longer visible









Treatment of Ulcerative Colitis

Goals of Therapy for UC

- Inducing remission
- Maintaining remission
- Restoring and maintaining nutrition
- Maintaining patient's quality of life
- Surgical intervention (selection of optimal time for surgery)

A) Medical Treatment

1) 5-Aminosalicylates

Used in mild to moderate disease.

Effective in induction and maintenance of remission.

Also, they may decrease the risk for CRC.

Preparations:

Generic Name	Proprietary Name	Delivery Mechanism	Location of Release	Typical Dosage
Sulfasalazine	Azulfidine	5-ASA azo bond to sulfapyridine	Colon	1-4 g/day divided twice daily
Mesalamine	Asacol	pH > 7	Ileum, colon	2.4-4.8 g/day divided three times daily
	Pentasa	Timed release	Small bowel, colon	2-4 g/day divided four times daily
	Lialda	pH > 7	Colon	2.4-4.8 g/day once daily
	Rowasa	Enema	Rectum, sigmoid colon	1-4 g/day
	Canasa	Suppository	Rectum	1 g/day
Balsalazide	Colazal	5-ASA azo bond to inert carrier	Colon	6.75 g/day divided three times daily
Olsalazine	Dipentum	5-ASA azo bond to 5-ASA	Colon	1-3 g/day divided twice daily

Side effects: rare

- Interstitial nephritis.
- Pulmonitis.
- Pericarditis.
- Rash.
- Pancreatitis.
- Worsening of colitis.

2) Corticosteroids

- Used in acute treatment of moderate to severe colitis.
- About one third of patients with ulcerative colitis require steroids.
- Only about 50% of patients will achieve a remission and about 30% will have a response.
- They should be tapered off once a satisfactory maintenance medication has been started.

Preparations:

- Prednisone 40-60 mg/day.
- Methylprednisolone 40-60 mg/day.
- Hydrocortisone 200-300 mg/day.
- Rectally administered steroid enemas provide therapy for flares of distal ulcerative colitis without the systemic side effects.

Side effects of systemic steroids

Skin/soft tissue

- Cushingoid appearance: moon facies, "buffalo hump"
- Abdominal striae
- Acne
- Hirsutism
- Edema

Psychiatric

- Sleep disturbance/activation
- Mood disturbance
- Psychosis

Neurologic

- Neuropathy
- Pseudotumor cerebri

Musculoskeletal

- Osteoporosis
- Aseptic necrosis of bone
- Myopathy

Endocrine

- Diabetes mellitus
- Adrenal cortex suppression and atrophy

Immunologic

- Lymphocytopenia
- Immunosuppression (opportunistic infection)
- False-negative skin test

Cardiovascular

- Hypertension

Ophthalmologic

- Cataract
- Narrow-angle glaucoma

Developmental

- Growth retardation

3) Thiopurines (Azathioprine & 6-mercaptopurine)

-Effective for the maintenance of remission but due to their slow onset of action, they are not appropriate as solo induction agents for patients with severe disease.

- Dose:

* Azathioprine 2 - 2.5 mg/kg/day.

* 6-mercaptopurine 1 - 1.5 mg/kg/day.

- Side effects:

- Leucopenia.

- Pancreatitis.

- Hepatitis.

- Nausea.

4) **Infliximab** (Remicade 100 mg vial)

- Its an IgG monoclonal antibody directed against TNF.
- Its effective for the induction and maintenance of remission.
- It offers a less toxic alternative to cyclosporine for patients with severe disease. Also, it can be used in patients who are steroid refractory or steroid dependent and for patients who are failing to respond to azathioprine & 6-mercaptopurine.
- Dose:
 - * Induction of remission: 5 mg/kg IV at weeks 0, 2, 6.
 - * Maintenance: 5 mg/kg IV every 8 weeks.

5) Cyclosporine

-Its used as last line medical therapy to treat hospitalized patients with severe ulcerative colitis.

- Dose:

* 2-4 mg/kg/day given as a continuous infusion.

- Side effects:

- Nephrotoxicity.

- Opportunistic infections.

- Seizures.

- Surgical options:

- Proctocolectomy and creation of IPAA.
- Proctocolectomy with end ileostomy.
- Proctocolectomy with continent ileostomy.

- Laparoscopic approach.

Surgery in UC : why & when?

- Uncontrollable colonic hemorrhage
- Failure to control severe attacks or toxic megacolon
- Colonic perforation
- Chronic symptoms despite medical therapy
- Medication side effects without disease control
- Dysplasia or Cancer
- Growth retardation

Surgery in UC : why & when?

Intractability:

- Colitis refractory to medical management
- Often due to side effects of medical treatments
- Most common indication for operation

Dysplasia/Carcinoma:

- high-grade dysplasia : absolute indication

Massive Colonic Bleeding:

- very infrequent; less than 5% of urgent UC colectomies

Toxic Megacolon:

- acute colitis accompanied by significant colonic dilatation
- high fever, severe abdominal pain, tachycardia, leukocytosis
- predisposed to perforation
- treatment: IVF resuscitation, antibiotics, steroids, immunosuppressives
- clinical deterioration despite above : urgent operation

Types of Operations

Total Proctocolectomy with End-Ileostomy:

- removes entire colon, rectum, and anus
- performed in one stage; avoids problems of multiple operations
- disadvantages: permanent stoma, problems with healing perineal wound

Total Abdominal Colectomy with Hartmann's Closure or Mucous Fistula:

- used in acutely sick patients (fulminant colitis, toxic megacolon)

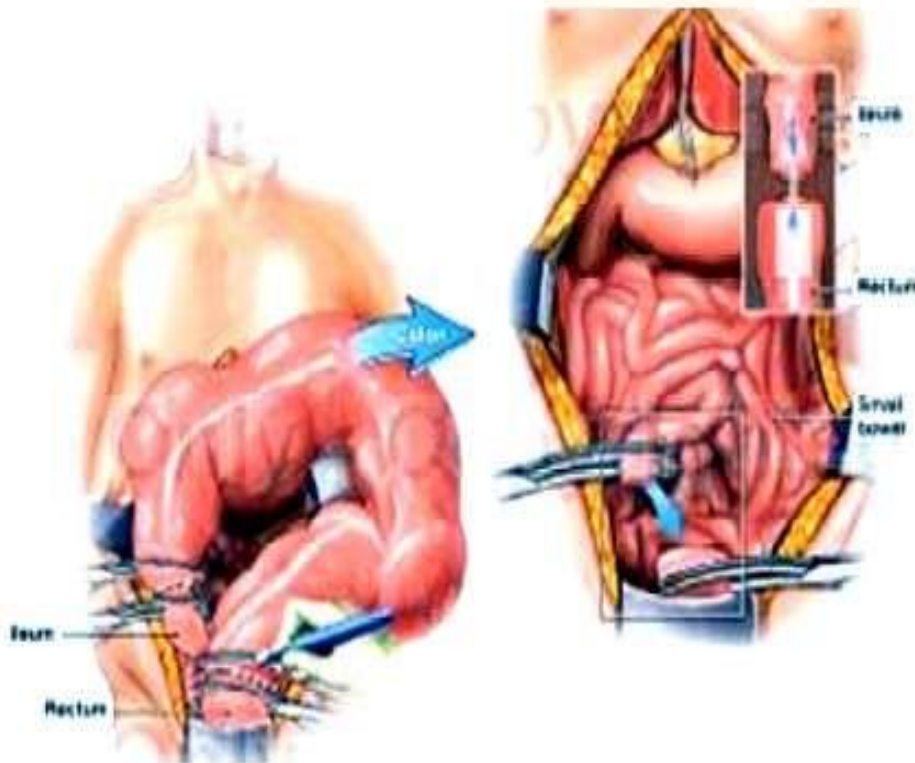
Total Proctocolectomy with Ileal Pouch-Anal Anastomosis:

- gold standard
- requires good anorectal function and sphincter tone
- generally performed on patients younger than 65

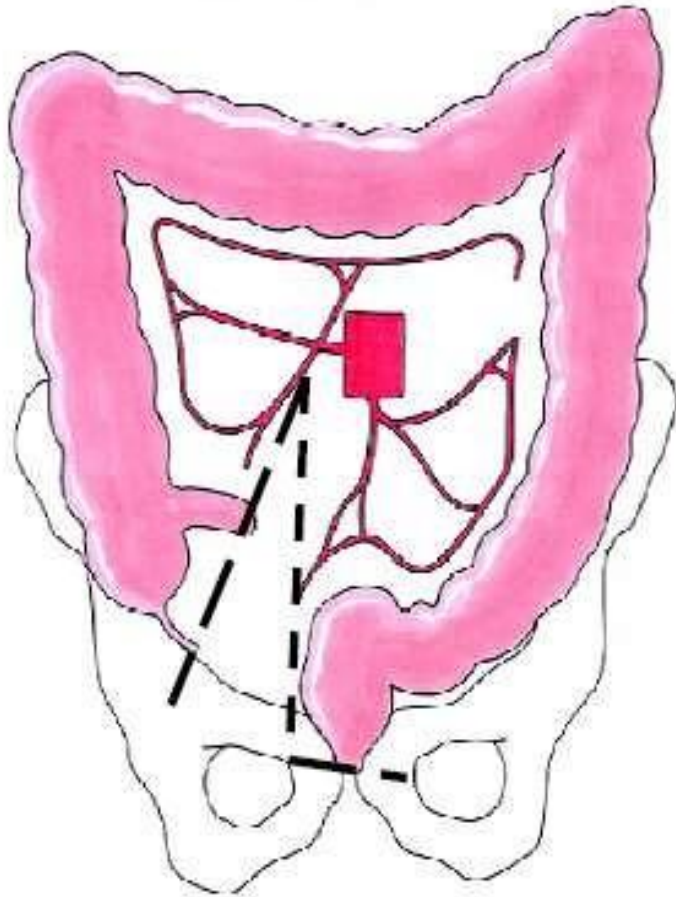
Types of Operation

Colectomy & ileorectal anastomosis

- Rectal sparing
- Normal sphincters
- No dysplasia
- Annual surveillance
- Preservation of fertility



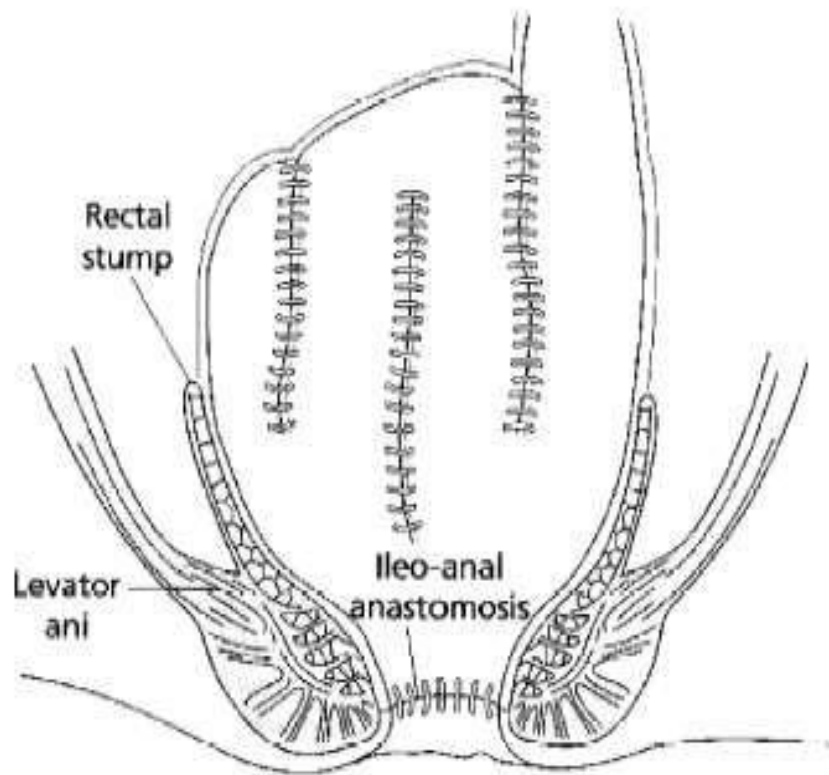
Types of Operation



Pan-proctocolectomy

- Diseased rectum
- Poor sphincters
- Avoid complications of ileoanal pouch
- Permanent ileostomy

Types of Operation



Restorative proctocolectomy

- Avoids permanent ileostomy
- Good sphincters
- Bowel function x4-8 per day
- Pouchitis
- Pouch failure

Complications of UC Surgery

- Mortality (<0.5%)
- 3-10 stools/24 hrs so bowel pattern not normal
- Impotence (1.5%)
- Pouchitis (10-60%)
- Small bowel obstruction (20%)
- Decrease in female fertility (56-98%)
- Pouch-vaginal fistula (4%)

Goals for Surgeon and Patient

Restore quality of life

IBD conclusion

- It is a chronic disorders
- Need to exclude other possibilities
- Need to differentiate between the two
- Need long term management with primary goal to induce then maintain remission and prevent complications of both the disease and drugs.

THANK YOU 😊