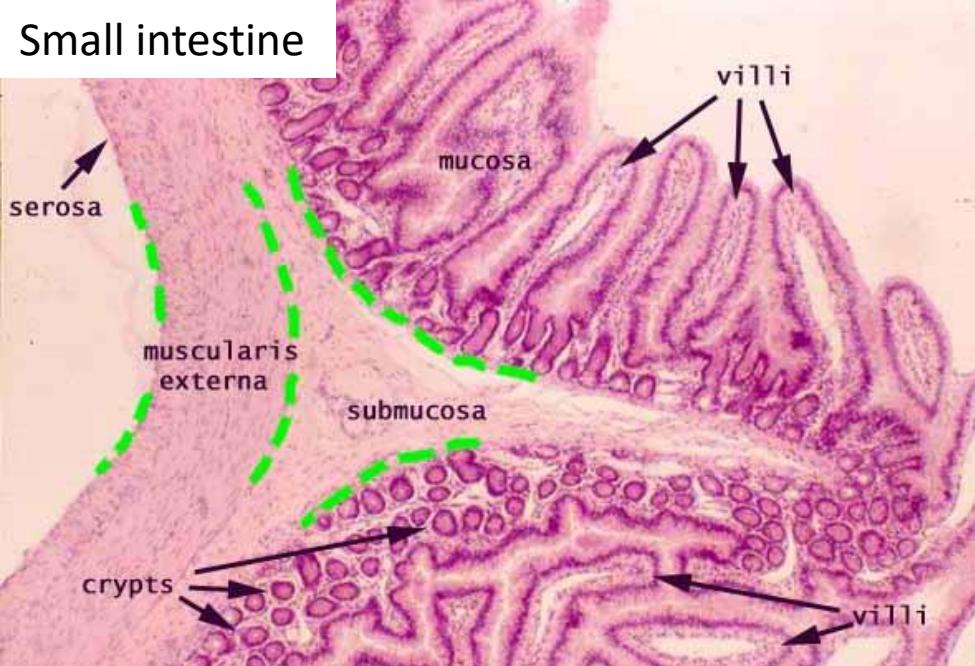


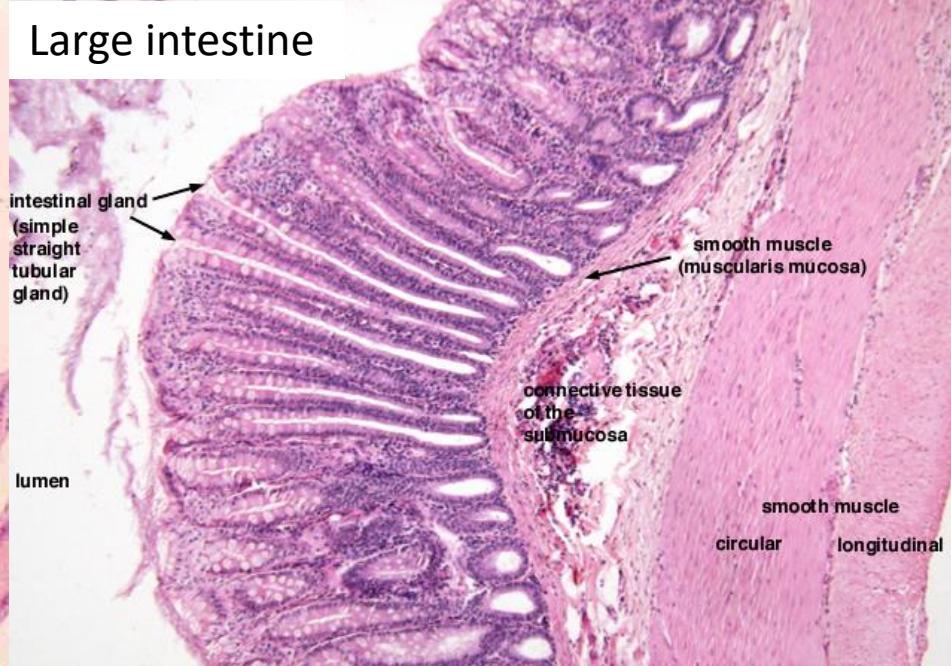
# Non-neoplastic Diseases of the Intestine

13.08.2018

## Small intestine



## Large intestine

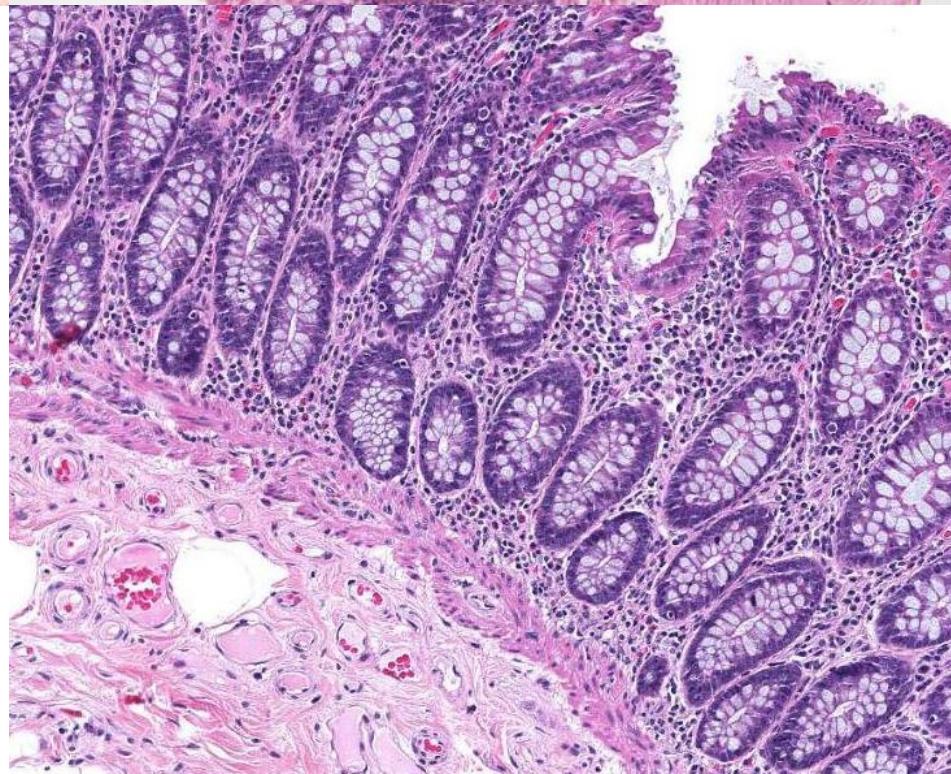


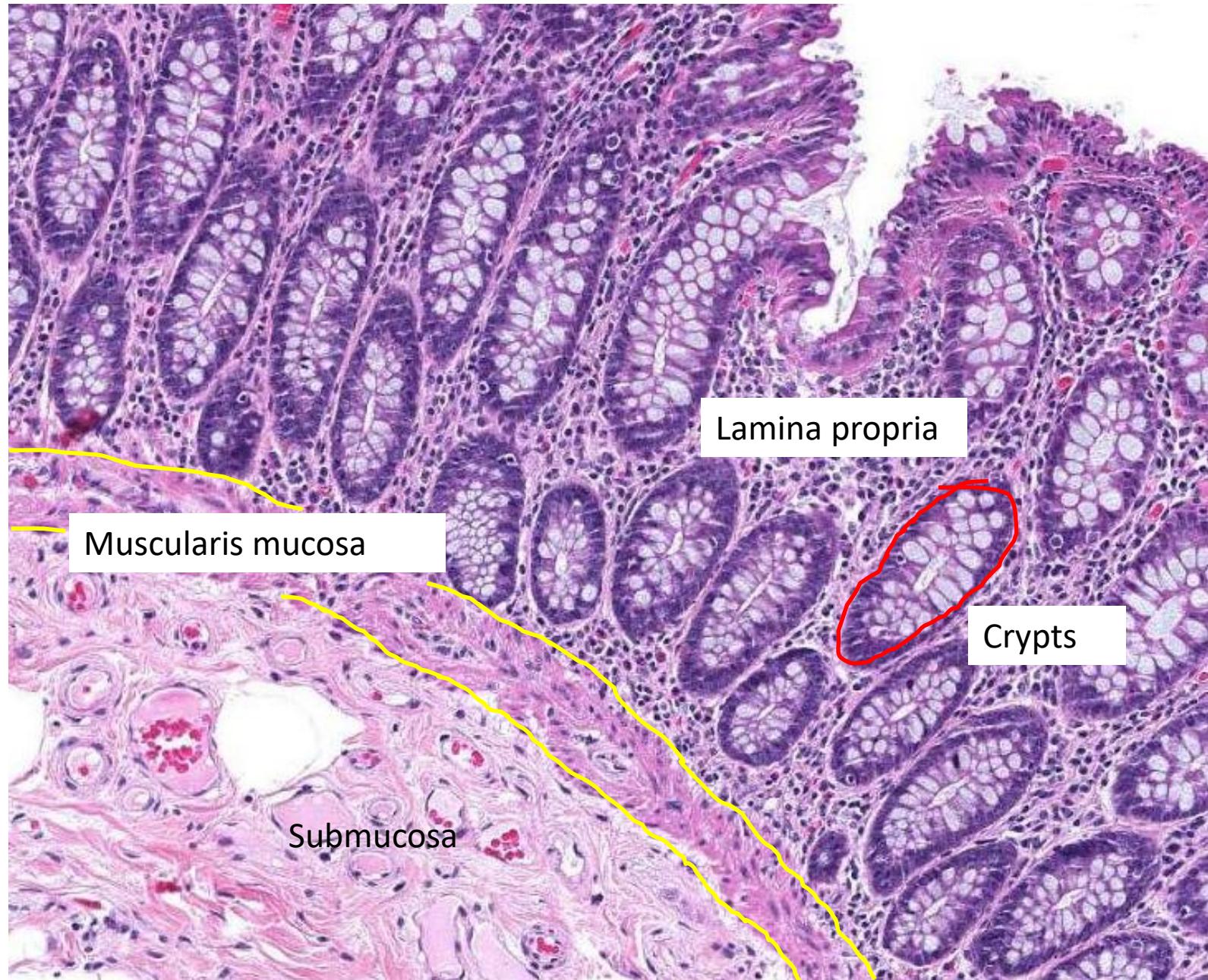
Mucosa – Crypts, lamina propria

Submucosa

Muscularis propria

Serosa





# Objectives

*At the end of this lecture, you should be able to*

- briefly describe the macroscopy and microscopy of the intestine in Inflammatory Bowel Disease (IBD):  
**Crohn's disease (CD) and ulcerative colitis (UC)**
- Briefly describe the pathology of
  - Ischemic bowel disease
  - Diverticular disease
  - Intestinal obstruction
  - Haemorrhoids
  - Angiodysplasia

# Inflammatory Bowel Disease (IBD)

- Chronic inflammatory disease with remissions and relapses/flare-ups
- Two closely related disorders

**Crohn's Disease (CD)**

**Ulcerative Colitis (UC)**

- Having overlapping features

- Clinical presentation - Non-specific

Blood and mucous diarrhoea

Abdominal pain

# Pathogenesis of IBD

- Complex
- Multifactorial
- Still not understood properly

- Cause ?
  - Inappropriate mucosal immune activation
- Incidence is increasing worldwide
- Reason?
  - “Hygiene hypothesis”

## Pathogenesis

- **Genetic factors**
  - Some individuals are more susceptible
  - Familial cases have been recognized
  - Susceptible genes, (eg. *NOD2*, *ATG16L1* and *IRGM* gene in CD) are related to recognition and response to intracellular pathogens

- **Mucosal immune response**
  - Exact mechanism ?
  - Immunosuppressants remain the mainstay of therapy
- **Epithelial defects**
  - Defects in intestinal epithelial tight junction barrier function
  - Defects in the extracellular barrier formed by secreted mucin
  - Abnormalities in Paneth cell granules which contain antibacterial peptides, defensins
- **Intestinal microbiota**
  - Precise role and mechanisms?
- Other factors

# CD and UC have overlapping clinical features

- Diagnosis is based on
  - Clinical features**
  - Radiological/endoscopic findings**
  - Operative findings**
  - Pathological findings**
- *You need “clinicopathological correlation”*

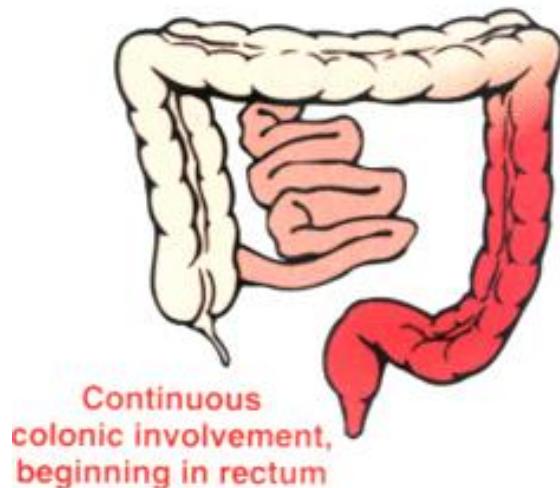
# CD and UC

- Features help to differentiate CD and UC
  - **distribution of the disease**
  - **morphology**

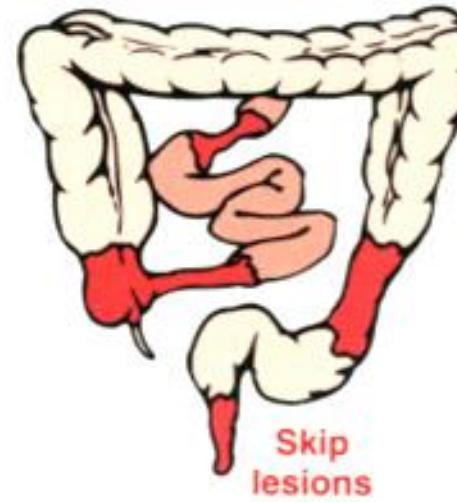
# UC

# CD

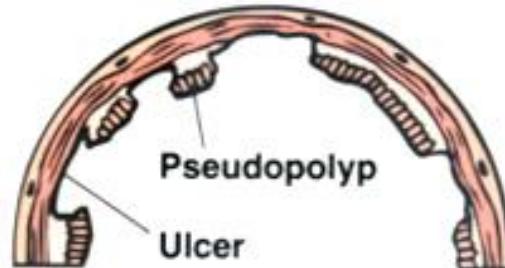
- Limited to the colon and rectum



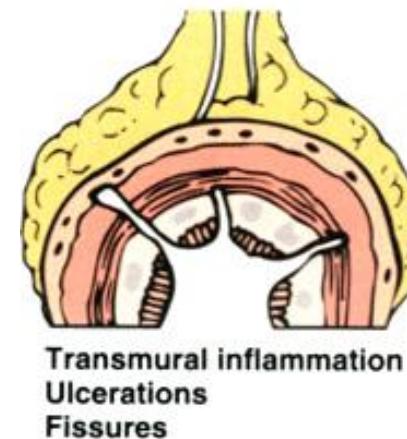
- May involve any area of the GIT



- Inflammation extends only into mucosa and submucosa



- Typically transmural / full thickness of the bowel wall



# CD - Macroscopy

- Can involve any part of the GIT : Mouth to anus
- May be limited to SI / colon or may involve both
- Common sites:  
terminal ileum, ileo-caecal valve and caecum

# CD - Macroscopy

- **Earliest lesions - Apthous ulcers**

Shallow pin point ulcers surrounded by erythema (A)

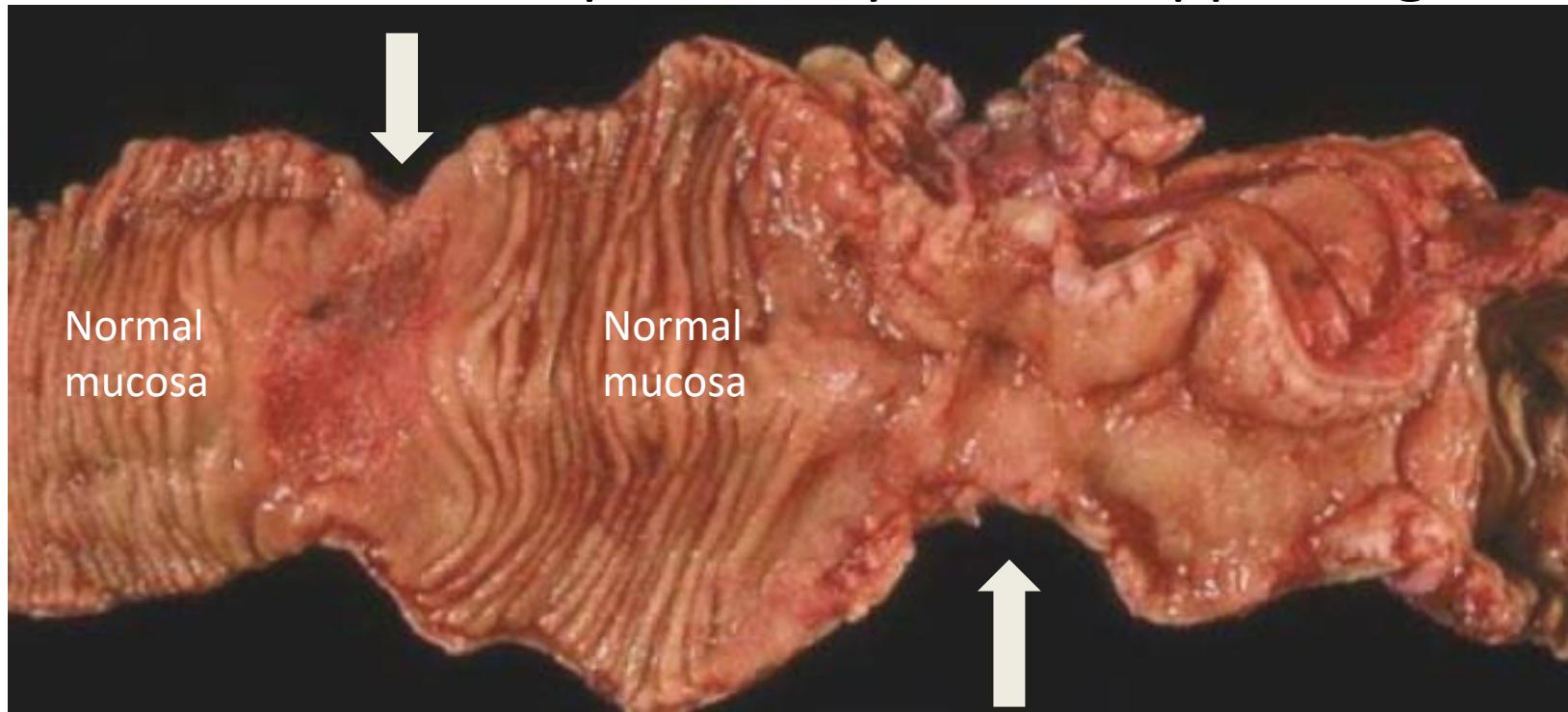
These ulcers overlie the lymphoid follicles

- Multiple apthous ulcers coalesce and form linear serpentine ulcers along the long axis of the bowel (B)



# CD - Macroscopy

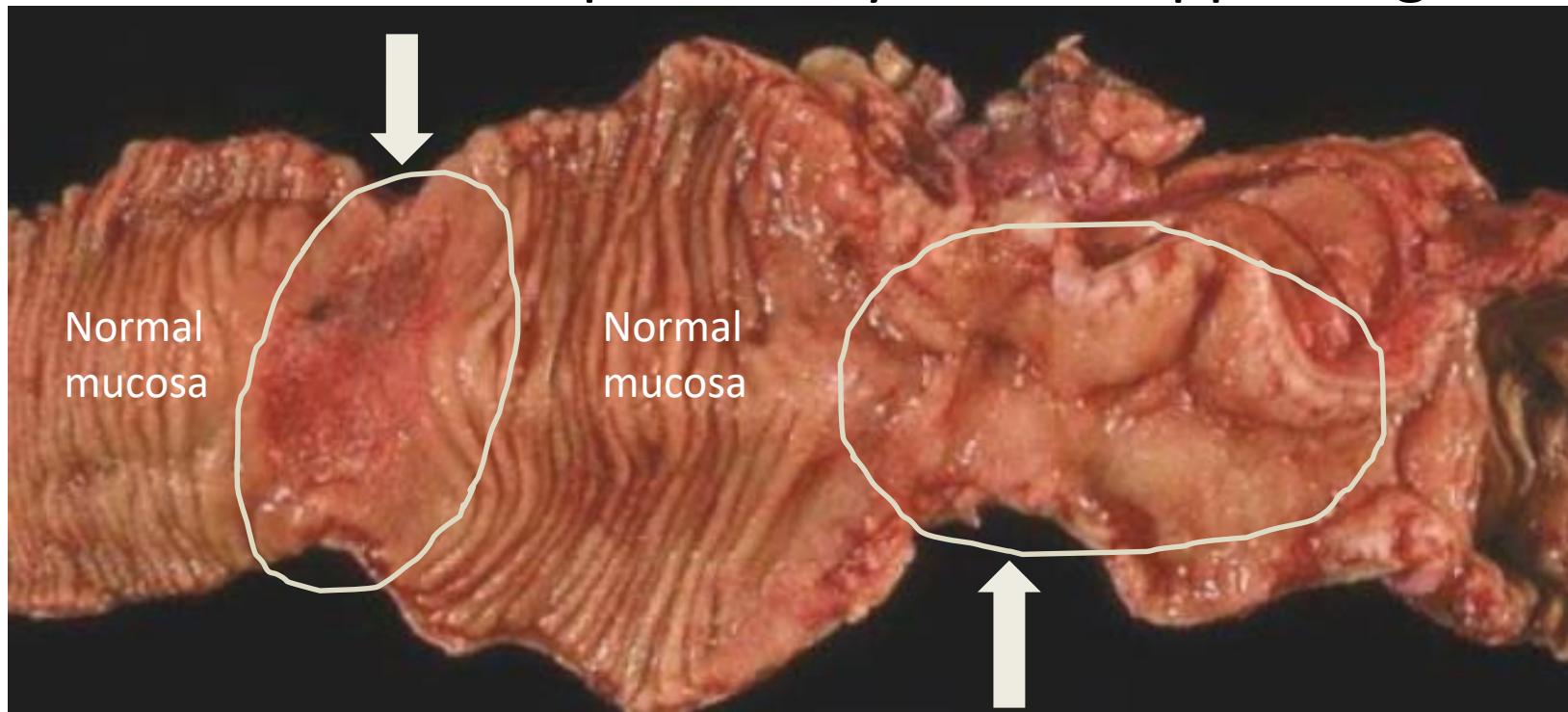
- Later develop multiple, separate, sharply demarcated **skip lesions** (white arrows) with oedematous mucosa with loss of normal mucosal texture
- These lesions are separated by normal appearing mucosa



Crohn disease

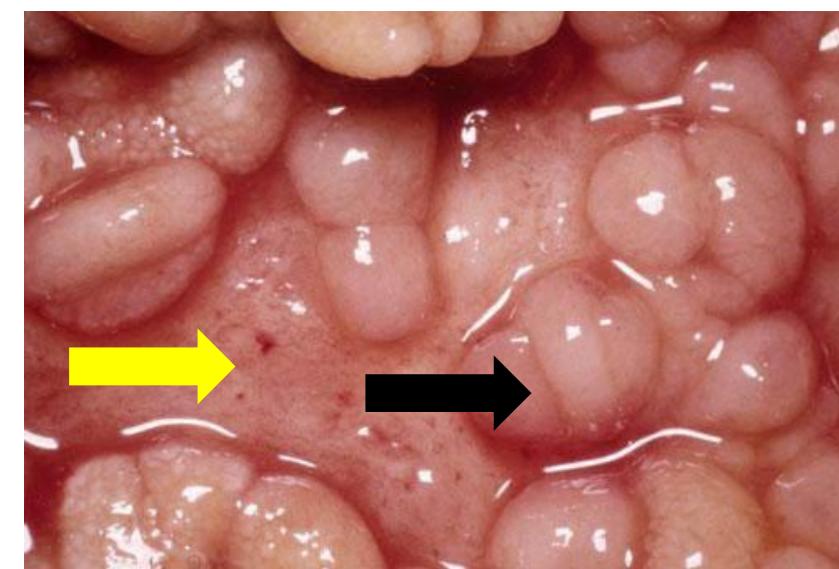
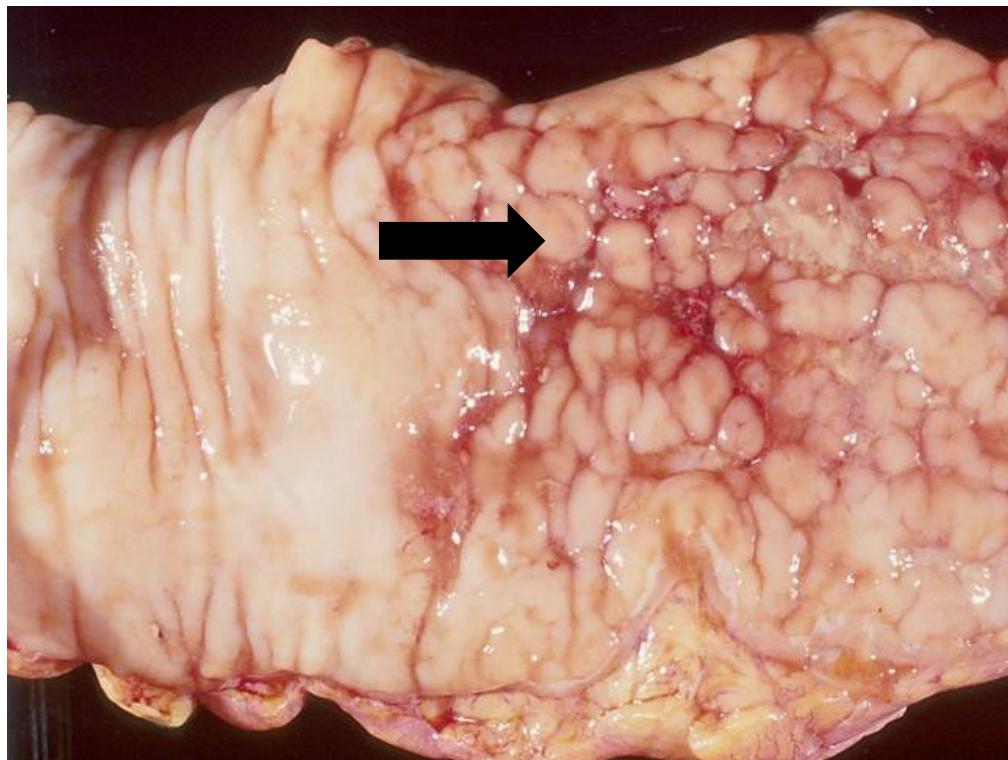
# CD - Macroscopy

- Later develop multiple, separate, sharply demarcated **skip lesions** (white arrows) with oedematous mucosa with loss of normal mucosal texture
- These lesions are separated by normal appearing mucosa

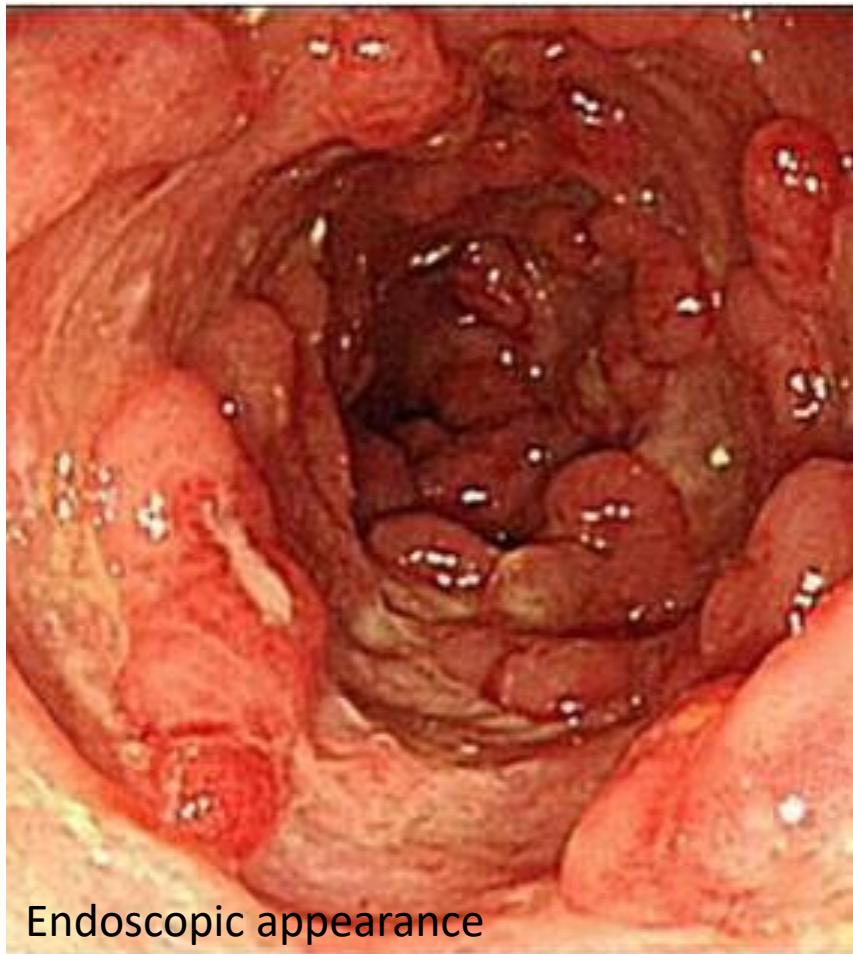


Crohn disease

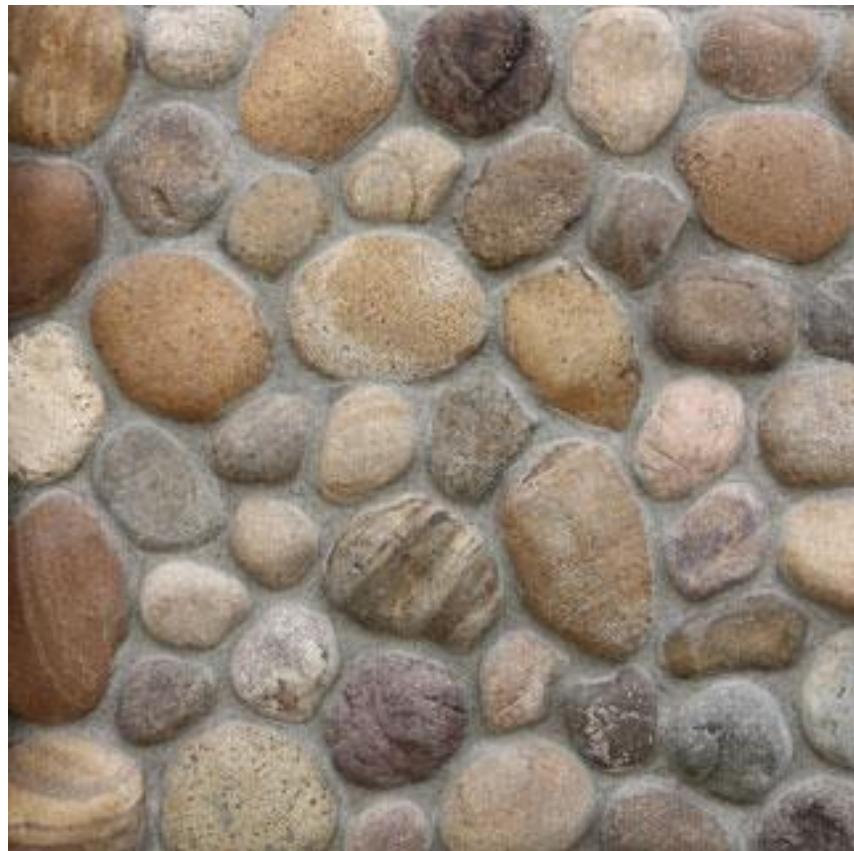
- Within the skip lesions there is uninvolved/spared mucosa ( black arrow )
  - Diseased tissue is depressed below the level of this uninvolved mucosa (yellow arrow)
  - giving rise to a “**Cobblestone appearance**”



# Cobblestone appearance

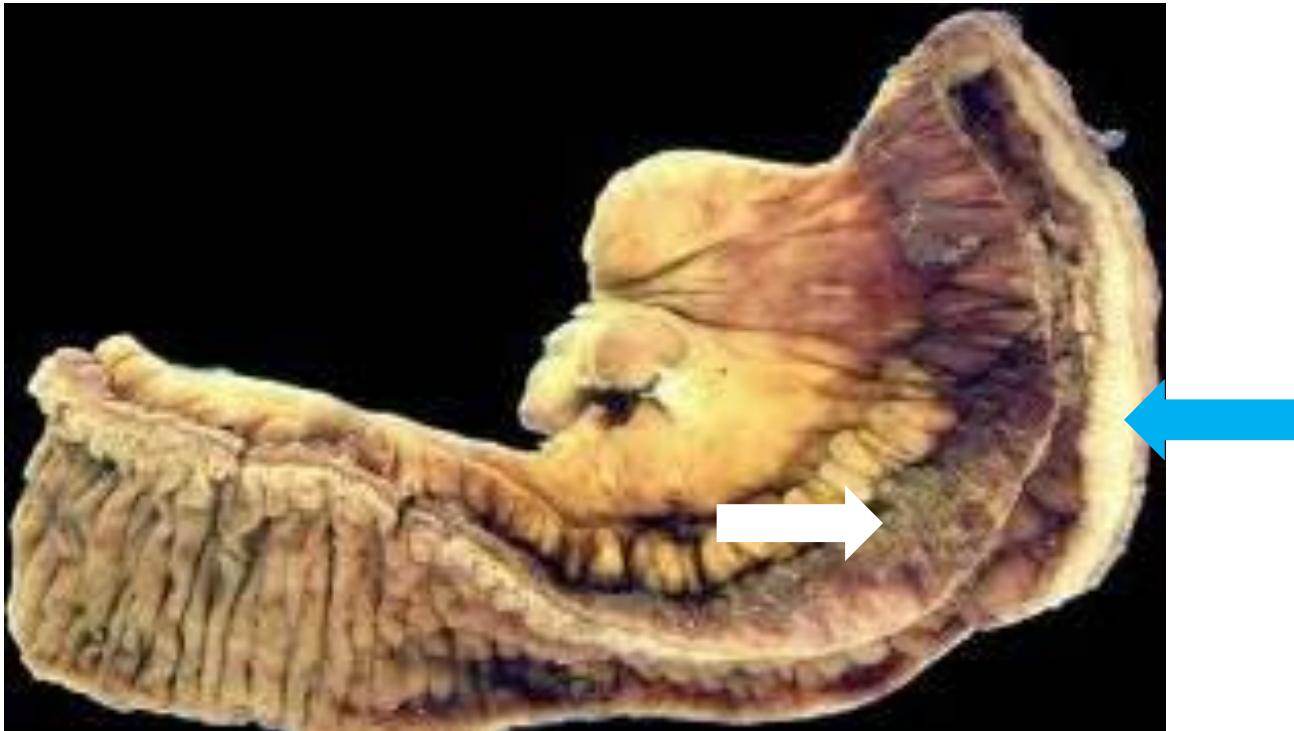


Endoscopic appearance



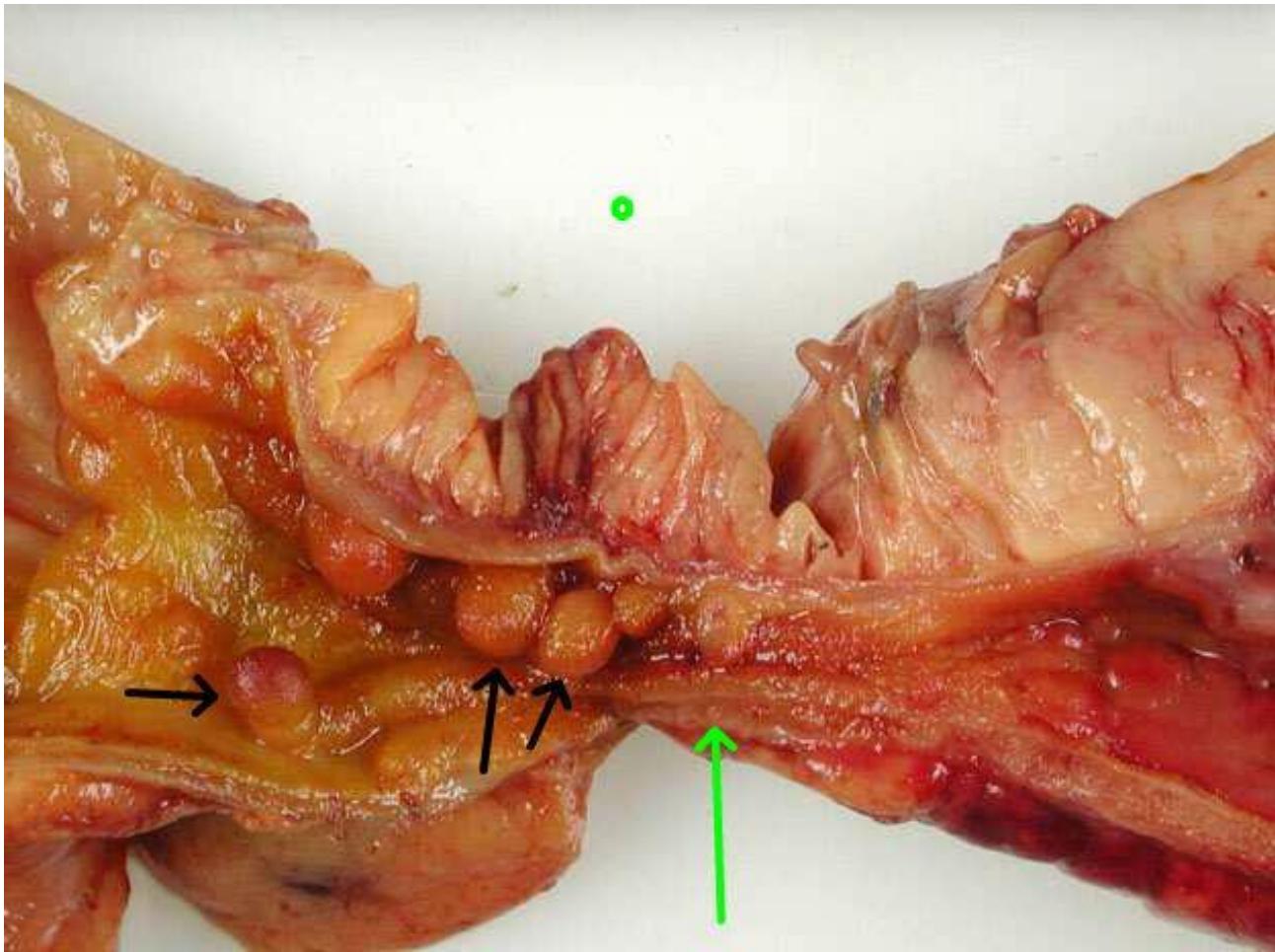
# CD - Macroscopy -

## Thickening of the bowel wall



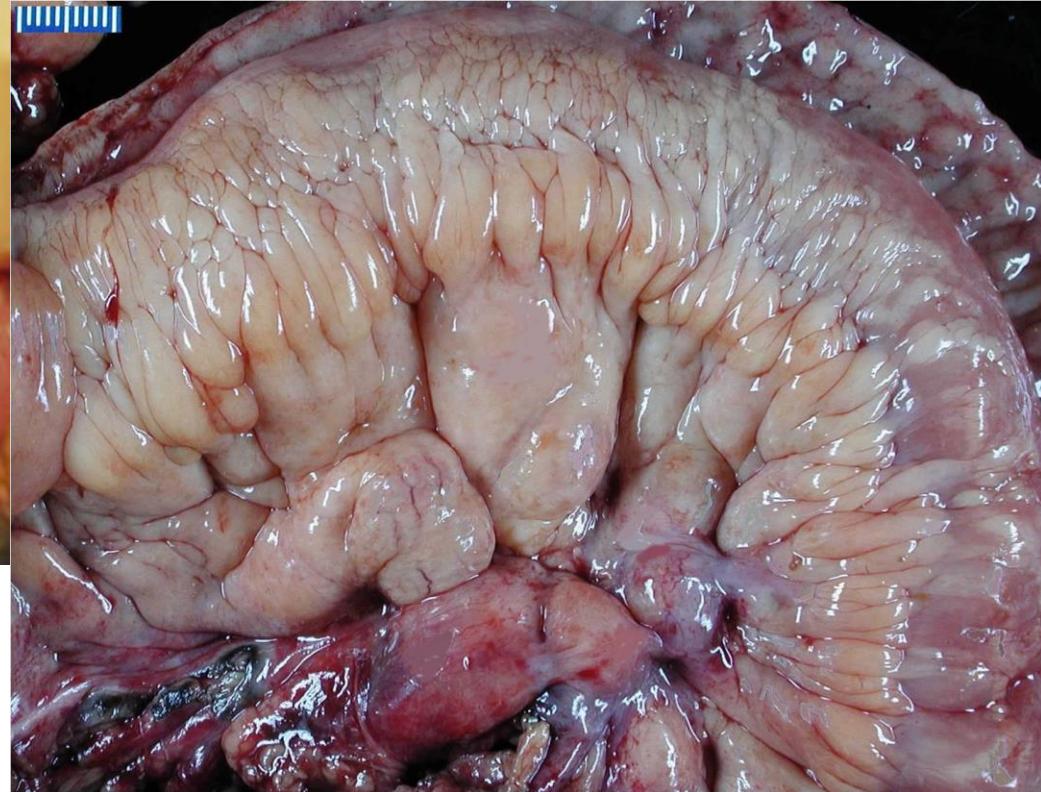
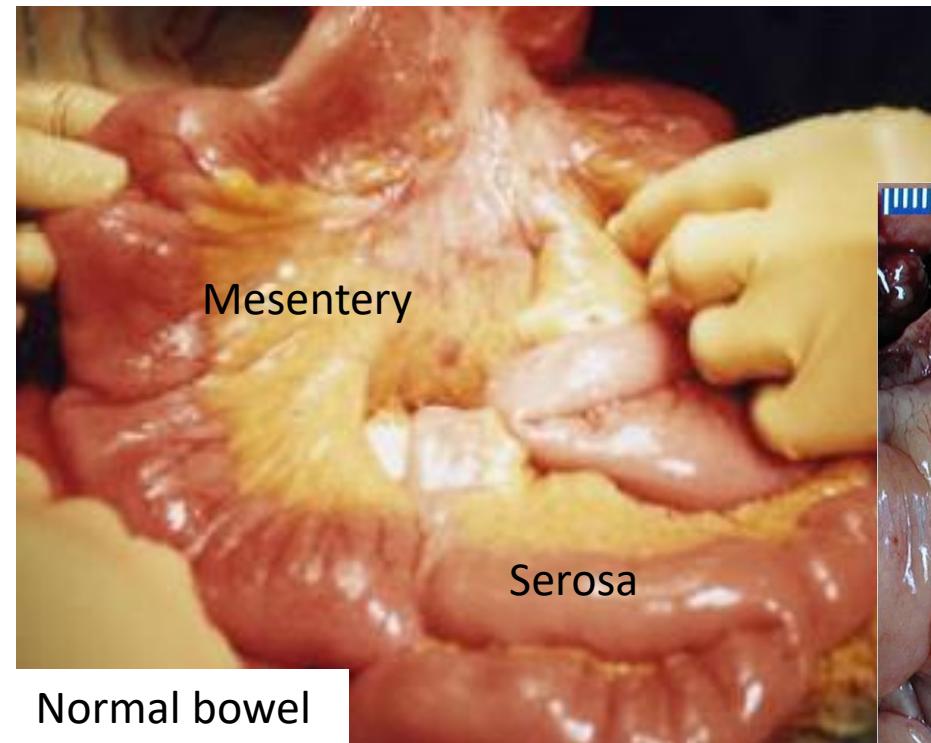
- Thickening is due to transmural inflammation, oedema, submucosal fibrosis and hypertrophy of the MP (blue arrow)
- Note the inflammatory exudate on the **serosal aspect** (white arrow)

# CD - Luminal narrowing and stricture formation (green arrow)



Crohn disease

# CD - Macroscopy - Creeping fat/fat wrapping

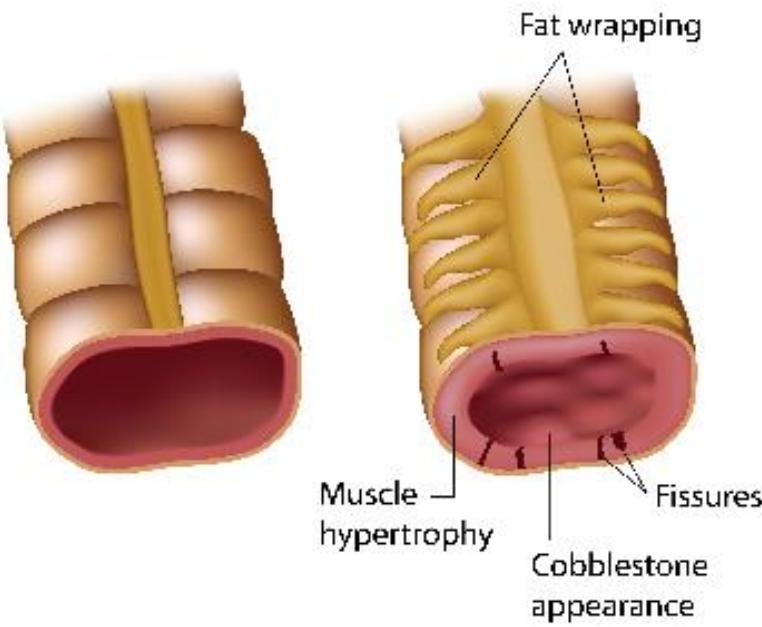


Mesenteric fat extends around the serosal surface  
of the bowel

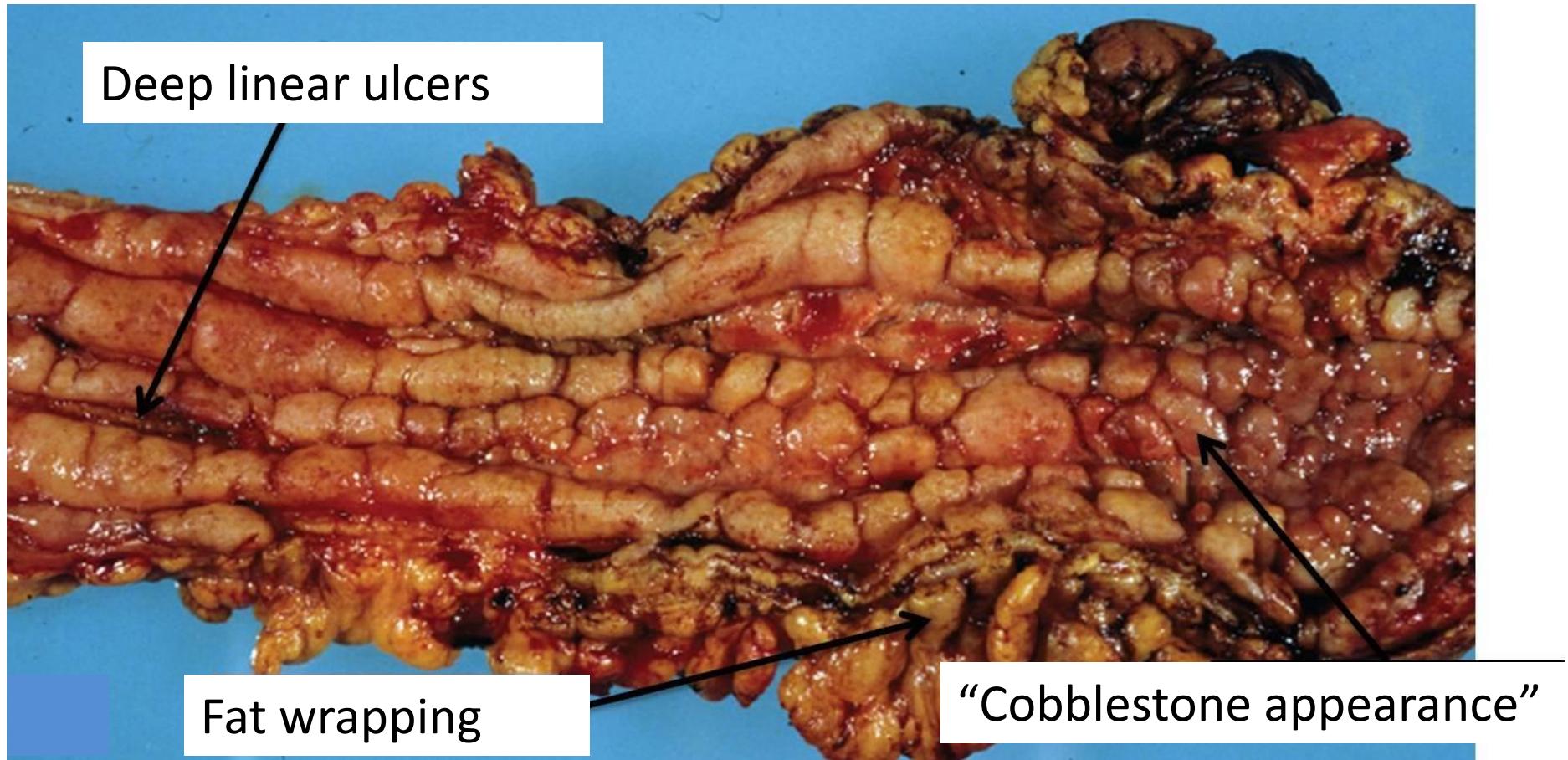
Crohn disease

# CD - Fissures

- Deep fissuring ulcers between mucosal folds
- When extend deep within the bowel wall
  - **Fistula tracts, bowel perforation, abscess formation, bowel adhesions**

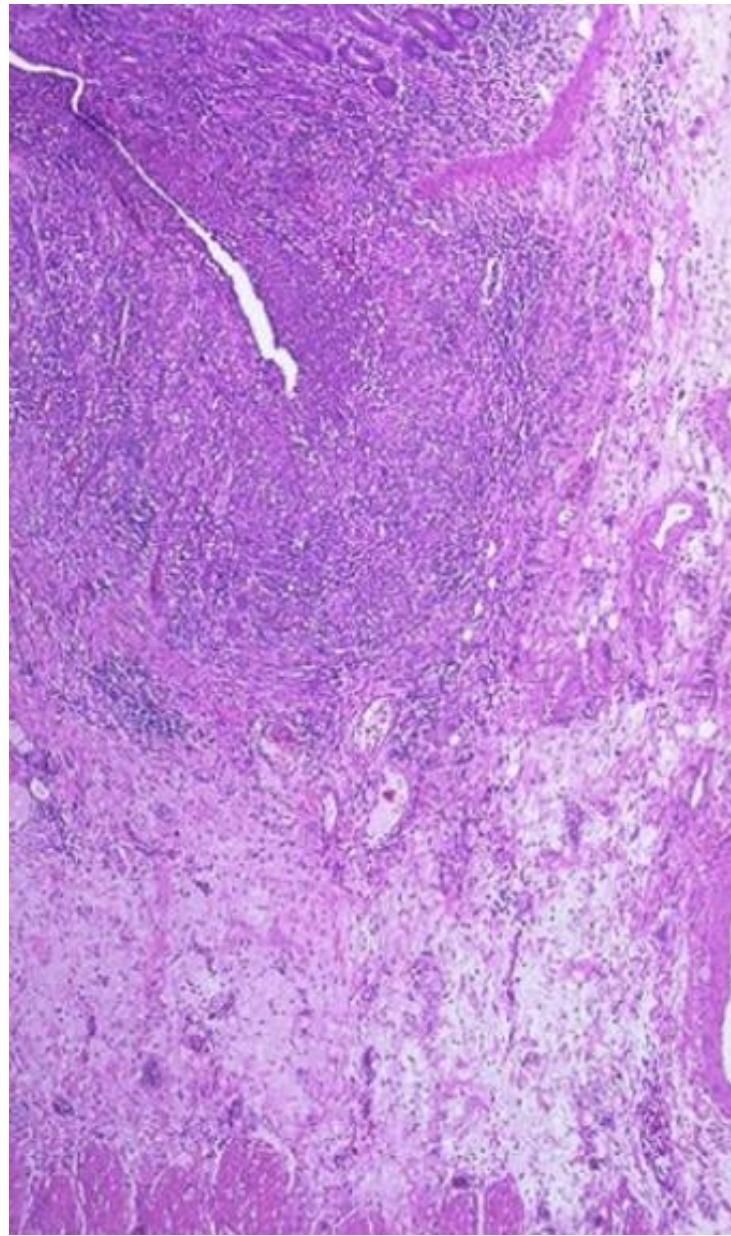


# Crohn disease - Macroscopy of the bowel



Mucosal surface of the bowel

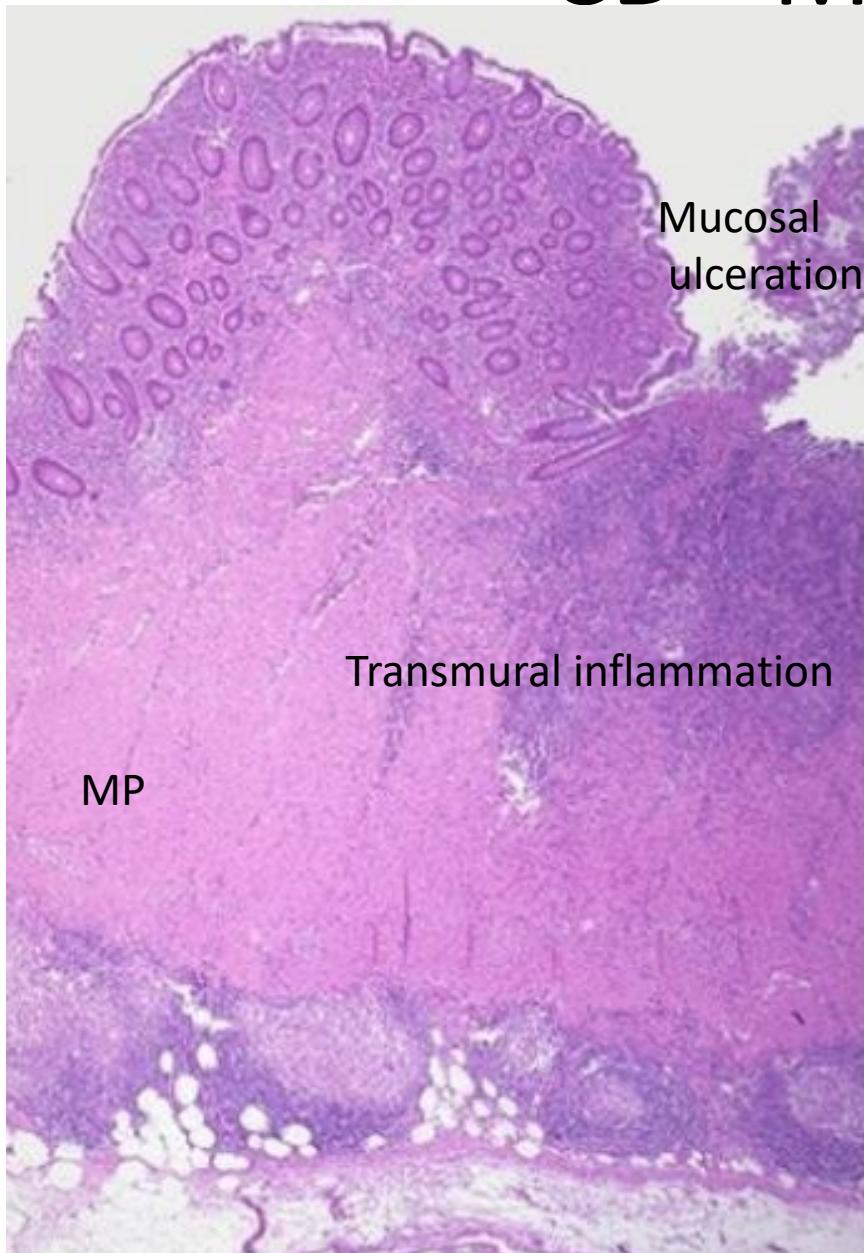
# CD - deep fissuring ulcers/ fissures



# CD - Transmural inflammation

- The inflammation characteristically involve the full thickness of the bowel wall
- This is not a feature that can be recognized by routine **mucosal** biopsies

# CD - Microscopy

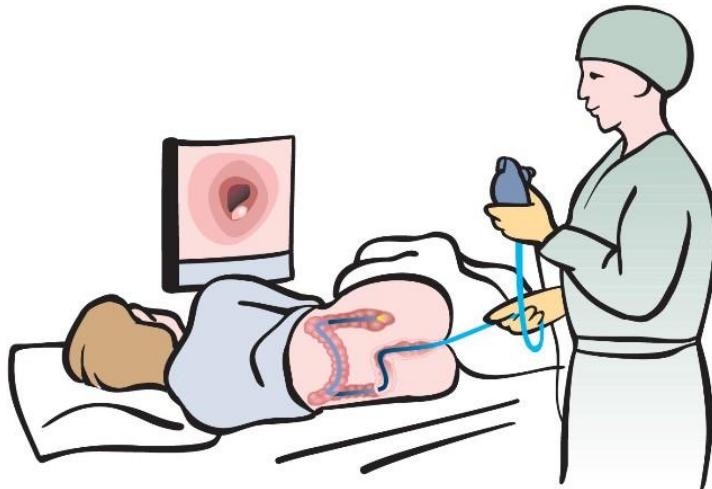


Transmural inflammation of the large bowel

There are lymphoid aggregates external to the muscularis propria (MP)

# Crohn Disease - Microscopy

- IBD patients undergo endoscopy and biopsy



- Multiple biopsies are taken
- A biopsy is usually around 3mm



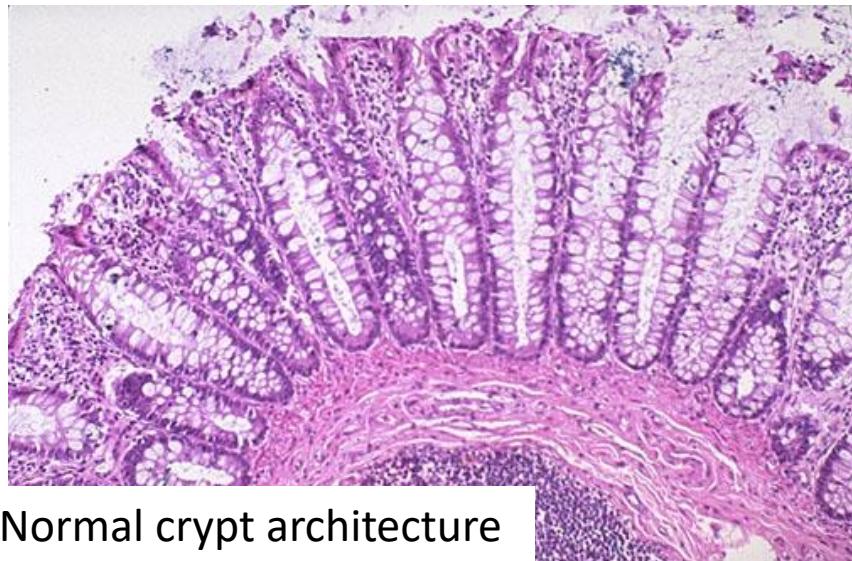
Crohn disease

# CD - Changes of the mucosa

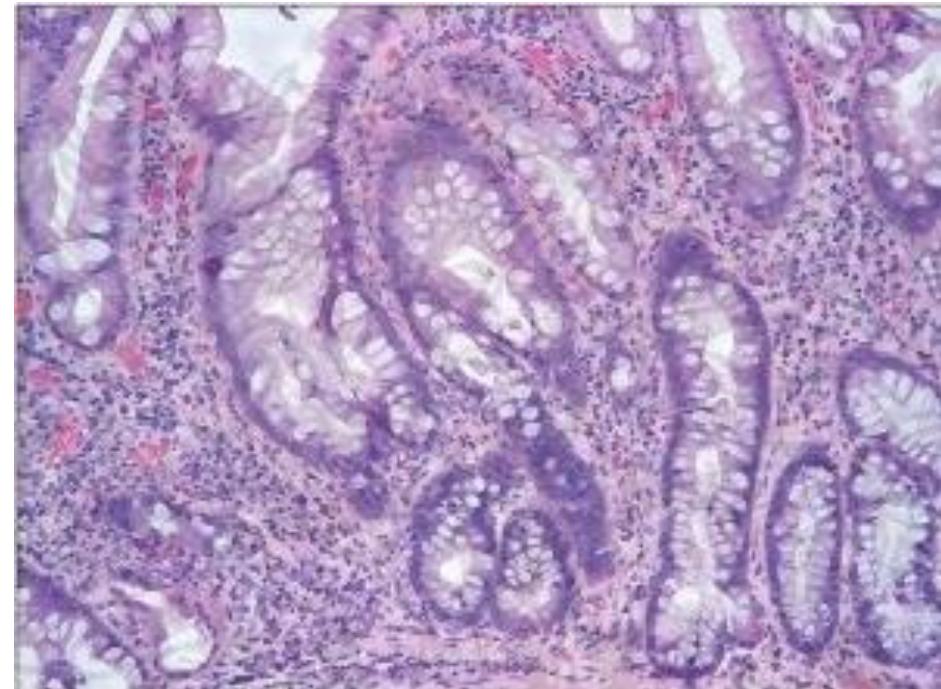
- Inflammation is transmural
- The mucosal changes are usually patchy

## CD - Mucosa - Distorted crypt architecture

Repeated attacks of inflammation cause crypt destruction and regeneration leading to irregular, branched crypts showing unusual orientation and also loss of crypts



Normal crypt architecture

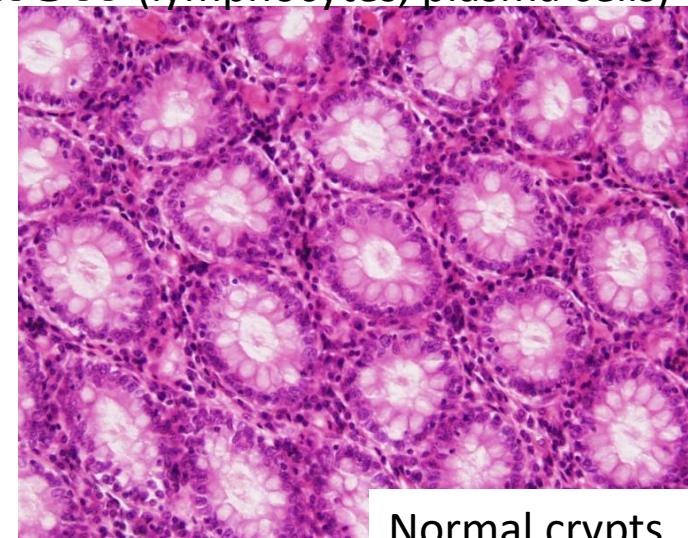


Crohn disease

# Patchy increase in LP inflammation (lymphocytes, plasma cells)

- **Cryptitis**

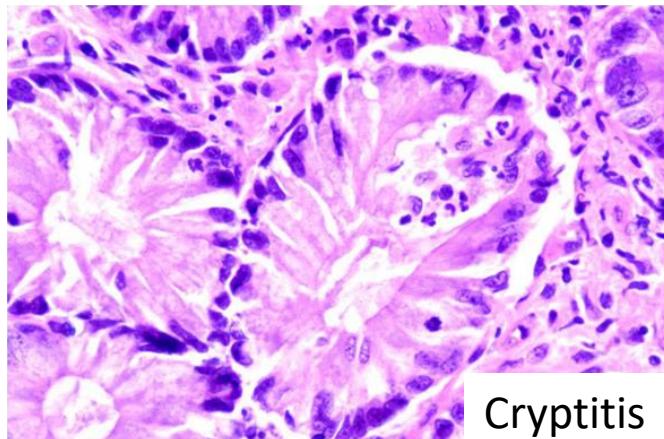
Neutrophils within damaged crypt epithelium



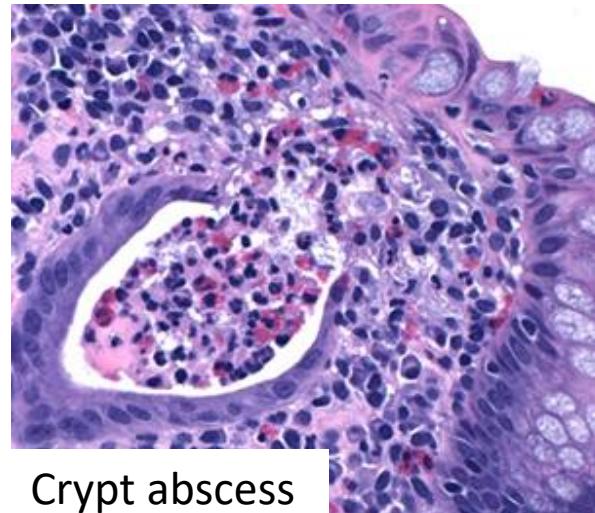
Normal crypts

- **Crypt abscesses**

- Clusters of neutrophils within crypts  
may lead to **crypt destruction**



Cryptitis

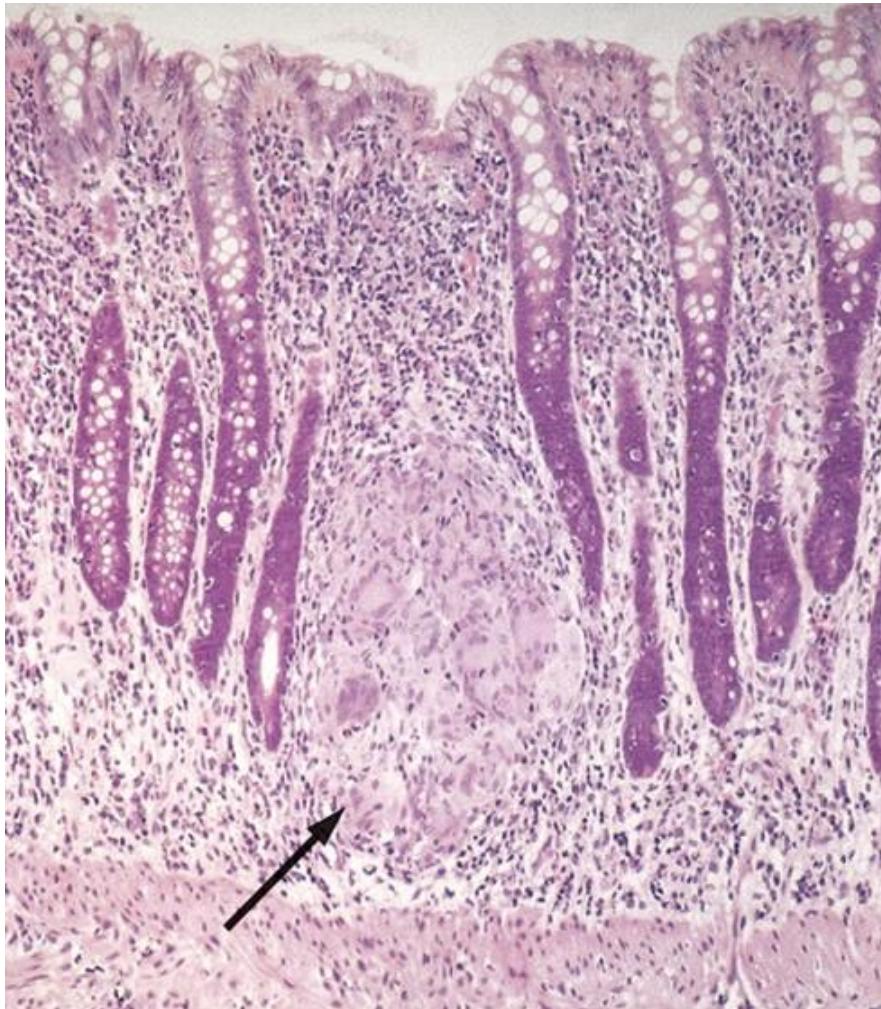


Crypt abscess

Crohn disease

- **Non - caseating granulomas**

- May present at any layer of the bowel wall
- May also present in mesenteric lymph nodes



Differential diagnosis?

# CD disease

## Other clinical presentations



Perioral ulcers/ fissures



Perianal ulcers/ fissures



# Extra-intestinal manifestations of CD

- Uveitis
- Migratory polyarthritis
- Sacroiliitis
- Ankylosing spondylitis
- Erythema nodosum
- Clubbing of fingertips

# Ulcerative colitis

# Ulcerative Colitis (UC)

- Limited to the rectum and colon
- Involves rectum and extends proximally in a continuous fashion

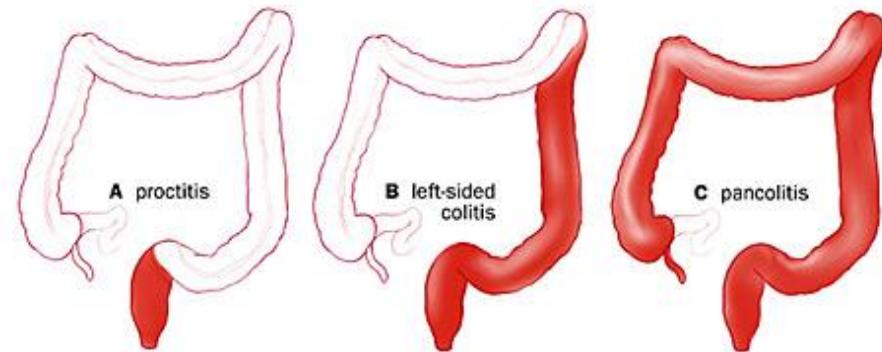
Rectum - Ulcerative proctitis

Rectum and sigmoid - Ulcerative proctosigmoiditis

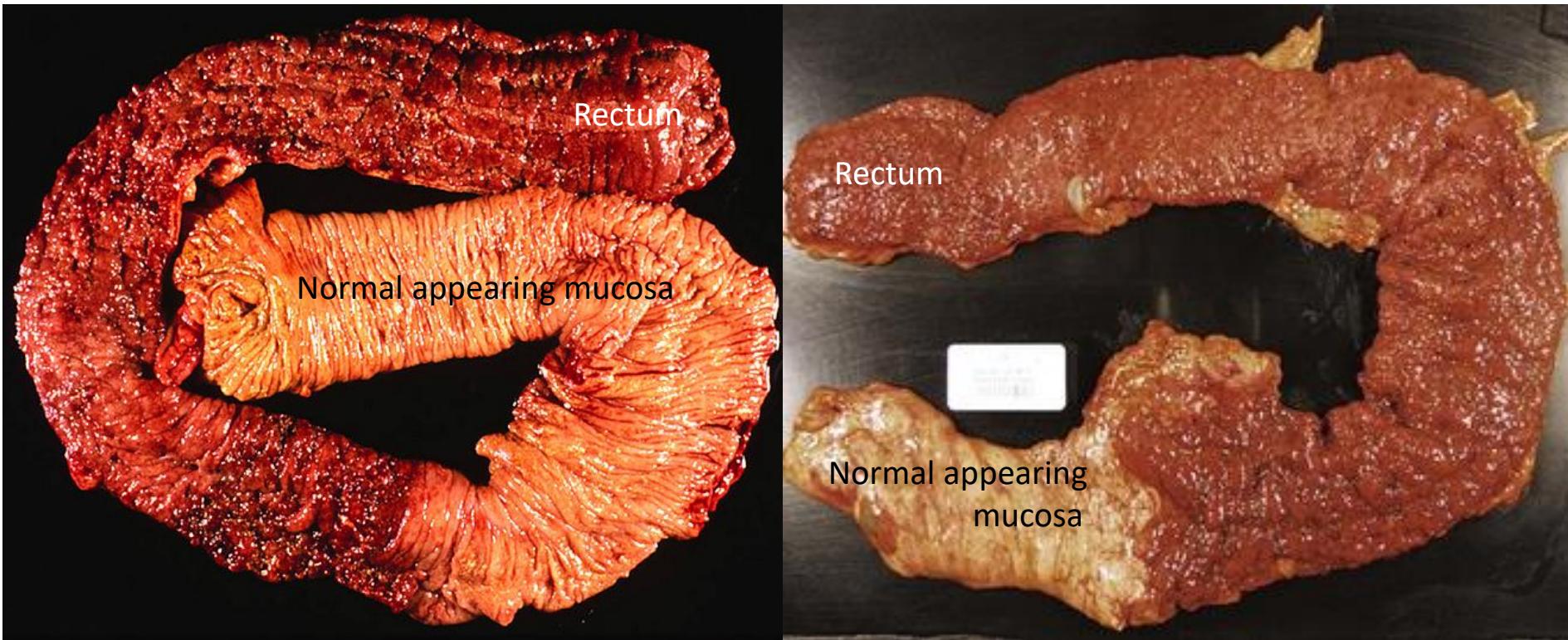
Left-sided disease

Entire colon - pan colitis

Distal ileum - Backwash ileitis



# UC - Macroscopy



Note the continuous involvement of the bowel from rectum

# UC - Macroscopy



Red and granular mucosal surface

# UC - Macroscopy

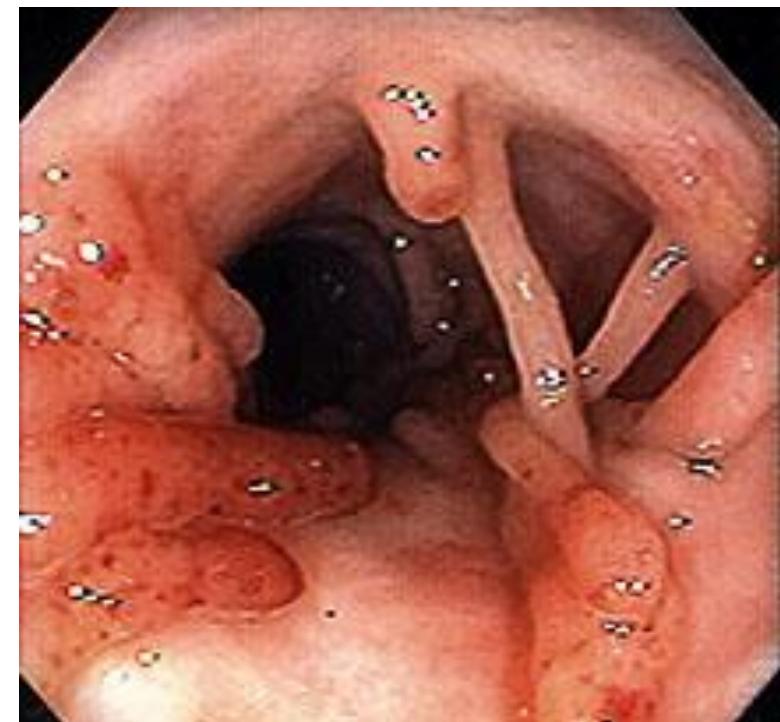


Note the broad based ulcers

# UC - Macroscopy



Regenerated mucosa creates  
**pseudopolyps**



These polyps may fuse to  
**create mucosal bridges**

Endoscopic appearance

- Chronic UC
  - Mucosal atrophy with flat and smooth mucosa lacking mucosal folds
- Toxic megacolon
  - Inflammation and inflammatory mediators can damage the muscularis propria and disturb the neuromuscular function
  - Carries a risk of perforation



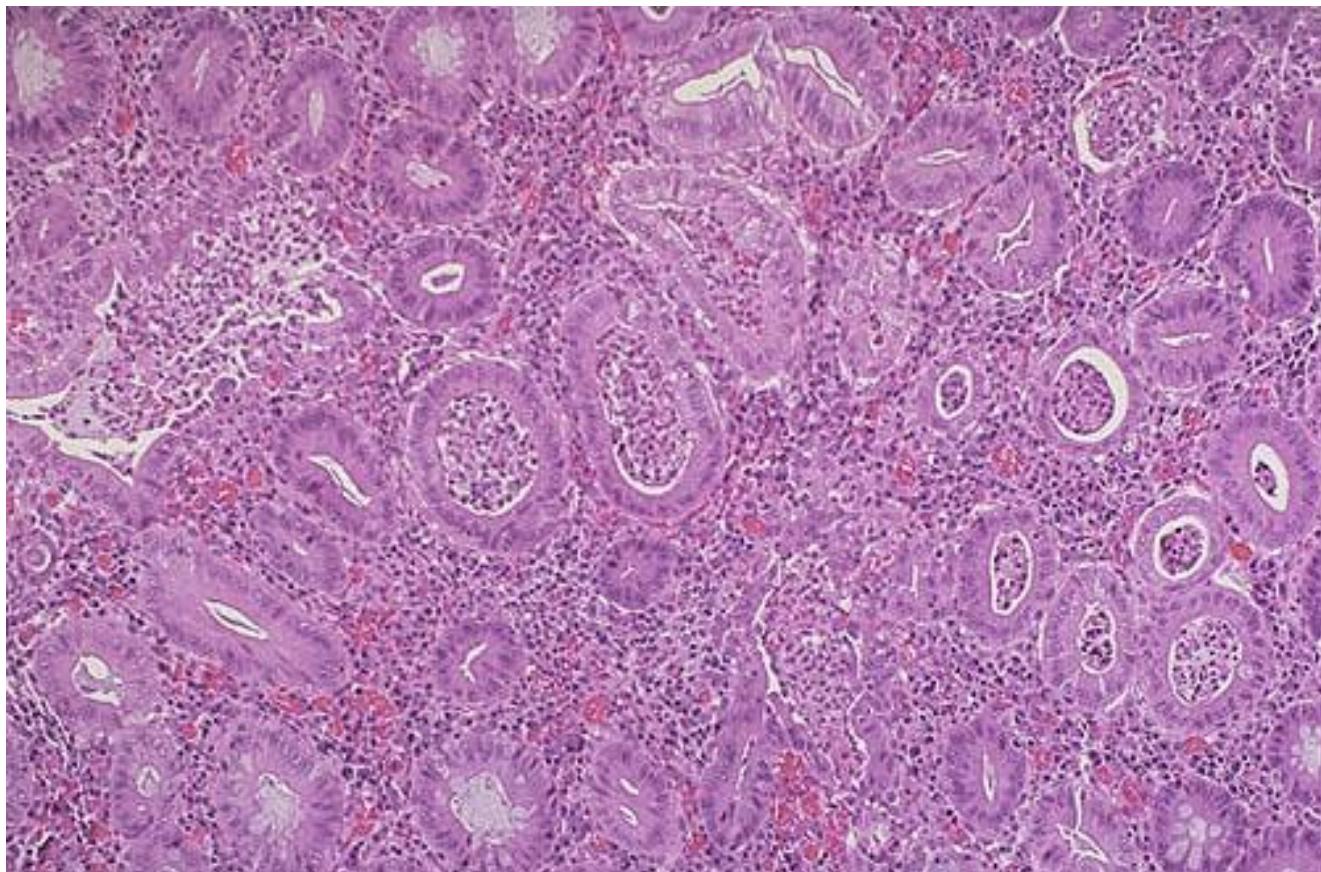
# UC - Microscopy

- The mucosal changes are more diffuse
- Distorted crypt architecture

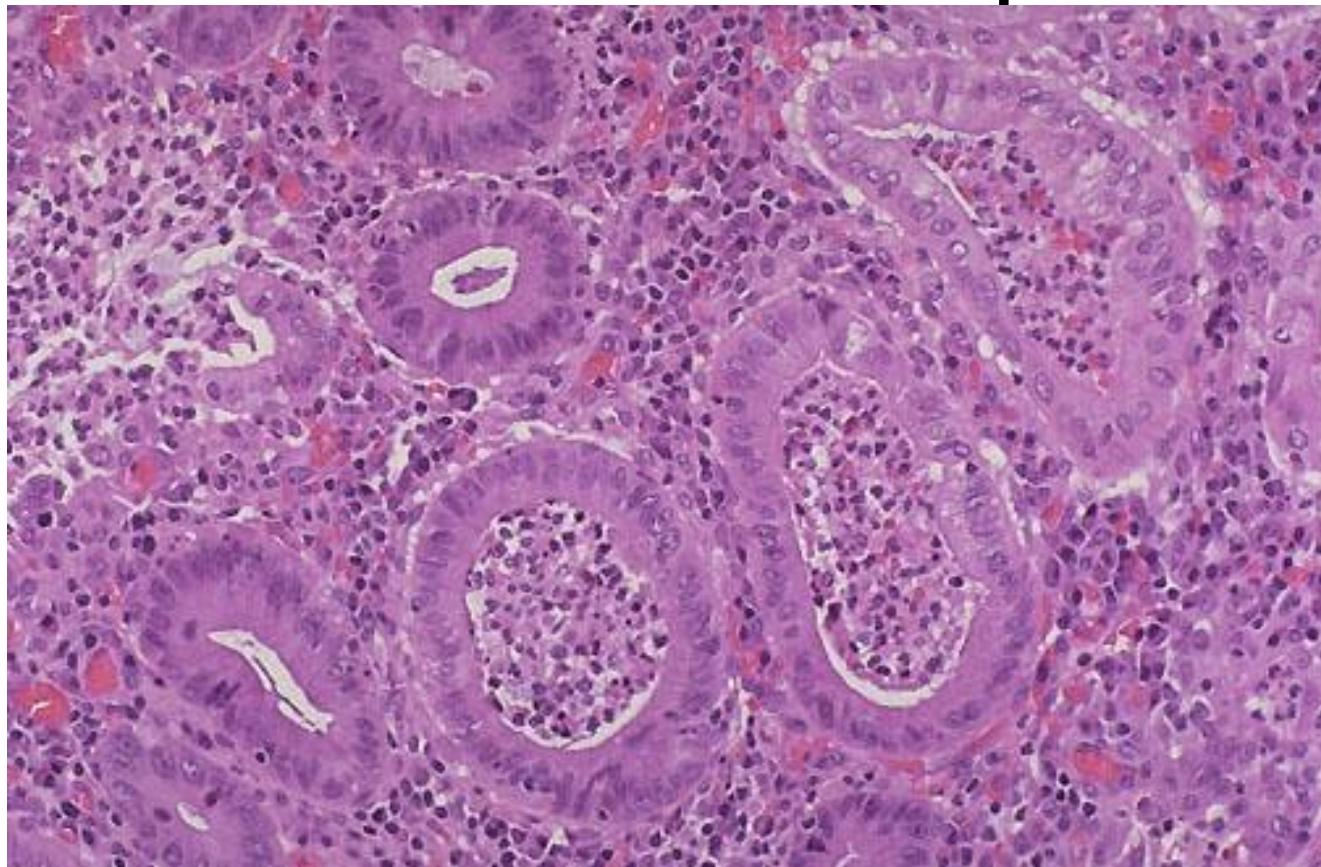


# UC - Microscopy

- Diffuse increase in lamina propria inflammation
- Cryptitis, crypt abscesses and crypt destruction
- Mucin depletion



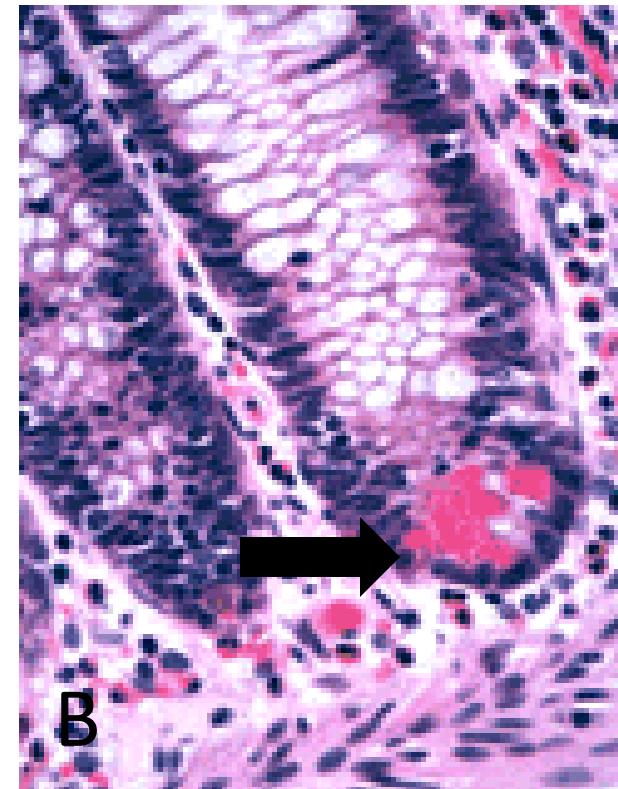
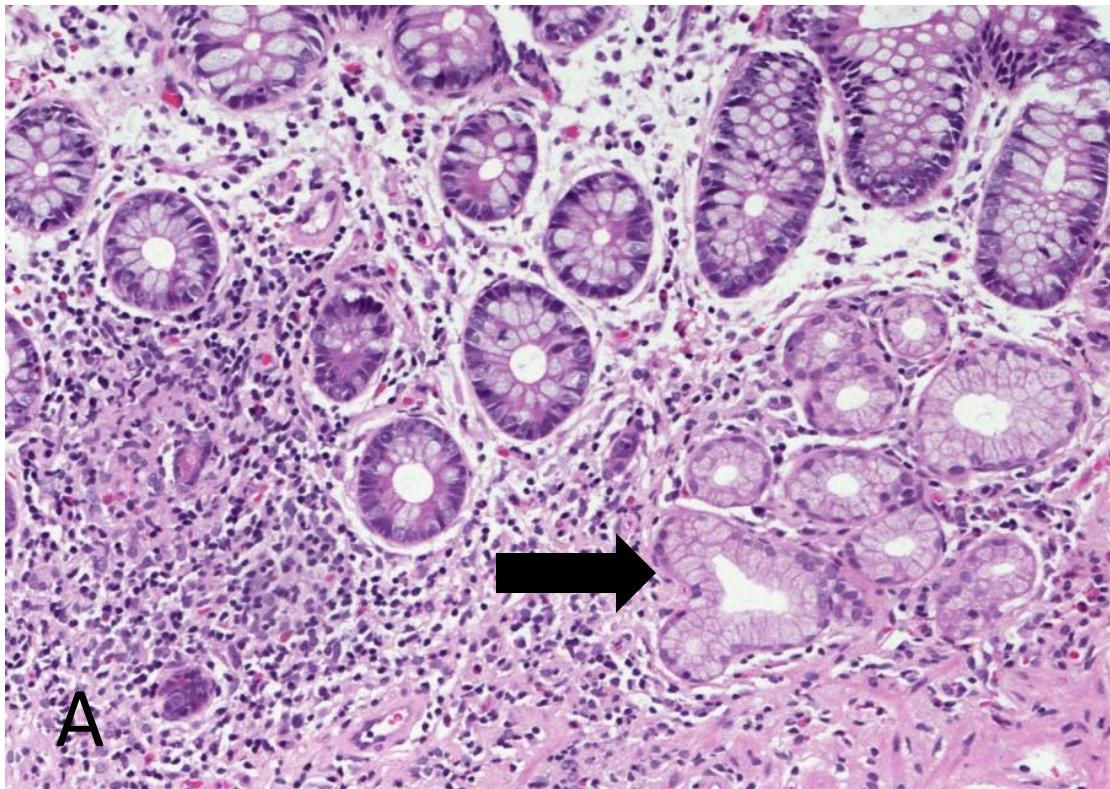
# Mucin depletion



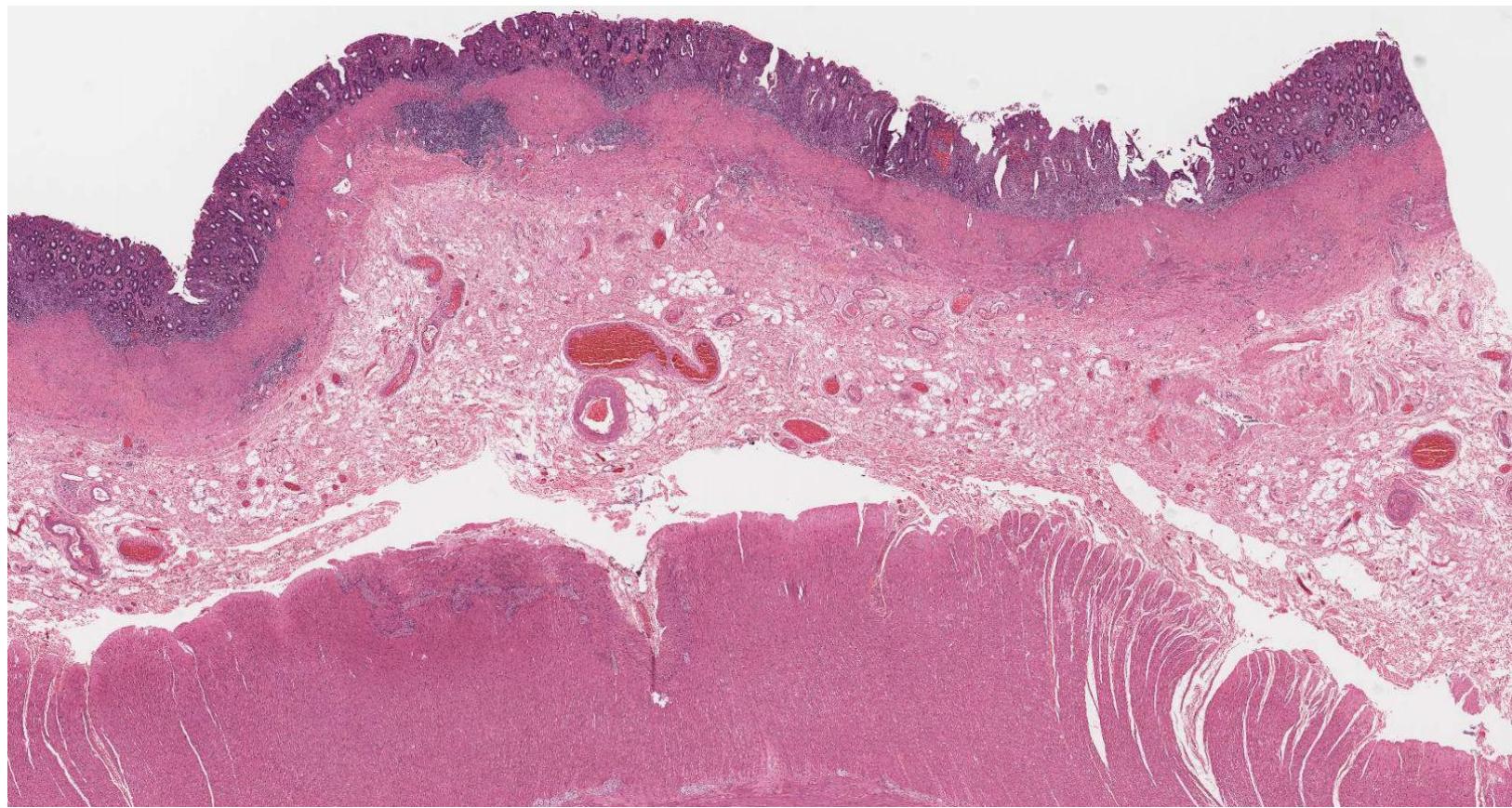
- Epithelial metaplasia

Pseudopyloric metaplasia (A)

Paneth cell metaplasia in the left colon (B)



- Inflammation is limited to mucosa and superficial submucosa
- Granulomas are not present



# Ulcerative Colitis (UC)

- Extra-intestinal manifestations overlap with that of CD

Migratory polyarthritis

Sacriilitis

Ankylosing spondylitis

Uveitis

Skin lesions

Pericholangitis

Primary sclerosing cholangitis

# Colitis associated neoplasia

- A long term complication of IBD
  - The risk increases with
    - the duration of the disease
    - pancolitis
    - greater frequency and severity of active disease  
(presence of neutrophils)
- Begins as dysplasia
- Need surveillance

# Ischaemic bowel disease

# Ischaemic bowel disease

- Bowel tolerates slowly progressive ischaemia
  - There is time to develop collaterals
- Acute compromise may lead to infarction

Blood supply to intestine – Read

- Infarction can involve  
**Mucosa and Submusosa**  
Secondary to acute / chronic hypoperfusion
- **Transmural /full thickness bowel ischemia**
  - Secondary to acute vascular obstruction
- Underlying pathologies for acute arterial obstruction  
Severe atherosclerosis , aortic aneurysms , hypercoagulable states, oral contraceptive use , embolization of cardiac vegetations aortic atheroma  
Cardiac failure, shock, dehydration, vasoconstrictive drugs  
Systemic vasculitis - Polyarteritis nodosa, Henoch-Schonlein purpura, Wegener granulomatosis

# Pathogenesis

- Intestinal ischaemia occurs in two phases
  - Hypoxic injury
  - Reperfusion injury associated with
    - free radicals
    - neutrophil infiltration
    - inflammatory mediators
    - activation of intracellular signalling pathways
- Severity, duration and the affected vessel decide the outcome of the ischaemia at a given site

- Susceptible regions  
“Watershed zones”
  - Intestinal segments at the ends of the arterial supplies  
Splenic flexure , sigmoid colon and rectum
  - Susceptible to localized ischaemic injury in generalized hypotension and hypoxaemia
- Surface epithelium is more vulnerable to ischemic injury than the crypts
  - Results in surface epithelial atrophy, necrosis/sloughing
  - Normal or hyperproliferative crypts

# Mucosal and submucosal infarction

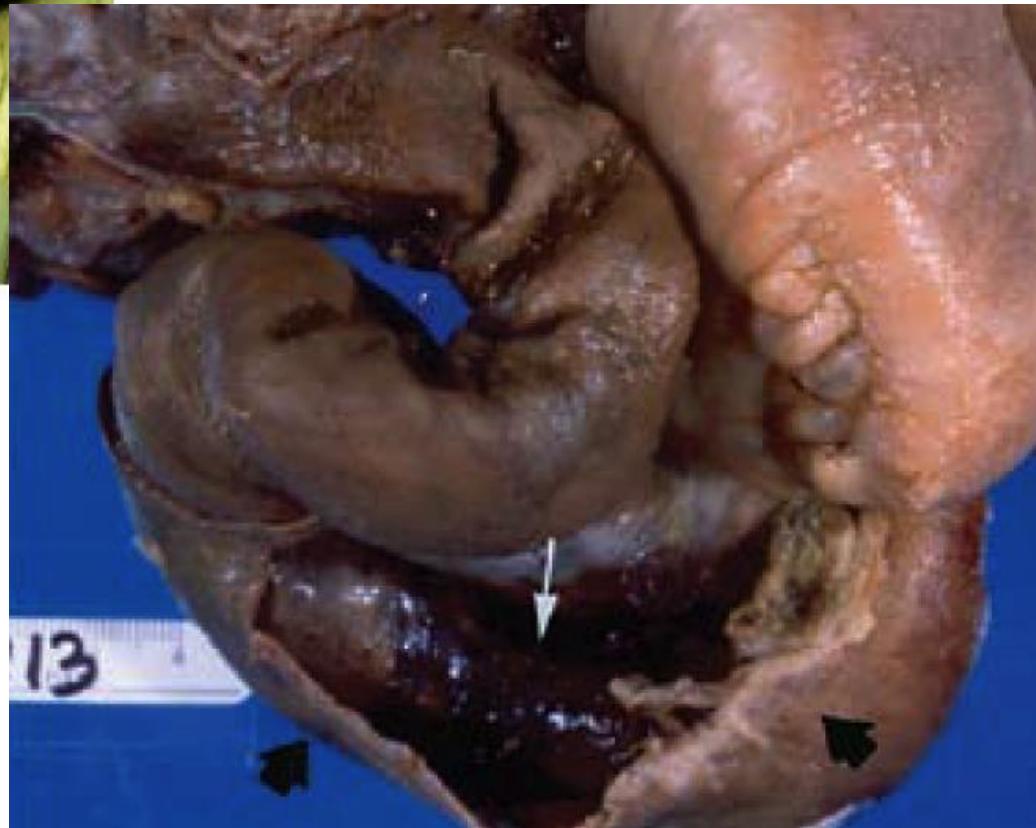
- Involves any part , stomach to anus
- More often segmental and patchy but may be continuous

## Macroscopy

- Mucosa
  - Haemorrhagic, ulcerated and dark red or purple in colour
- Bowel wall
  - Thickened due to oedema in musosa, submucosa
- In severe cases - extensive mucosal and submucosal haemorrhage and necrosis
- Serosal haemorrhage and serositis is generally absent

# Transmural infarction

- Commonest site - Splenic flexure
- Ischaemic bowel segment is sharply demarcated from the adjacent normal bowel
- Infarcted bowel
  - initially congested, and dusky to purple in colour
  - later , blood tinged mucus or frank blood accumulate in the lumen
  - Bowel wall become oedematous, thickened and rubbery



13

- Coagulative necrosis occurs within 1-4 days and may result in perforation
- Serosa shows purulent exudates and deposition of fibrin

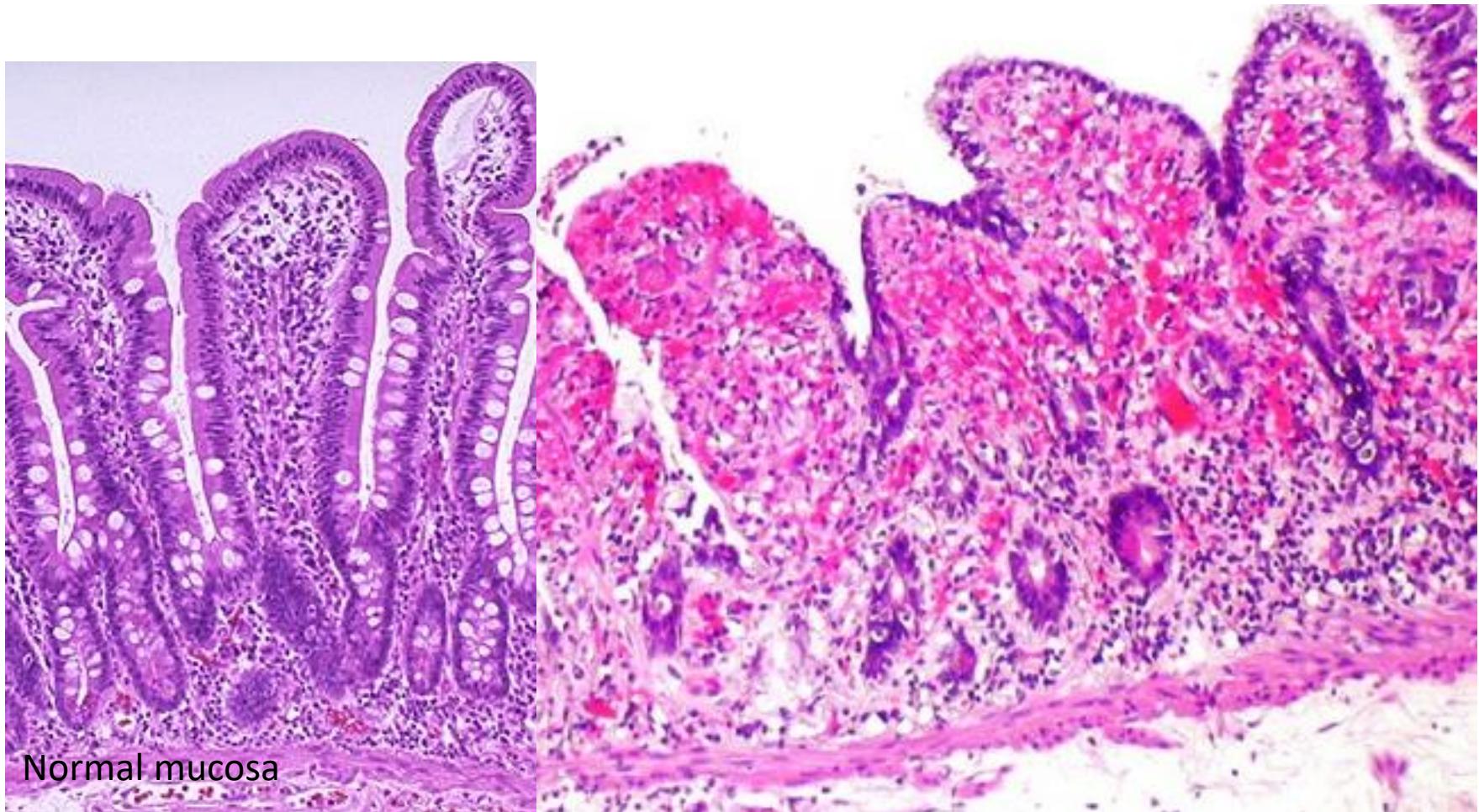
## Microscopy

- Atrophy / sloughing of surface epithelium
- Crypts may be hyperproliferative
- Neutrophil infiltrate
- Haemorrhage may be present

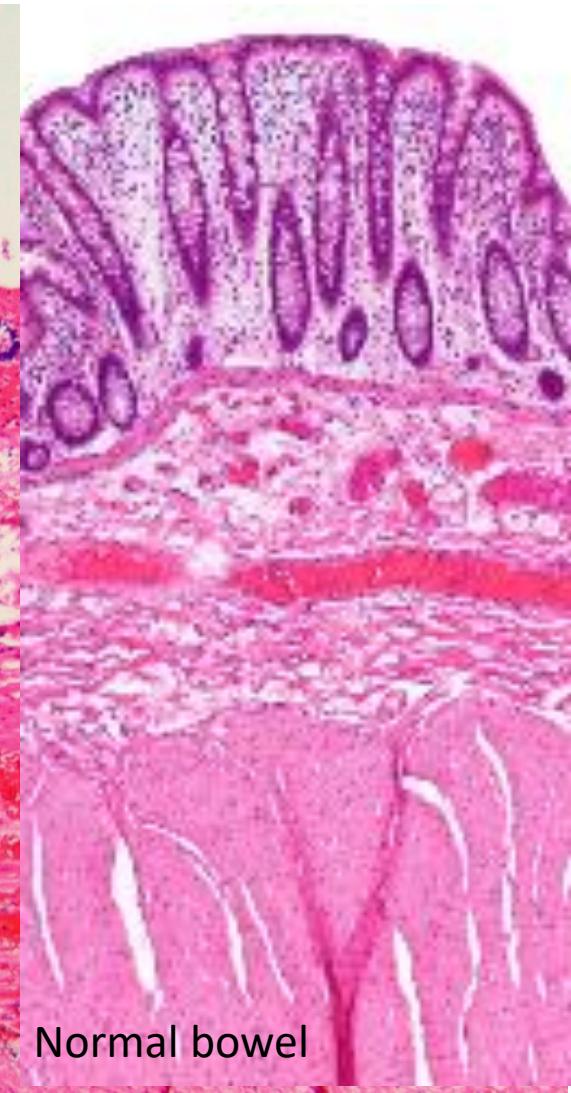
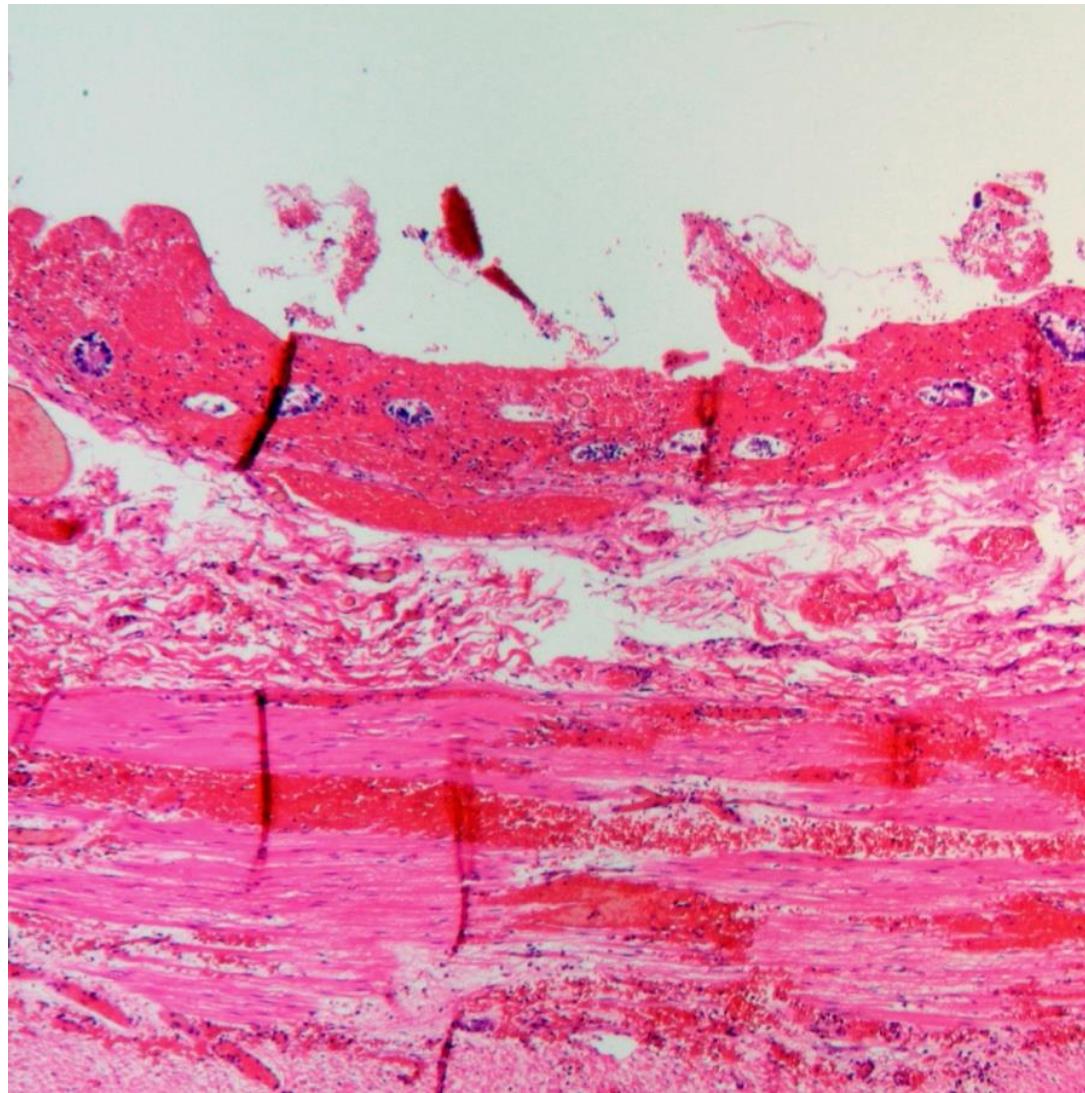
## Chronic ischaemia

- Fibrosis and scarring of the lamina propria

- Sloughing of surface epithelium
- Viable crypts
- Neutrophil infiltrate



# Transmural haemorrhagic infarct



Normal bowel

# Diverticular disease

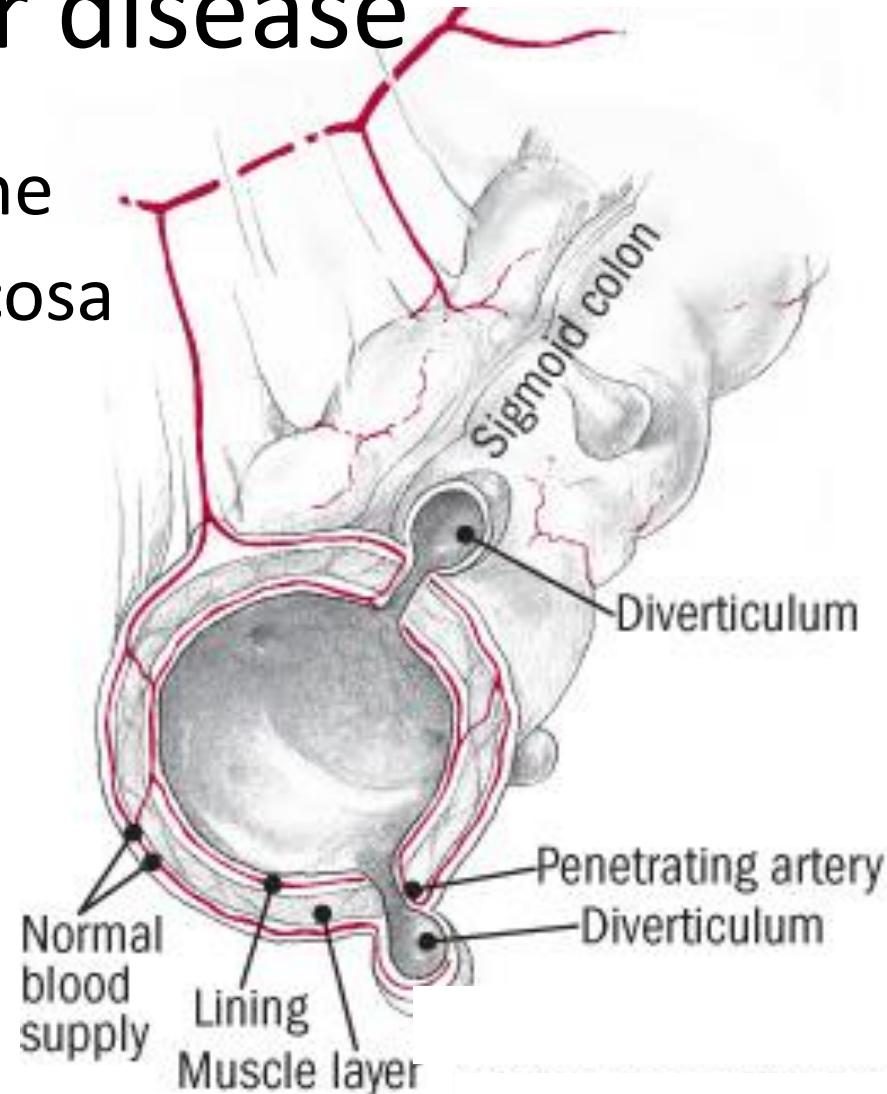
# Diverticular disease

- Acquired outpouchings of the colonic mucosa and submucosa
- Rare before 30 years

## Pathogenesis

Structure of the colonic muscularis propria - Read

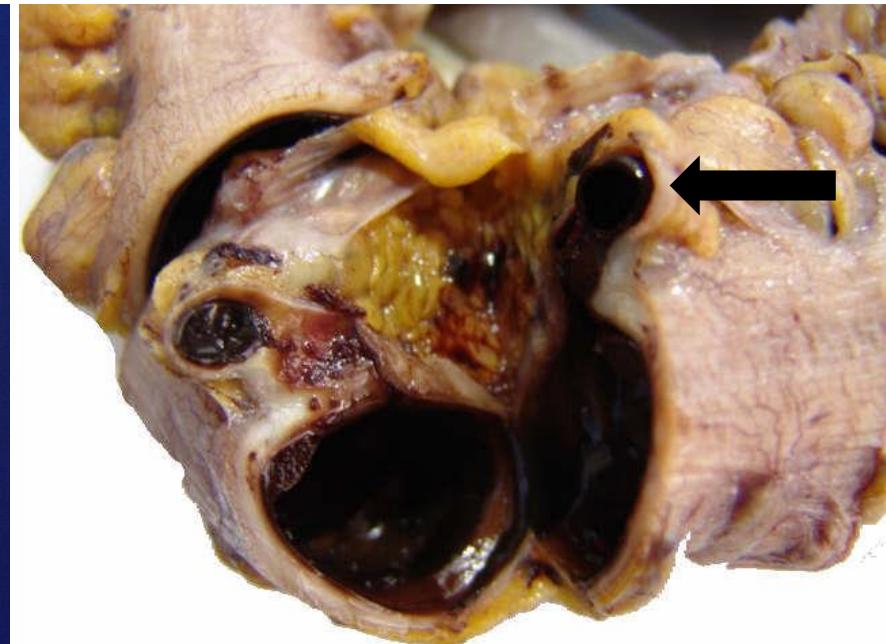
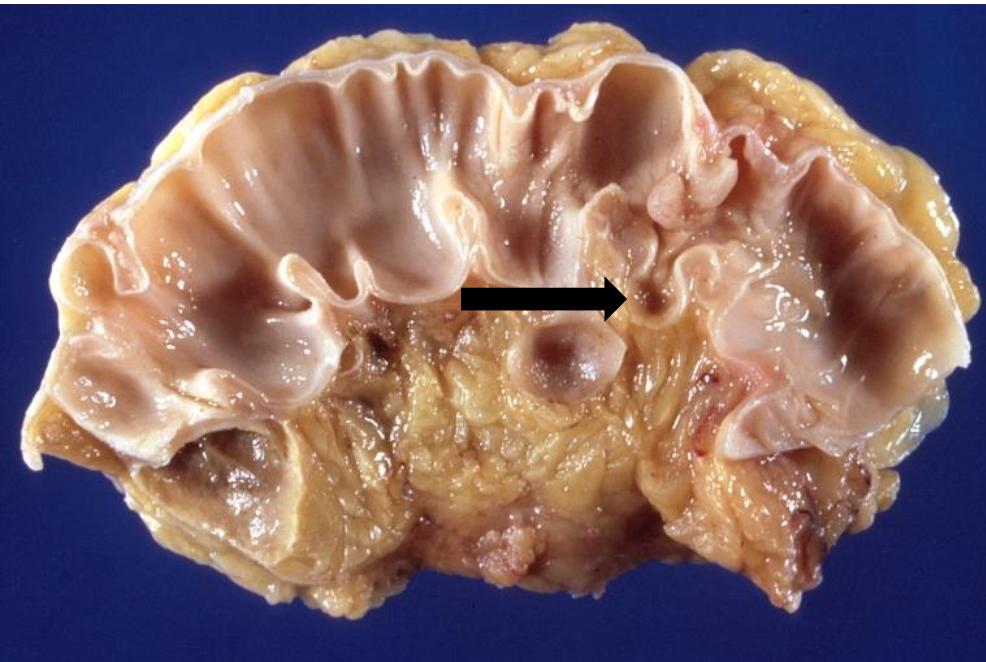
\*Gaps at the sites where neuromuscular bundles penetrate the inner circular muscle wall



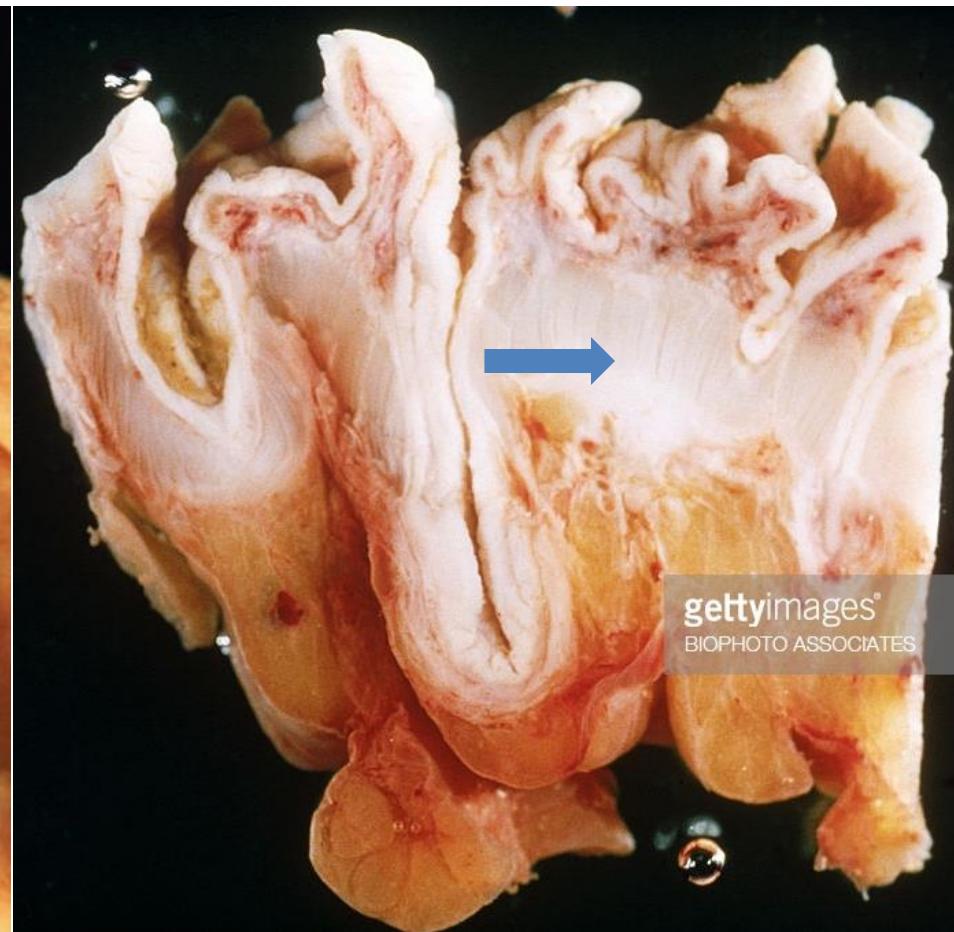
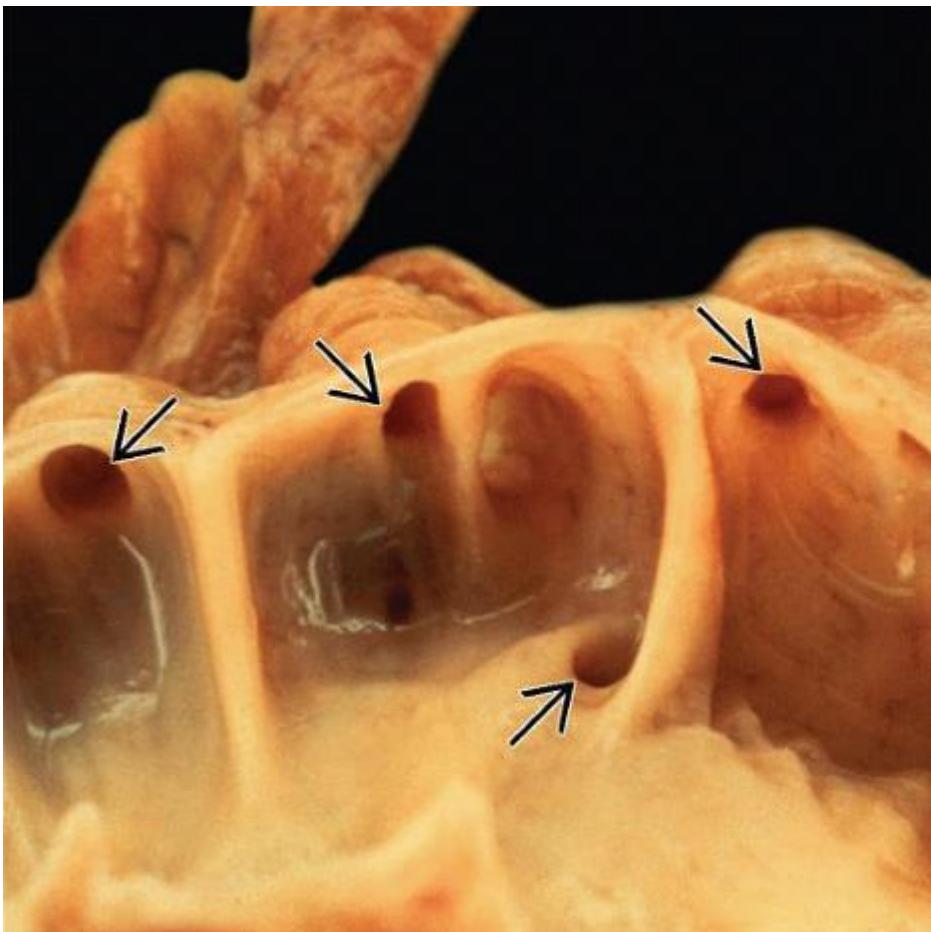
Trigger - Elevated intraluminal pressure

# Diverticular disease - Macroscopy

- Multiple, small flask-like thin-walled outpouchings of the bowel (0.5-1cm)
- Regularly distributed on either side of taeniae coli
- Surrounded by appendices epiploicae
- Fibrotic thickening of the bowel wall



# Diverticular disease – Macroscopy



gettyimages®  
BIOPHOTO ASSOCIATES

Diverticular openings from mucosal surface

Fibrotic thickening of the muscularis propria

# Microscopy

- Thin walls are lined by atrophic or flattened mucosa
- Compressed submucosa
- Attenuated or totally absent muscular propria
- Hypertrophy of the circular muscle layer



## Complications

### Diverticulitis

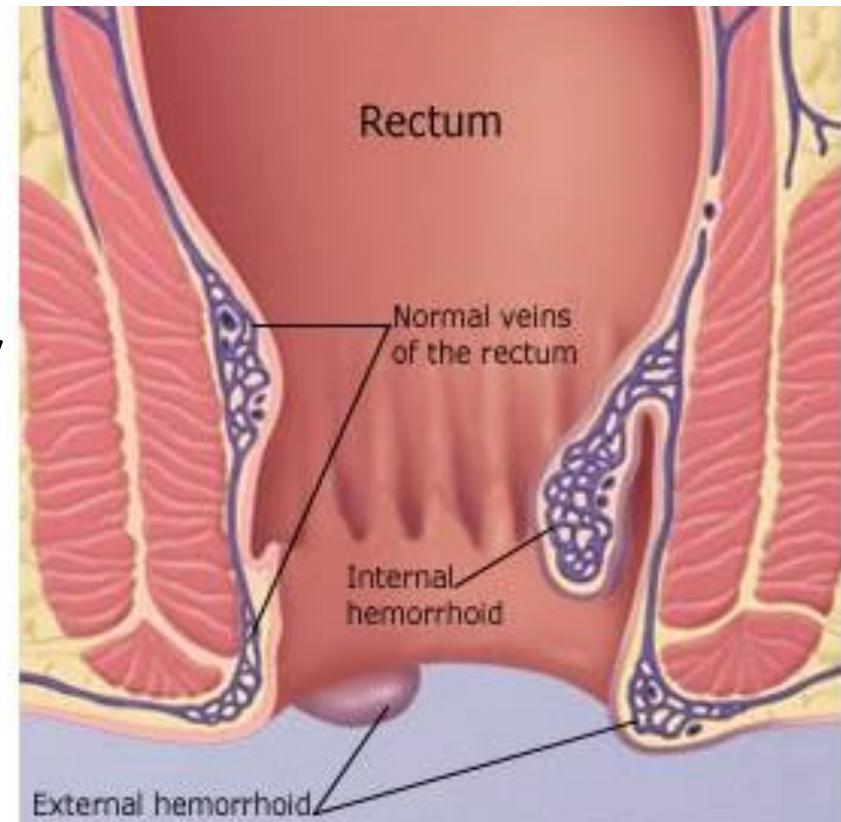
Perforation leads to pericolonic abscesses, sinus tracts, peritonitis

# Haemorrhoids

# Haemorrhoids

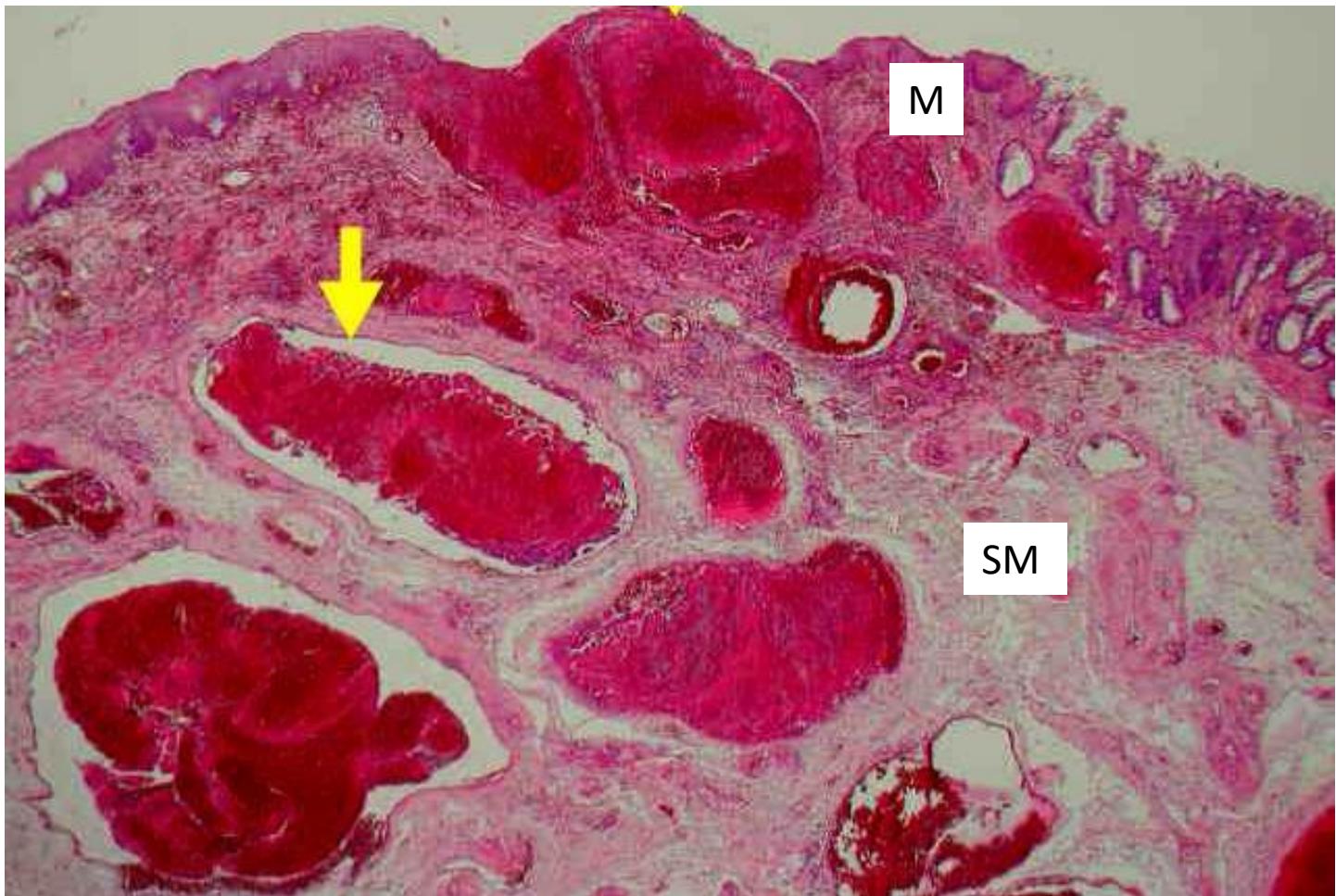
## Pathogenesis

- Develop secondary to elevated venous pressure within the haemorrhoidal plexus
- Predisposing factors
  - Constipation followed by straining
  - Venous stasis of pregnancy



# Haemorrhoids - Microscopy

- Dilated and congested , thin wall submucosal vessels
- May be inflamed, ulcerated or thrombosed



# Intestinal obstruction

# Intestinal obstruction

## Underlying pathologies

- **Mechanical obstruction**

Hernias

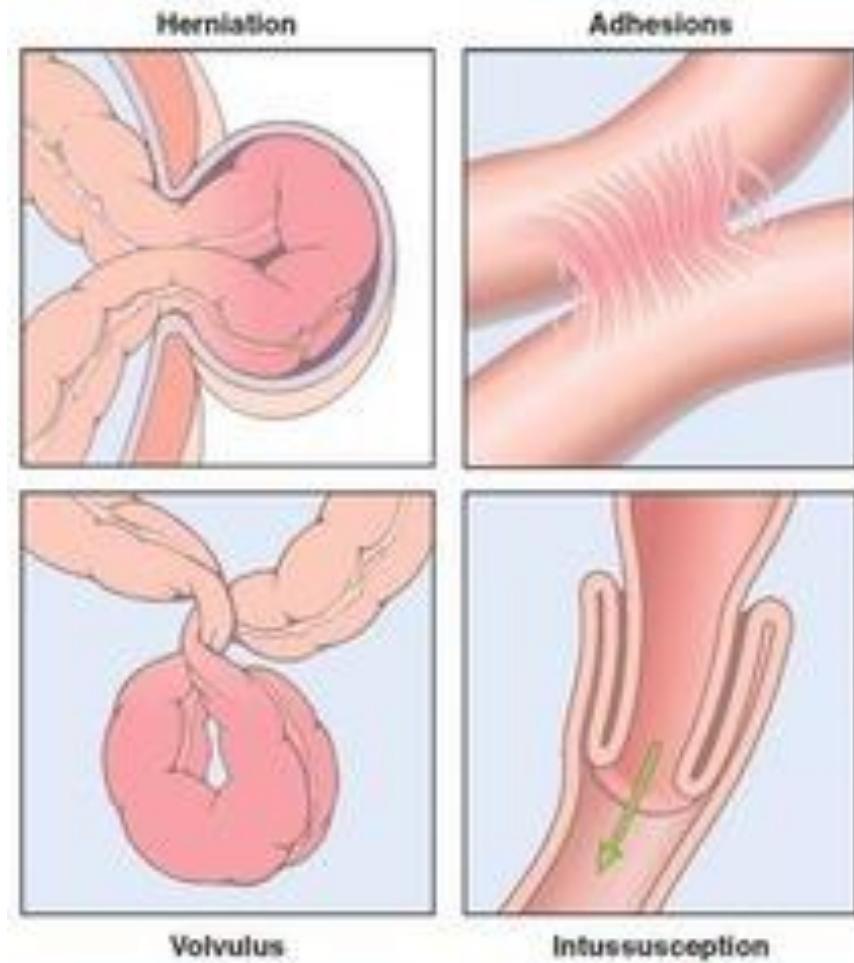
Intestinal adhesions

Intussusception

Volvulus

Tumours

Infarction



# Hernia

Weakness / defect in the peritoneal cavity



Protrusion of a serosa -lined pouch of peritoneum – **Hernia sac**

Sites - Inguinal canal , femoral canal, umbilicus , at surgical scars

Viscera can protrude – **External herniation** (SI, LI or omentum)

Pressure at the neck of the pouch



Impairs venous drainage of the entrapped viscera



Stasis and oedema – Increase the bulk of the herniated loop



Permanent entrapment/ incarceration



Arterial and venous compromise / strangulation



Results in **infarction**

- **Adhesions** due to
  - Surgical procedures
  - Infection
  - Peritoneal inflammation
  - Endometriosis

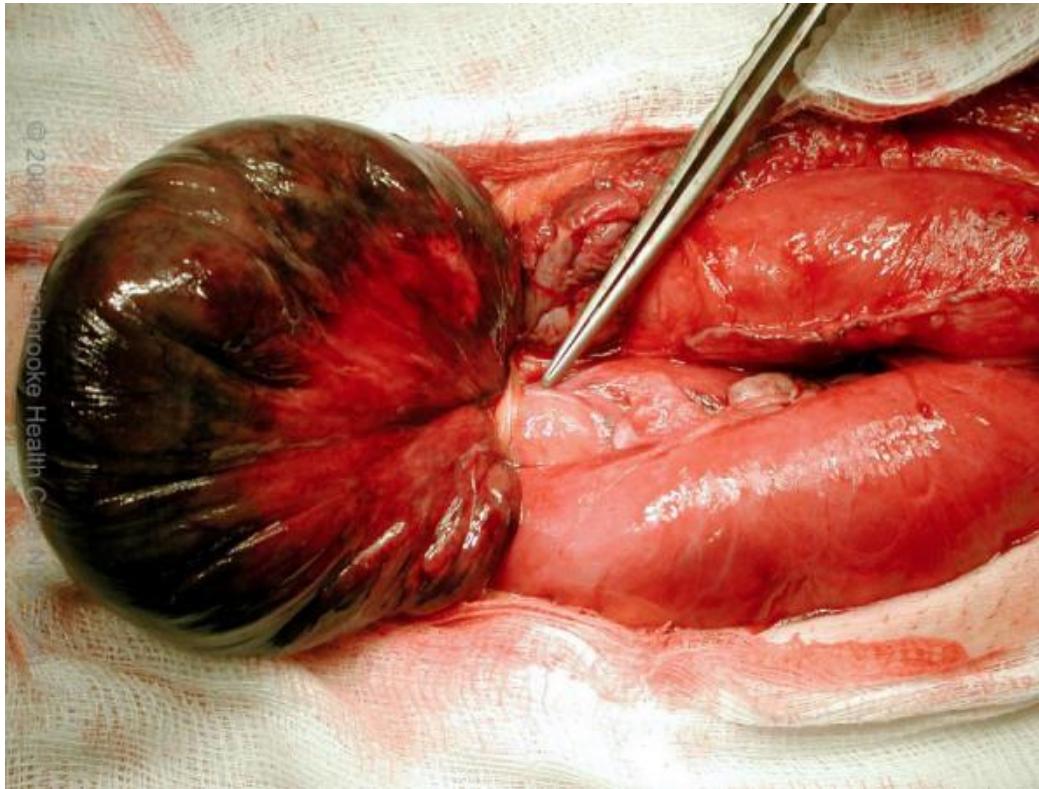


- May occur between bowel segments , abdominal wall and operative sites
- Create fibrous bands, closed loops and viscera can slide and get entrapped - internal herniation

## **Sequale**

Obstruction and strangulation

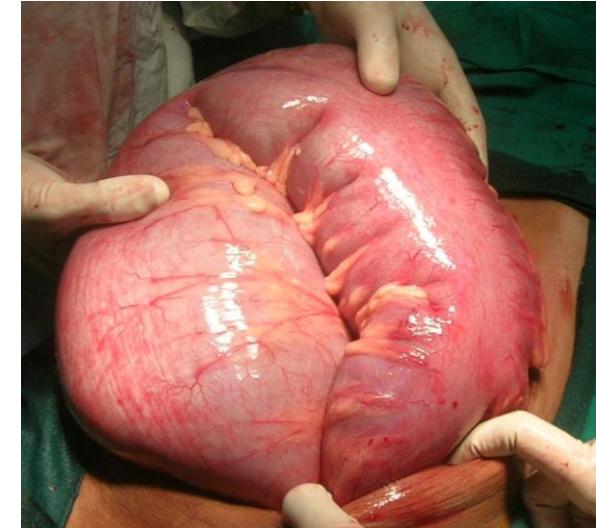
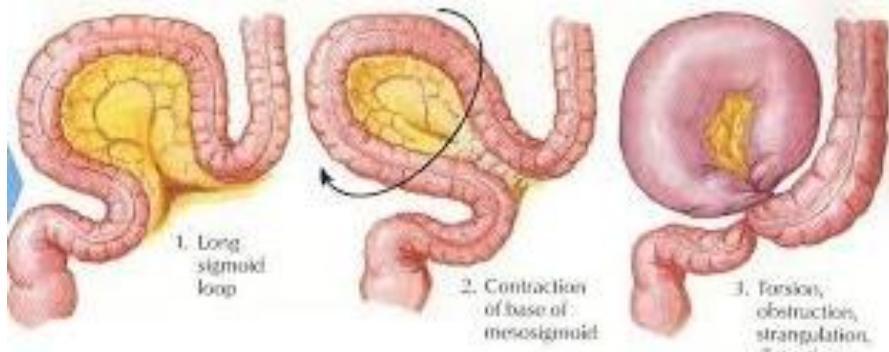
# Strangulated inguinal hernia



Gangrenous small bowel with closed loop obstruction caused by an omental band adhesion

# Volvulus

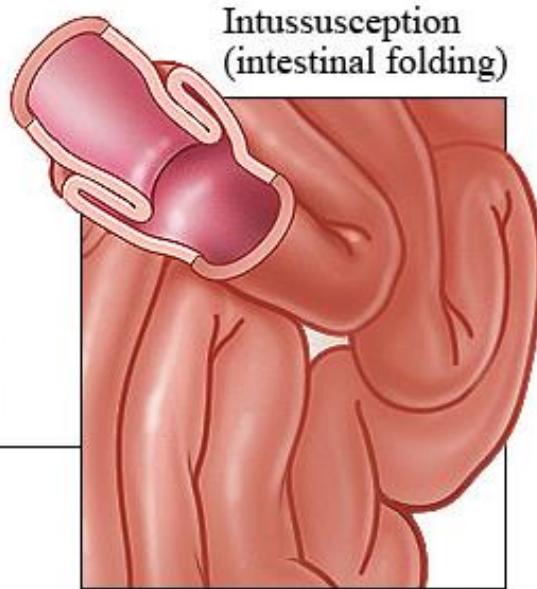
- Complete twisting of a loop of bowel about its mesenteric base



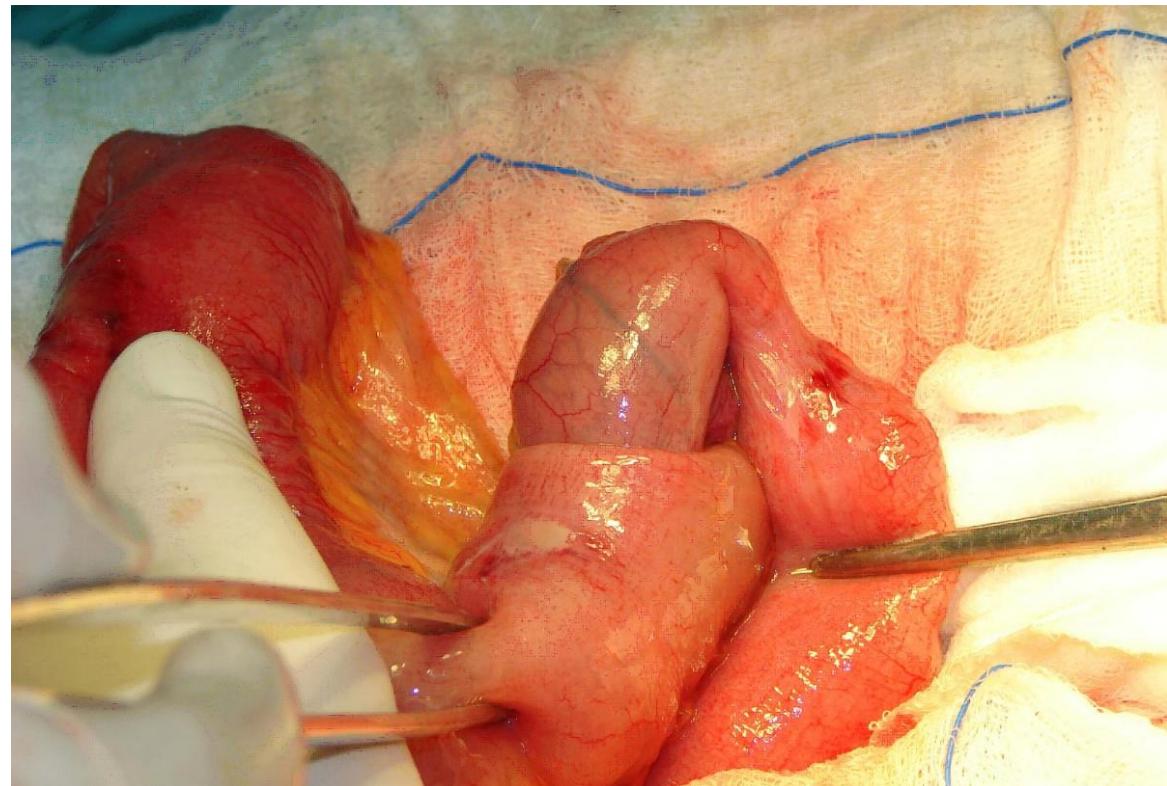
- Commonest at sigmoid colon  
Also in caecum, SI, stomach  
Rarely - transverse colon
- Produce both obstruction and ischaemia and infarction

- **Intussusception**

Segment of intestine constricted by a wave of peristalsis, telescopes into the immediate distal bowel segment



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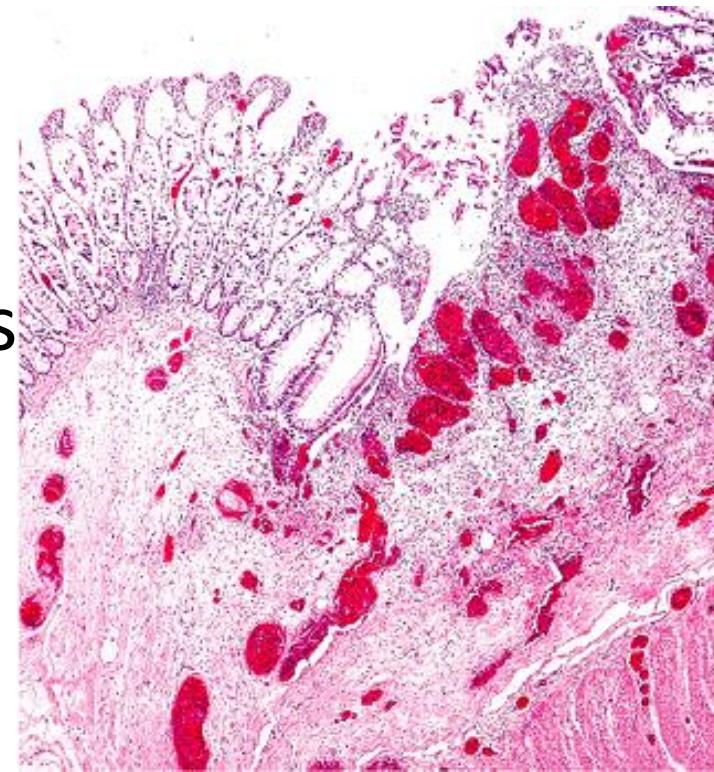


# Angiodysplasia

- Malformed submucosal and mucosal blood vessels
- Commonest at caecum/ right colon
- Clinical importance - **severe lower GI haemorrhage**
- Pathogenesis is attributed to mechanical and congenital factors

## Microscopy

- Ectatic , tortuous veins, venules and capillaries in submucosa and mucosa



# Summary

*Now you should be able to*

- briefly describe the macroscopy and microscopy of the intestine in Inflammatory Bowel Disease (IBD):  
**Crohn's disease (CD) and ulcerative colitis (UC)**
- Briefly describe the pathology of
  - Ischemic bowel disease
  - Diverticular disease
  - Intestinal obstruction
  - Haemorrhoids
  - Angiodysplasia

# Assignments

- List the macroscopic and microscopic differenced between UC and CD
- Read - Congenital abnormalities
  - Duplication of intestine
  - Meckel diverticulum
  - Hirschprung disease