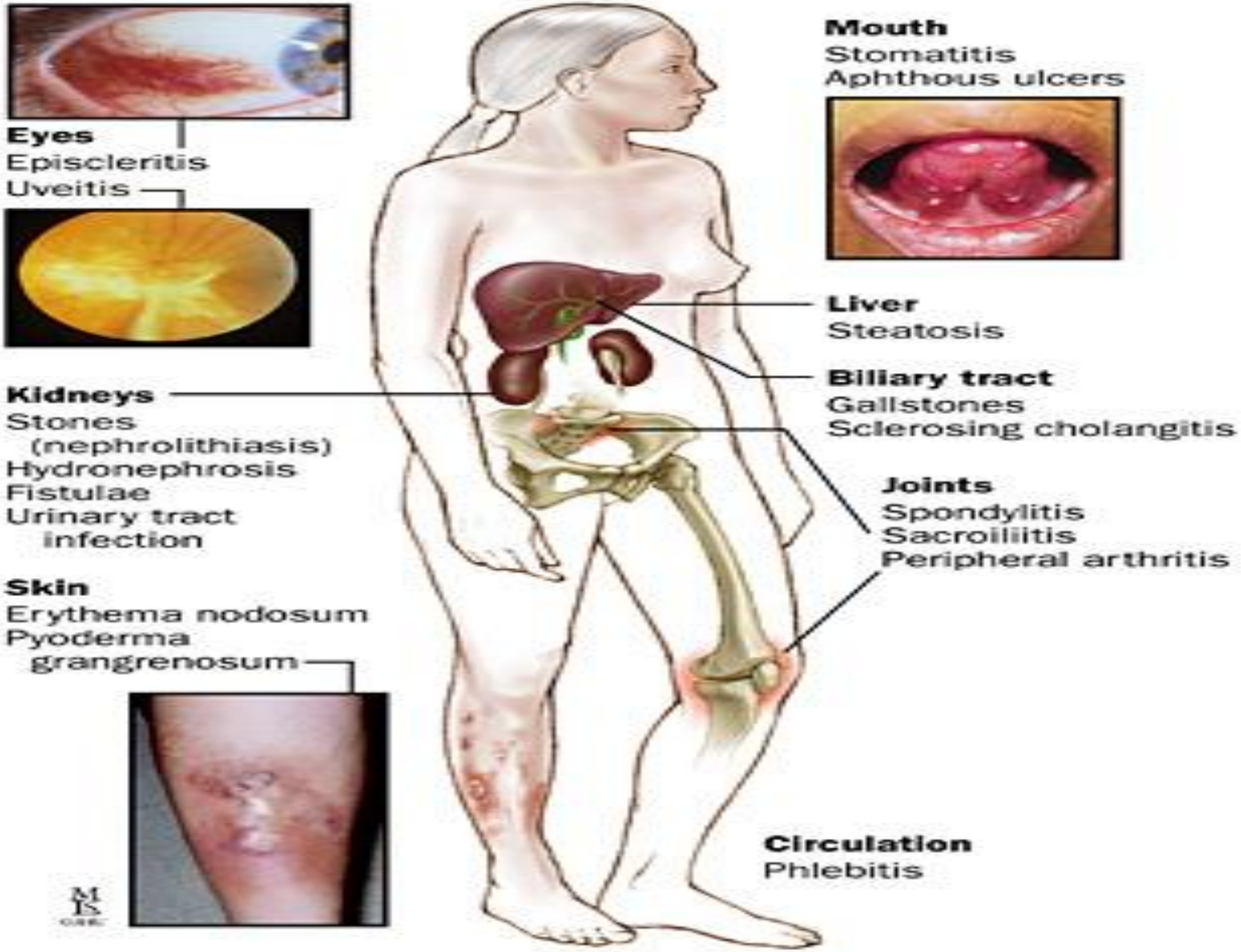
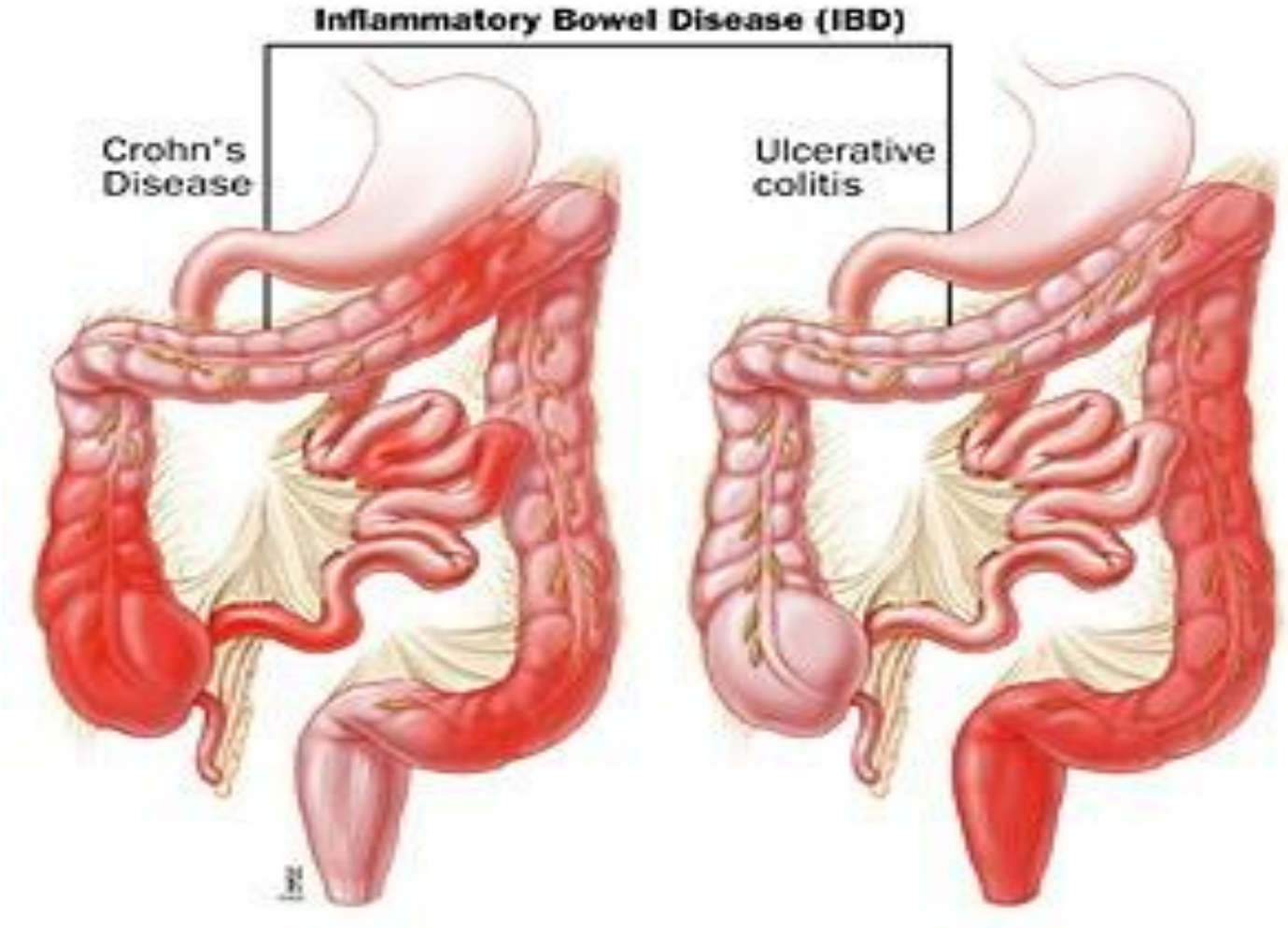
INFLAMMATORY BOWEL DISEASE (IBD)

- It is a chronic condition resulting from inappropriate mucosal immune activation.
- The disorders under IBD are,
  (1) Ulcerative colitis (U.C.)
  (2) Crohn's disease (C.D.)
- U.C. is limited to the colon & rectum. It extends only into mucosa & submucosa.
- C.D.(regional enteritis) may involve any area of G.I.T. and is typically transmural.

- Both CD and UC are chronic relapsing inflammatory disorders of obscure origin.
- CD is autoimmune disease - may affect any portion of GIT from esophagus to anus, - most often involves distal small intestine and colon.
- UC is chronic inflammatory disease limited to colon and rectum.
- Both exibits extraintestinal inflammatory manifestation.


Eyes
Episcleritis
Uveitis
Mouth
Stomatitis
Aphthous ulcers
Liver
Steatosis
Biliary tract
Gallstones
Sclerosing cholangitis
Kidneys
Stones
(nephrolithiasis)
Hydronephrosis
Fistulae
Urinary tract
infection
Joints
Spondylitis
Sacroiliitis
Peripheral arthritis
Skin
Erythema nodosum
Pyoderma
gangrenosum
Circulation
Phlebitis


Inflammatory Bowel Disease (IBD)
Crohn's Disease
Ulcerative colitis

- ETIOPATHOGENESIS SAME FOR BOTH DISEASES.

PATHOGENESIS :

Precise causes are not defined yet.

It is believed that IBD results from

(a) alteration in host interaction with intestinal microbiota.

(b) Intestinal epithelial dysfunction.

(c) Aberrant mucosal immune response.

(d) Altered mucosal microbiome composition.

GENETICS :

- Familial aggregations observed repeatedly.
- Ten fold incresed risk for 1st degree relatives
- Crohn's concordance in monozygotic twins – 50 % (similar regions affection)
- U.C. : Monozygotic twins – 15 %
- Concordance for dizygotic twins < 10 % (in both)
- 160 genes associated with IBD have been identified.
- NOD2 gene (nucleotide oligomerisation binding domain) is most strongly associated with C.D.

- Other 2 genes associated with Crohn's disease are ATG 16 LI (Autophagy related 16 like) and IRGM (Immunity related GTPaseM).

- All 3 are involved in recognition and response to intracellular pathogens.

- Genomic search has revealed disease associated loci of IBD are present in chromosome 16, 12 ,7, 3, and 1, although no consistent genetic abnormalities.

- HLA studies show that ulcerative colitis is more common in DR2-related genes. Crohn disease is more common in DR5, DQ1 alleles.

DEFENCE FACTORS :

- Paneth cells contain antimicrobial protein - defensins responsible for innate immunity against bacterial infection.
- IgA antibody for surface epithelial protection.
- MALT Responsible for intestinal immune system.

MUCOSAL IMMUNE RESPONSE :

- Too much T-cell activation and too little control by regulatory T lymphocytes.
- Lesions caused by CD4+Tcells and their products.
- Crohn disease- due to TH17 cells.

  TH17 cells produces IFN-Y, IL 2,which induces

  1 Chronic delayed type hypersensitive reaction.

  2 Non caseating granuloma.

- UC caused by excessive actvation of TH2 cells
- TH2 cells secrets IL4, IL5, IL13.
- Not clear that autoantibodies play pathogenic role.

  So inappropriate mucosal immune activation and defective immunoregulation leads to IBD.

  (Immunosuppression is treatment of choice.)

EPITHELIAL DEFECTS :

- Defects in intestinal epithelial tight junction barrier function in C.D. (NOD2 polymorphism). so innate & aquired mucosal immunity is activated.
- Polymorphism of ECM1 (Inhibit metallo proteinase 9) are linked to U.C.
- Polymorphism in HNFA (transcription factor) associated with U.C.(also associated with MODY)

MICROBIOTA :

- 10^{12} Organisms / ml in colon.
- NOD2 association suggests role of microbes.
- Antiflagelin antibodies are common in C.D.

Probiotics(benefitial) bacteria benefit IBD patients.

Microbes exacerbate immune reaction by

1 Providing antigens

2 Inducing cytokines.

3 Contribute to T cell activities.

Strong immune respose against normal flora.

CHAIN OF EVENT

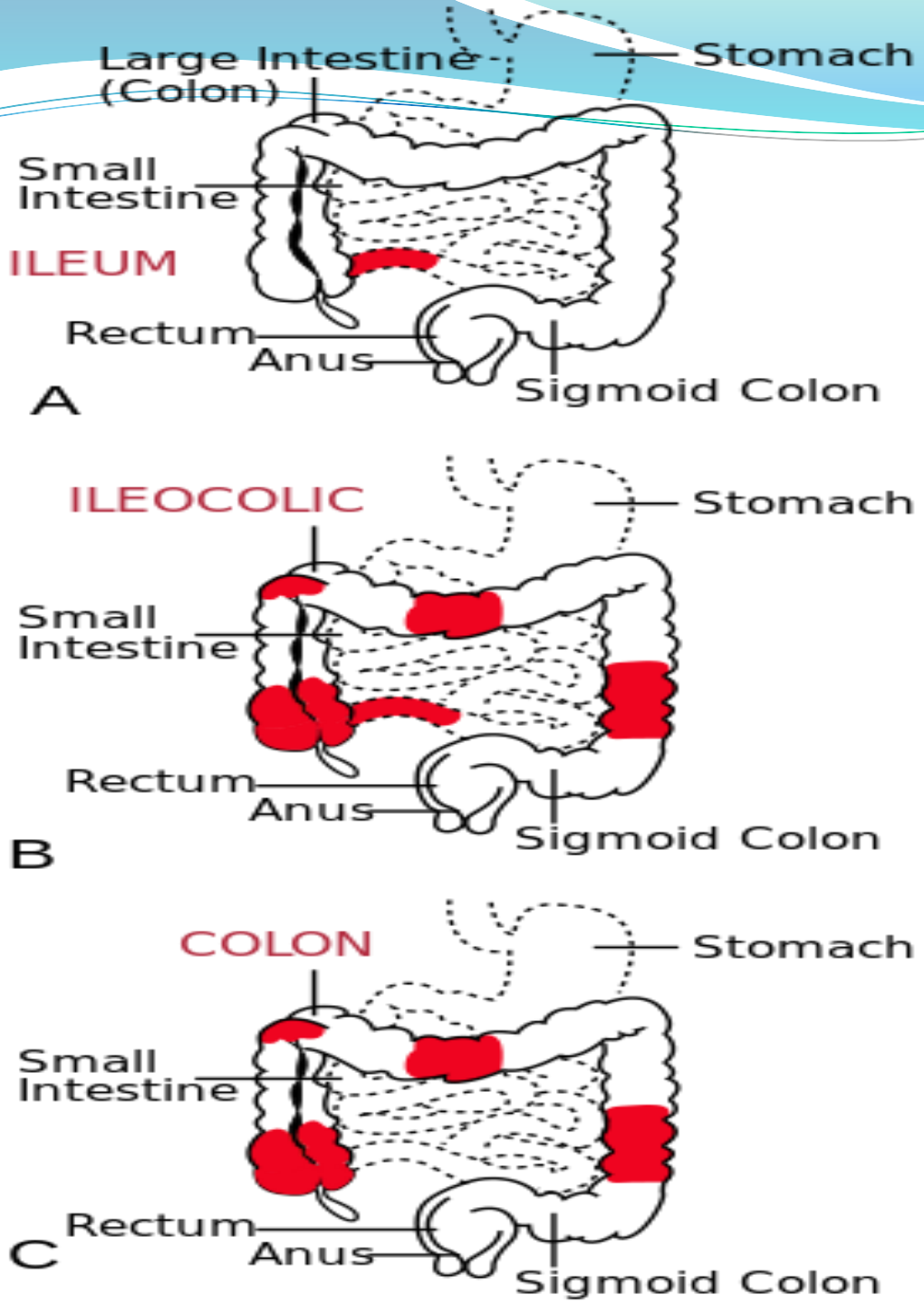
- Defective barrier function of intestinal epithelium.
- Allow luminal flora to gain access to mucosal lymphoid tissue.
- Trigger immune responses

CROHN'S DISEASE

- First described by Crohn and his collegue in 1932.
- When 1st described thought that bowl involvement limited to terminal ileum so designated as terminal ileitis.
- Segmental involment of small bowel leaving intervening unaffected (skip) segment hence another name " regional enteritis."
- Predominant involvement of colon "granulomatous colitis"
- Sharply delimited and typically transmural involvement of bowel by inflammatory process with mucosal damage.

MORPHOLOGY :

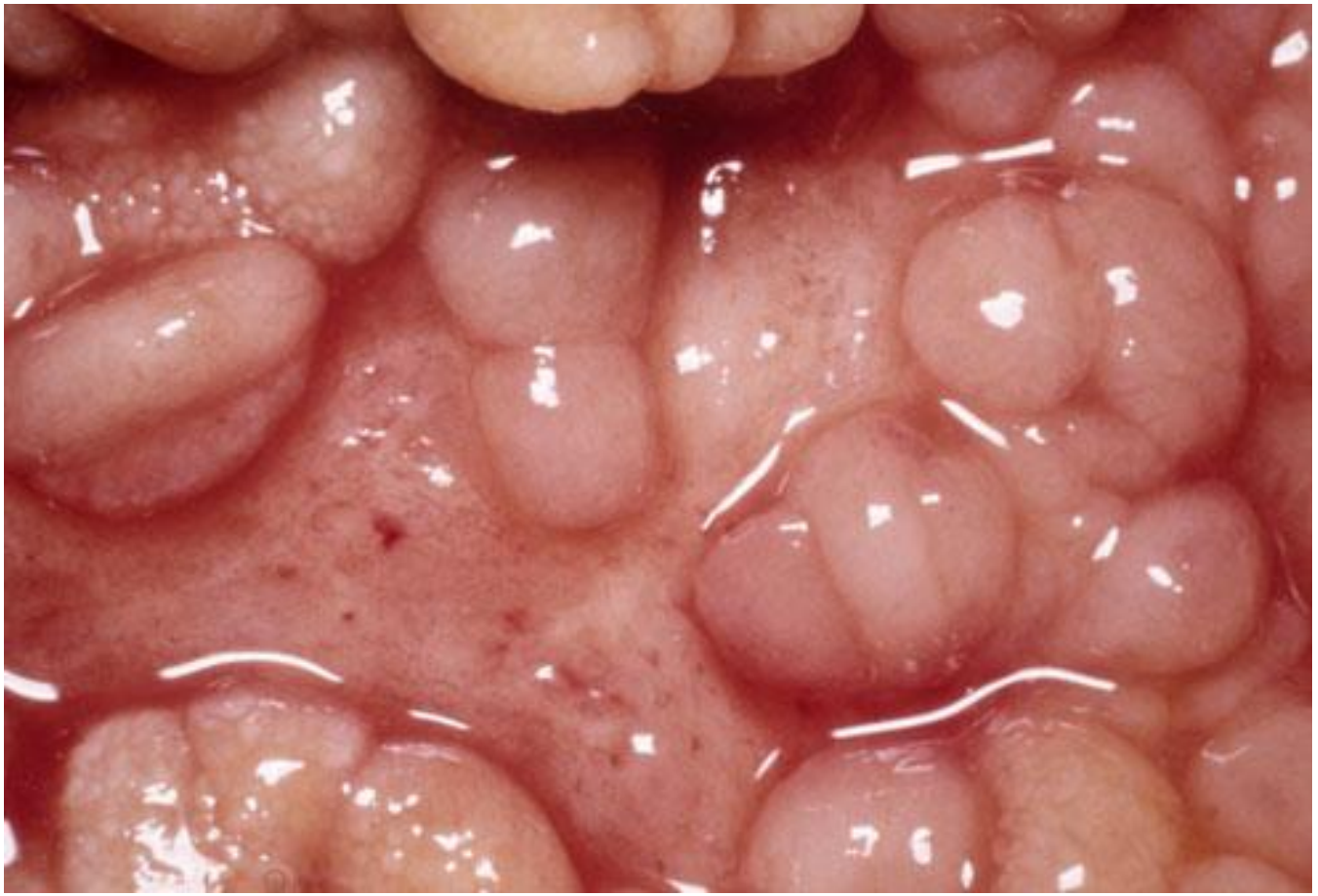
- Terminal ileum,ileocecal valve & cecum-most commonly affected.
- - 40 % small intestine alone
  - 30 % both small intestine & colon
  - 30 % colon alone
- Duodenum, stomach, esophagus, mouth rarely involved.
- Multiple,separate,sharply outlined areas are affected , known as SKIP LESIONS (characteristic of C.D.)


Large Intestine
(Colon)
Stomach
Small
Intestine
ILEUM
Rectum
Anus
Sigmoid Colon
A
ILEOCOLIC
Stomach
Small
Intestine
Rectum
Anus
Sigmoid Colon
B
COLON
Stomach
Small
Intestine
Rectum
Anus
Sigmoid Colon
C

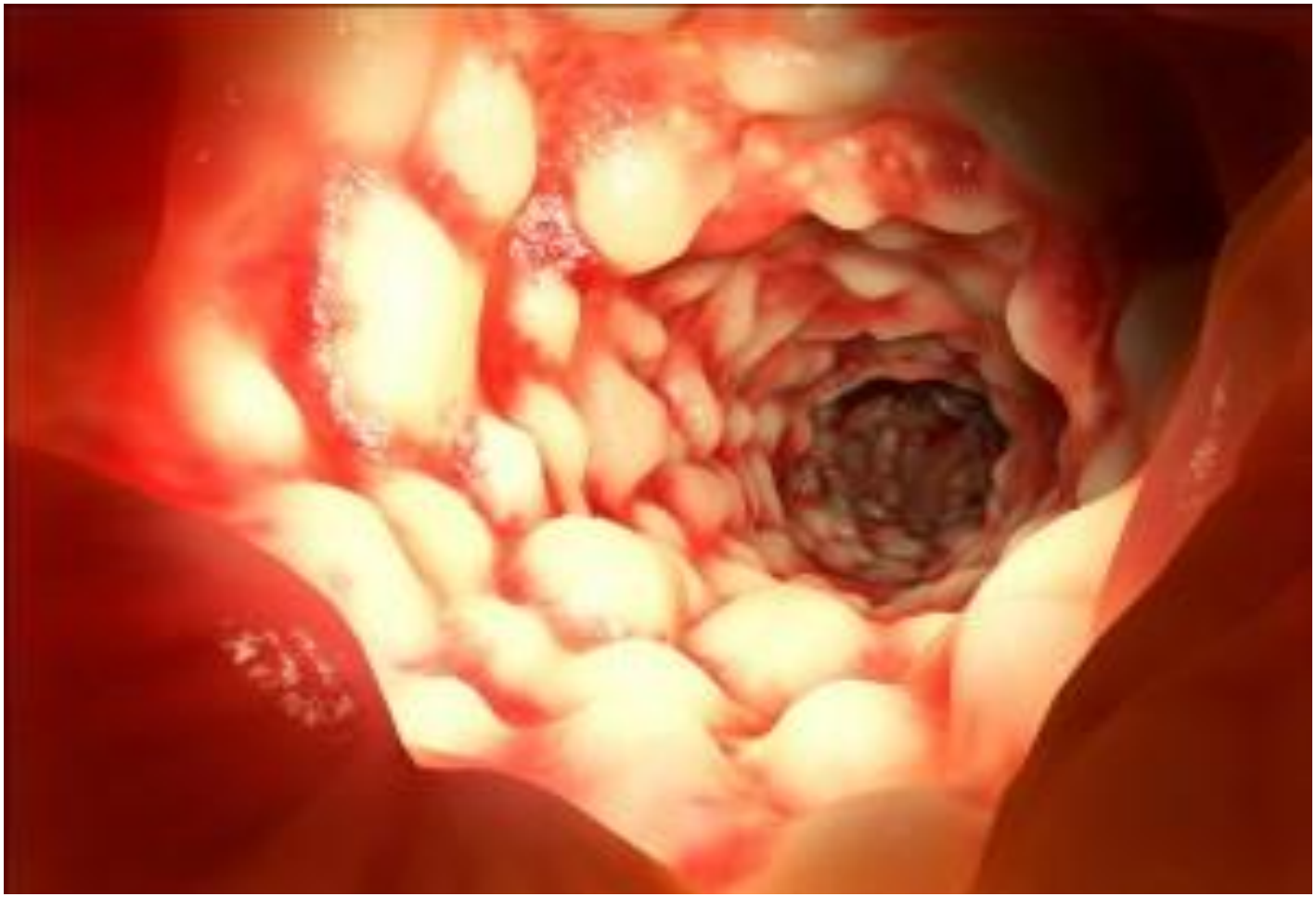
- Serosa- Granular, dull gray, mesentric fat wraps around bowel surface.(creeping fat).
- Mesentry- Thickened, edematous, some time fibrotic.
- Intestinal wall- rubbery and thick due to inflammation, fibrosis and hypertrophy.
- Lumen is narrowed, evident on x-ray film as 'string sign'- A thin stream of barium passing through diseased segment.

- Apthous ulcer earliest then multiple lesions coalesce to form serpentine ulcer along the axis of bowel.
- edema & loss of normal mucosal texture with sparing of interspersed mucosa. (cobblestone appearance ; i.e. alternate depressed & elevated mucosa)

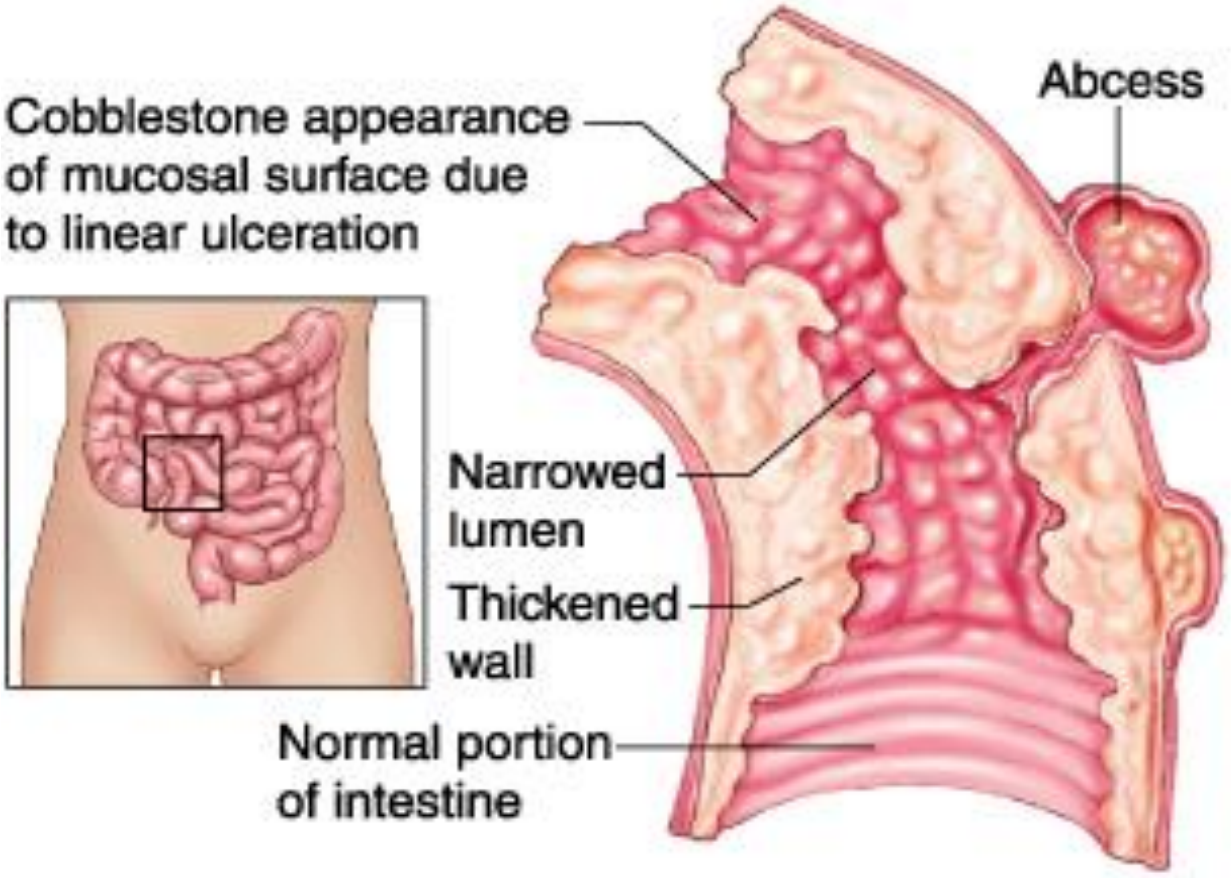
Cobblestone appearance



Cobblestone appearance



Cobblestone appearance

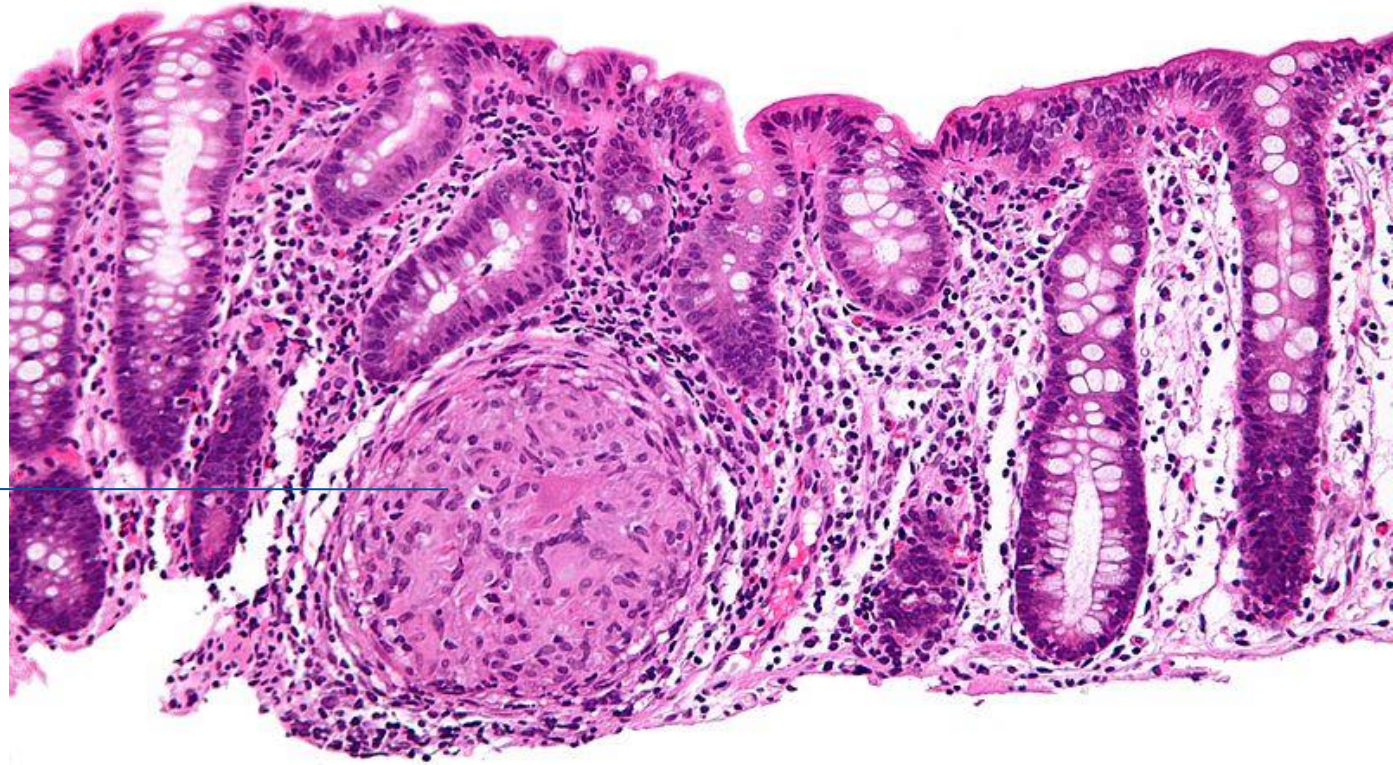


- fissures , fistulas & perforations can occur.
- Strictures are common due to inflammation, fibrosis & muscular hypertrophy.
- Neutrophils infiltrate & damage crypt epithelium → Crypt abscess.(neutrophils within a crypt)

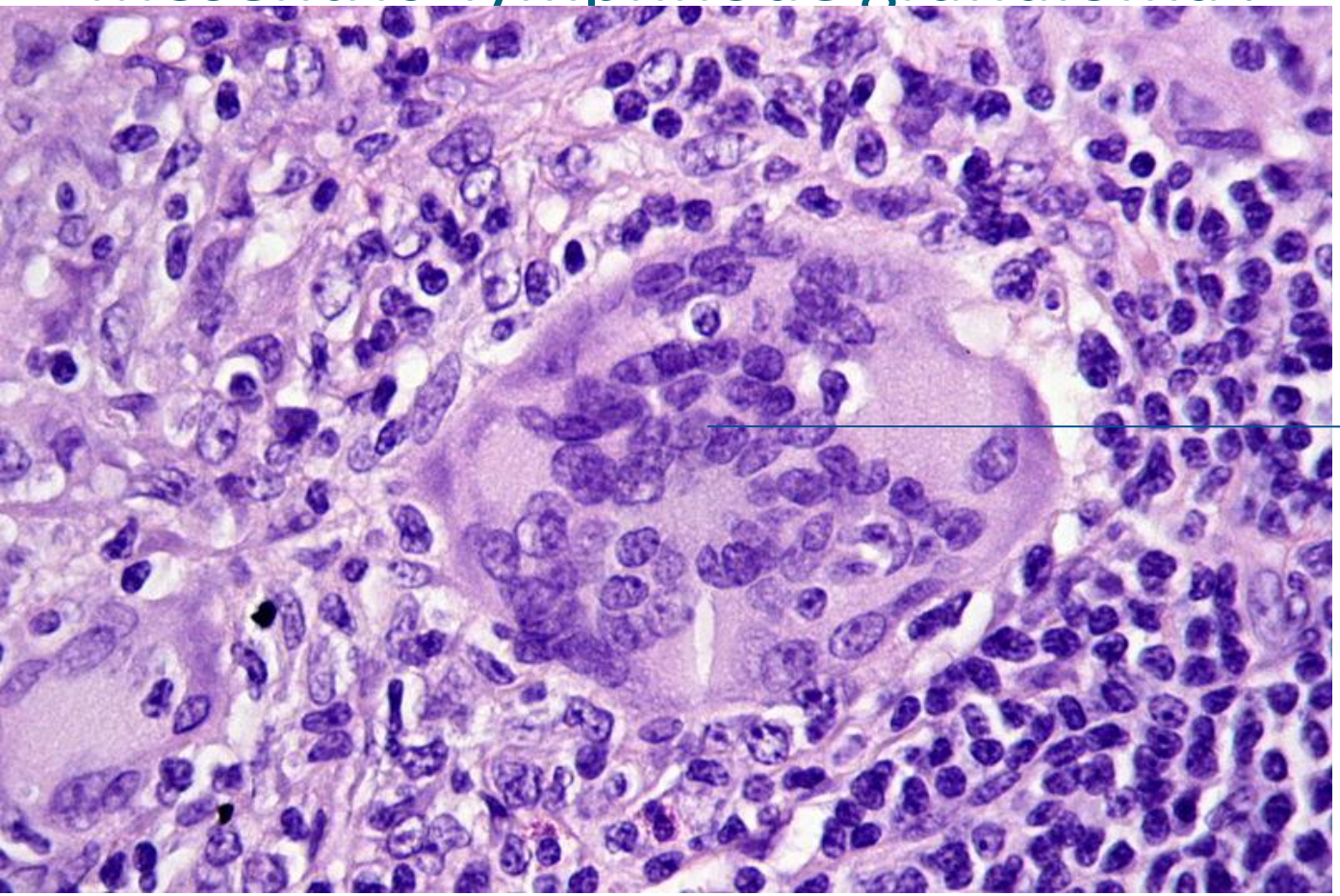
- Repeated destruction & regeneration leads to distortion of mucosal architecture.
  (a) bizzare branching crypts with unusual orientation to one another.
  (b) gastric gland metaplasia , paneth cell metaplasia (on left colon).
- All lead to mucosal atrophy, loss of crypts.

- NON-CASEATING GRANULOMA –
  - hall mark of Crohn's Disease.
  - occur in 35 % of cases.
  - in any layer.
  - sometimes granuloma are found in mesenteric lymph nodes.
  - cutaneous granuloma known as metastatic crohn's disease.(misnomer)

Granuloma in intestinal wall



Mesentric lymphnode granuloma :



EPIDEMIOLOGY:

- Occurs throughout world.
- Primarily in western developed population.
- Age - at any age.
- Peak - 2nd to 3rd decade.
- Minor peak- 6th to 7th decade of life.
- Female are affected more than male. (F > M)
- Smoking is strong exogenous risk factor.

CLINICAL FEATURES :

- Intermittent attacks of mild diarrhoea , fever, abdominal pain.
- in 20 % of patients, pain mimic acute appendicitis.
- asymptomatic periods follow symptomatic periods which last for weeks to months.

- Reactivation of disease associated with physical or emotional stress, dietary items & cigarette smoking.
- smoking is strong exogenous factor for C.D.
- Iron deficiency anemia (colon involvement).
- Hypoalbuminemia , malabsorption of vitamins & bile salt (small bowel disease).
- Fibrosing strictures of terminal ileum.
- Fistula involving urinary bladder, vagina, abdominal or perianal skin.

- Perforation & peritoneal abscess.
- Extra intestinal menifestations like uveitis, migratery polyarthritis ,sacroilitis,ankylosing spondylitis , clubbing of fingers.
- Pericholangitis & primary sclerosing cholangitis.
- ↑ risk of colonic adenocarcinoma with long standing IBD.

THANK YOU

DR. Rajul Shah