Inflammatory Bowel disease: → It is an immune mediate chronic intestinal inflammatory condition. It is triggered by the host immune Response to intestinal mucosa.

⇒ IBD etiology:

→ Genetic predisposition
→ Mucosal immune system.
→ Environmental trigger.
→ Oral contraceptive use – ↑ Risk of crohn disease.

(Appendectomy is protective Against UC ~~but not~~ higher Risk of CD)

GENECTIC FACTORS:

- Crohns > Ulcerative colitis
- IBD genes.

⇒ 1) Defective NOD2 (nucleotide oligomerization binding domain 2 / CARD15 code for NOD2/CARD2

2) Mutation of ATG16L1 (Autophagy Related 16 like) & IRGM } for chrons disease

NOD2 codes for protein which is Required for normal Recognition & Response Against microbes in lumen

function → Prevent entry of microbe
→ Regulate innate immune Res
→ Prevent excessive immune Response

ENVIRONMENTAL & HOST FACTORS:

- Smoking, NSAIDS, Bacteria
- Diet
- Inadequate immune Regulation of ATG16L1

ATG16L1

MUCOSAL IMMUNE RESPONES.

- Defective Immune Response → Activate T cells in the lamina propria
- Secrete excess inflammatory cytokines
- Imbalance b/w pro inflammatory And Anti inflammatory Mediators.

uncontrolled inflammation.

PATHOGENESIS:

- Trans epithelial influx of bacteria / Antigens → Activate Immune Response
- Antigen presented to CD4+T helper cells.
- T cell Activation and differentiation (IL-6, 12, 23)
- ~~Changes in the microbiota in the luminal tumen.~~

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TH2, TH17.

TH1 - IFN gamma → TNF - Activate macrophage
- Tight function permeability, which further increase the flux of luminal material.
- establish a self amplifying cycle

→ TH2, IL-4, 5, 13, 17, 13 - Stimulate mucosal inflammation.
→ TH17, IL-17, 21 - Neutrophil - Recruitment.
→ Abnormal mucosal immune Response (CD4+T cell and its differentiation into TH1, TH2 TH17 type.

① CROHN'S DISEASES.
- Regional enteritis
- Chronic Relapsing and Remitting progressive inflammatory bowel disease
- Can involve Any portion of GI tract.
- Multifocal.
Most common → Ileocecal valve, caecum, perianal region
- The presence of multiple, separate sharply delineated area of disease skip lesion - characteristics
- Mucosal lesion:
when endoscopy is done.
1st phase - Aphthus ulcer
2nd phase - serpentine ulcer (snake like)
↓
Fissure, fistula perforation
→ Mucosal edema
⇒ cobble stone Appearance. (islands of normal mucosa between ulcer)
Remaining wall become - thickened
Stricture formation - hour glass - Radiological sign
- Adherence
extensive transmural disease - mesentric fat frequently encircle around the mucosal surface ÷ creeping fat

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↳ mesentric fat become adherent to serosal surface may encircle Around Antimesentric serosal surface reducing pattern.

Radiology - string sing
(Barium study) →

epithelial
Lamina propria
Muscularis mucosae
M
SM
MP
Serosa

MICROSCOPIC FEATURES:
- Distortion of mucosal Architecture. - bizarre branching
- Non caseating granulomas. - hall mark.
- Transmural inflammation (skip lesions)
- Ulceration
- cryptitis, crypt Abscess, crypt distruction
- epithelial metaplasia, Paneth cell Metaplasia
→ Mucosal Aphthous ulcers. Aniply. Paneth
→ cryptitis

GRANULOMA: → crypt Abscess. → clutus of neutrophils within crypt.

CLINICAL FEATURES:

Extra intestinal Manifestation
→ Uveitis
→ migratory polyarthritis
→ Sacroiliitis
→ erythema nodosum.

→ Acute Onset Resembling Appendicitis.
→ Chronic ill health
→ Recurrent attacks of Abdominal pain & diarrhea
→ Low grade fever
→ Tender mass in Right iliac fossa.

Risks → fistulas, colon cancer, Ileus, Malnutrition, Anaemia, Systemic Amyloidosis.

SISTER INCEF

(2) ULCERATIVE COLOTIS:

→ With exacerbation & Remissions.
→ Mucosa And submucosa.
→ No skip lesion
→ Rectum And colon (Able LD)
Associated with bloody diarrhea

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Red And granular colonic Mucosa. (Resemble sandpaper)
→ Extensive mixed-based ulcer.
→ Isolated islands of Regeneration mucosa often bulge into the lumen to create small elevation - pseudopolyps
→ chronic ulcer - mucosal Atrophy.
→ mural thickening is absent, the ulcered surface is normal if stricture does not occur.
→ Bowel wall is not thickened, the mucosa is normal, if stricture develop.
→ Toxic Megacolon - Risk of perforation.

HISTOLOGICAL FEATURES:
- Inflammatory generally is limited to the mucosa And superficial Submucosa.
- Mucosal edema, congestion and haemorrhages.
- Ulceration, inflammatory infiltrate, cryptitis, crypt distortion & crypt Abscess.
- chronic inflammatory cell.

- Inactive / Resolution Phase: ↓ Activity, crypt Regeneration.
- Chronic phase: Distortion of crypt Architecture
Chronic inflammation, mucosal Atrophy, metaplasia, Dysplasia.

→ Loss of goblet cell & mucus depletion.

Symptoms: → Dysplastic changes in epithelium may appear & progress to carcinoma

→ Bloody stool
→ Diarrhea
→ Rectal pain
→ Abdominal pain
→ weight loss
→ chronic fatigue
→ eye pain
→ Dehydration
→ Anemia
→ Joint Pain

Complication
→ Toxic megacolon
→ Colorectal cancer
→ Bowel ↓.

Indeterminate Colitis
→ cannot differentiate b/w colitis &

PATHOGENESIS OF IBD:

Activated Tcell in the lamina propria are involved in pathogenesis of IBD

Events

1) Transepithelial influx of luminal bac components.
(They enter through ulcerated mucosa)
↓
Presentation of microbial Antigen to CD4+ helper Tcell
↓
differentiation into three types of CD4+ Thelper effector

TH1 by IL-2 → TH2 by IL-4 → TH17 IL-23.

TH1 → secrete IFNγ → ↑ permeability of epithelial cell → ↑ entry of bac.
↓
self Amplifying cycle.

TH2 → induce superficial inflammation of the mucosa.

TH17 → neutrophils.