

Le Malattie Infiammatorie Intestinali

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22 Maggio, 2018

Roberto De Giorgio

Inflammatory bowel disease (IBD)

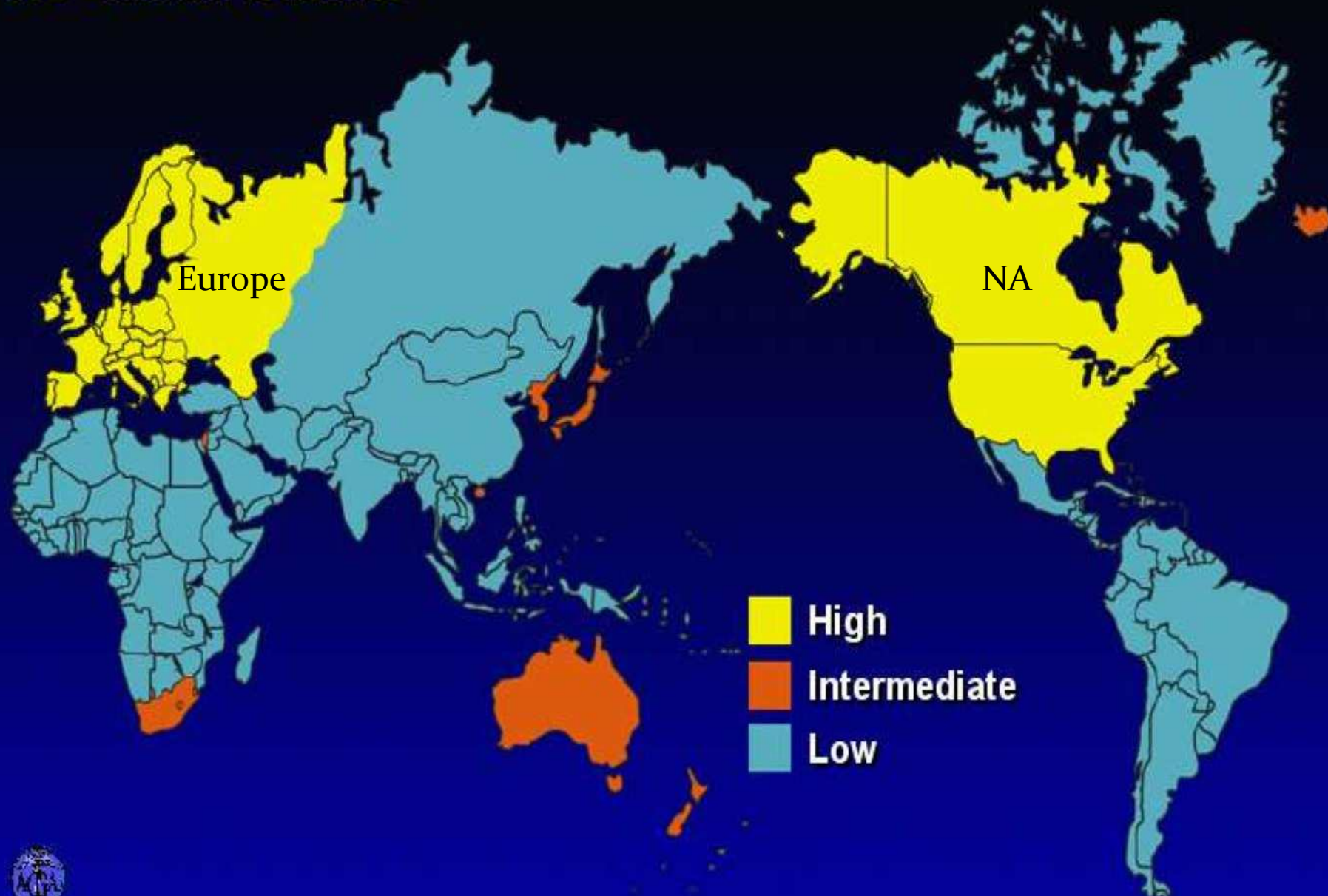
Malattie infiammatorie croniche intestinali (MICI)

Malattie infiammatorie cronica idiopatiche la cui origine è attribuibile ad una inappropriata risposta del sistema immunitario a vari antigeni (probabilmente alcuni di questi potrebbero derivare dal *gut microbiota* o meglio da alterazioni dello stesso)

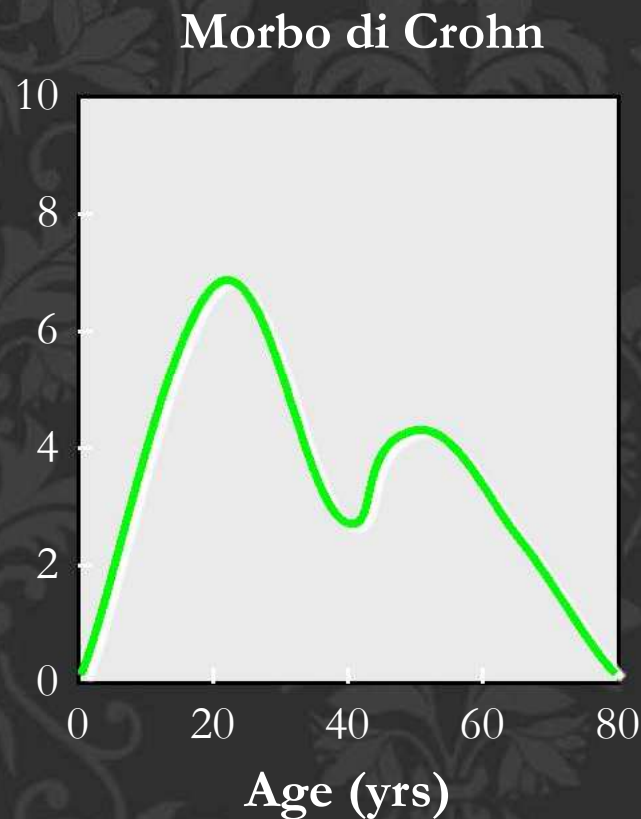
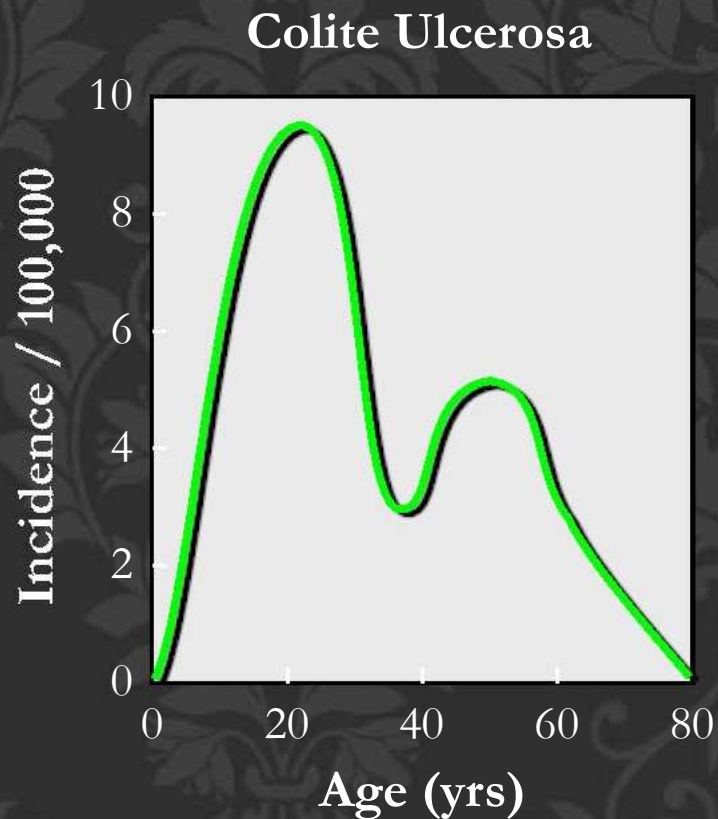
Fenotipi clinici delle IBD:

- Colite ulcerosa (UC)
- Morbo di Crohn (CD)
- Colite Indeterminata

IBD - Global Prevalence

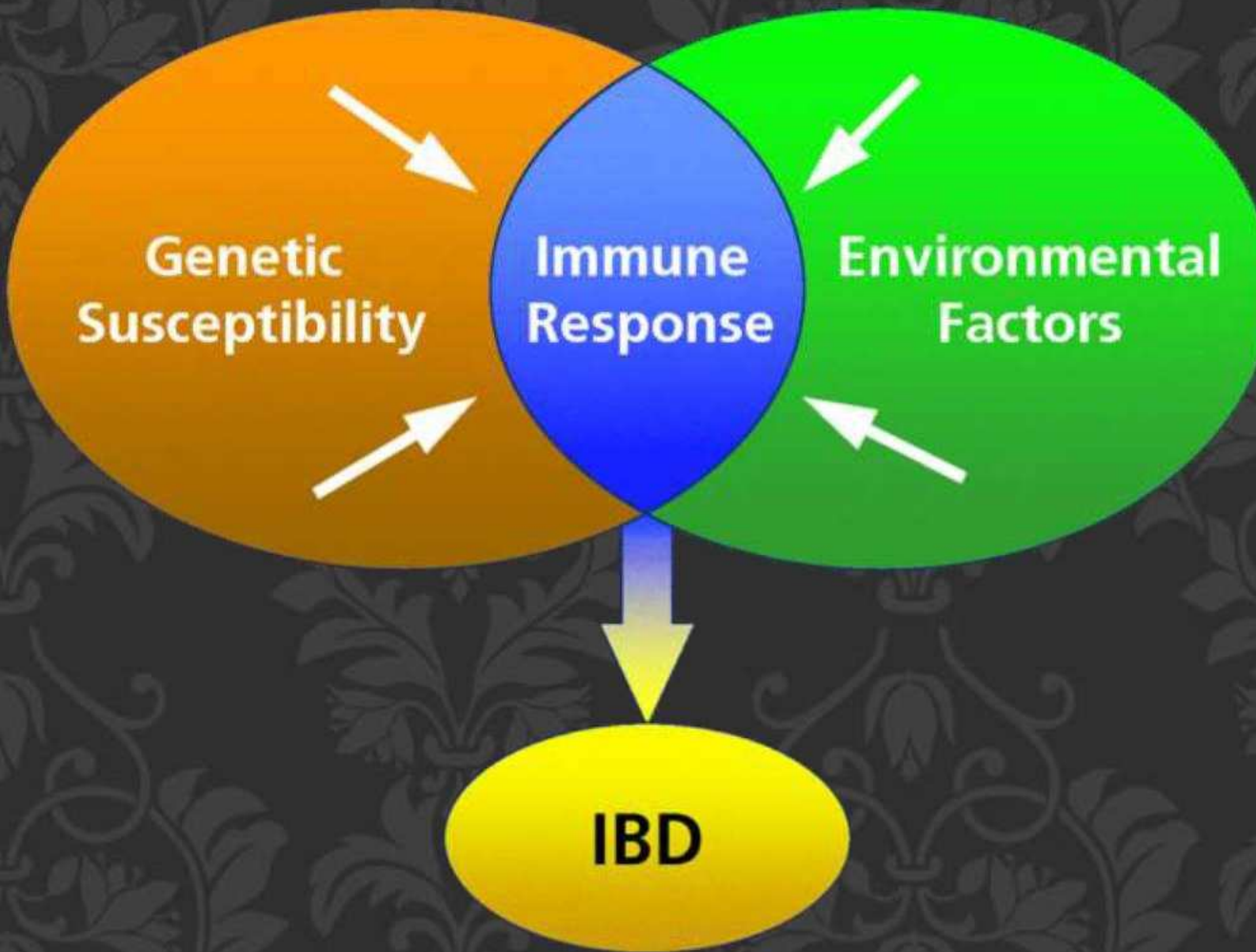


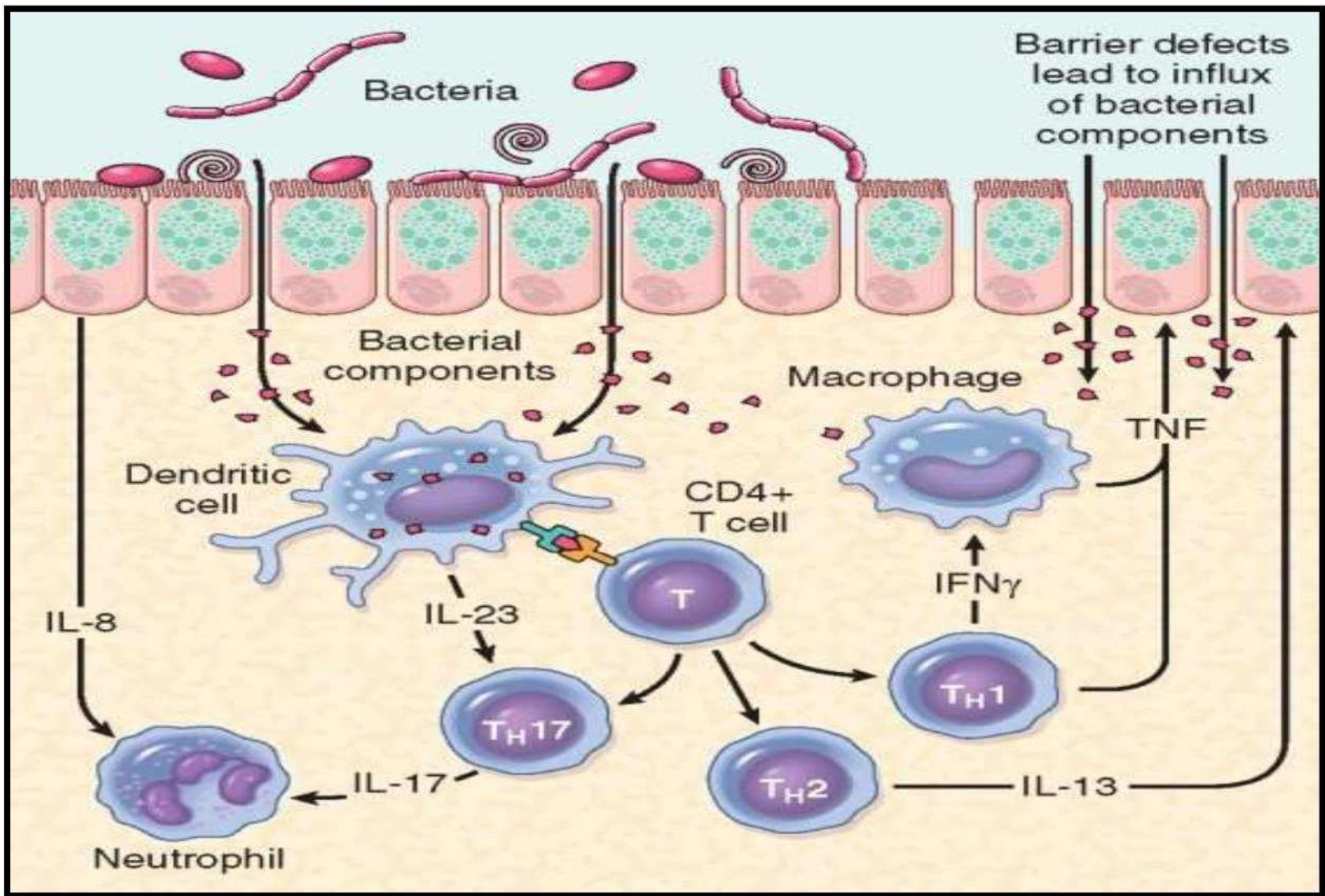
Incidenza delle IBD



L'incidenza della UC e CD ha 2 picchi di età:
2-3 decade e 6 decade

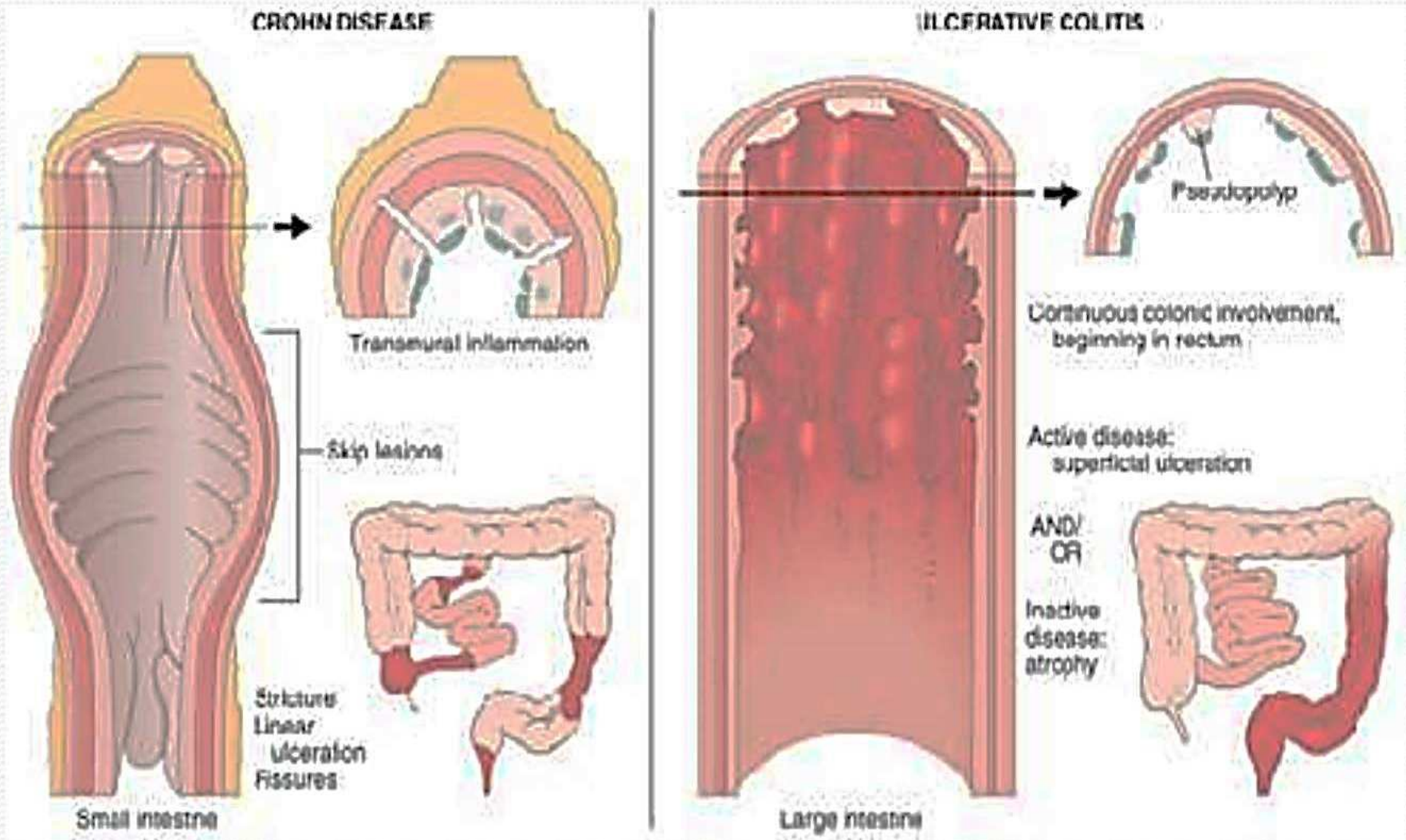
Possibili fattori eziopatogenetici delle IBD



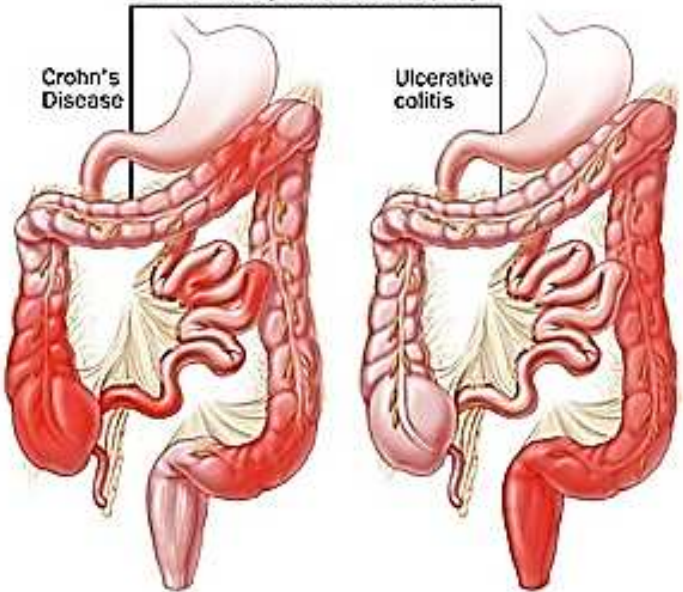


Modello 'olistico' della patogenesi delle IBD (aspetti comuni di UC e CD)

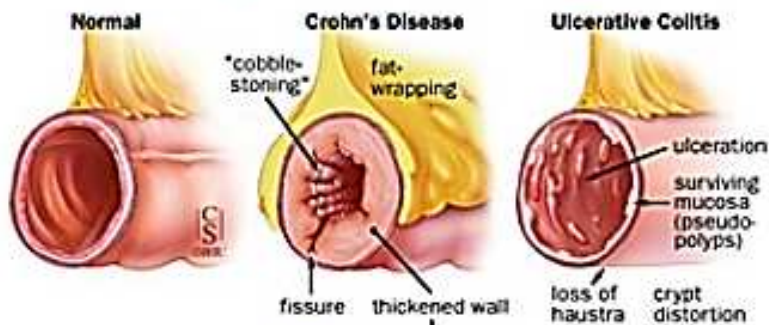
Caratteristiche anatomo-cliniche del Crohn e della Colite ulcerosa



Inflammatory Bowel Disease (IBD)

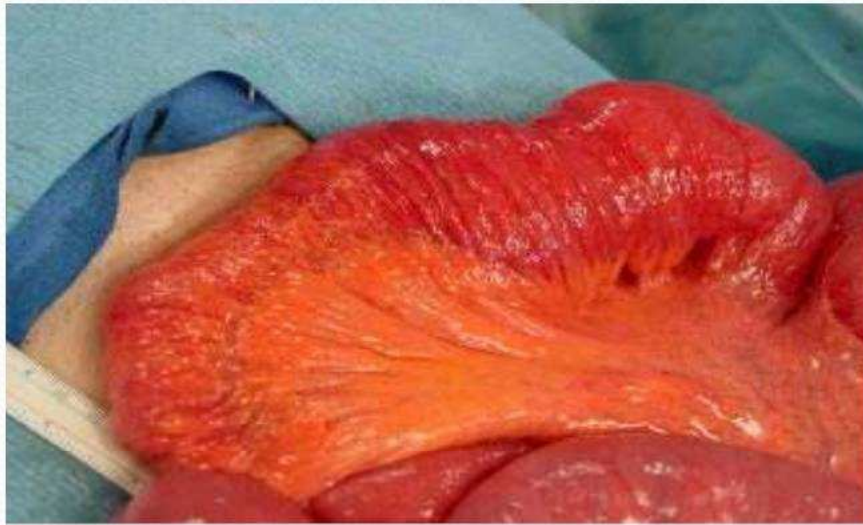


**Aspetti anatomo-
patologici distintivi
tra CD e UC**

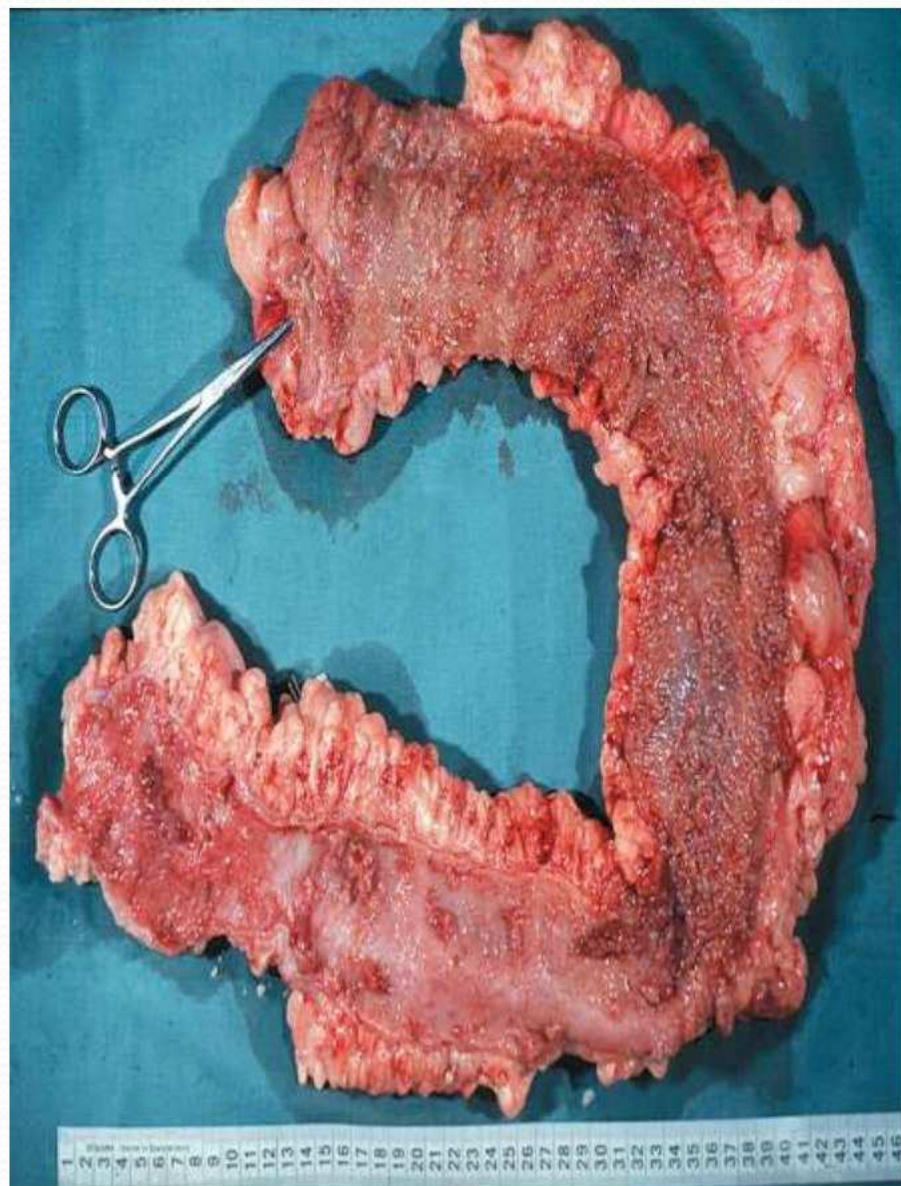


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Anatomia patologica macroscopica del Crohn



Anatomia patologica macroscopica della Colite ulcerosa



Presentazione clinica delle IBD

A- sintomi

- Diarrea ematica / rettorragia
- Muco nelle feci
- Tenesmo
- Dolore addominale
- Febbre
- Anoressia
- Nausea / vomito

B- Segni (CD)

- Calo ponderale
- Lesioni aftoidi del cavo orale
- Glossite
- Cheilite angolare
- Defecamento (se la malattia non è stata ben trattata)
- Ddolore addominale alla palpazione in fossa iliaca dx
- Ragadi e fistole perianali

B- Segni (UC)

- Stato di idratazione e volemia (P.A., polso, obiettività)
- Febbre !!!
- Dolore addominale diffuso;
attenzione se Blumberg +
(segno di irritazione peritoneale)
- Pesplorazione rettale con
presenza di sangue nel guanto

Caratteristiche distintive del CD vs. UC

	CD	UC
Diarrhea	Often porridge like (sometimes steatorrhea)	Typically with mucus and blood
Tenesmus	Less common	More common
Fever	Common	Common; may indicate severe outcome !
Fistulae	Common	Seldom
Weight loss	Often	More seldom
Malignant potential	With colonic involvement	Yes
Toxic megacolon	No	Yes
Post-surgical FU	Recurrence is common	No recurrence

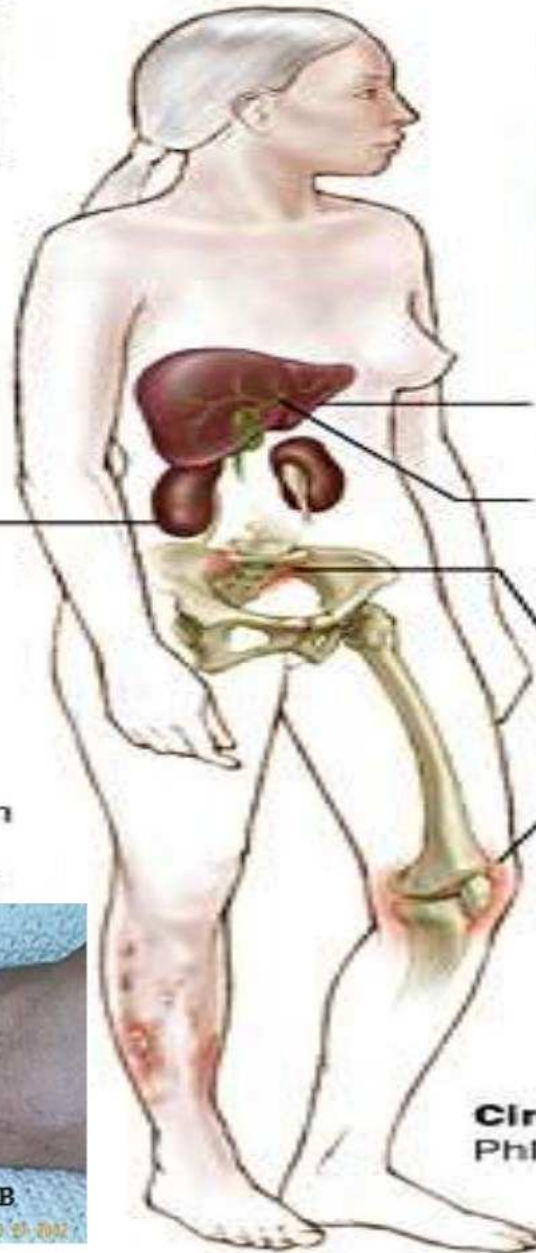


Eyes
Episcleritis
Uveitis



Kidneys
Stones
(nephrolithiasis)
Hydronephrosis
Fistulae
Urinary tract
infection

Skin
Erythema nodosum
Pyoderma
gangrenosum



Mouth
Stomatitis
Aphthous ulcers



Liver
Steatosis

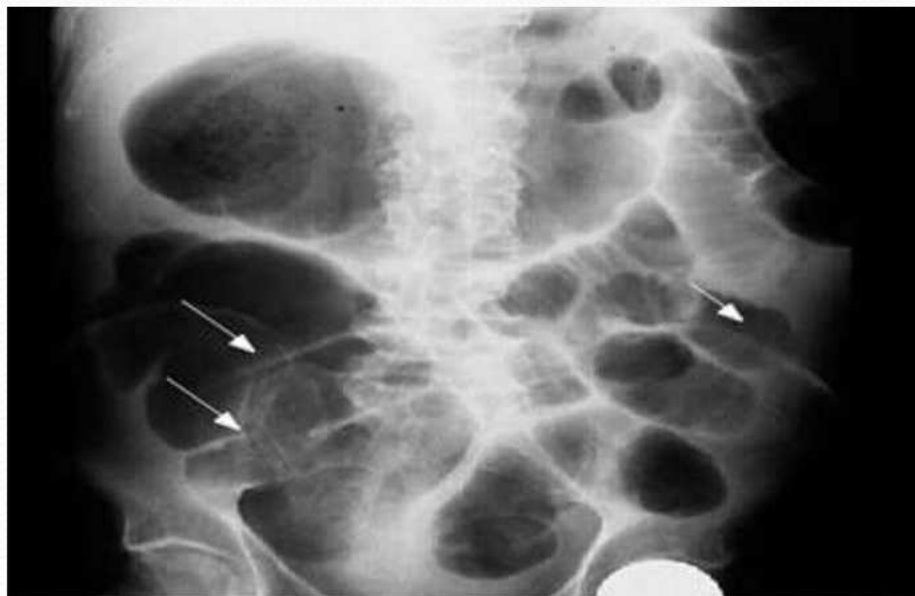
Biliary tract
Gallstones
Sclerosing cholangitis

Joints
Spondylitis
Sacroiliitis
Peripheral arthritis

Circulation
Phlebitis

Complicazioni della UC

- Emorragie
- Perforazione
- Megacolon tossico (colon trasverso di 5-6 cm di diametro con perdita dell'austratura !!!)
- Cancerizzazione: con attività di malattia >8 anni



Complicazioni del CD

- Stenosi con conseguente occlusione intestinale meccanica
- Ascessualizzazioni
- Fistole
- ❖ Cancerizzazione: rischio legato alla severità e alla durata della malattia



watering-can perineum secondario a una forma severa di CD con interessamento perianale.

Valutazione del grado di attività clinica delle **IBD**

- **A** Ulcerative colitis Clinical Activity Index (UCCAI)
- **B** Crohn's Disease clinical Activity Indices:
 - I – Harvey-Bradshaw index
 - II - Crohn's Disease Activity Index (CDAI)

Ulcerative colitis Clinical Activity Index (UC-CAI)

Criteria per la valutazione della severità della UC

Criteria	Mild Disease	Severe Disease	Fulminant Disease
Stools	< 4 / day	> 6 / day	> 10 / day
Blood in stool	Intermittent	Frequent	Continuous
Temperature	Normal	> 37.5°C	> 37.5°C
Pulse	Normal	> 90 beats/min	> 90 beats/min
Hemoglobin	Normal	< 75% of normal	Transfusion required
ESR / VES	≤30 mm/hr	> 30 mm/hr	> 30 mm/hr
Colonic features on radiography	–	Air, edematous wall	Dilatation
Clinical signs	–	Abdominal tenderness	Abdominal distention and tenderness

CD Clinical Activity Indices

I - Harvey-Bradshaw index

- **A-general well-being** (0 = very well, 1 = slightly below average, 2 = poor, 3 = very poor, 4 = terrible)
- **B- abdominal pain** (0 = none, 1 = mild, 2 = moderate, 3 = severe) .
- **C- number of liquid stools per day.**
- **D- abdominal mass** (0 = none, 1 = dubious, 2 = definite, 3 = tender) .
- **E- Complications**, with one point for each.

Uno score < **5** indica **remissione clinica**

Crohn's Disease Activity Index (CDAI)

Clinical or laboratory variable	Weighting factor
Number of liquid or soft stools each day for seven days	X 2
Abdominal pain (graded from 0-3 on severity) each day for seven days	X 5
General well-being, subjectively assessed from 0 (well) to 4 (terrible) each day for seven days	X 7
Presence of complications*	X 20
Taking Lomotil or opiates for diarrhea	X 30
Presence of an abdominal mass (0 as none, 2 as questionable, 5 as definite)	X 10
Hematocrit of <0.47 in men and <0.42 in women	X 6
Percentage deviation from standard weight	X 1

CD in remission < 150

CD severa > 450

Principali indici di laboratorio

- ✓ Emocromo: Hb, GB e PLT
- ✓ Valutazione nutrizionale: Vit B12, Sideremia, **Ferritina**, Folati, Vit D3, Protidemia, etc

VES: buona correlazione con l'attività di malattia nella UC;
pare meno efficace nel CD

PCR: buon marker per l'attività di malattia IBD; può essere usato con biomarker per monitorare la risposta al trattamento

Markers Sierologici Anticorpali

- 1-Anti-neutrophil cytoplasmic antibodies (cANCA)
- 2-Antibodies to outer membrane **porin** (Anti-OmpC)

Biomarkers nelle Feci

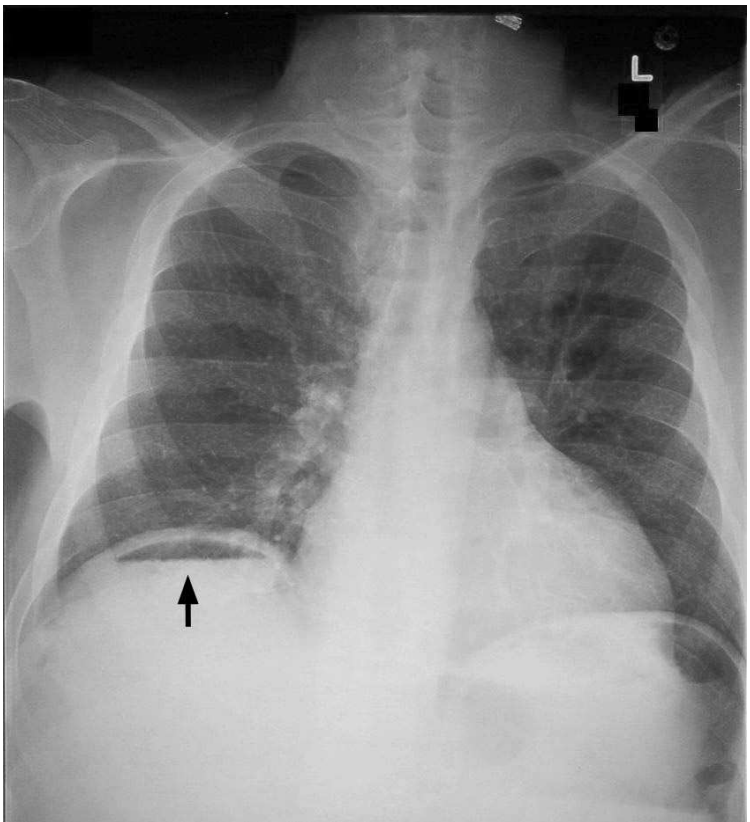
Calprotectina: si misura tramite ELISA;
marker sensibile di infiammazione

Lattoferrina: si misura con ELISA;
Marker sensibile d'infiammazione

S100A12: si misura sia nelle feci che nel siero;
il dosaggio fecale è più sensibile e specifico
per IBD

Radiologia convenzionale

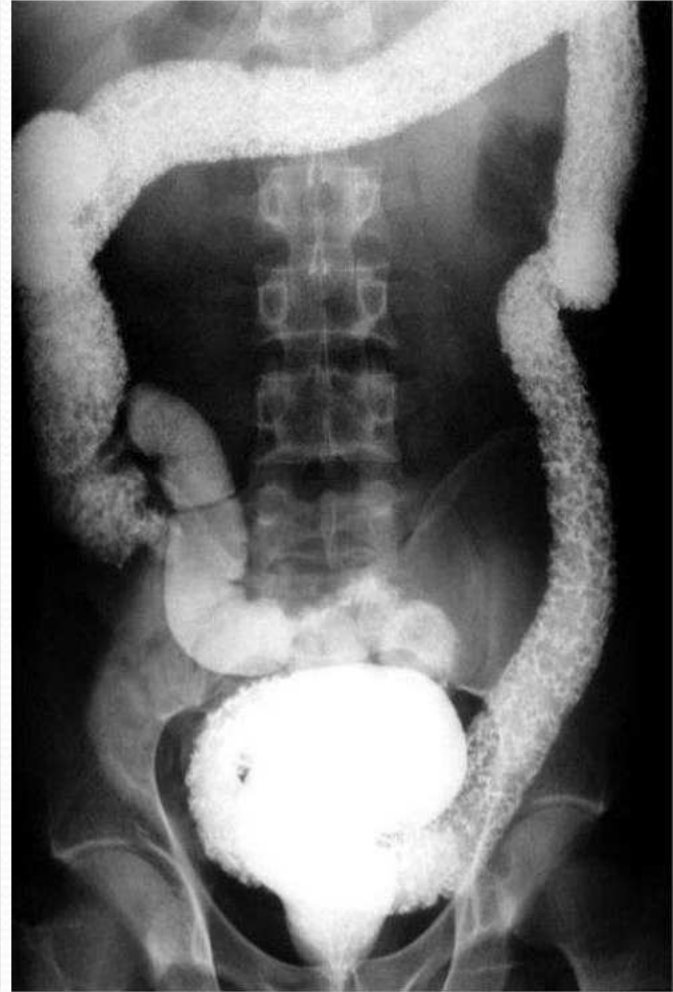
- 1- Valutare sub-occlusione / occlusione intestinale; pneumoperitoneo; megacolon tossico
- 2- RX con mdc (bario)



Clisma opaco



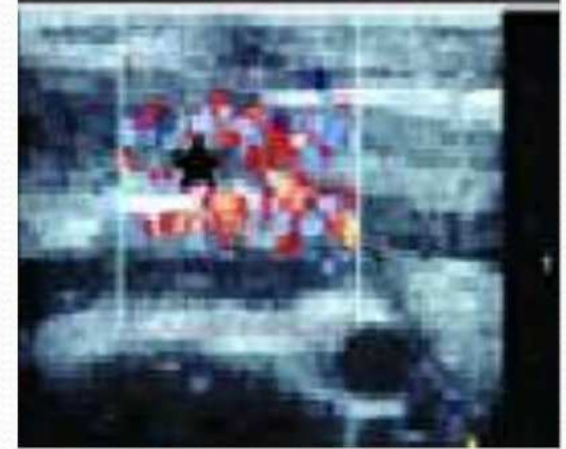
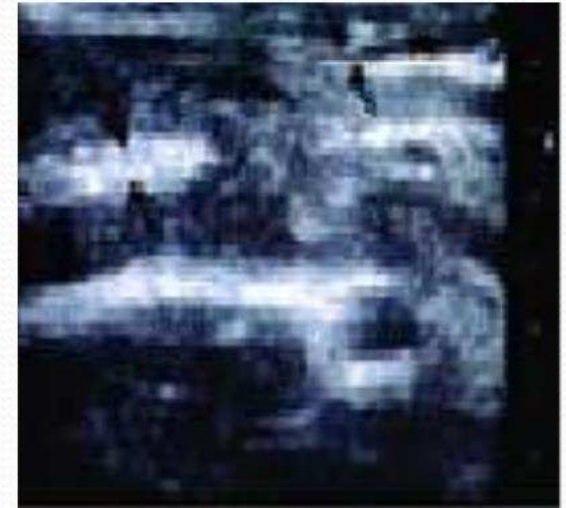
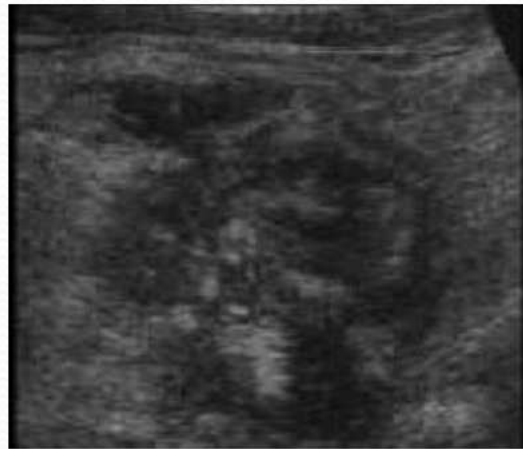
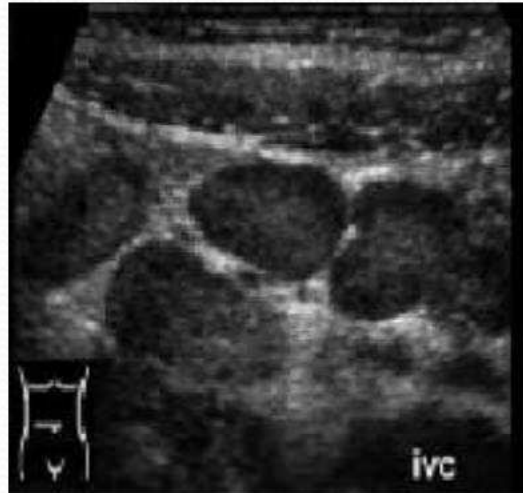
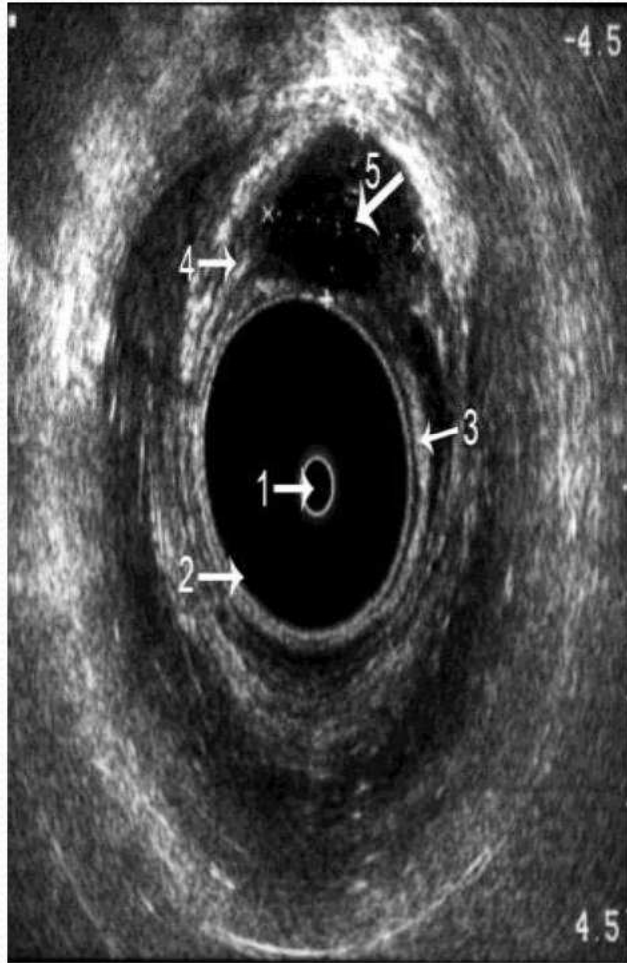
ULCERATIVE COLITIS WITH LEAD PIPE COLON



ULCERATIVE COLITIS WITH PSEUDO-POLYP.



Abdominal Ultrasonography



Endoscopic Ultrasound

Abdominal Ultrasonography

Computed tomography



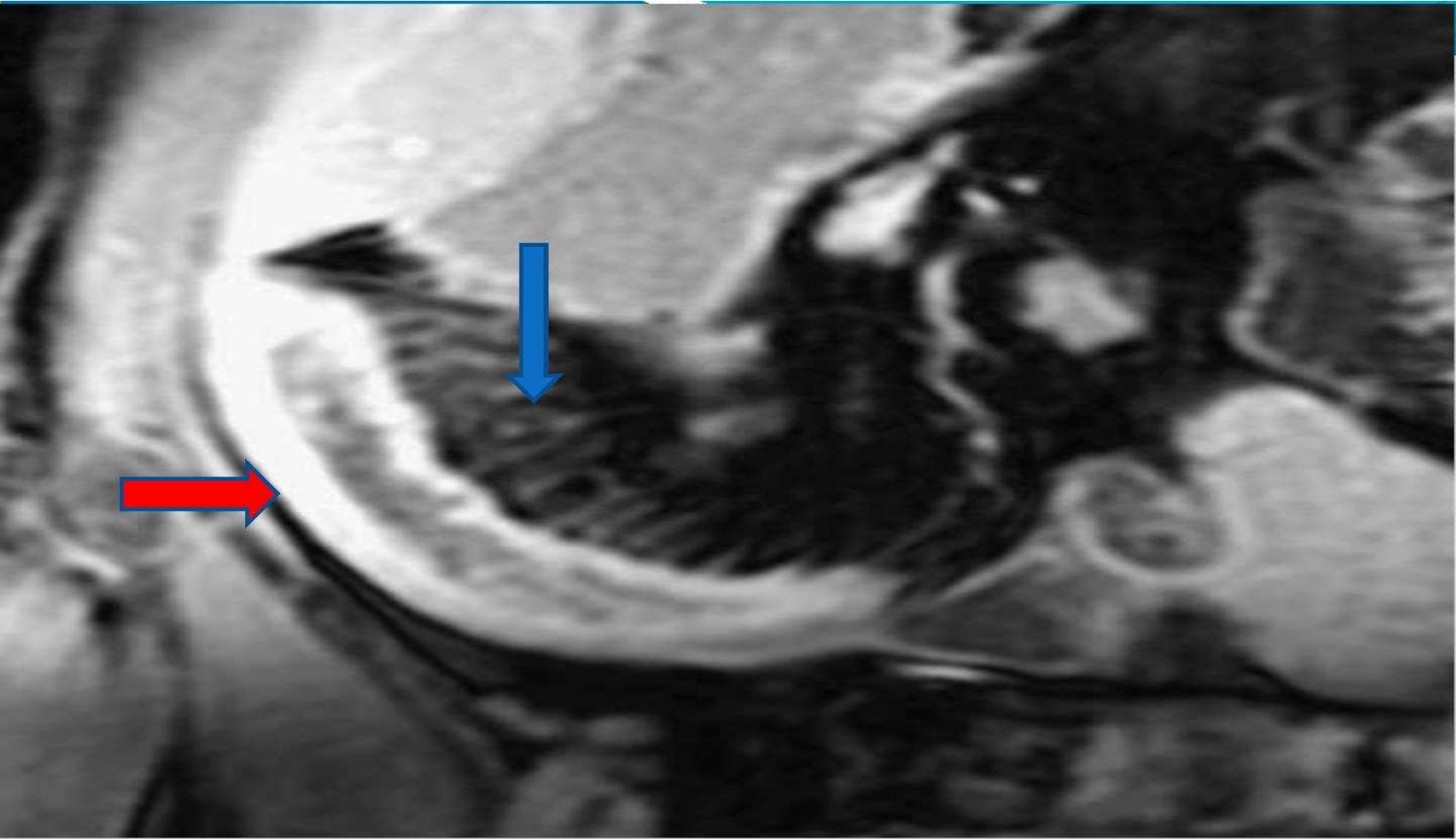
Mural enhancement



Comb sign

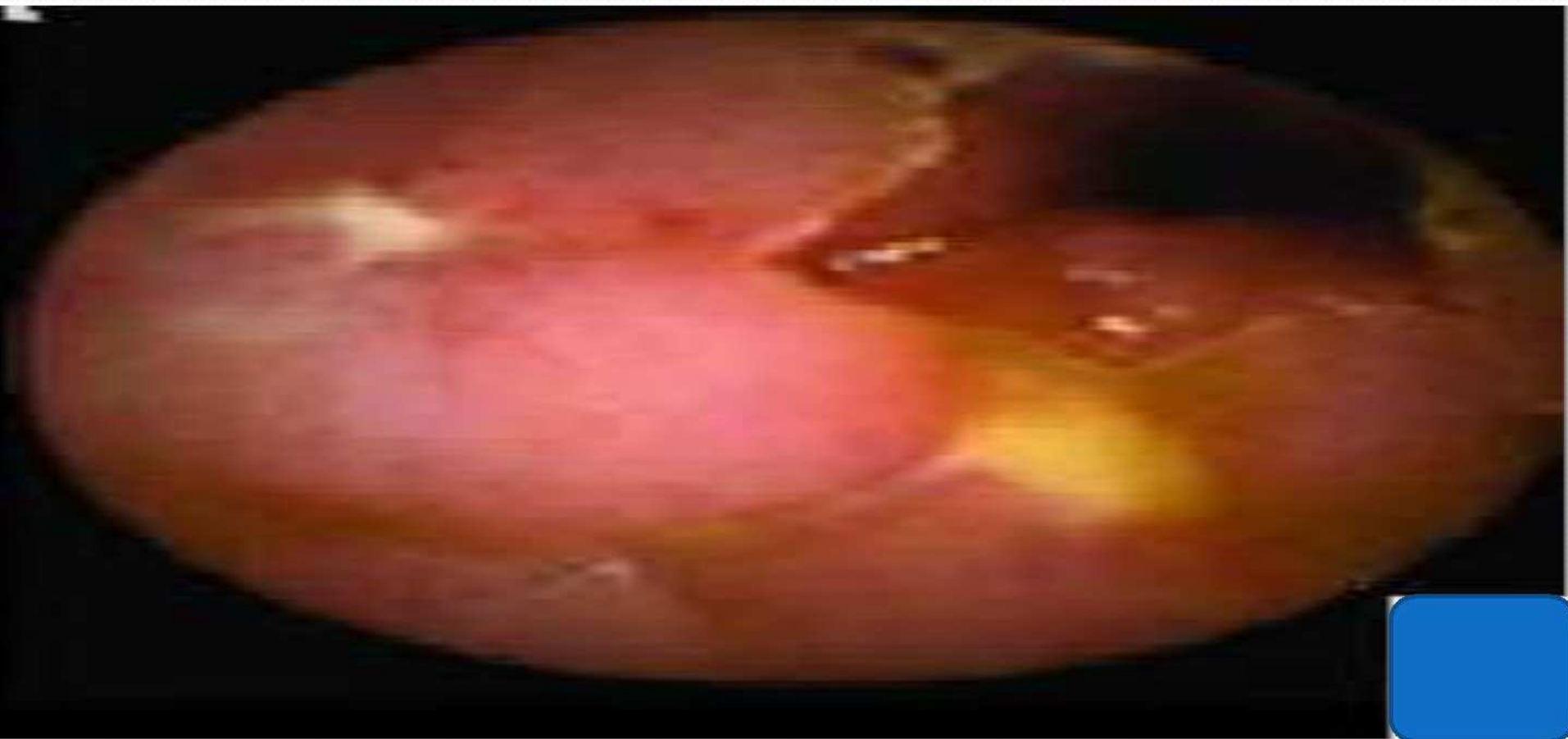


Intestinal stricture with prestenoic dilatation.



Wireless capsule endoscopy (Videocapsula)

Enteroscopia

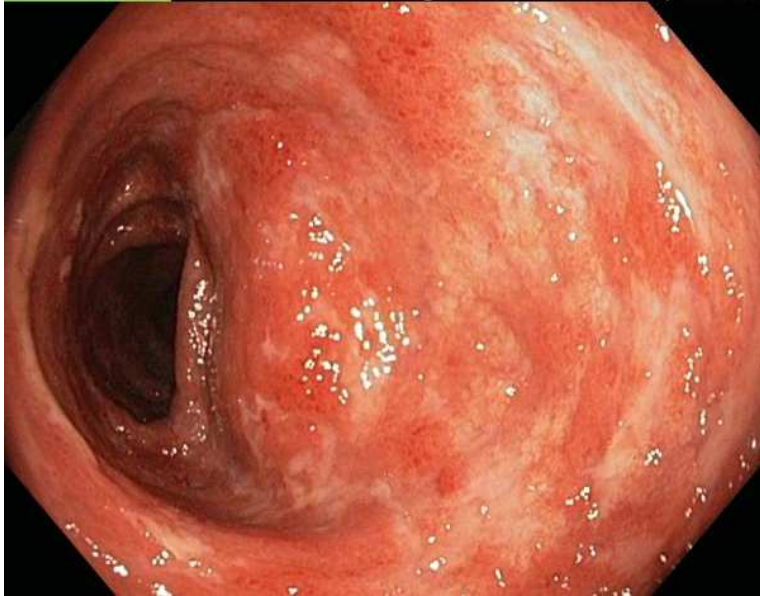


Medicine Nucleare

Tc-99m 'Leucociti marcati': superiore alle tecniche radiologiche per determinare l'estensione e attività di IBD; utile per la distinzione tra CD e UC.

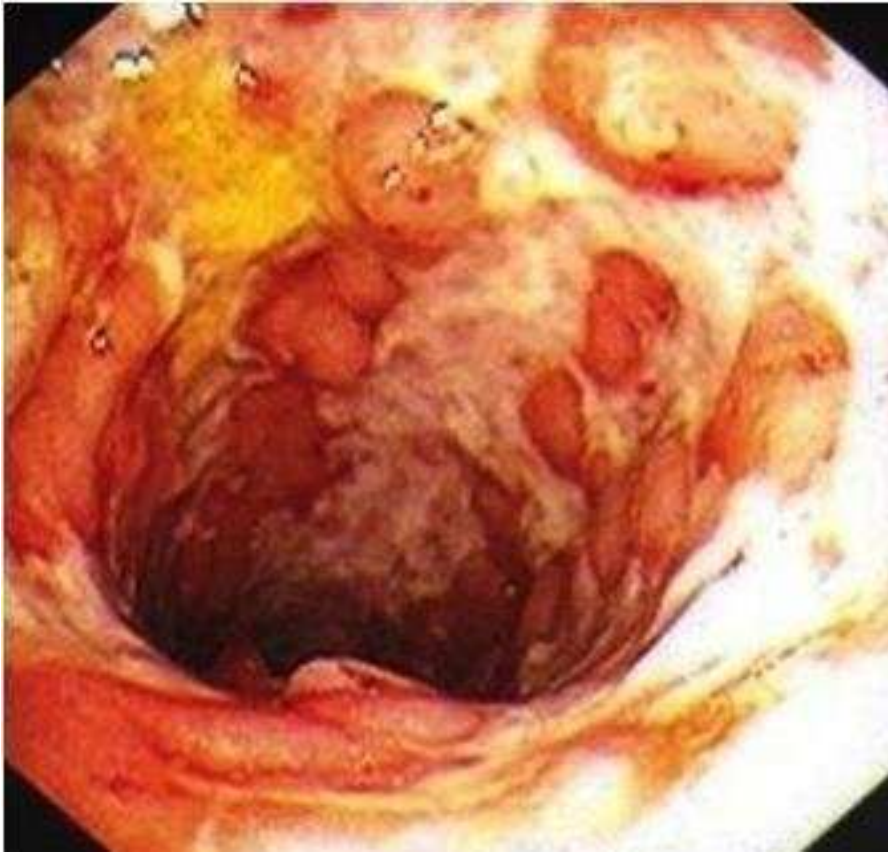
PET / CT e PET / MRI: migliorano ulteriormente la localizzazione di IBD riducendo i falsi positivi

Aspetti endoscopici delle IBD - *UC*



- Edema
- Eritema / perdita della vascolarizzazione
- Fragilità della mucosa
- Erosioni
- Essudato muco-purulento
- Sanguinamento spontaneo
- Ulcere

Aspetti endoscopici delle IBD - *CD*



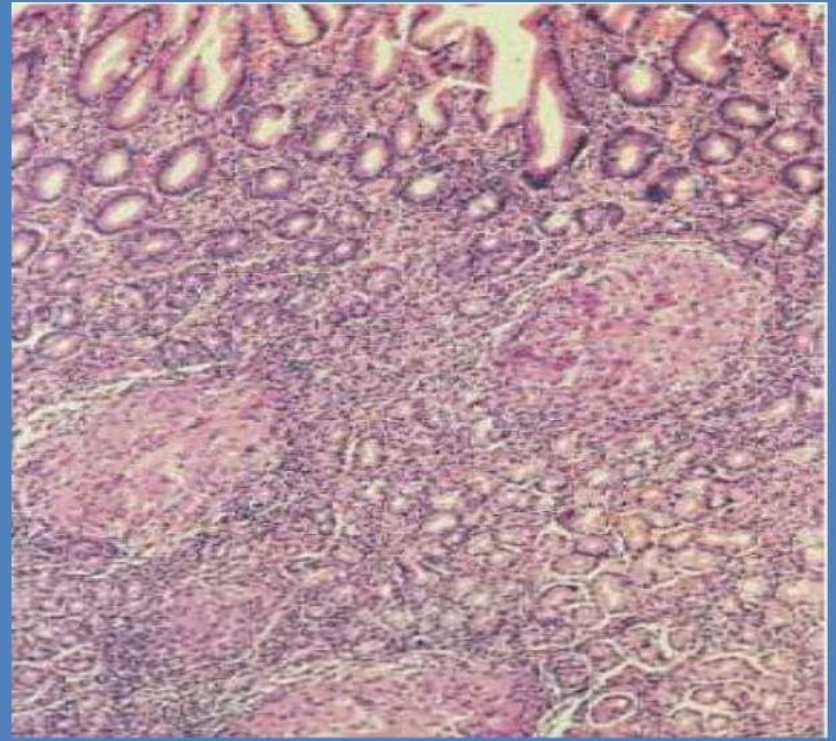
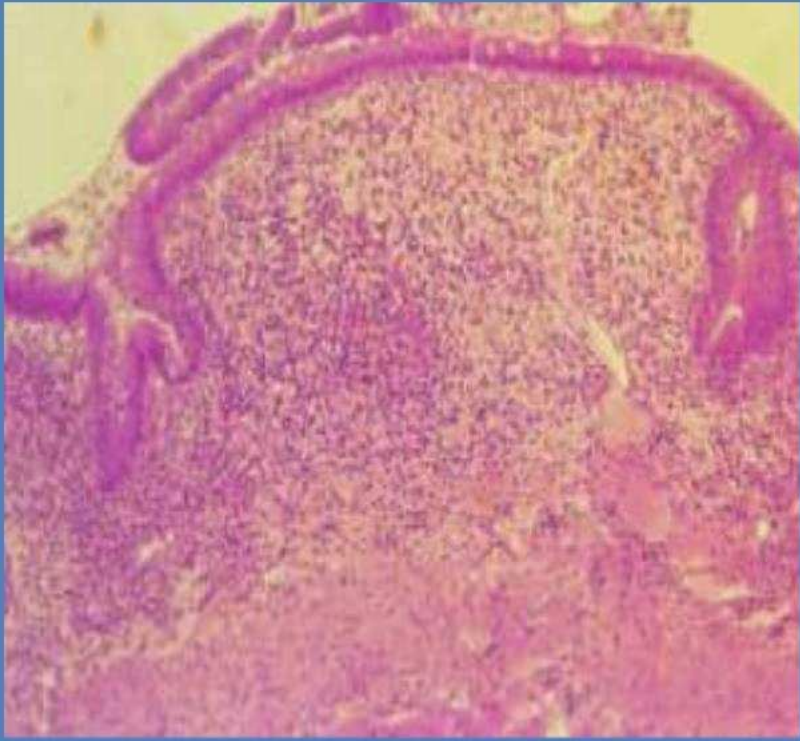
- Edema localizzato, eritema
- Ulcere serpiginose profonde
- Ulcerazioni aftoidi
- Ulcere coalescenti che danno luogo all'aspetto 'cobblestone', «mucosa ad acciottolato»

Valutazione istologica di attività nella UC

Grade 0	Structural (architectural change) Subgrades : 0.0 No abnormality 0.1 Mild abnormality 0.2 Mild or moderate diffuse or multifocal abnormalities 0.3 Severe diffuse or multifocal abnormalities
Grade 1	Chronic inflammatory infiltrate Subgrades 1.0 No increase 1.1 Mild but unequivocal increase 1.2 Moderate increase 1.3 Marked increase
Grade 2	Lamina propria neutrophils and eosinophils 2A Eosinophils 2B Neutrophils
Grade 3	Neutrophils in epithelium
Grade 4	Crypt destruction (crypt abscesses)
Grade 5	Erosion or ulceration

Valutazione istologica di attività nel CD

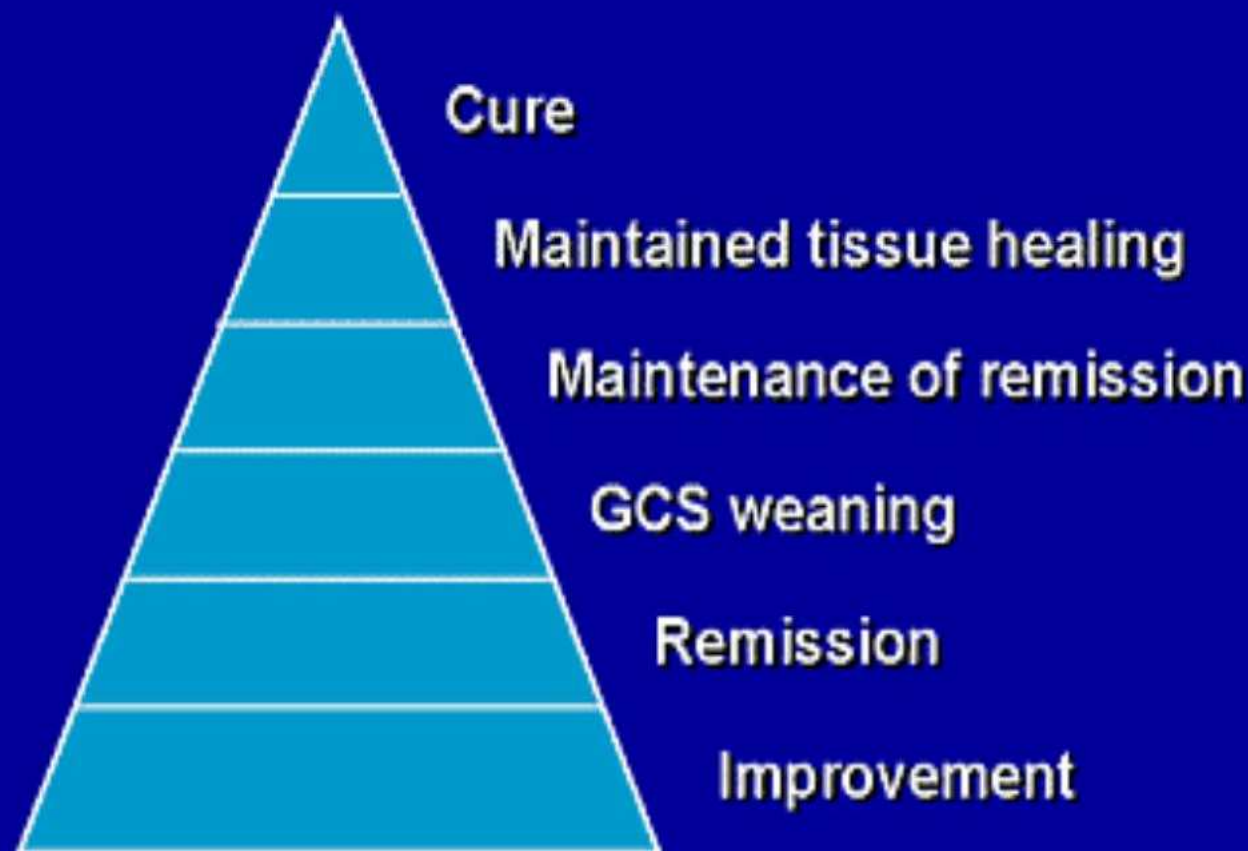
Histologic findings	Score
Epithelial damage	0-2
Architectural changes	0-2
Mononuclear infiltrate in LP	0-2
PMN infiltrate in epithelium	0-3
Erosion / ulcers	0-1
Granulomas	0-1
Proportion of biopsies affected	0-3



Diagnosi differenziale

- ✓ Colite ischemica
- ✓ TBC intestinale
- ✓ Colite attinica
- ✓ Malformazioni artero-venose
- ✓ Enteropatia da NSAIDs
- ✓ Malattia di Behcet
- ✓ Cancro colon-retto

Treatment Goals in Inflammatory Bowel Disease



GCS = glucocorticosteroid

General Care



- ✓ Proper resuscitation.
- ✓ Hospitalization.
- ✓ Bowel rest to reduce the volume of diarrhea.
- ✓ Blood products should be administered to treat significant anemia or coagulopathy.
- ✓ Pain relievers. Acetaminophen.
- ✓ Iron supplements.
- ✓ Nutrition (TPN).
- ❖ Avoid (Narcotics, antidiarrheal agents and anticholinergic) can precipitate toxic dilation of the colon.

Drug Therapies

1- 5-Aminosalicylates (5-ASA)

2- Glucocorticoids (steroids)

3- Antibiotics

4- Immunosuppressants

Thiopurines

Azathioprine

6-mercaptopurin

Methotrexate

Cyclosporine

5- Biological Therapy

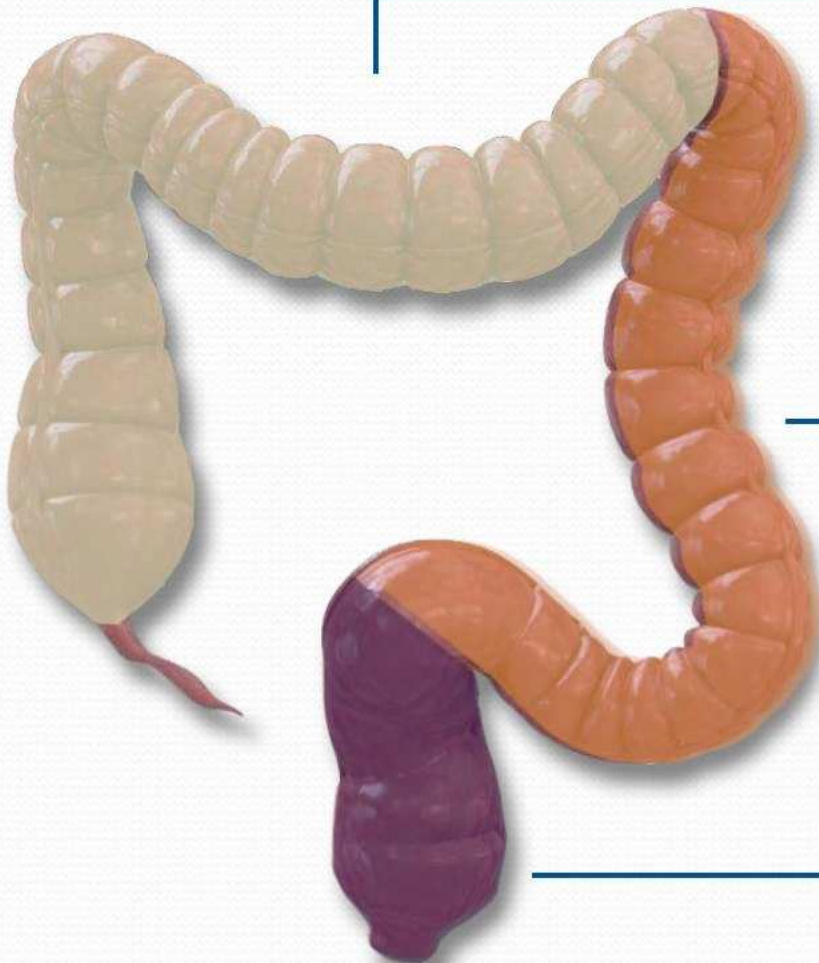
Infliximab



1- 5-ASA; Sulfasalazine (Supp. , enemas or Oral)

i t u

A A Preparations



Oral

aries by agent: may be released in the
stal/terminal ileum, or colon¹

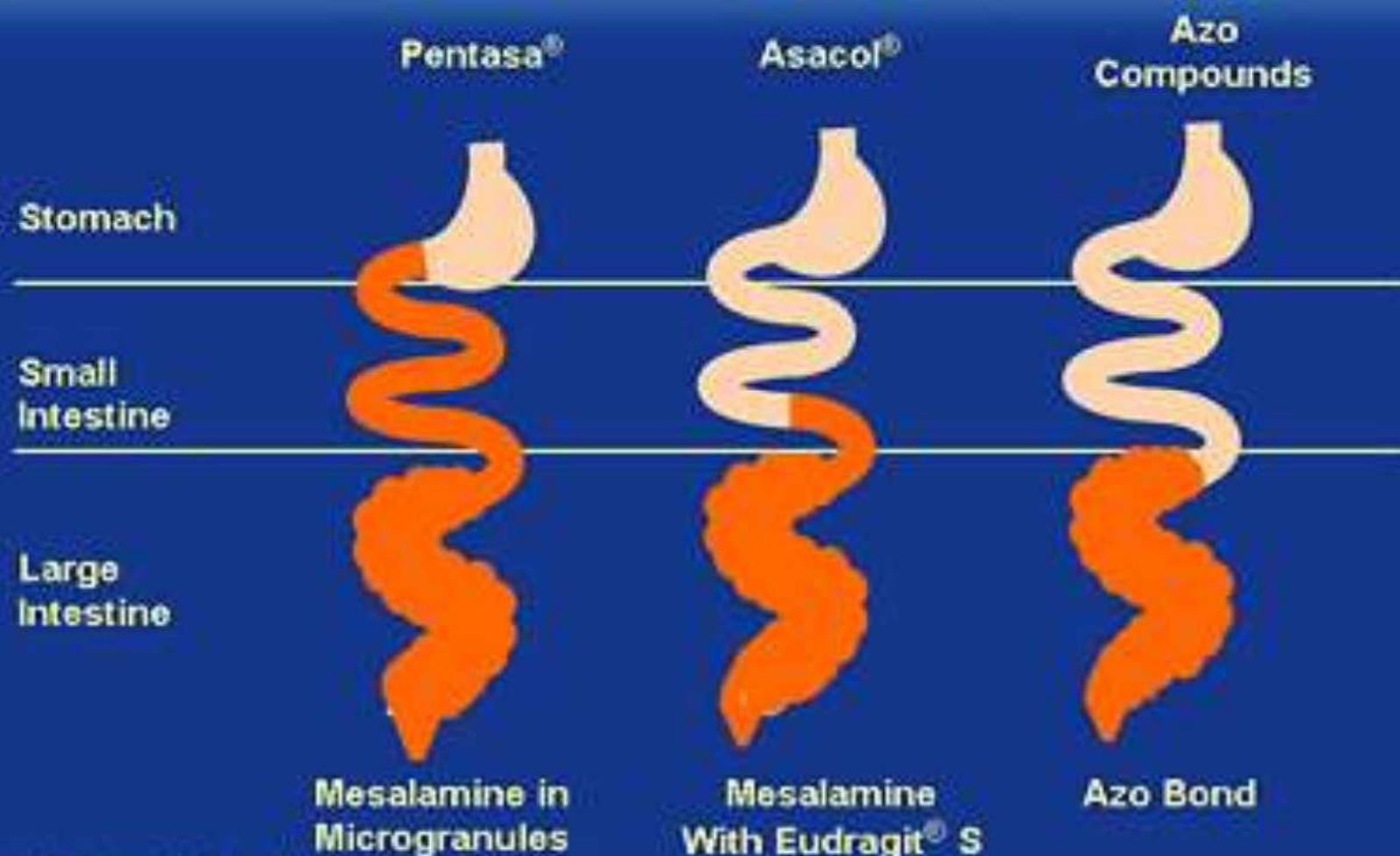
Liquid Enemas

- May reach the splenic flexure²⁻⁴
- Do not frequently concentrate in the rectum³

Suppositories

ach the upper rectum^{2,5}
(-20 cm beyond the anal verge)

Oral 5-ASA Release Sites



5-ASA = 5-aminosalicylic acid.

Asacol is a registered trademark of Medeva Pharma Schweiz AG.

Pentasa is a registered trademark of Ferring A/S Corporation.

Eudragit is a registered trademark of Rohm GmbH.

2 - Hydrocortisone or Methylprednisolone (IV , Oral or enema)

- Fast symptom relief
- 40 to 60 mg/day in a continuous I.V. infusion
- 5 to 10 days
- Not advised for prolonged use (120 day max)
- Does not improve long term surgery rates

3 - Ciprofloxacin +/- Metronidazole

- Effectiveness arguable but often seen used anyway

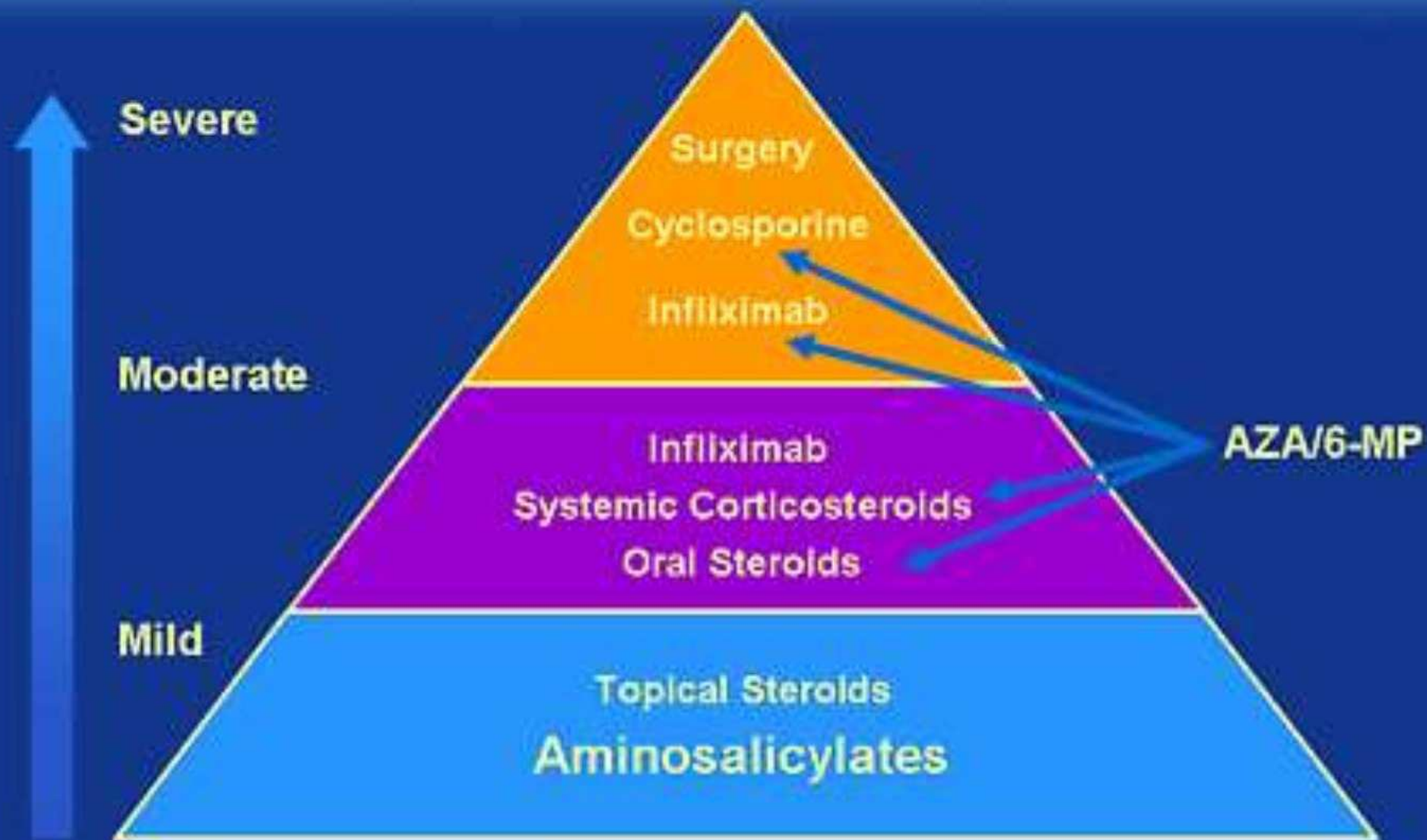
4 - IV Cyclosporine 2-4 mg/kg

- Effective for induction of remission but not long-term maintenance
- Patients who did not respond to I.V. steroid
- If no improvement within 4 to 5 days or if complete remission is not achieved by 10 to 14 days, surgical treatment is advised. (32)

5 - **Infliximab** is currently approved for use in IBD

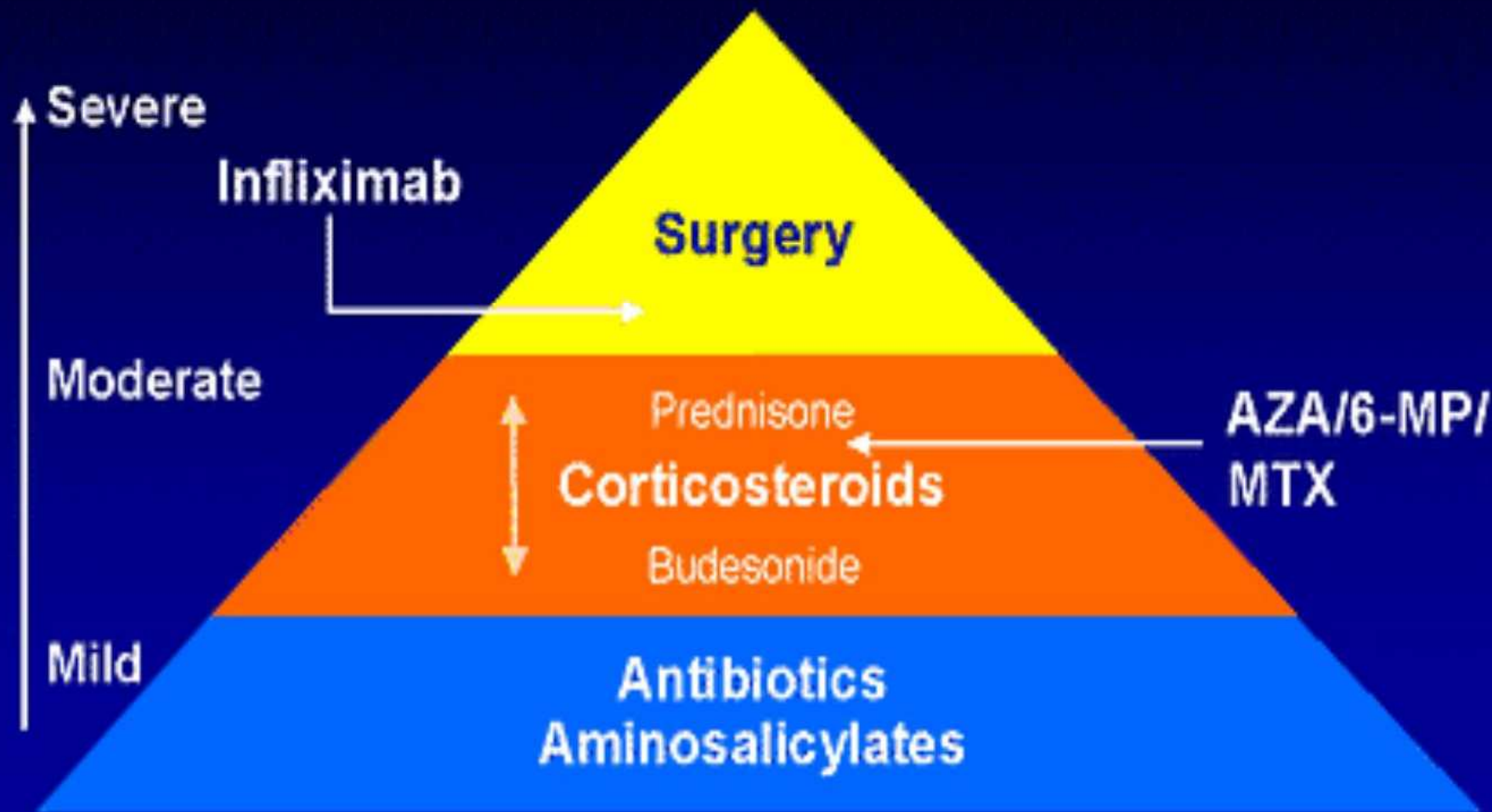
- **Induction**- 3 separate infusions of 5 mg/kg for moderate to severe IBD at weeks 0, 2, and 6
- **Maintenance**- infusions every 8 weeks

Therapeutic Pyramid for Active UC



AZA/6-MP = azathioprine/6-mercaptopurine

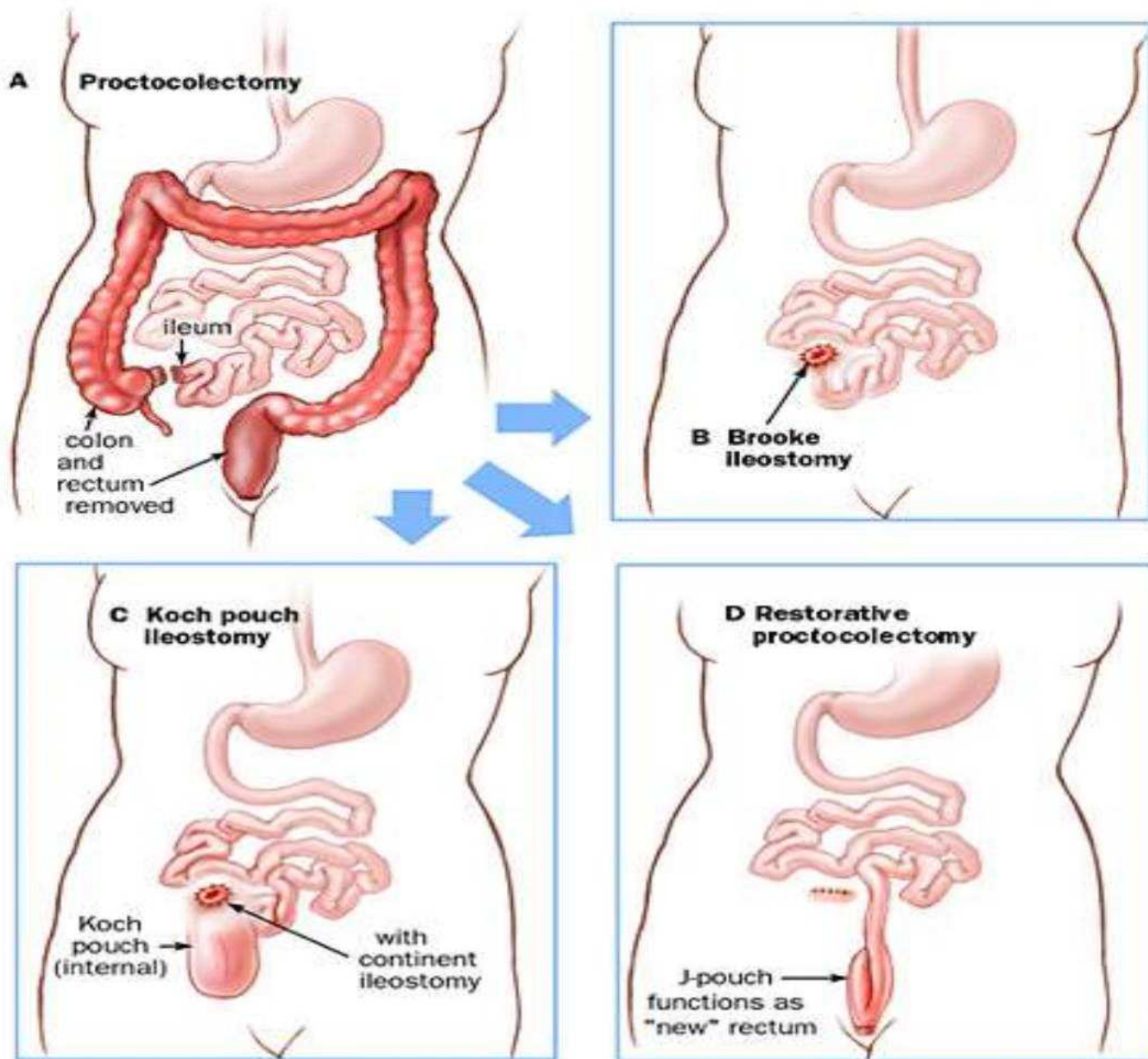
Current "Step-Up" Approach to Crohn's Disease (CD) Therapy



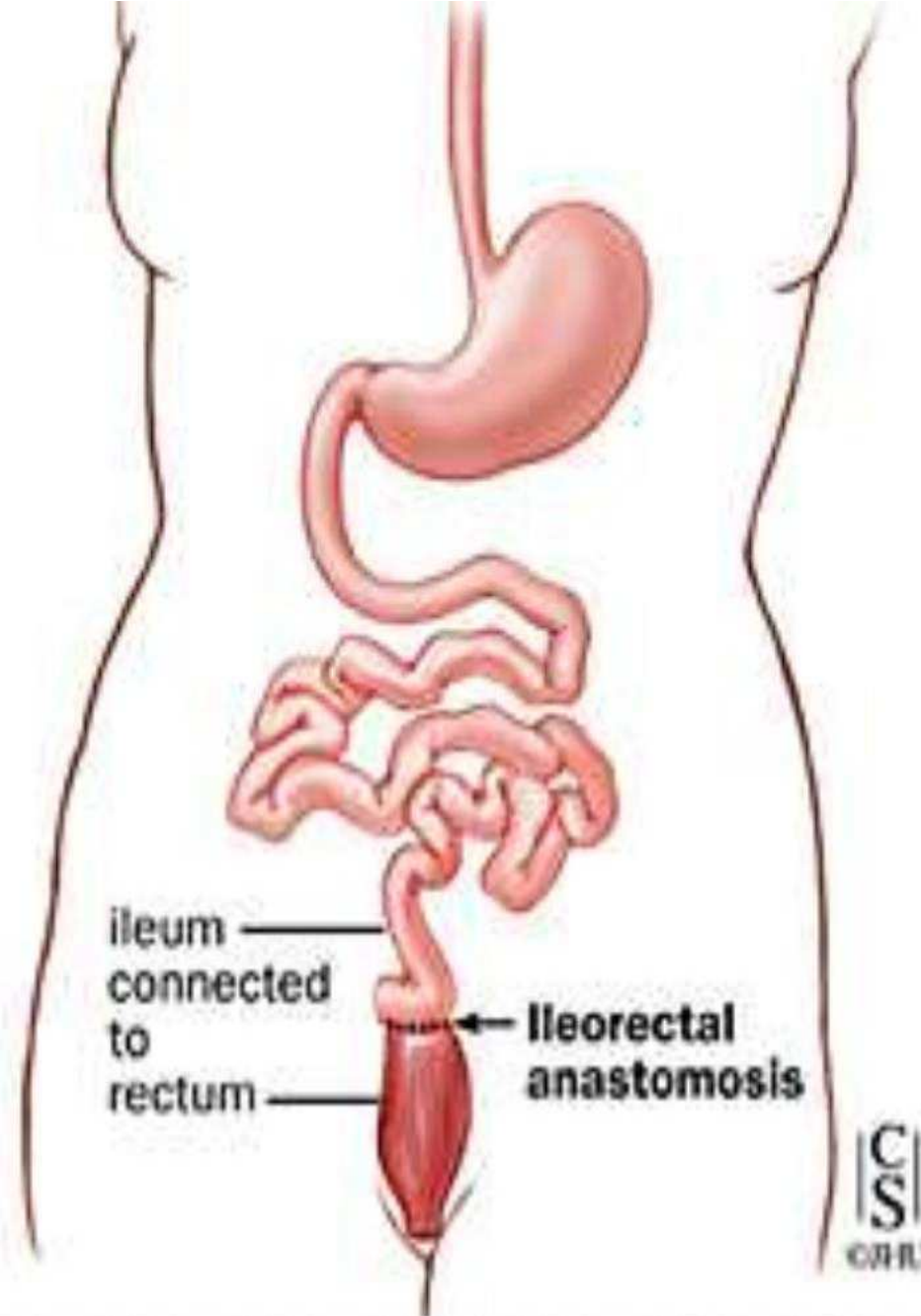
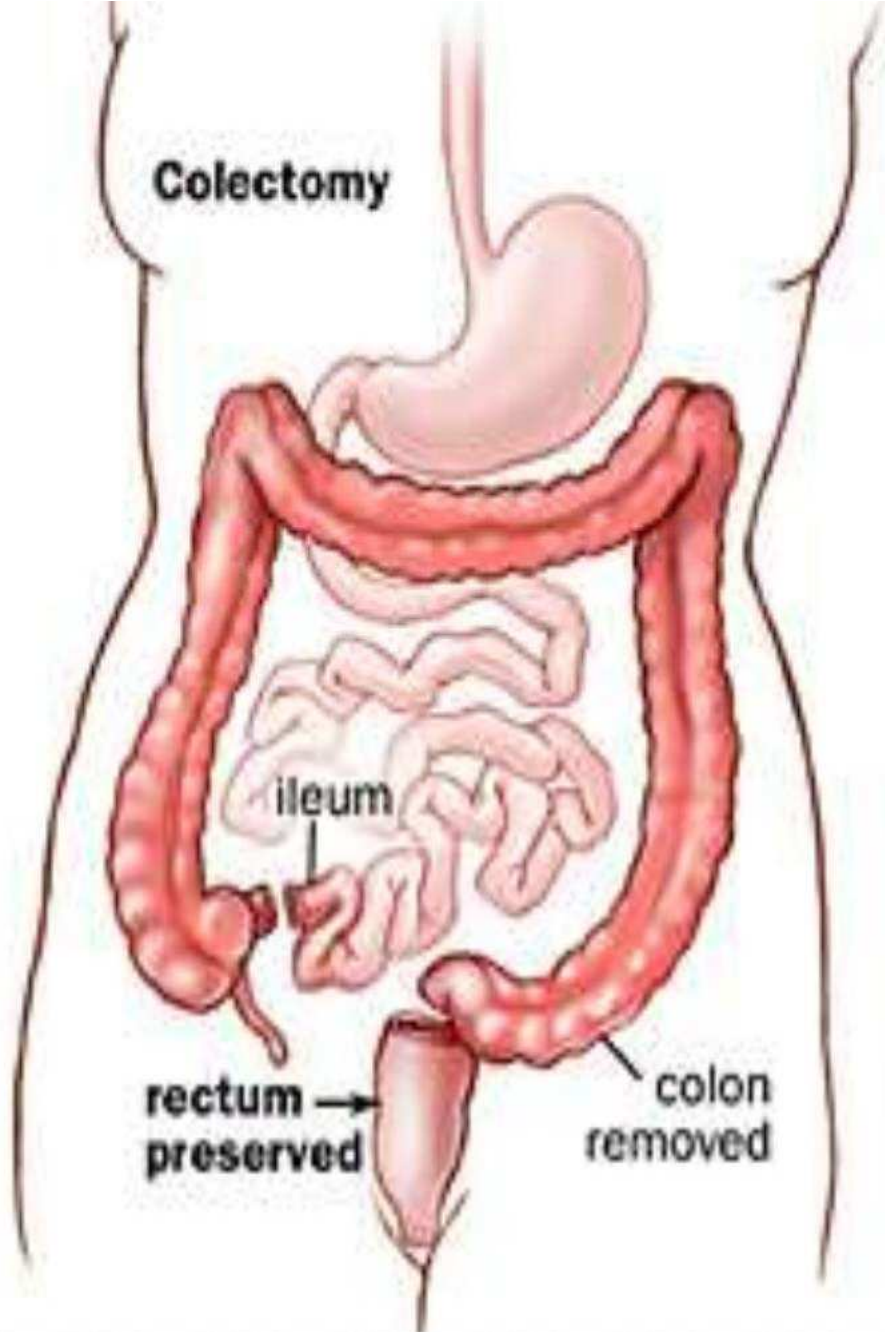
Indications for surgery in ulcerative colitis

Urgent Surgery	Elective Surgery
Ongoing hemorrhage	Failure of medical therapy
Toxic megacolon	Intolerable side effect of medical therapy
Colonic perforation	Development of dysplasia
Fulminant ulcerative colitis	Carcinoma
	Colonic stricture
	Growth retardation in children

*Current Surgical Therapy 9th Edition



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Indications for surgery in Crohn's Disease

Urgent Surgery	Elective Surgery
Perforation	Stricture
Abscess	Fistula
Uncontrollable hemorrhage	Malignancy
Toxic megacolon	Malnutrition
Bowel obstruction	Poorly controlled despite management
	Extra-intestinal manifestations

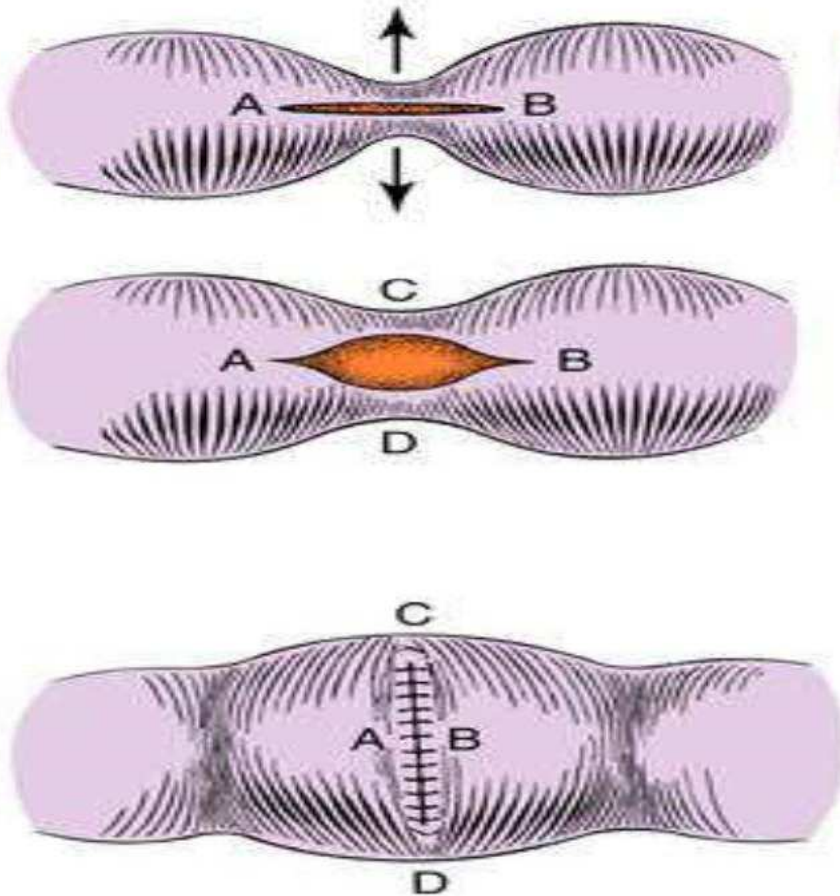
*Medical Management of the Surgical Patient: A Textbook of Perioperative Medicine

*ASCRS – American Society of Colon and Rectal Surgeons

Surgical treatment

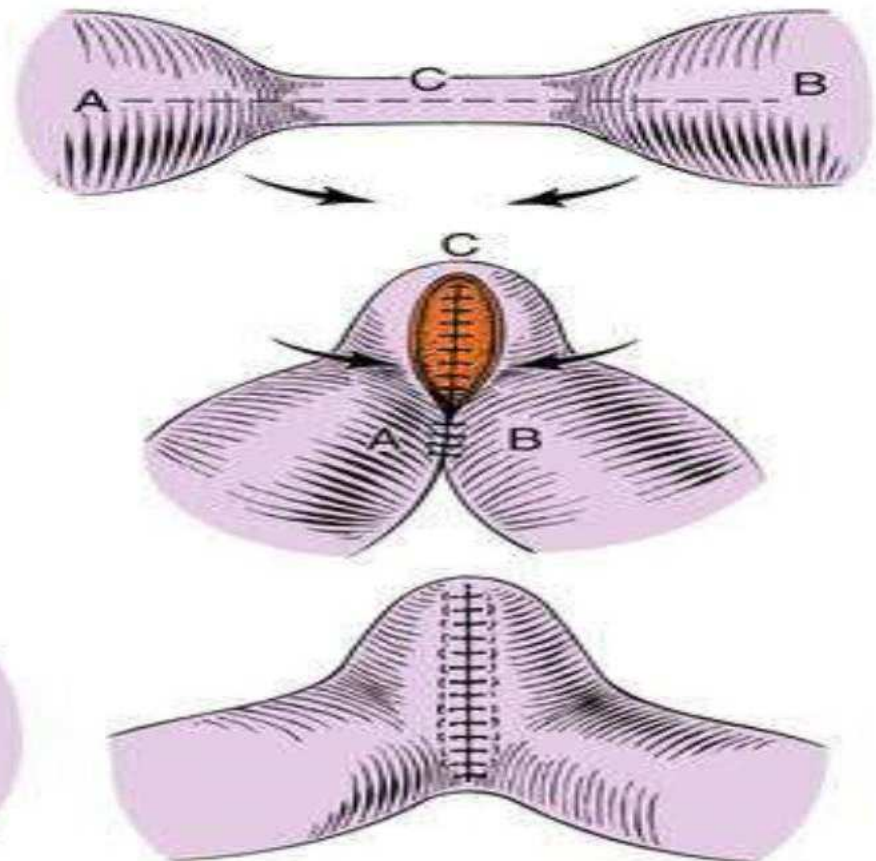
Strictureplasty

Short stricture

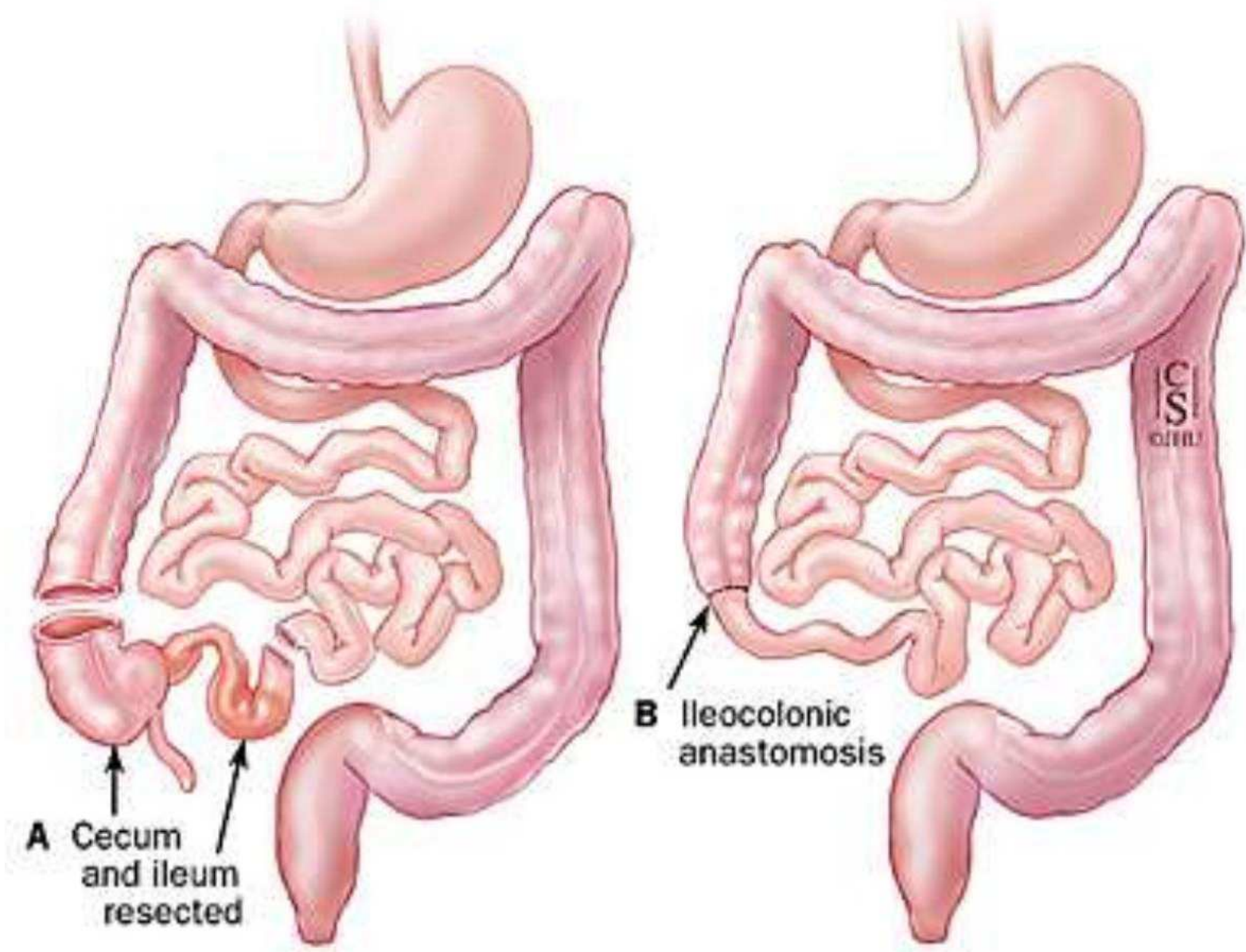


Heineke-Miculicz type

Long stricture



Finney type



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