An Introduction To

Inflammatory Bowel Disease

Inflammatory Bowel Disease

- Outline
  - What is the Disease?
  - Epidemiology
  - Pathophysiology
  - Ulcerative Colitis
  - Crohn's Disease

Inflammatory Bowel Disease

- Two chronic diseases that cause ulceration & inflammation of the intestines
  - Ulcerative Colitis
  - Crohn's Disease.

Inflammatory Bowel Disease

- Two chronic diseases that cause ulceration & inflammation of the intestines
- They have some features in common but there are some important differences
- 20% of patients have clinical picture that falls in between (indeterminate colitis)

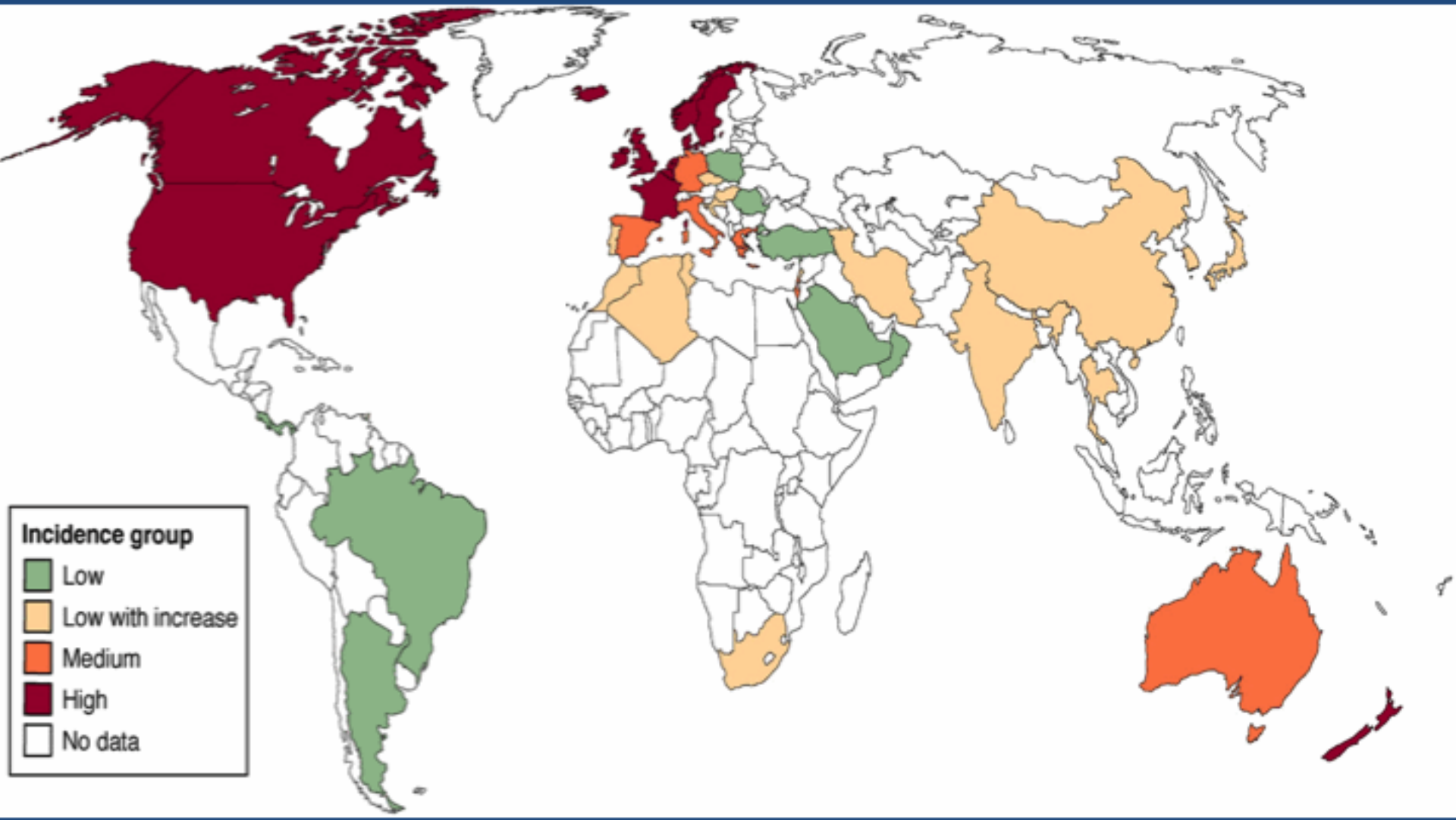
Epidemiology

- Most numbers are North American
- Increasingly diagnosed in Saudi Arabia

Epidemiology of inflammatory bowel disease

Incidence, per 100,000 (North America)	3-14 (CD)
	2-14 (UC)
Prevalence, per 100,000 (North America)	26-199 (CD)
	27-246 (UC)
Geography	Northern Countries > Southern Countries
Age of onset	Peak: 15-30
	Second Peak 50-80 (CD)
Sex	M = F
Race	Whites > Blacks
Ethnic	Jewish > Non-Jewish
Smoking	Associated with CD: protective in UC
Appendectomy	May be protective in UC
Possible genetic associations	Chromosome 16 (CD)
	Chromosome 3, 5, 7, 12, 19 (UC and CD), TNF-(CD); IL-1A (CD), IL-23 receptor (CD and UC), ATG I6L1 (CD), HLA-A2; HLA-DR1; DQw5 (CD), HLA-DR2 (UC)

Global Rising Incidence of IBD



Cosnes et al, 2011

Pathophysiology

- Unclear
- A number of factors may be involved.
  - Host Factors
  - Environmental Factors

Pathophysiology

- Host Factors
  - Genetics (Twins, Relatives, & children)

Pathophysiology

- Environmental Factors
  - Smoking (Crohn's Vs Ulcerative)
  - Infection

Pathophysiology

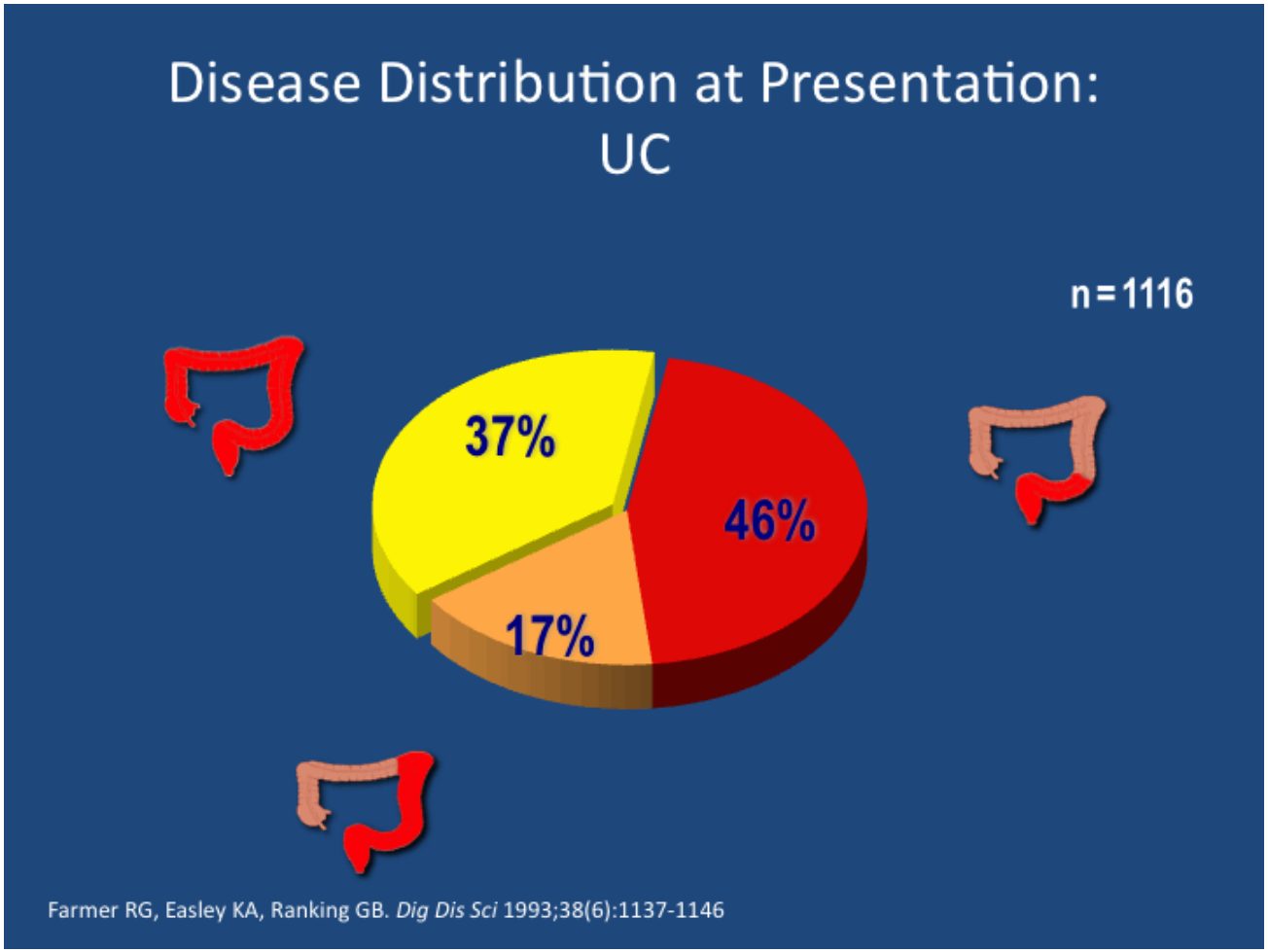
- Current Theory:

There is a genetic defect that affects the immune system, so that it attacks the bowel wall in response to stimulation by an offending antigen, like a bacteria, a virus, or a protein in the food

Ulcerative Colitis

- An inflammatory disease of the large intestine
- Recurring Inflammation and ulceration of the mucosa of the large intestine
- Almost always involve the rectum and extend proximally

Ulcerative Colitis

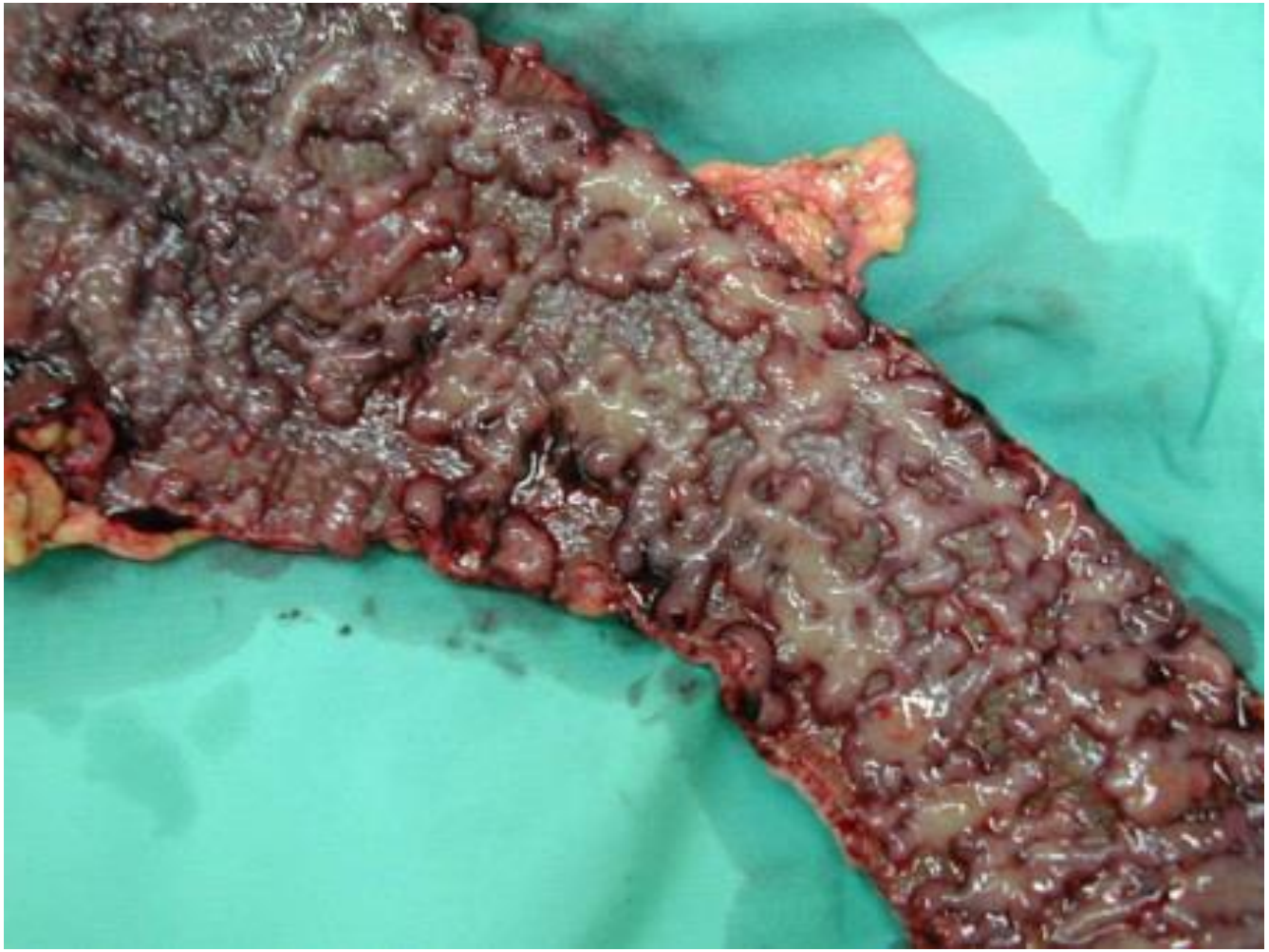


Farmer RG, Easley KA, Ranking GB. *Dig Dis Sci* 1993;38(6):1137-1146

Ulcerative Colitis

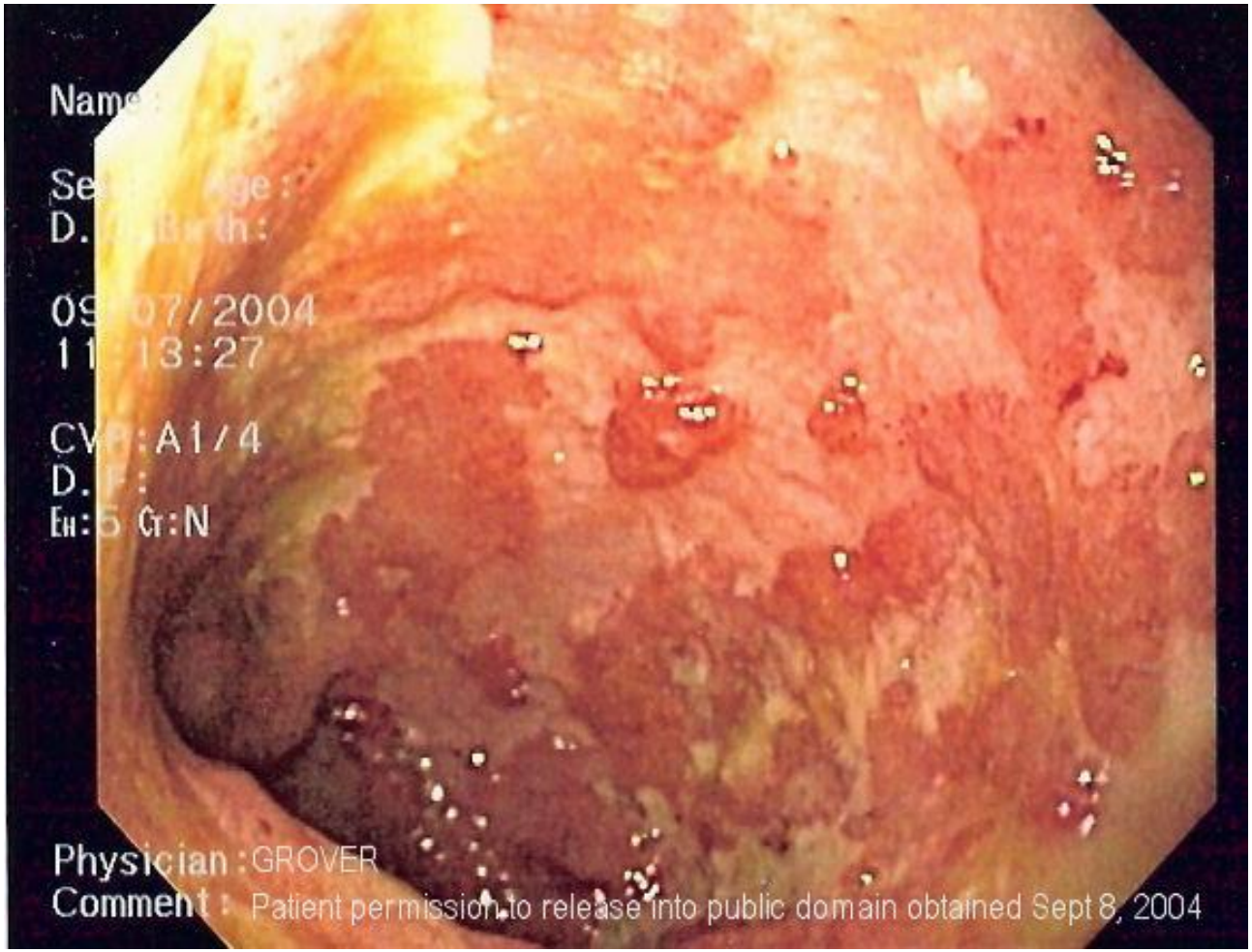
- Macroscopic Appearance
  - Erythematous mucosa, has a granular surface, looks like sand paper
  - In more severe diseases hemorrhagic, edematous and ulcerated
  - In fulminant disease a toxic colitis or a toxic megacolon may develop

Ulcerative Colitis



Ulcerative Colitis

Ulcerative Colitis



Ulcerative Colitis

- Microscopic Appearance
  - Crypt abscesses
  - Branching of crypts,
  - Atrophy of glands
  - Loss of mucin in goblet cells

Ulcerative Colitis Presentation

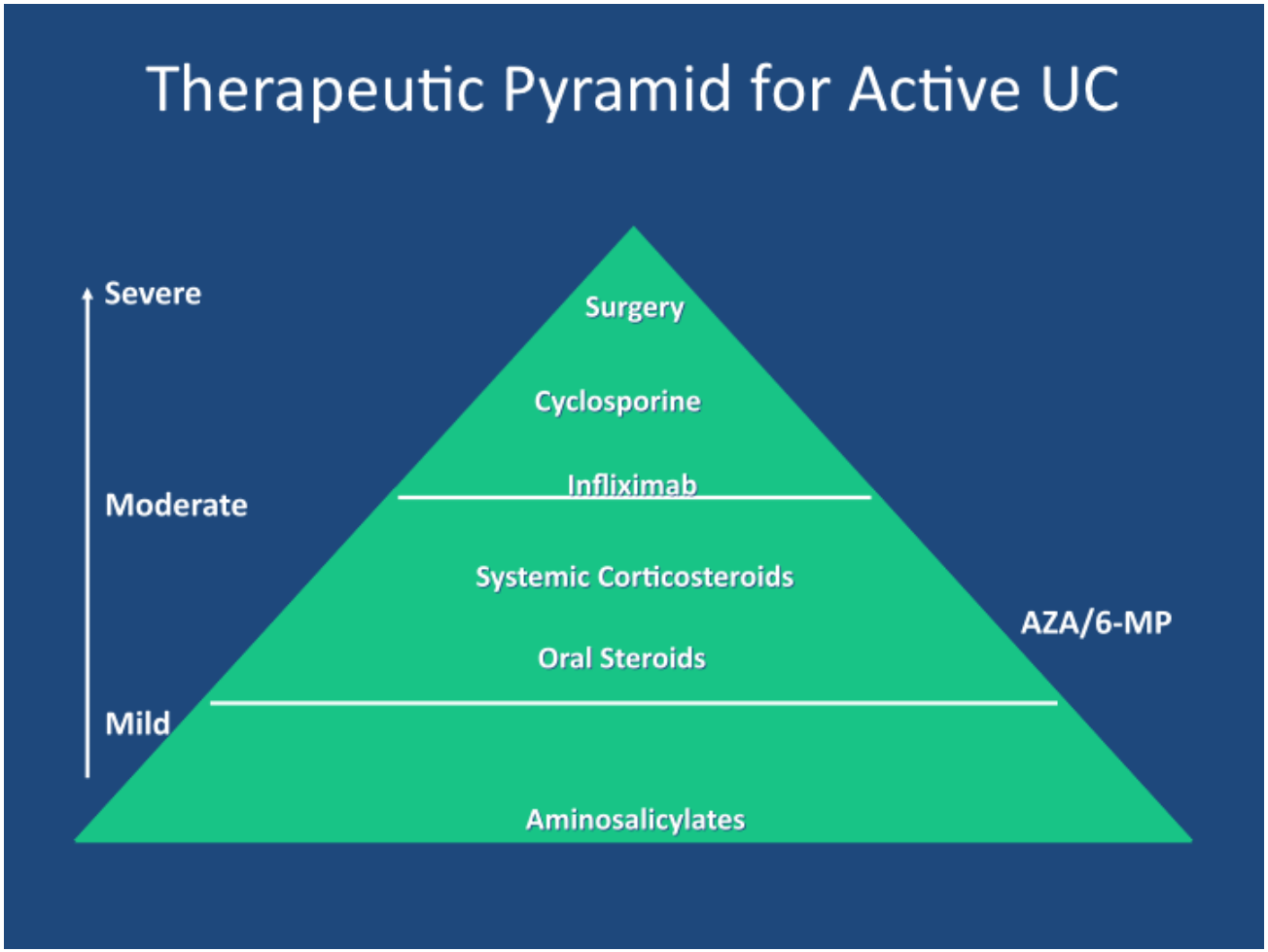
- The major symptoms of UC are:
  - Diarrhea (4 to more than 10)
  - Rectal bleeding
  - Tenesmus & Passage of mucus
  - Crampy abdominal pain & Fever
- Exam is often normal unless complications occur.

Ulcerative Colitis Complications

- Hemorrhage
- Toxic megacolon
- Perforation
- Stricture
- Cancer

Ulcerative Colitis

- Extra-intestinal manifestations
  - Uveitis and Episcleritis
  - Erythema Nodosum and Pyoderma Gangrenosum
  - Arthritis
  - Ankylosing Spondylitis
  - Sclerosing cholangitis


Therapeutic Pyramid for Active UC
Severe
Moderate
Mild
Surgery
Cyclosporine
Infliximab
Systemic Corticosteroids
AZA/6-MP
Oral Steroids
Aminosalicylates

Goals of Therapy for IBD

- Inducing remission

- Maintaining remission

Treatment of Ulcerative colitis

- Mainly medical treatment

Medical therapy of active ulcerative colitis according to disease severity

Disease severity	Medication	Daily dose
Mild-to-moderate disease		
	Sulfasalazine	1 to 1.5 g PO four times daily
	Mesalamine	
	Delayed release EC tablet:	
	- Asacol*	800 to 1600 mg PO three times daily
	- Lialda*	2.4 or 4.8 g PO once daily (2.4 g initially; 4.8 g if no complete response)
	Extended release capsule:	
	- Apriso*	1.5 g orally (four Apriso* capsules) in the morning once daily
	Controlled release capsule:	
	- Pentasa*	500 to 1000 mg PO four times daily
	Olsalazine	1 to 1.5 g PO twice daily
	Balsalazide	2.25 g PO three times daily
	Mesalamine suppository	1000 mg at night
	Hydrocortisone foam 10% (rectal)	90 mg (one applicatorful) at night or twice daily
	Mesalamine enema	4 g at night
	Hydrocortisone enema	100 mg at night
	Sulfasalazine/oral 5-ASA plus 5-ASA enemas/steroid enema	
	Prednisone	40 to 60 mg PO once daily
Severe active disease		
On steroids recently	Methylprednisolone	48 to 60 mg IV once daily
	Hydrocortisone	100 mg IV every 6 hours or as continuous infusion
	Cyclosporine	See topic review for dosing
	Infliximab	See topic on "Anti-tumor necrosis factor therapy in ulcerative colitis"
Toxic megacolon	Intravenous corticosteroids	See topic on "Toxic megacolon"
	Broad-spectrum antibiotics	
Chronic active disease (steroid refractory)	Mercaptopurine	See topic on "Azathioprine and 6-mercaptopurine in ulcerative colitis"
	Azathioprine	
	Infliximab	See topic on "Anti-tumor necrosis factor therapy in ulcerative colitis"

5-ASA: mesalamine, olsalazine, or balsalazide; anti-TNF: anti-tumor necrosis factor; UC: ulcerative colitis; EC: enteric coated.
* United States brand names.

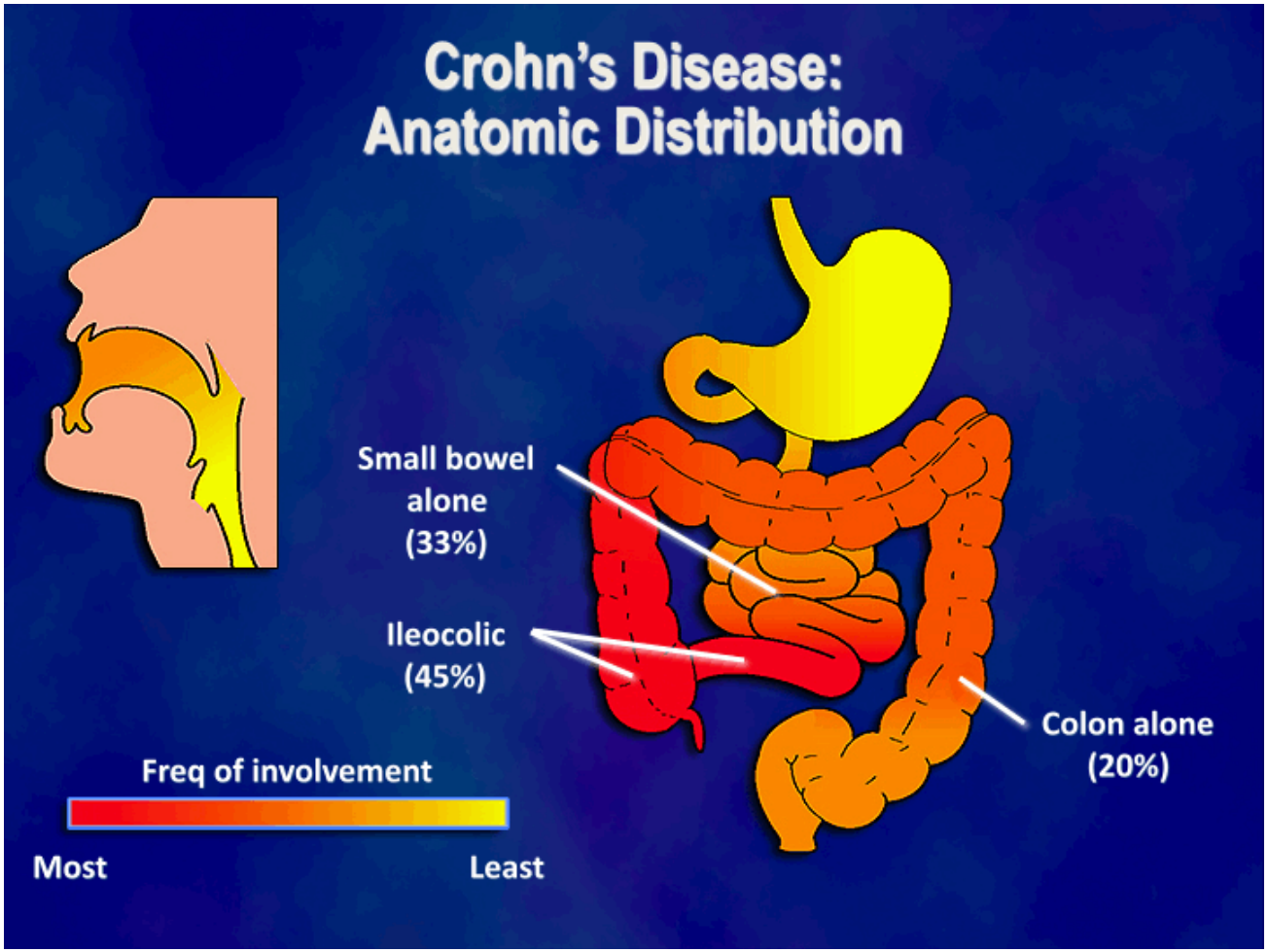
Ulcerative Colitis Treatment

- Mainly medical treatment
- Surgical treatment:
  - Failure of medical management
  - Treating complications
  - Prophylaxis for cancer
  - Cure after colectomy

Crohn's Disease

- An inflammatory disease that affects any part of the GI tract
- Recurring transmural Inflammation of the bowel
- About 80% have small bowel involvement, mostly the terminal ileum

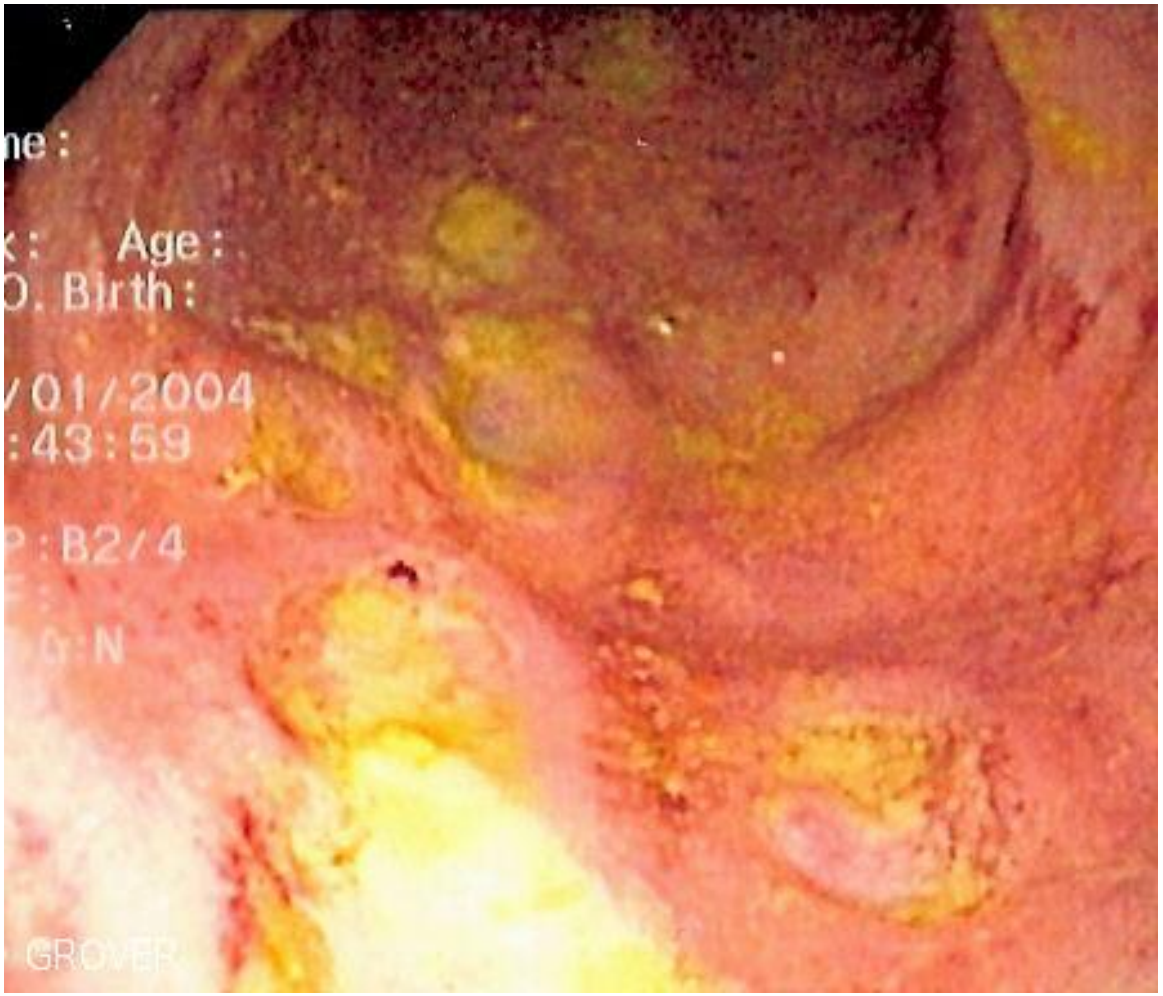
Crohn's Disease



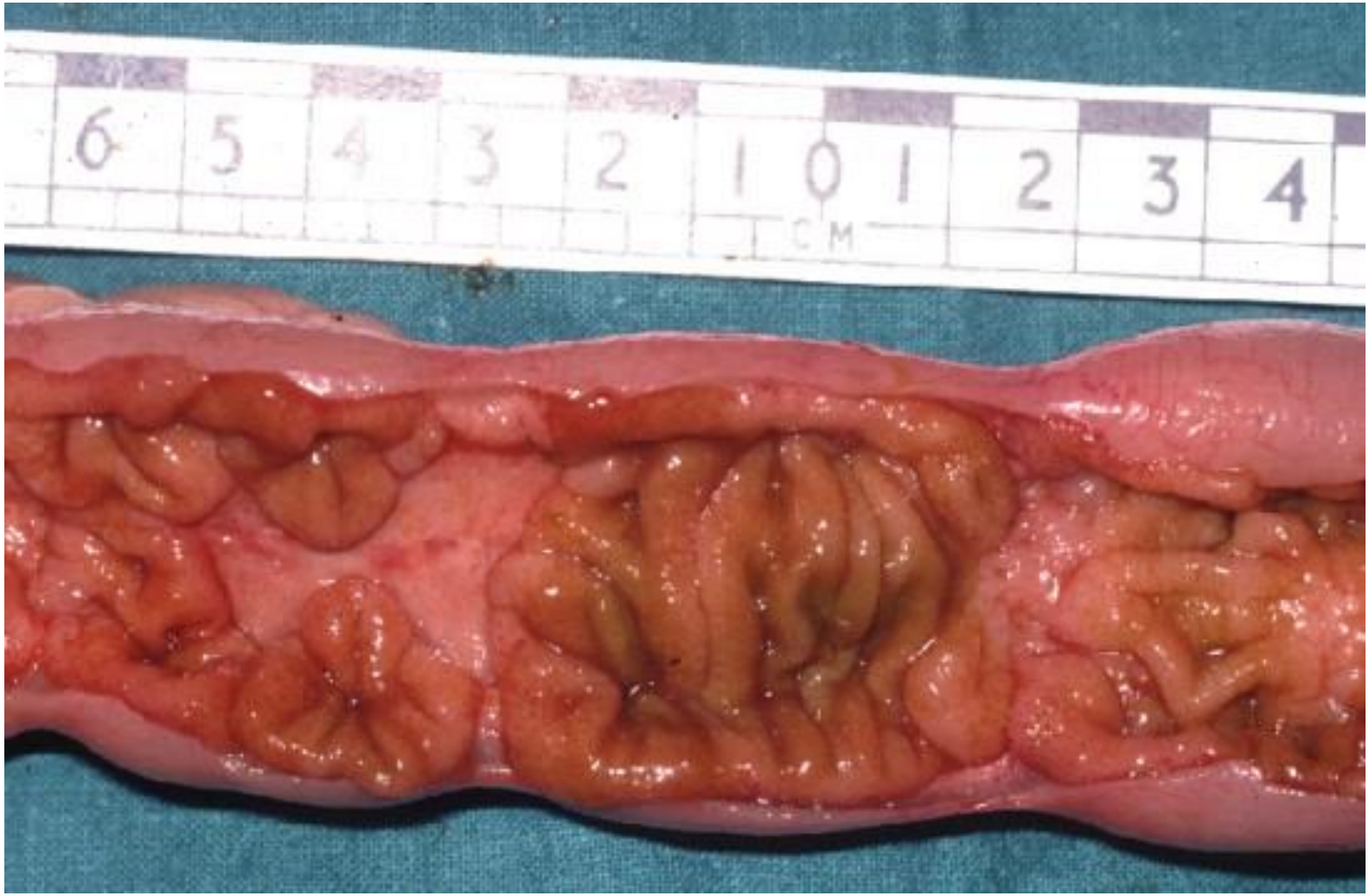
Crohn's Disease

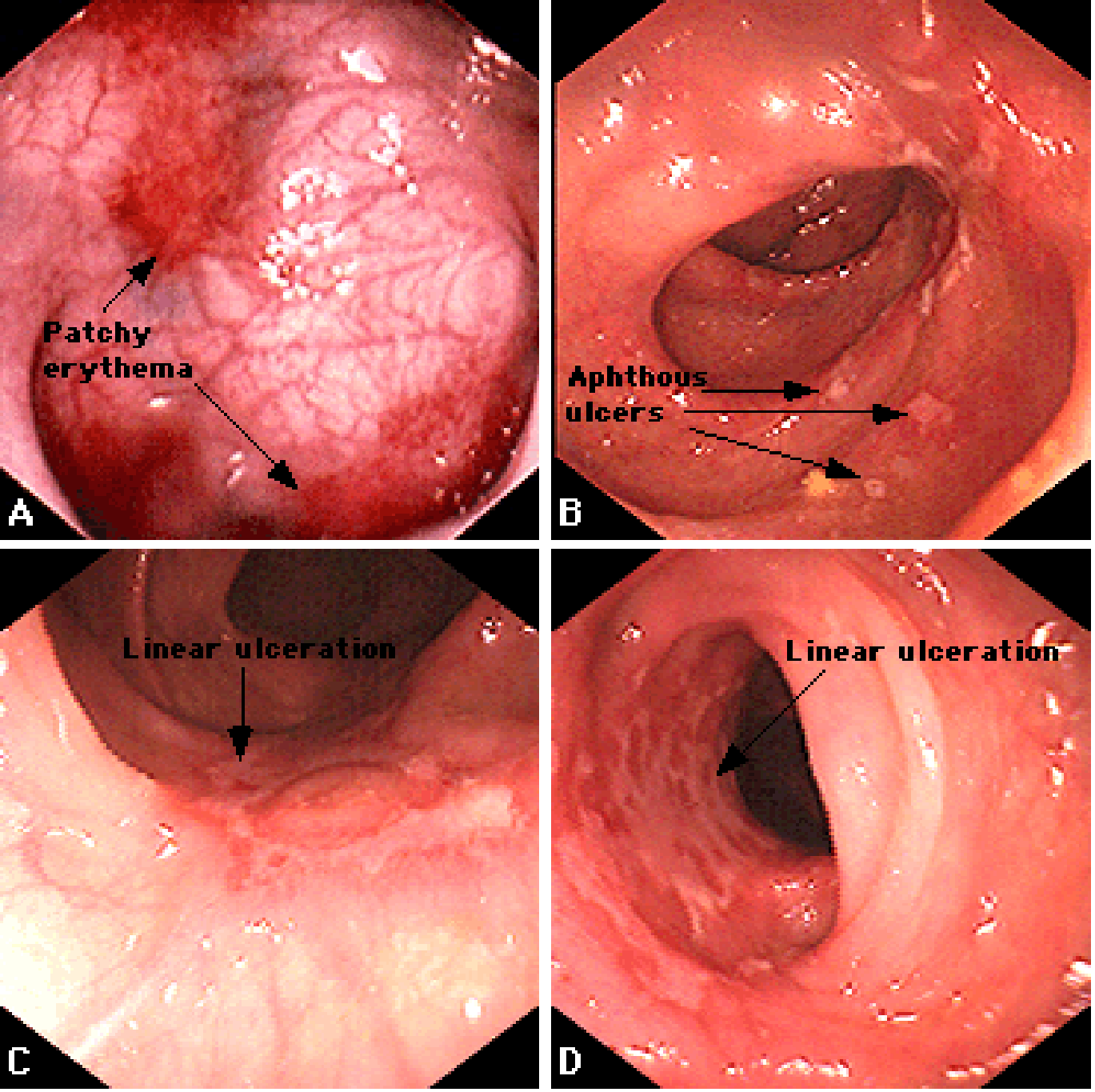
- Macroscopic Appearance
  - Mild disease has aphthus or small superfecial ulcers
  - In more severe diseases there is the characteristic cobblestone appearance
  - Thickening of the bowel wall with creaping fat

Crohn's Disease



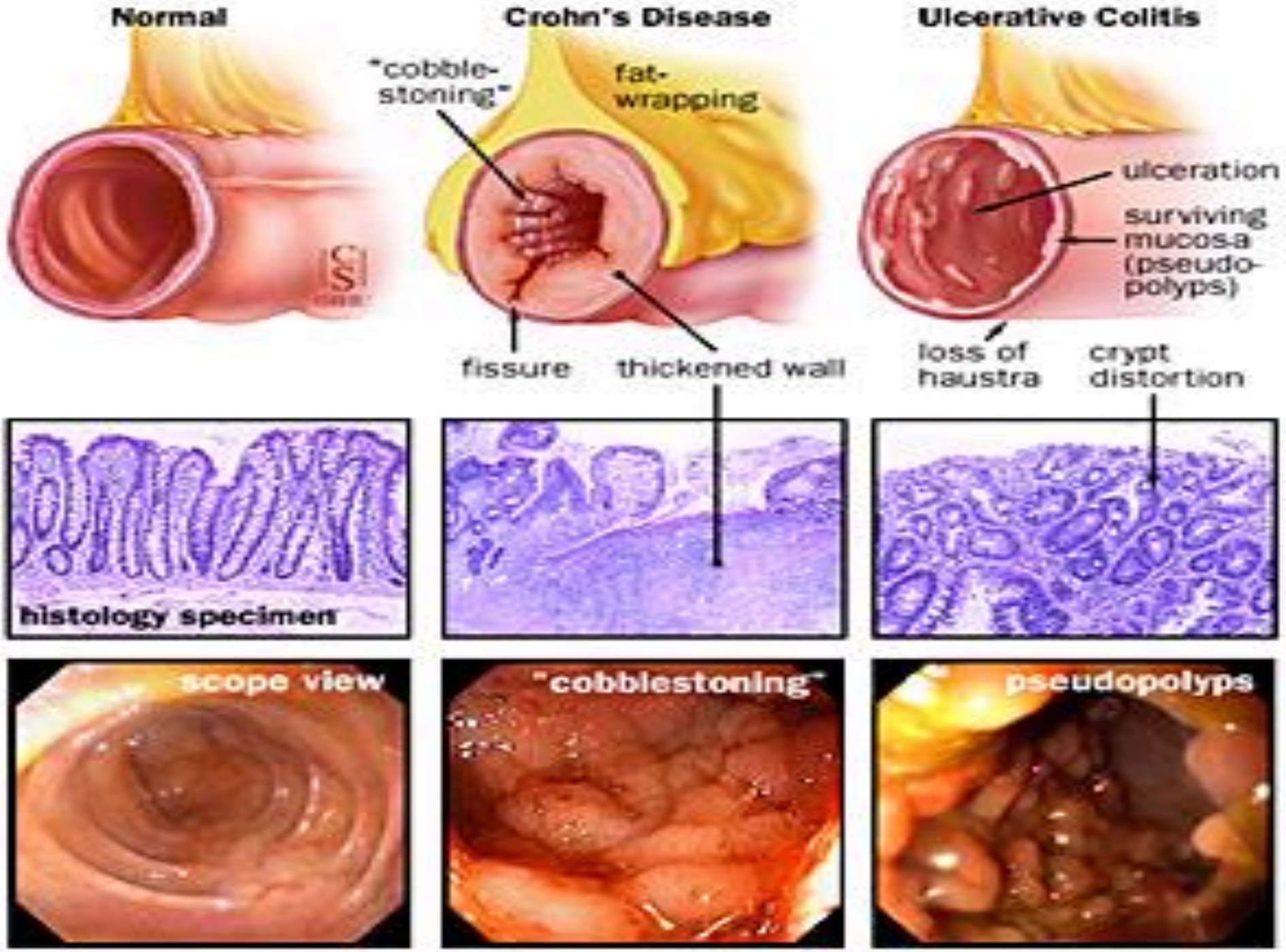
Crohn's Disease

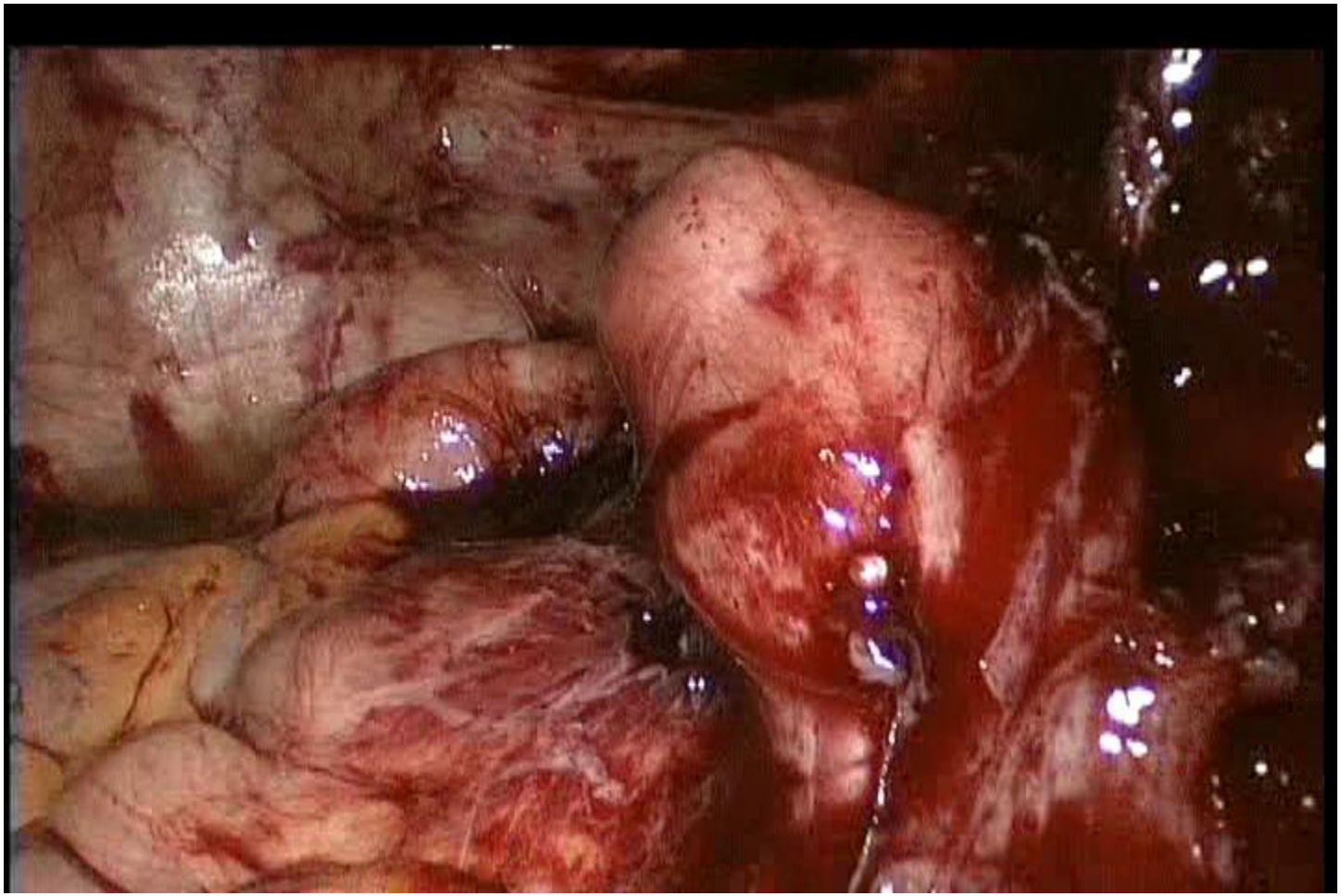


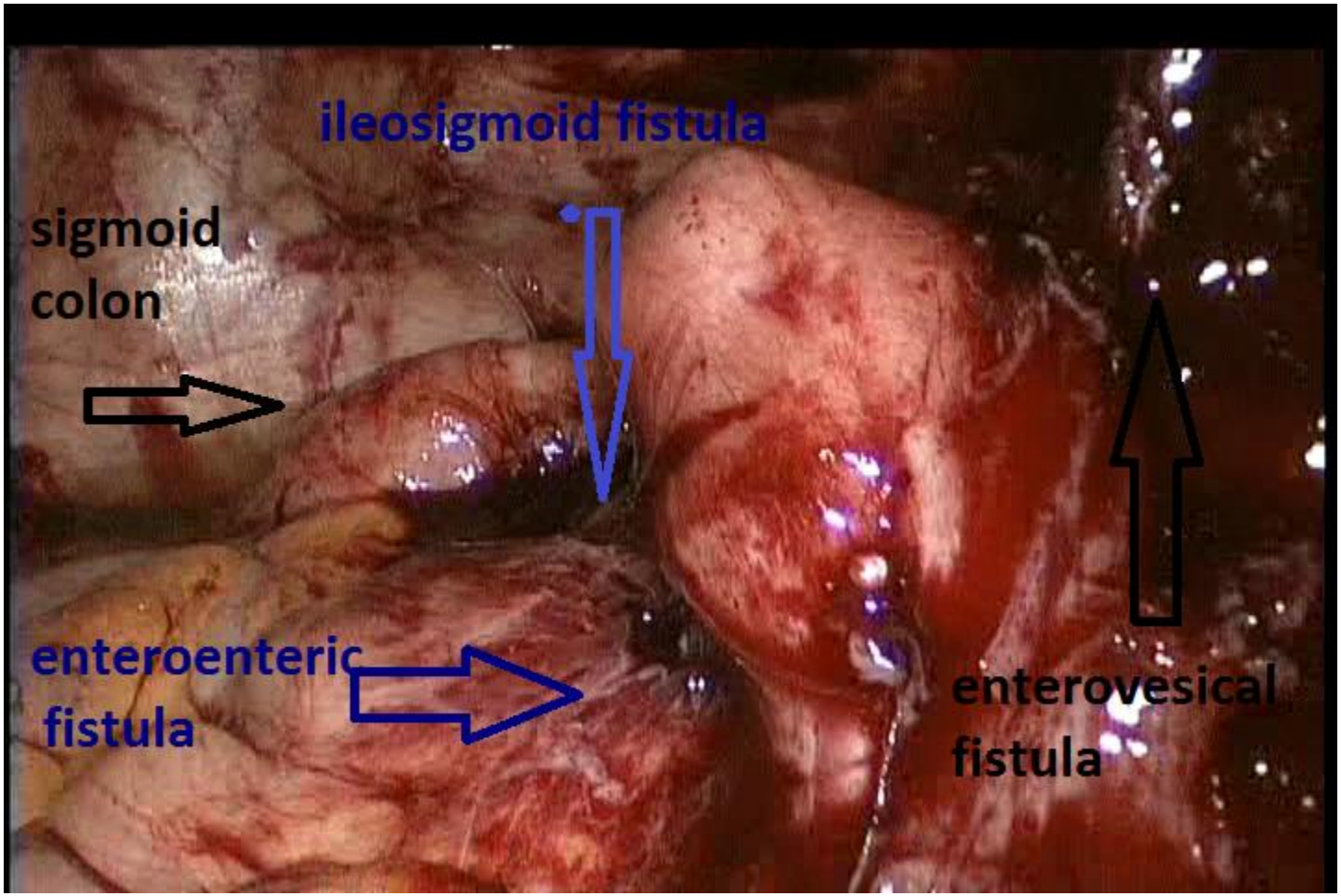


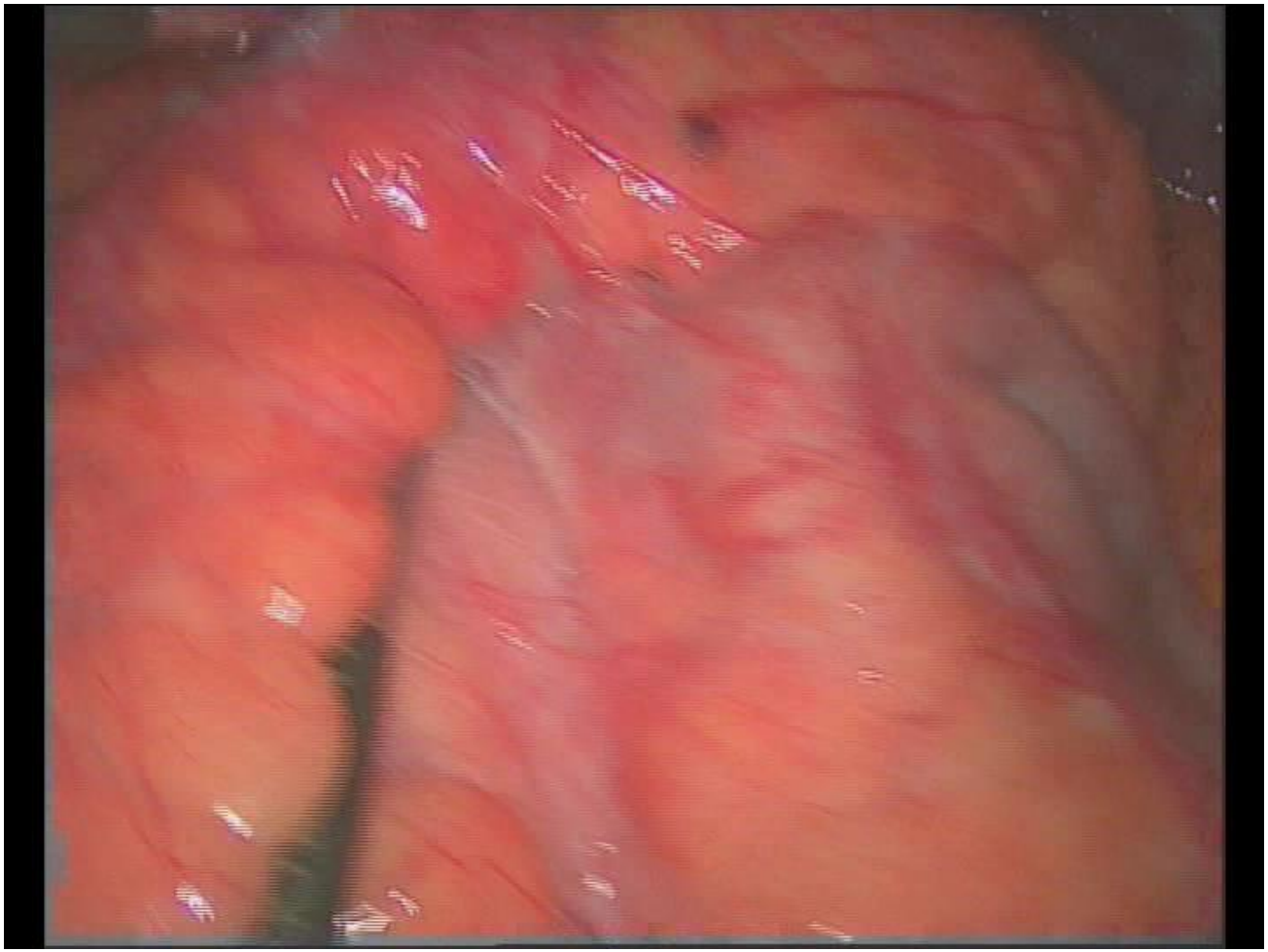
Endoscopic progression of Crohn's disease

Ulcers are the dominant endoscopic feature in Crohn's disease. These tend to be linear and discontinuous, or "skip lesions". Early changes may be only patchy erythema (panel A) or aphthoid ulcers (panel B). Linear ulcers (panel C) are seen with more advanced disease, culminating in very deep and long serpiginous ulcers (panel D). Courtesy of James B McGee, MD.


Normal
Crohn's Disease
Ulcerative Colitis
"cobble-stoning"
fat-wrapping
ulceration
surviving mucosa (pseudo-polyps)
fissure
thickened wall
loss of haustra
crypt distortion
histology specimen
scope view
"cobblestoning"
pseudopolyps




ileosigmoid fistula
sigmoid colon
enteroenteric fistula
enterovesical fistula



Crohn's Disease

- Microscopic Appearance
  - Transmural inflammation
  - Focal ulcerations
  - Acute and chronic inflammation
  - Granulomas may be noted in up to 30 percent of patients

Crohn's Disease Presentation

- The major presentations of CD are:
  - Crampy abdominal pain
  - Diarrhea
  - Weight loss
  - Colitis and Perianal disease
  - Dudenal Disease

Crohn's Disease Complications

- Phlegmons & abcesses
- Fistulas
- Stricture
- Malabsorption
- Perianal disease
- Cancer risk

Crohn's Disease

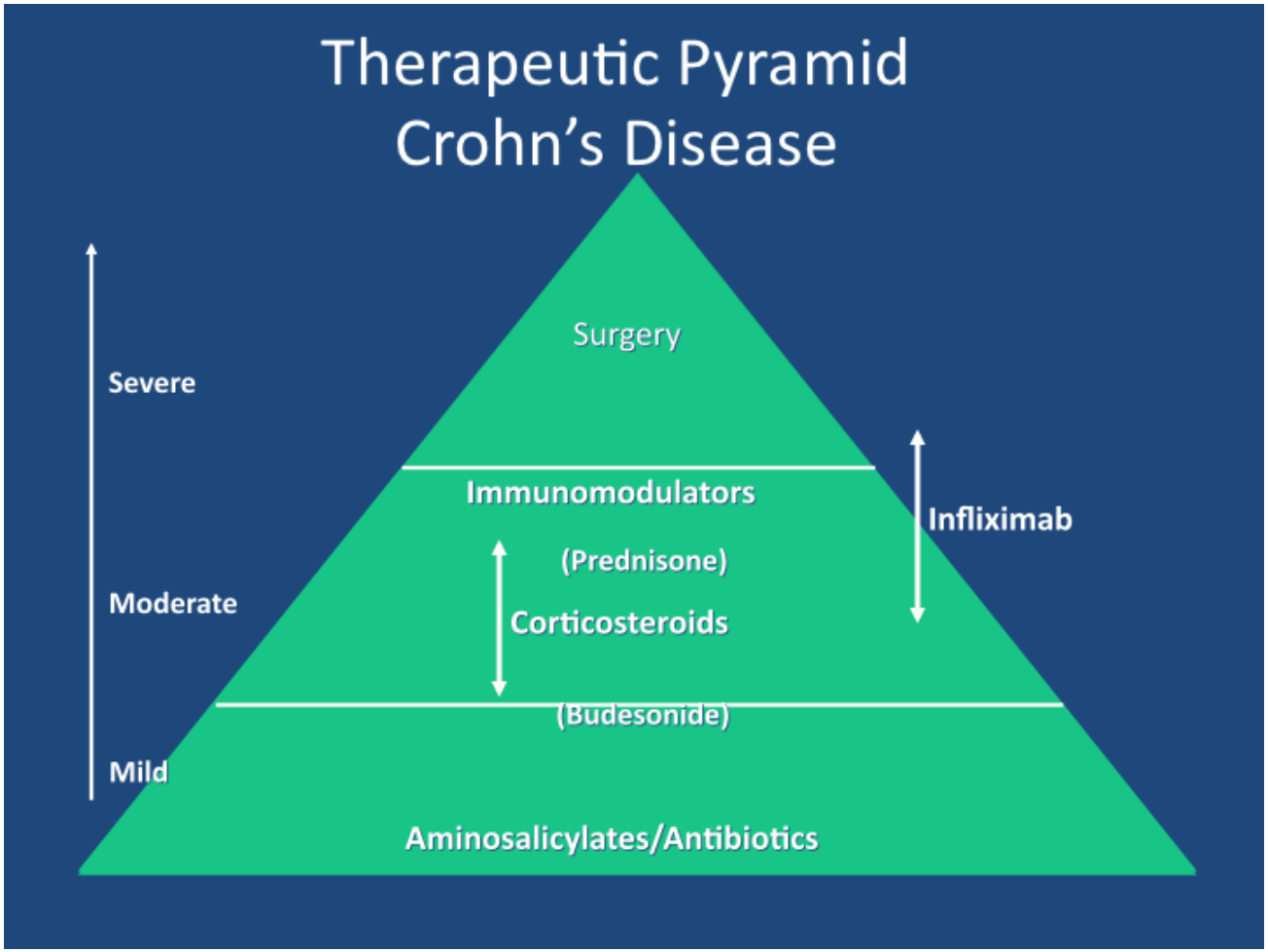
- Extra-intestinal manifestations
  - Uveitis and Episcleritis
  - Erythema Nodosum and Pyoderma Gangrenosum
  - Sclerosing cholangitis
  - Renal stones
  - Gall stones
  - Amyloidosis

Crohn's Disease Treatment

- Mainly medical treatment:
  - Oral 5-aminosalicylates (sulfasalazine)
  - Antibiotics (Cipro, Metronidazole)
  - Glucocorticoids (Prednisone)
  - Immunomodulators (Azathioprine)
  - Biologic therapies (infliximab)

Crohn's Disease Treatment

- Mainly medical treatment
- Surgical treatment:
  - Failure of medical management
  - Treating complications
  - Not a Cure


Therapeutic Pyramid
Crohn's Disease
Severe
Moderate
Mild
Surgery
Immunomodulators
(Prednisone)
Corticosteroids
(Budesonide)
Aminosalicylates/Antibiotics
Infliximab

Inflammatory Bowel Disease

	UC	*Crohn's disease*
Blood in stool	Yes	Occasionally
Mucus	Yes	Occasionally
Systemic symptoms	Occasionally	Frequently
Pain	Occasionally	Frequently
Abdominal mass	Rarely	Yes
Perineal disease	No	Frequently

Inflammatory Bowel Disease

	UC	*Crohn's disease*
Fistulas	No	Yes
Small intestine obstruction	No	Frequently
Colonic obstruction	Rarely	Frequently
Response to antibiotic	No	Yes
Recurrence after surgery	No	Yes

Inflammatory Bowel Disease

	UC	*Crohn's disease*
Rectal sparing	Rarely	Frequently
Continuous disease	Yes	Occasionally
„cobblestoning"	No	Yes
Granuloma on biopsy	No	Occasionally

Inflammatory Bowel Disease

Questions?