IBD Management in PSC

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Inflammatory Bowel Disease

- Chronic inflammatory condition of the gastrointestinal tract of unclear cause

- Two types
  - Ulcerative Colitis (UC)
  - Crohn's Disease (CD)

Loftus EV Jr., et al. Gastroenterology 1998;114:1161
Andres PG, et al. Gastroenterol Clin North Am 1999;28:255

Inflammatory Bowel Disease

- Disease usually starts - 2nd to 3rd decade of life

- Incidence
  - UC - 8 to 12 per 100,000
  - CD - 5 per 100,000

Loftus EV Jr., et al. Gastroenterology 1998;114:1161
Andres PG, et al. Gastroenterol Clin North Am 1999;28:255

IBD Symptoms

- Abdominal pain
- Bloody diarrhea
- Weight loss

Su C, Lichtenstein GR. Ulcerative Colitis. In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia:Saunders;2006(109):2508

Differential Diagnosis Of IBD

- Irritable bowel syndrome
- Infectious ileitis/colitis
  - Ileo-colonic TB
- Neoplasm
  - Lymphoma
  - Carcinoma
- Medication related
  - NSAID-related
- Ischemic colitis
- Appendicitis
- Diverticulitis
- Radiation enteritis/colitis
- Eosinophilic gastroenteritis
- Microscopic colitis
- Sarcoidosis
- Acute self-limited colitis

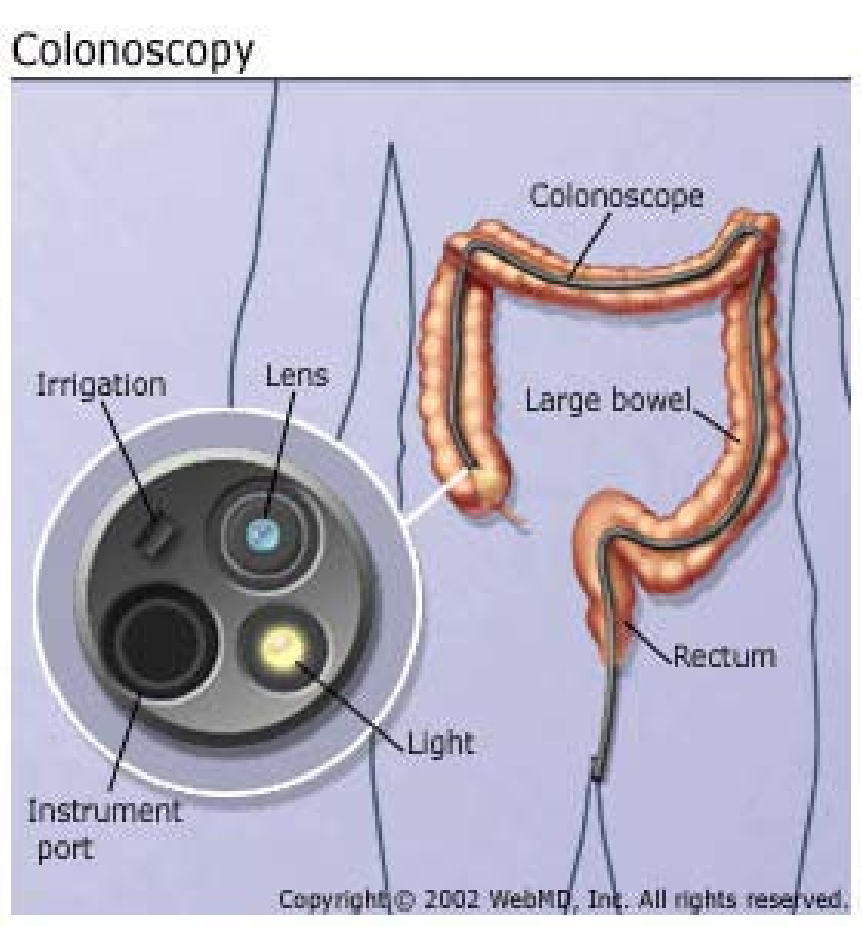
Su C, Lichtenstein GR. Ulcerative Colitis. In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia:Saunders;2006(109):2508

How Is IBD Diagnosed?

- Blood tests
- Stool test to rule out infection as a cause
- Radiology exams- X-Rays, CT scan
- Endoscopy with biopsies- gold standard

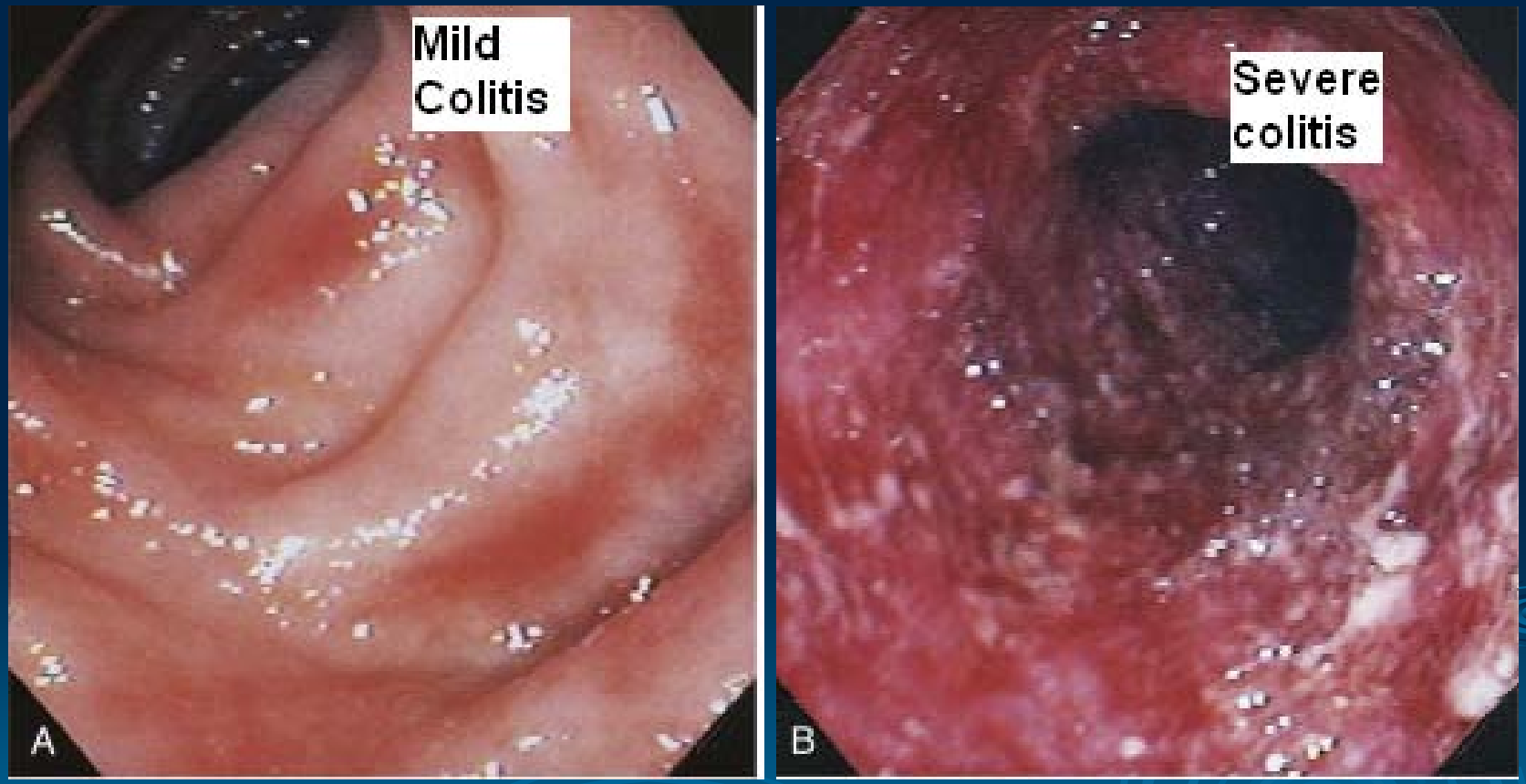
Su C, Lichtenstein GR. Ulcerative Colitis. In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia:Saunders;2006(109):2508

Colonoscopy



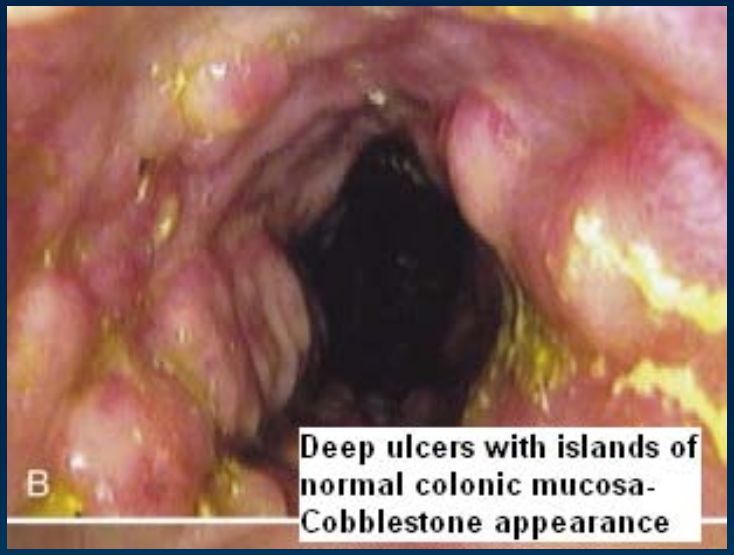
http://www.webmd.com/digestive-disorders/colonoscopy
www.gastrointestinalatlas.com

Colonoscopy Findings in UC

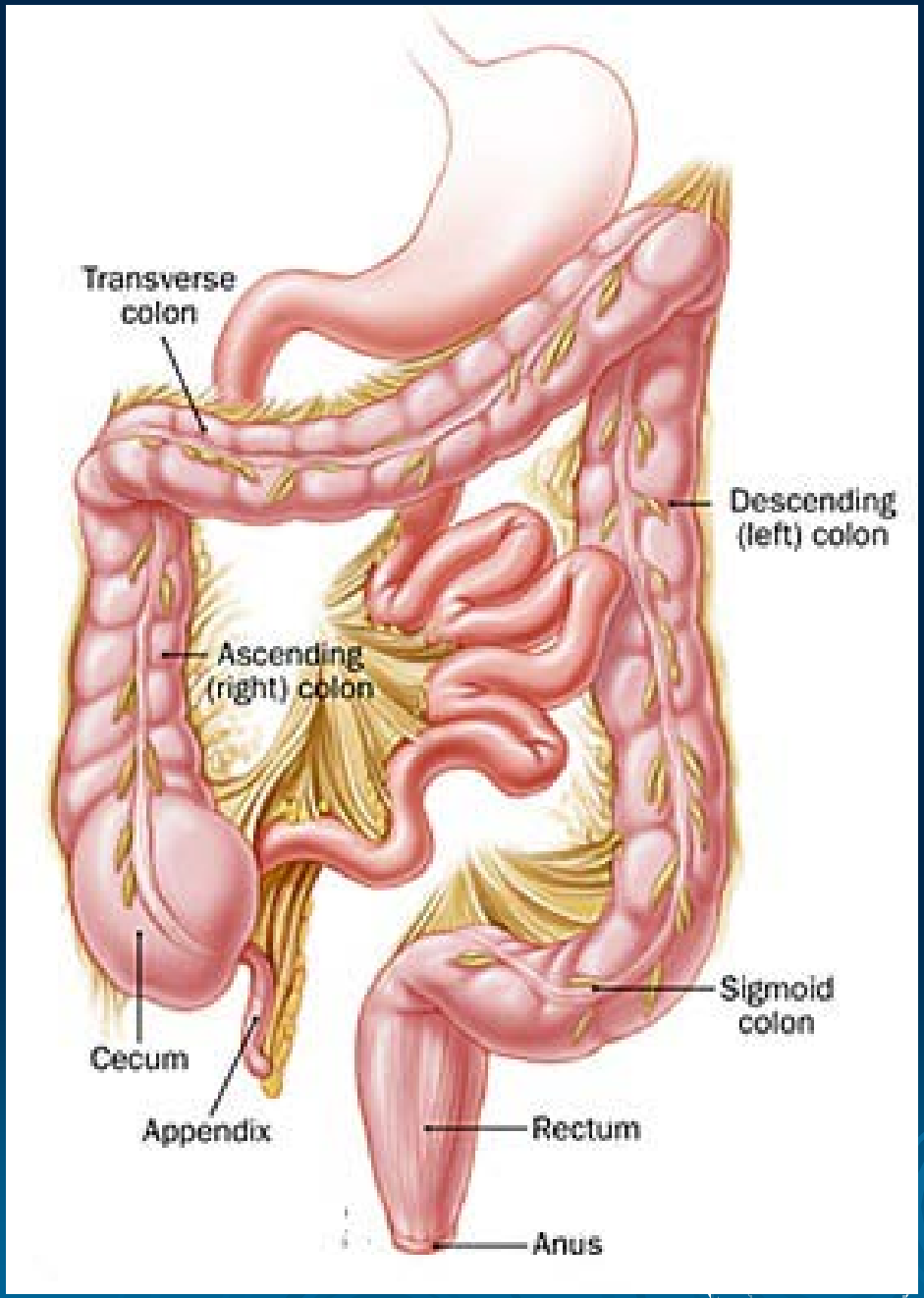


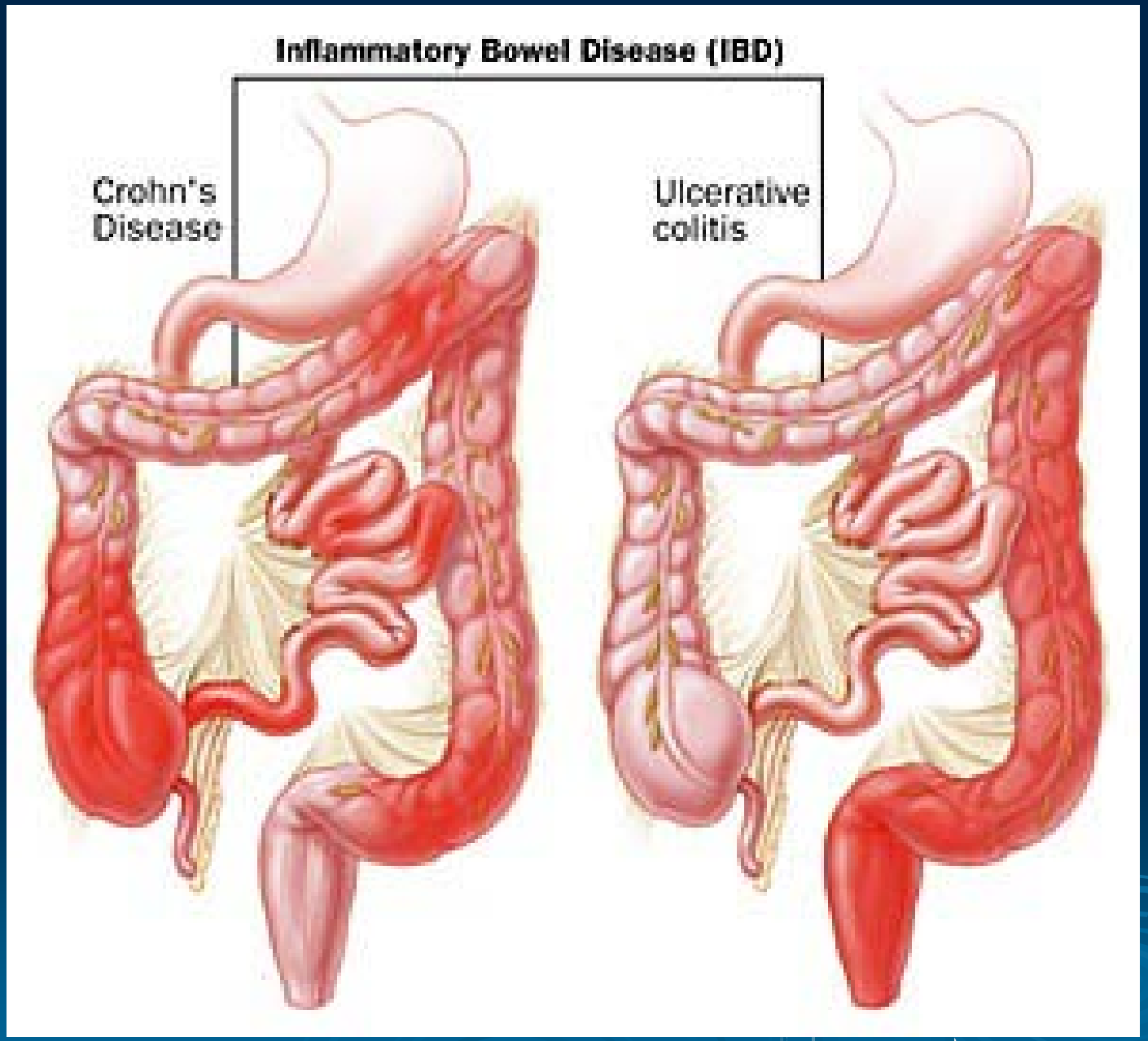
Su C, Lichtenstein GR. Ulcerative Colitis. In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia:Saunders;2006(109):2511

Colonoscopy Findings In CD

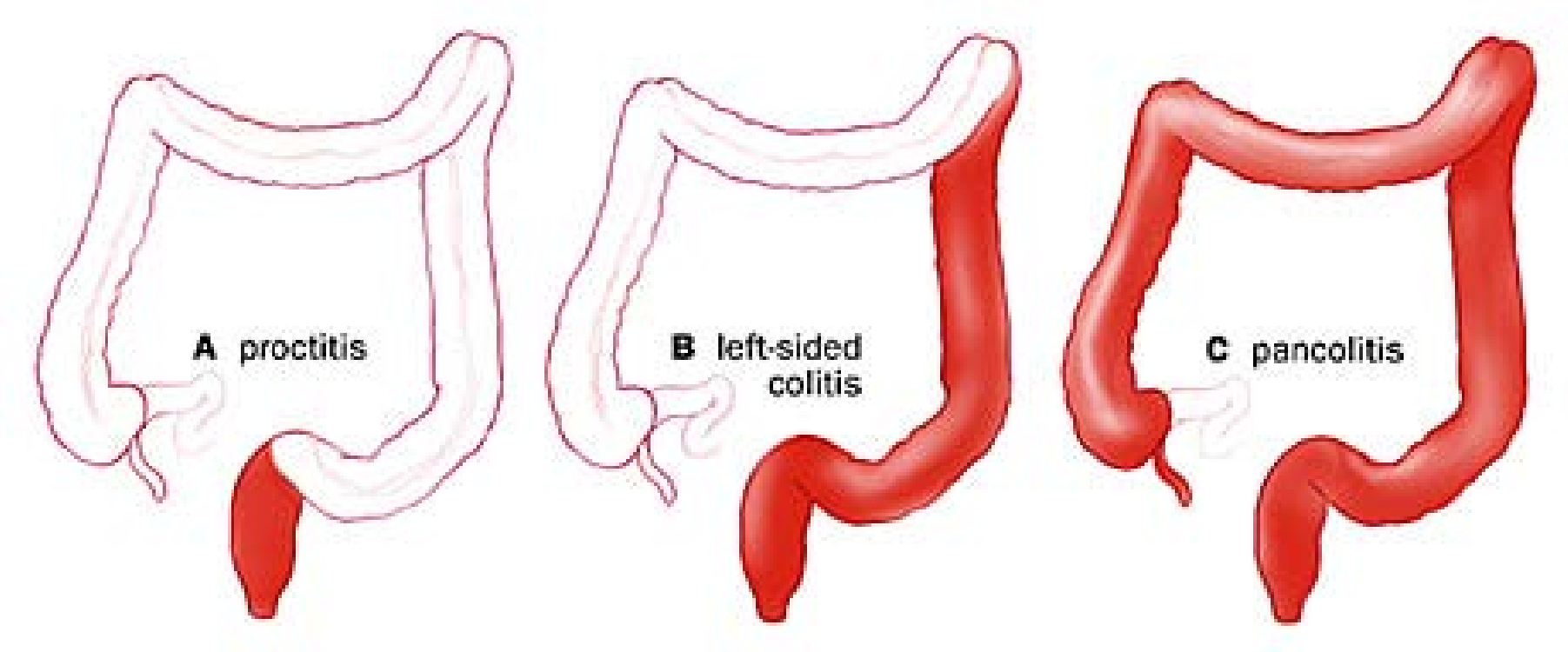


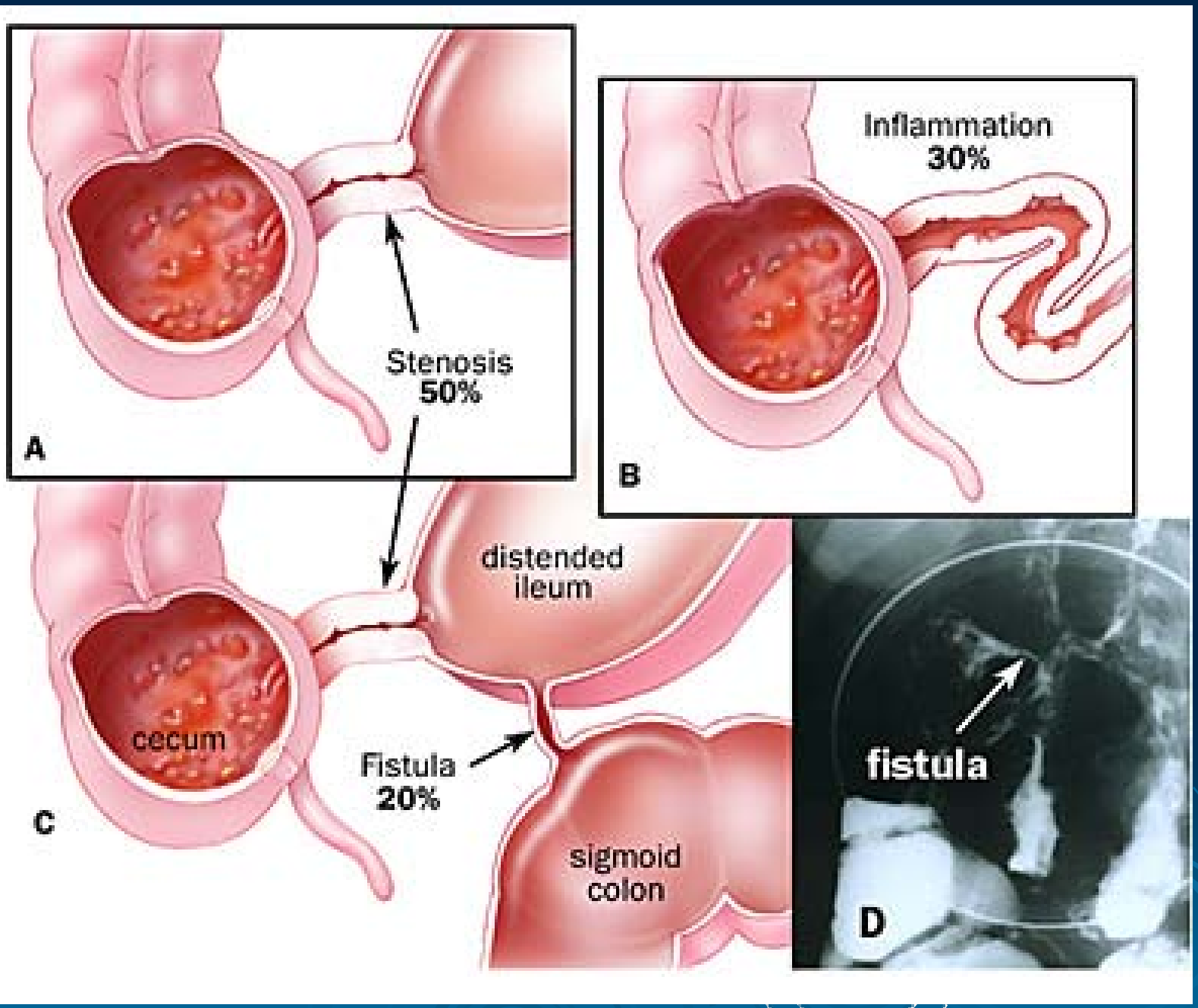
Sands BE. In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia:Saunders;2006(109):2476


Transverse colon
Descending (left) colon
Ascending (right) colon
Sigmoid colon
Cecum
Appendix
Rectum
Anus


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

Patterns Of UC




Stenosis
50%
A
Inflammation
30%
B
distended
ileum
cecum
Fistula
20%
C
sigmoid
colon
fistula
D

Differences Between CD And UC

	UC	CD
Bowel involvement	Continuous involvement	Skip lesions
Depth of disease	Confined to surface	Extends deep through the wall
Rectum	Involved 95%	Spared
Terminal ileum	Spared	Involved 70%
Small bowel	Not affected	Affected 30%
	-	Fistula, perianal disease
Surgery/colectomy	Curative	Symptom relief
Prevalence in PSC	Common	Rare

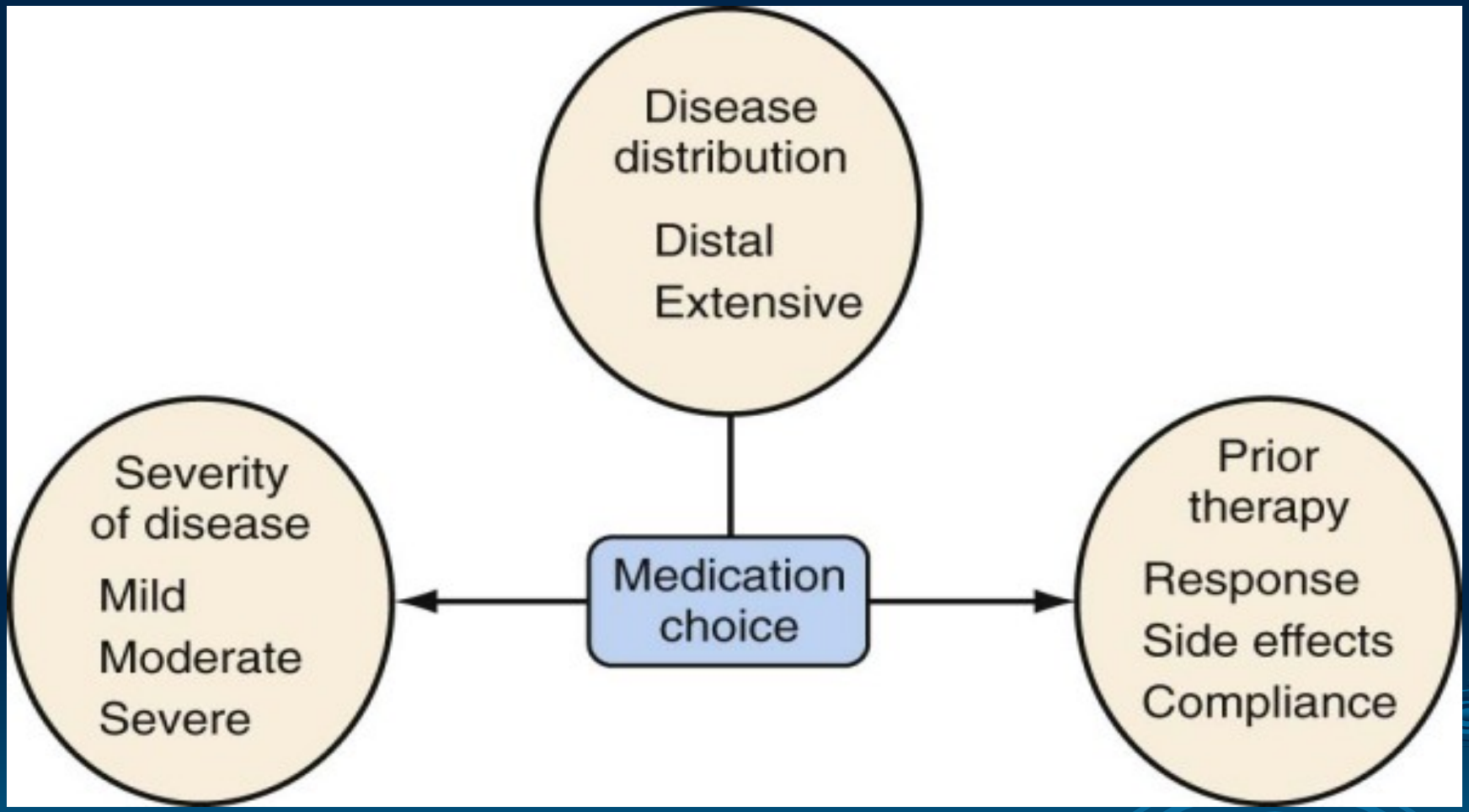
Treatment of UC & CD
Goals Of Therapy

- Induce remission (disease control)
- Maintain remission
- Avoid treatment-related side effects
- Maintain adequate nutritional status
- Prevent/address long term disease-related complications
  - Cancer screening, osteoporosis

Available Medications For IBD

- 5-ASA preparations (Asacol, Mesalamine, Lialda, Pentasa etc)
- Immunomodulators (Azathioprine, 6-Mercaptopurine, Methotrexate)
- Steroids
- Cyclosporine
- Biologics (Remicade, Humira etc)

Choosing The Right Drug



Su C, Lichtenstein GR. Ulcerative Colitis. In: Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed. Philadelphia:Saunders;2006(109):2518

Common Reasons For Flare (Disease exacerbation)

- Medication non-compliance
- Smoking (esp. Crohn's)
- NSAIDs (Ibuprofen, Aleve, Motrin etc)
- Infections (Upper respiratory, enteric)
- Natural disease progression

Surgery In IBD

Indications For Surgery In IBD

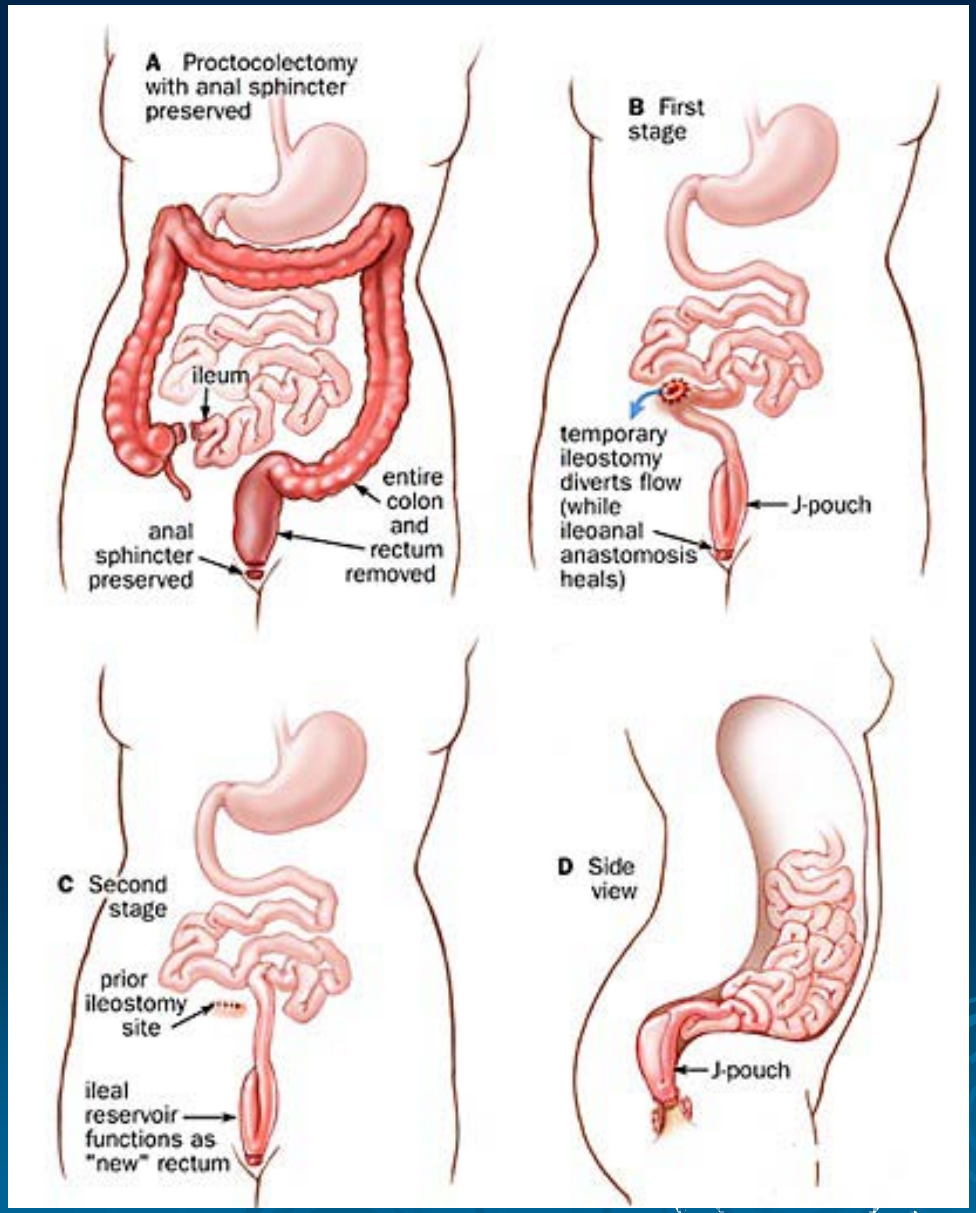
- Colon cancer
- Non response/inadequate response to maximal medical therapy
- Conditions that are unlikely to respond to medications – abscess (pus collection), fistula, stricture causing obstruction.

Types Of Surgeries In IBD

- For UC
  - Colon resection (proctocolectomy) with pouch creation (Ileal Pouch Anal Anastomosis or IPAA) is the preferred surgery

- For CD- depends on the indication
  - Abscess drainage
  - Resection of a narrowed segment of bowel
  - Resection of a fistula

Proctocolectomy With Ileal Pouch Anal Anastomosis (IPAA)



Colorectal Cancer Risk In IBD

- Risk is 5 - 15 fold higher than general population
- Cancers
  - Multiple at same time
  - Arise from flat mucosa

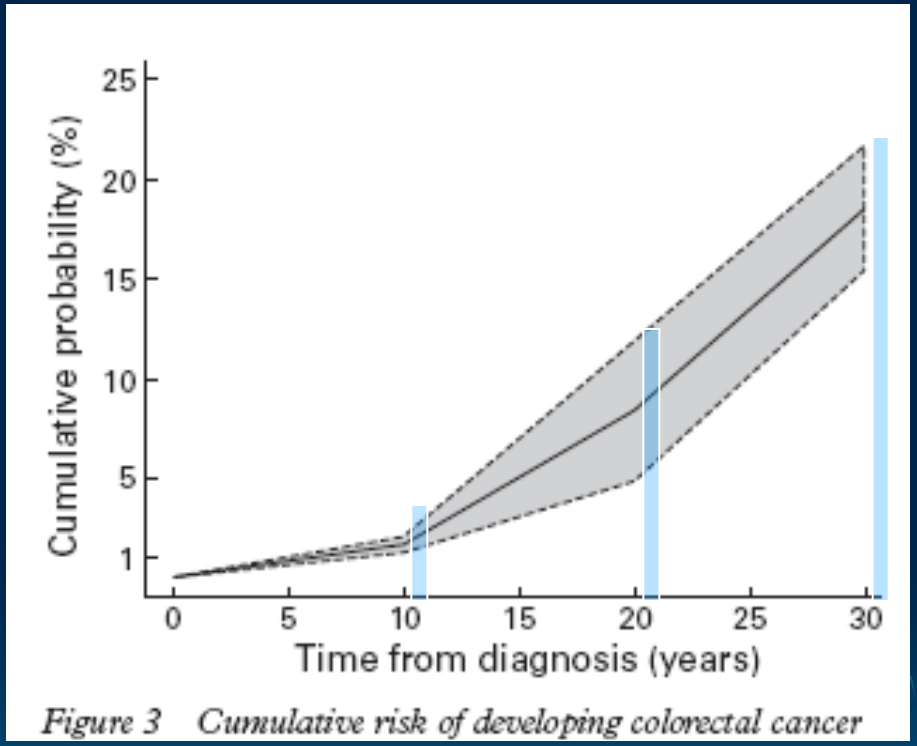


Figure 3 Cumulative risk of developing colorectal cancer

Greenstein AJ, et al. Gastroenterology 1979; 77: 290
Sugita A, et al. Gut 1991; 32: 167
Eaden JA, et al. Gut 2001; 48(4): 526

Prevention/Treatment Of Osteoporosis In IBD

- Oral calcium/vitamin D supplementation
  - May be sufficient with normal BMD (DEXA scan)
- Bisphosphonate therapy (Fosamax, Boniva etc) may be needed if
  - On steroid therapy
  - Personal/family history of fractures

Bernstein CN, et al. Am J Gastroenterol 2003;98(5):1094
Habtezion A, et al. Inflamm Bowel Dis 2002;8(2):87
Van Staa TP, et al. Rheumatology(Oxford) 2000;39(12):1383

Reproductive Issues In IBD

- Fertility is similar to general population in pre-surgical UC and CD patients
- Some surgeries may affect fertility
- Pelvic inflammation in CD may decrease fertility
- Reversible sperm abnormalities with sulfasalazine use in 60% patients

Mahadevan U. Med Clin N Am 2010;94:53
Dejaco C, et al. Gastroenterology 2001;121:1048

Pregnancy And IBD

IBD in pregnancy

- Disease unchanged in 1/3 patients
- Remission in 1/3
- Disease flare in 1/3
  - Non-adherence to medical therapy

Pregnancy outcome

- No difference in pregnancy outcomes if disease in remission
- With relapse, risk of
  - Low birth weight
  - Preterm delivery

Korelitz BI. Gastroenterol Clin N Am 1998;27:213
Hou JK, Mahadevan U. Clin Gastroenterol Hepatol 2009;7:244
Mahadevan U. Sandborn WJ. Gastroenterology2007;132:1106
Reddy D, et al. Am J Gastroenterol 2008;103:1203

Will My Child Get IBD?

Scenario	Risk to child
Mother with UC	1.6%
Mother with CD	5.2%
Both parents with IBD	36%

Mahadevan U. Med Clin N Am 2010;94:53

IBD IN PSC

IBD In PSC

- 70- 80% of PSC patients develop IBD
  - Only 2 to 7.5% IBD patients develop PSC
- PSC patients are more likely to have UC (85-90%) versus CD (5-15%)
- Either PSC or IBD may manifest first

Broome U et al. Semin Liv Dis. 2006; 26:31.
Olsson R et al. Gastroenterology. 1991; 100:1319.

Unique Features Of IBD In PSC

- Continuous colon involvement (like UC)
  - But rectum spared (unlike UC)
  - Terminal ileum involved (like CD)
- Runs a mild, sometimes asymptomatic course
- Higher risk of colonic dysplasia and cancer

Chapman R et al. Hepatology 2010; 51(2): 660

IBD Treatment in PSC-IBD

- Not different from treatment of IBD without PSC
- Under treatment more likely due to quiescent nature of IBD in PSC

How Does Coexisting IBD Impact Course Of PSC ?

- No differences seen w.r.t
  - Clinical features of PSC
  - Radiologic features of PSC
  - Biopsy (histopathology) features of PSC

Ludwig J et al. Hepatology 1981
MacCarty RL et al. Radiology 1985
Broome U et al. Gut 1996
Navaneethan U et al. Inflamm Bowel Disease 2009

Colorectal Cancer Risk In PSC-IBD

UC Duration	At 10 years	At 20 years	At 25 years
UC only	2%	5%	10%
UC + PSC	9%	31%	50%

More right sided cancers are seen for unclear reasons

Broome U et al. Hepatology 1995
Claessen MMH et al. Inflamm Bowel Dis 2009; 15:1331

Does The Risk of Colon Cancer Decrease with Liver Transplant?

	Colon Rectal Cancer
PSC-IBD with Liver Transplant (43)	34%
PSC-IBD (30)	30%
Liver transplant for non-PSC indication (43)	0

Ursodiol did not prevent colorectal cancer

Hanoueneh,, I et al. Inflamm Bowel Dis 2011

Are There Medications That Can Prevention Colon Cancer ?

- Ursodiol use is not routinely recommended anymore
- Folic acid supplementation may help
- Role of 5-ASA drugs unclear at this time

Chapman R et al. Hepatology 2010; 51(2): 660.
Giovannucci E et al. Ann Intern Med 1998;129:517.

Current Approach To Colorectal Cancer In IBD

- IBD alone (UC or Crohn's colitis)
  - Surveillance colonoscopies every 1-2 years after 8-10 years of IBD
- IBD with PSC
  - Surveillance colonoscopies every year starting in the first year of diagnosis

Chapman R et al. Hepatology 2010; 51(2): 660
Kornbluth A et al. Am J Gas10troenterol 2010.; 105:501

Outcomes of Common Surgeries In PSC-IBD

- Proctocolectomy with IPAA for colorectal cancer
- Liver transplant (OLT) for advanced PSC

Impact Of PSC On IPAA Outcomes

- Compared to patients without PSC
  - Pouch function is not different
  - Quality of life is not different
  - There is more pouchitis (9-90% Vs. 7-47%)
  - Long-term mortality may be higher
    - But this is usually due to worsening PSC

Gorgun E et al. Surgery 2005; 138:631.
Rahman M et al. Int J Colorectal Dis 2011;

Impact of IPAA On PSC

- Finnish study of 30 PSC-IBD pts followed for median 11 years after IPAA showed

PSC activity on liver biopsy	No. (%)
No change	11 (37%)
Better/Decreased	15 (50%)
Worse/Increased	4 (13%)

Leppisto A et al. Int J Colorectal Dis 2009; 24:1169

How Does Liver Transplant For PSC Impact The Course Of IBD ?

Study	Outcome
Jorgensen, KK et al. Norway, 2011	Less colitis in liver transplant group
Moncrief, KJ et al. Canada, 2010	In 67% colitis remained unchanged In 6.1% colitis improved In 26.5% colitis worsened
Dvordik, I et al. US, 2002	Accelerated IBD progression seen in the liver transplant group
De Vrie, W et al. Holland, 2002	No observed differences

Summary

- PSC-IBD may be a separate entity with several unique features
- IBD should actively be sought in patients with PSC even if they are asymptomatic, and aggressive colon cancer surveillance should be undertaken
- Further studies into the pathogenesis of PSC-IBD may help manage increased cancer risk better

On The Horizon

- Colonoscopy imaging technology aimed at earlier colon cancer diagnosis
- Blood tests to identify high-risk IBD patients (serology)
- Drug trials of chemoprevention for colon cancer - needed

Thank You!