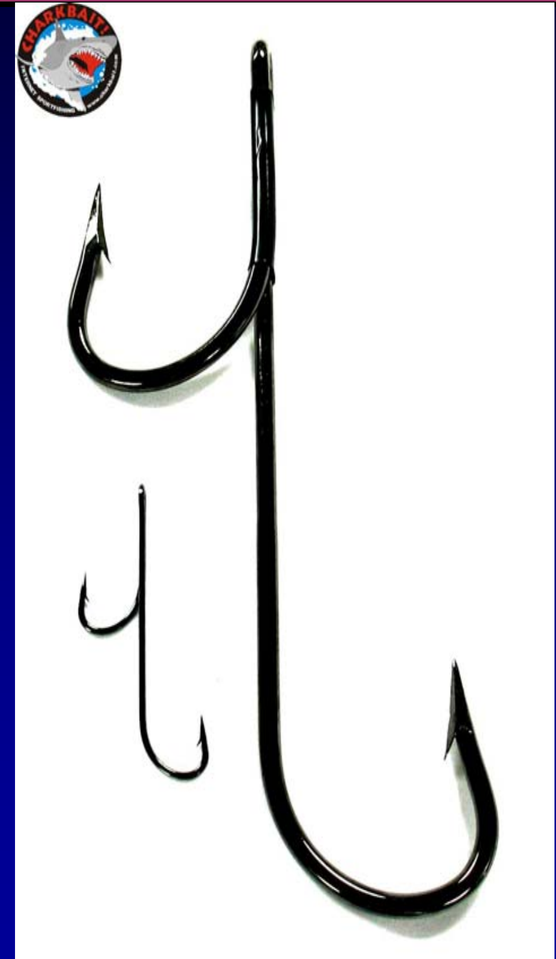
Double Trouble: PSC and Inflammatory Bowel Disease

Michael F. Picco, M.D., Ph.D.
Assistant Professor of Medicine
Mayo Medical School
Mayo Clinic-Jacksonville



What is Inflammatory Bowel Disease?

- Chronic disorder affecting the digestive tract that can have many different symptoms including diarrhea, weight loss and abdominal pain
- Types
  - Crohn's Disease
  - Ulcerative Colitis

What Causes Inflammatory Bowel Disease (IBD)?

- The exact cause of IBD is unknown.
- At least 3 major factors may be involved
  - Genetics (a family history)
  - Abnormal immune system
  - Environmental triggers (eg, smoking, oral contraceptives, NSAIDs)

Andres PG et al. *Gastroenterol Clin N Am* 1999;28:255.

How does your physician make the diagnosis of IBD?

- Clinical history
- Physical examination
- Laboratory tests
- Endoscopic findings
- Radiographic findings
- Biopsy Results

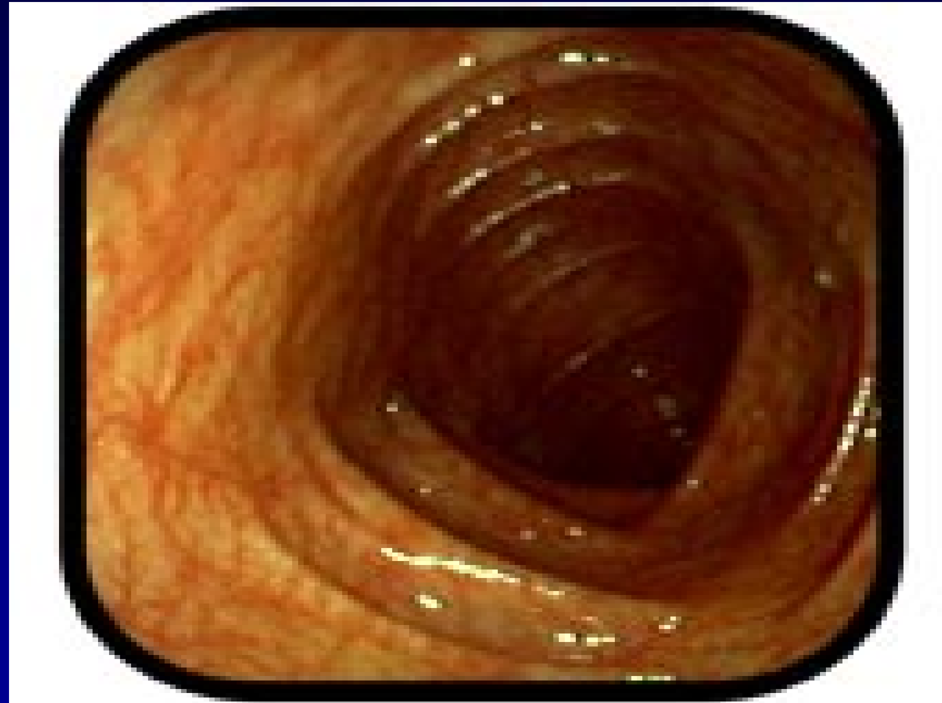
How is IBD Diagnosed?

- Physical exam
- Stool sample
  - Bleeding or infection in the intestines?
- Blood tests
  - Anemia indicates bleeding in the intestines.

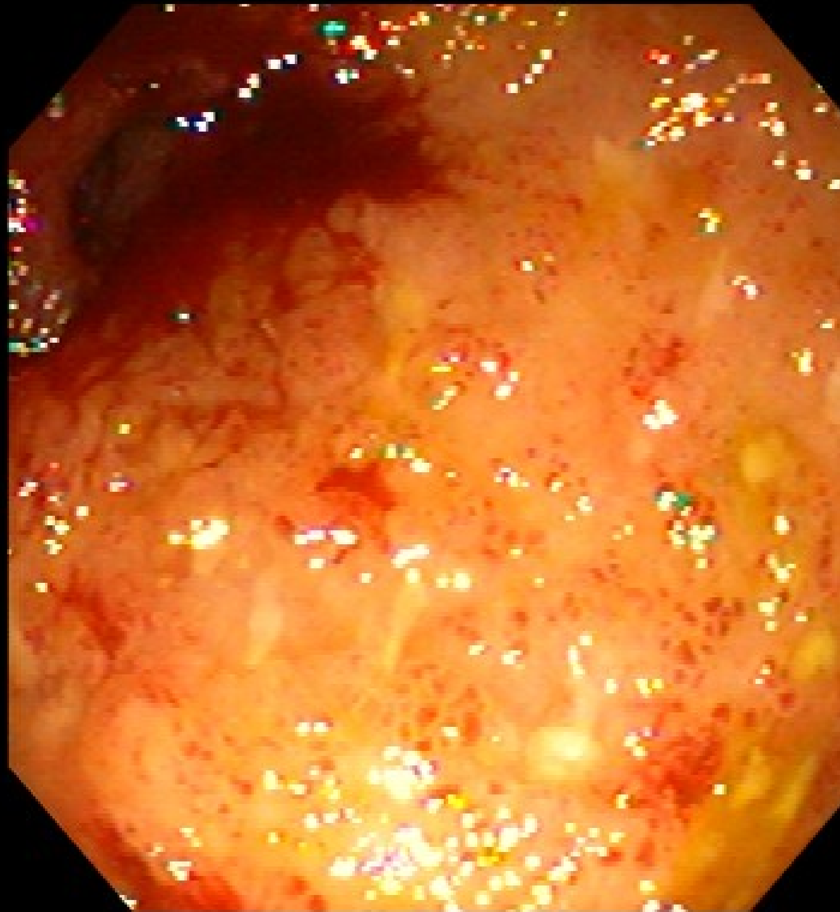
IBD Diagnosis (cont.)

- Small bowel series or CT scan
  - Patient swallows barium, a chalky solution that coats the GI tract, and undergoes x-ray to find abnormalities.
- Colonoscopy
  - A long, flexible tube is inserted through the anus and into the large intestine, allowing the doctor to view inside the GI tract.

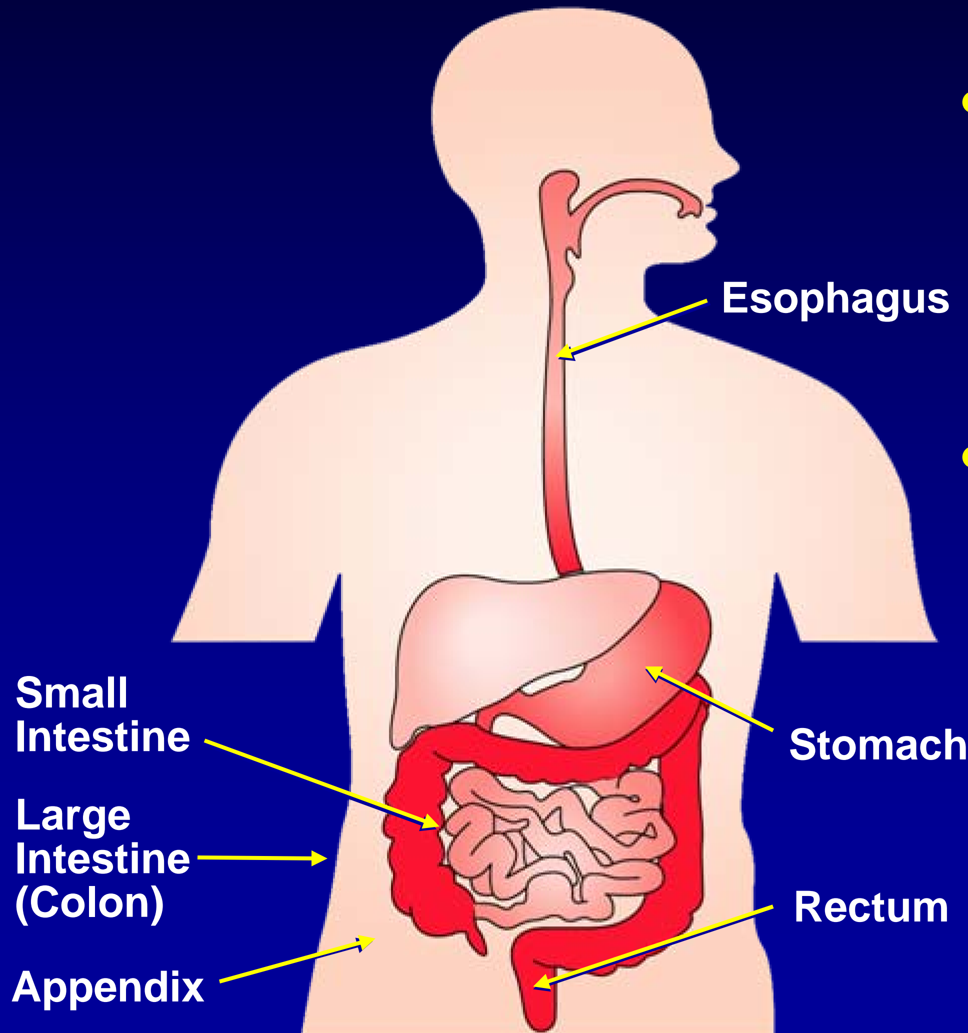
Normal Colon



Inflammatory Crohn's Disease

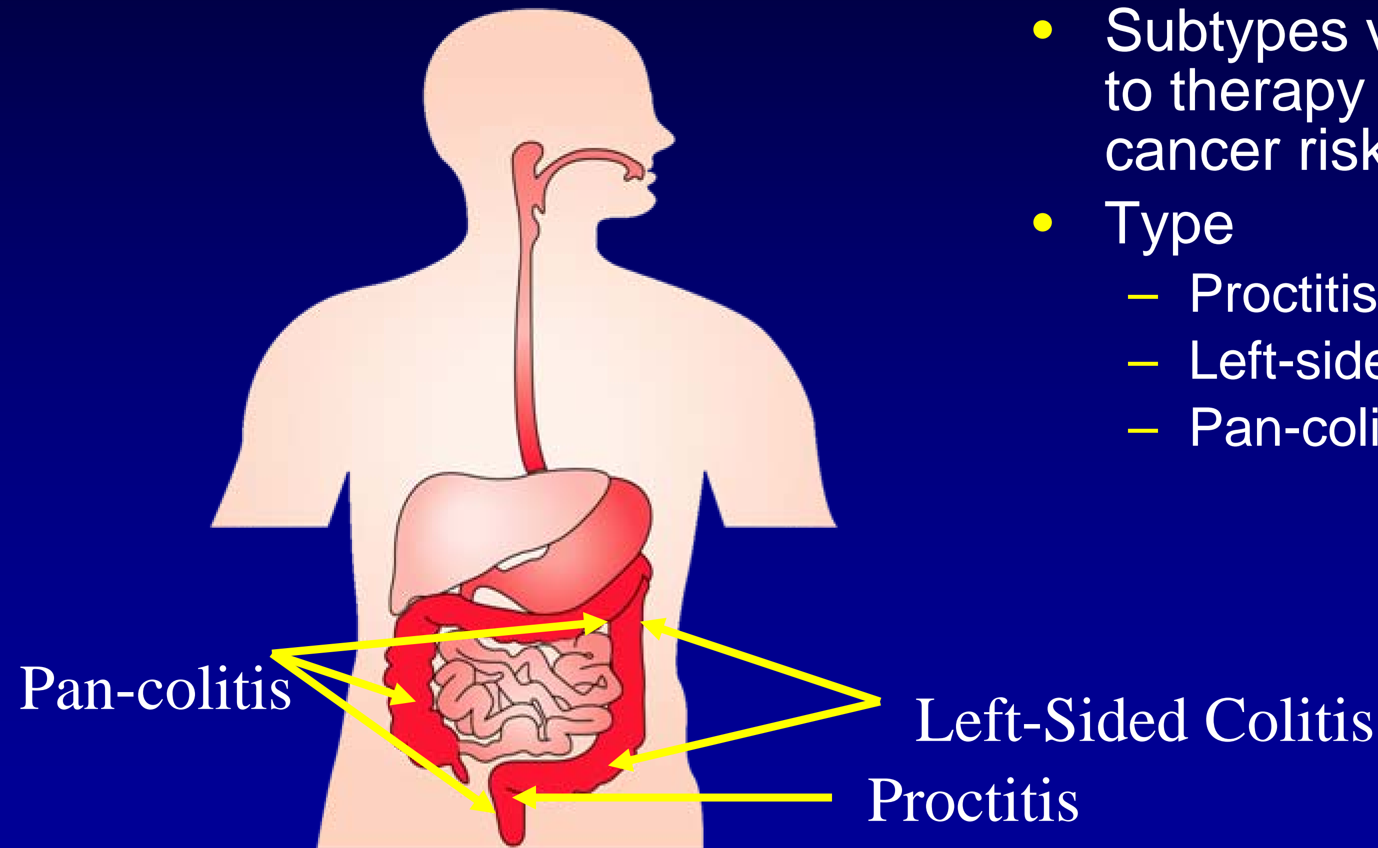


What Is Ulcerative Colitis?



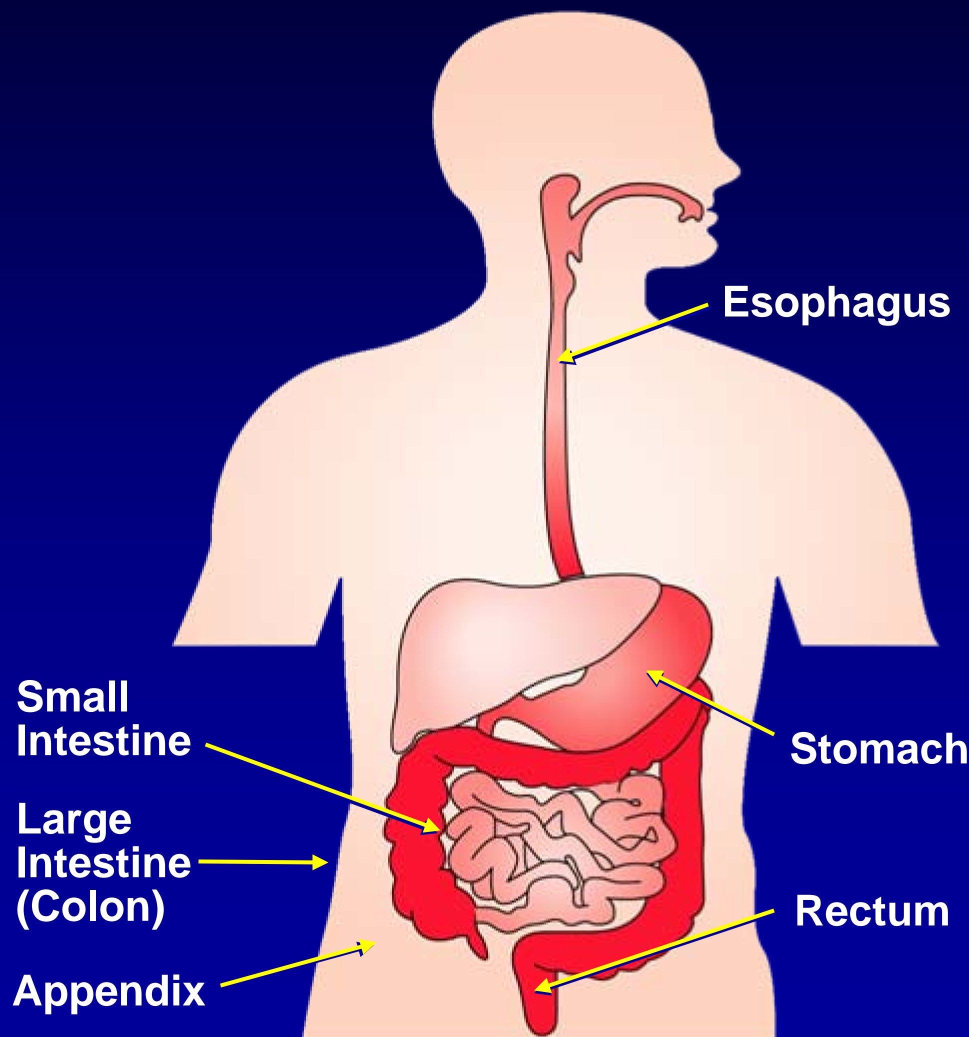
- Ulcerative colitis is an inflammatory bowel disorder that affects only the colon.
- The inflammation is confined to the lining of the colon

Ulcerative Colitis



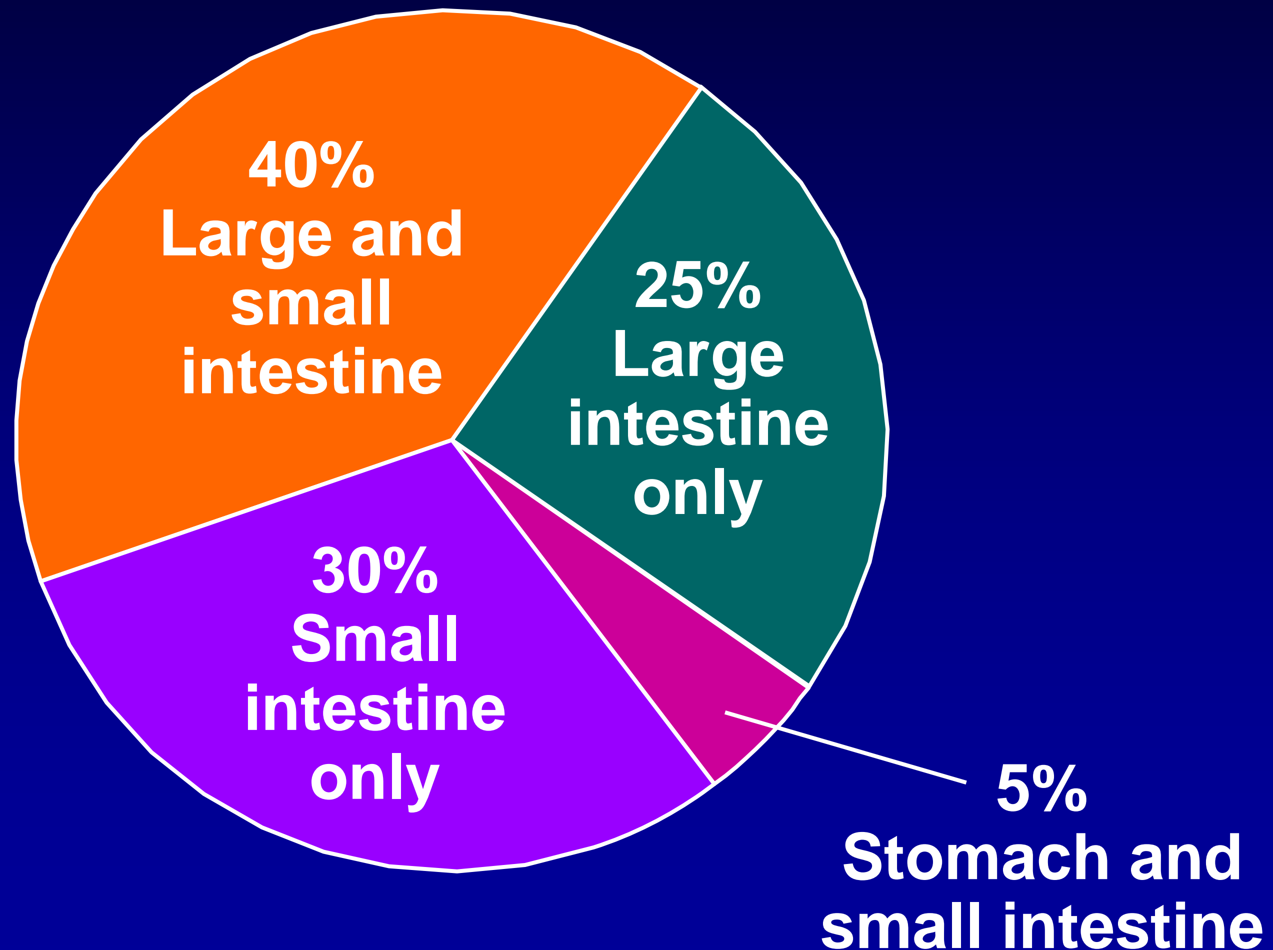
- Subtypes vary in response to therapy and colorectal cancer risk.
- Type
  - Proctitis
  - Left-sided colitis
  - Pan-colitis

What Is Crohn's Disease?

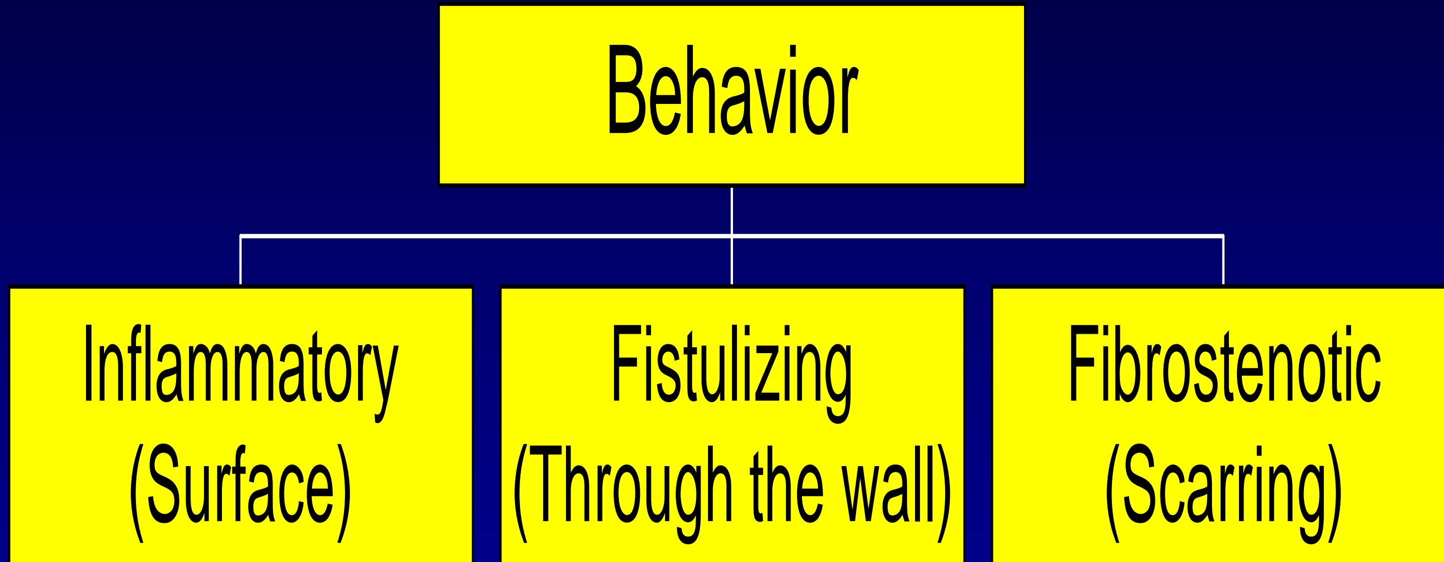


- Crohn's disease (CD) is an inflammatory bowel disorder that may affect any part of the gastro-intestinal (GI) tract
- The inflammation penetrates the lining of the GI tract and often causes ulcers to form

Crohn's Disease Can Occur in Different Places in the GI Tract

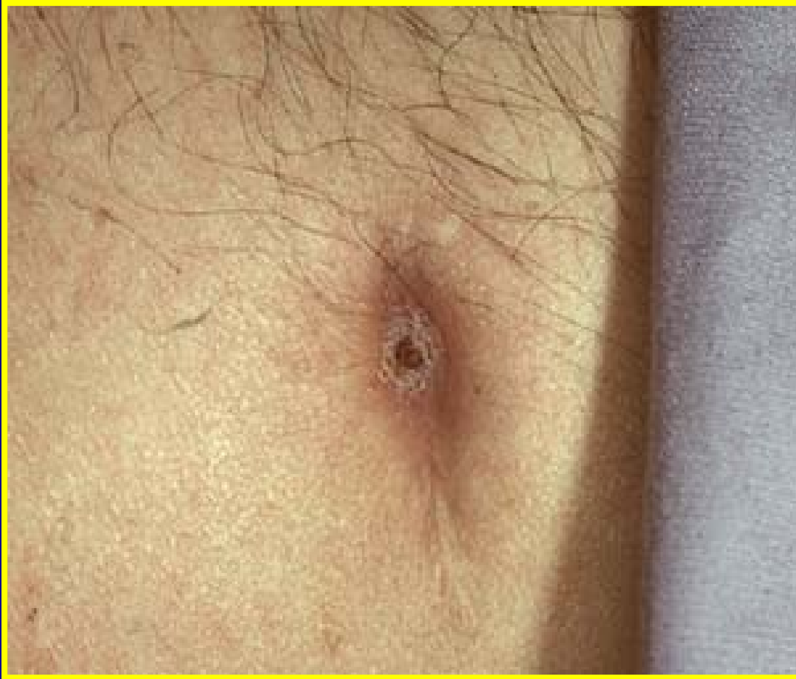


Crohn's Disease
How does it act?

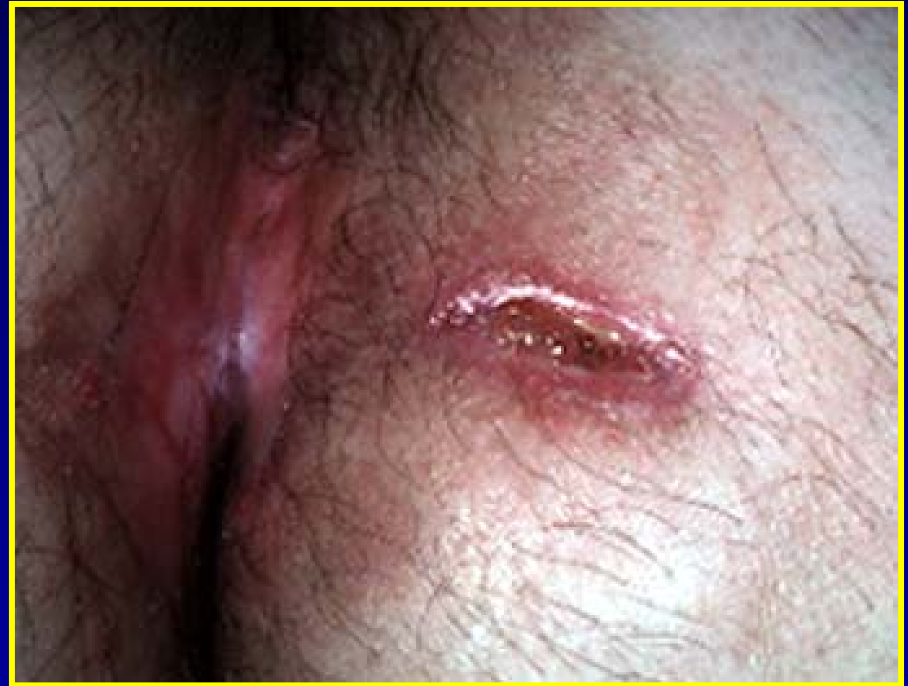


Complications of CD: Fistulas

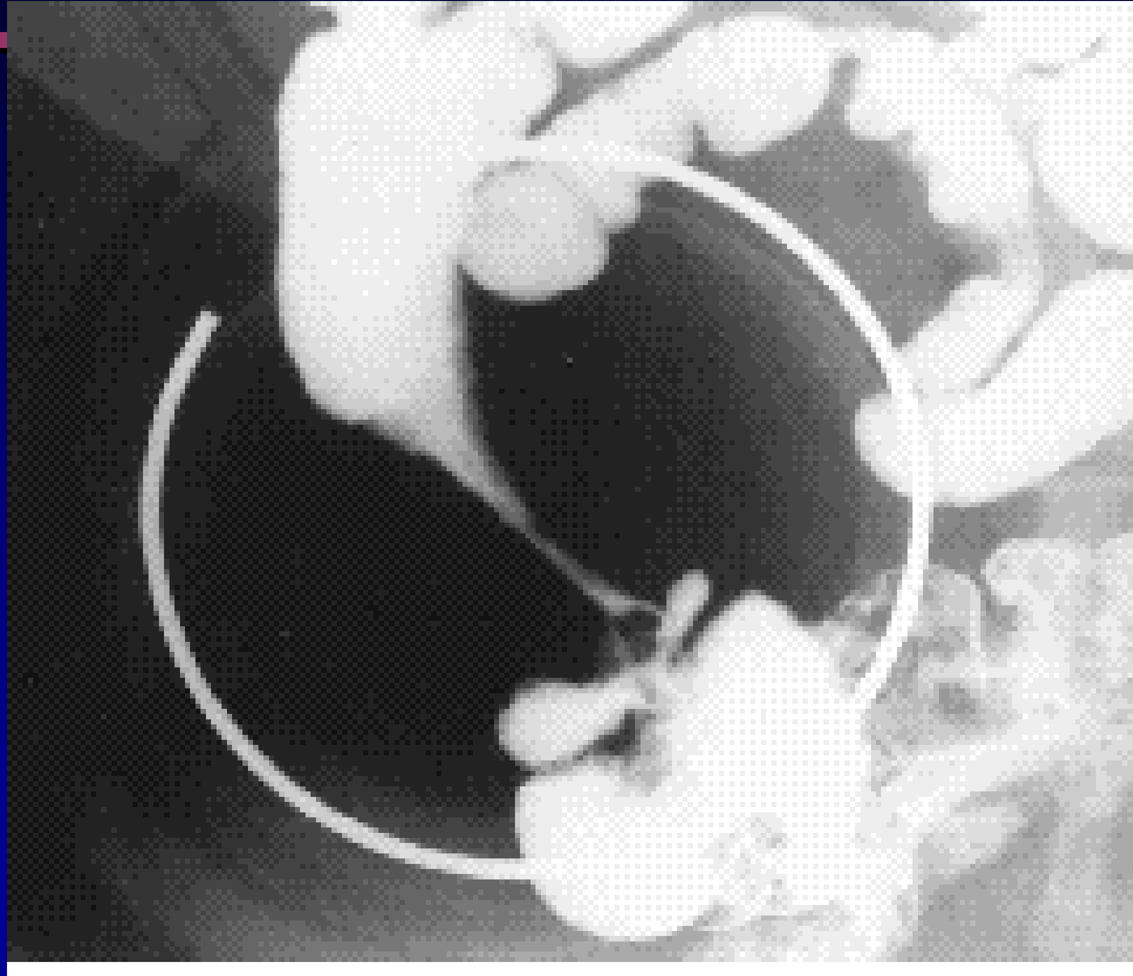
Abdominal Fistula



Perianal Fistula



Narrowing or Scarring in CD



Goals of Treatment

- INDUCE REMISSION
- MAINTAIN REMISSION

Goals of Treatment

- Relieve symptoms
- Prevent recurrence of symptoms
- Prevent or cure complications
- Control inflammation in the GI tract
- Improve quality of life
- Correct nutritional problems
- Reduce the need for surgery

Treatment of IBD

- No cure has yet been found for IBD.
- Choice of treatment depends on disease location and severity.
- Treatment may include:
  - Medications
  - Nutritional therapy
  - Surgery
- Conventional treatment is most effective in relieving symptoms short term, not preventing relapse of symptoms long term.

Treatment Options in IBD

- Aminosalicylates (5-ASA)
- Antibiotics
- Steroids
  - Standard steroids (eg, prednisone)
  - Controlled ileal-release budesonide
- Immunosuppressants
  - Azathioprine (AZA) and 6-mercaptopurine (6-MP)
  - Methotrexate (MTX)
- Biologics

Conventional Treatments: Induction of Clinical Response/Remission

Drug	*Response*
5-ASA	43%–64%
Oral prednisone	60%–78%
AZA/6-MP	36%–91%*
MTX	39%
Placebo	8%–50%

*Response only after 8 to 12 weeks

Stein RB et al. *Gastroenterol Clin North Am.* 1999;28:297.

Facts About Surgery

Who Undergoes Surgery?

- Patients with symptoms not relieved by medication
- Patients with serious complications, eg, abscesses, fistulas, intestinal blockage, or uncontrolled bleeding
- Patients with early warning signs of cancer

What Does It Do?

- Relieves symptoms
- Does not prevent relapse in CD

How Is It Performed?

- Depends on the reason.

What Else to Expect…

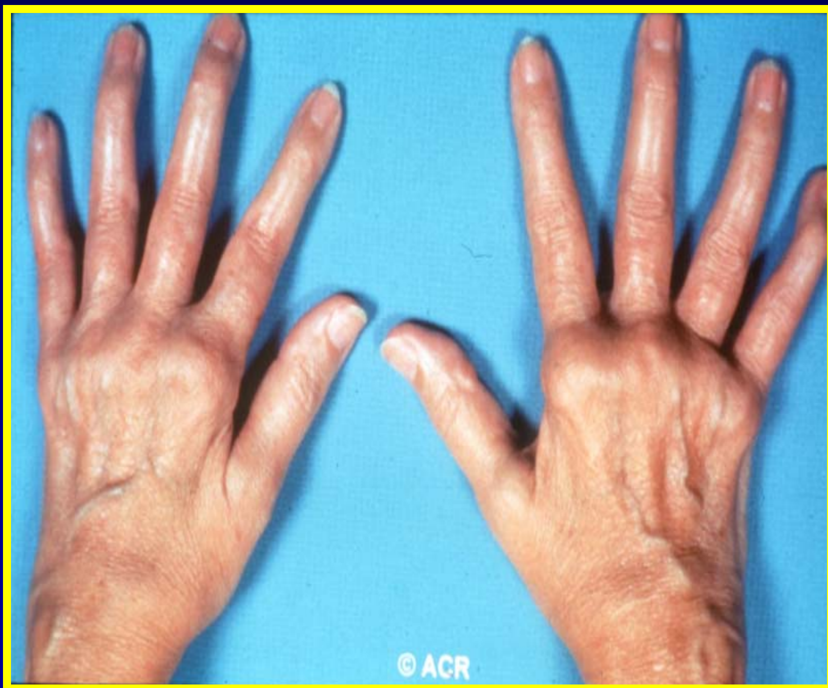
- IBD is a chronic (lifelong) disease.
- The course of IBD is unpredictable. Symptoms may come and go, often without rhyme or reason.
- Ulcerative colitis can be cured with surgery but Crohn’s disease can not be.

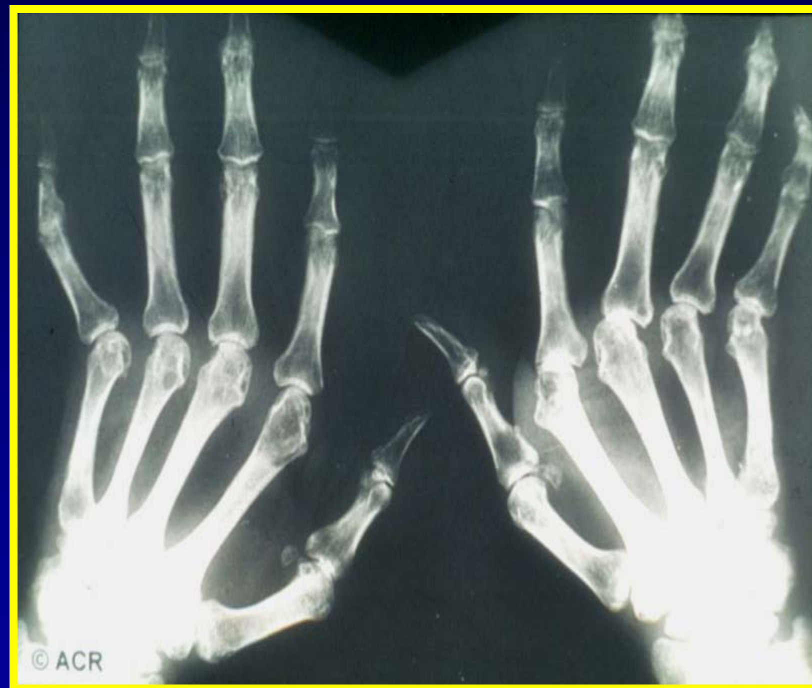
Complications Outside the Bowel in IBD

Scleritis in IBD

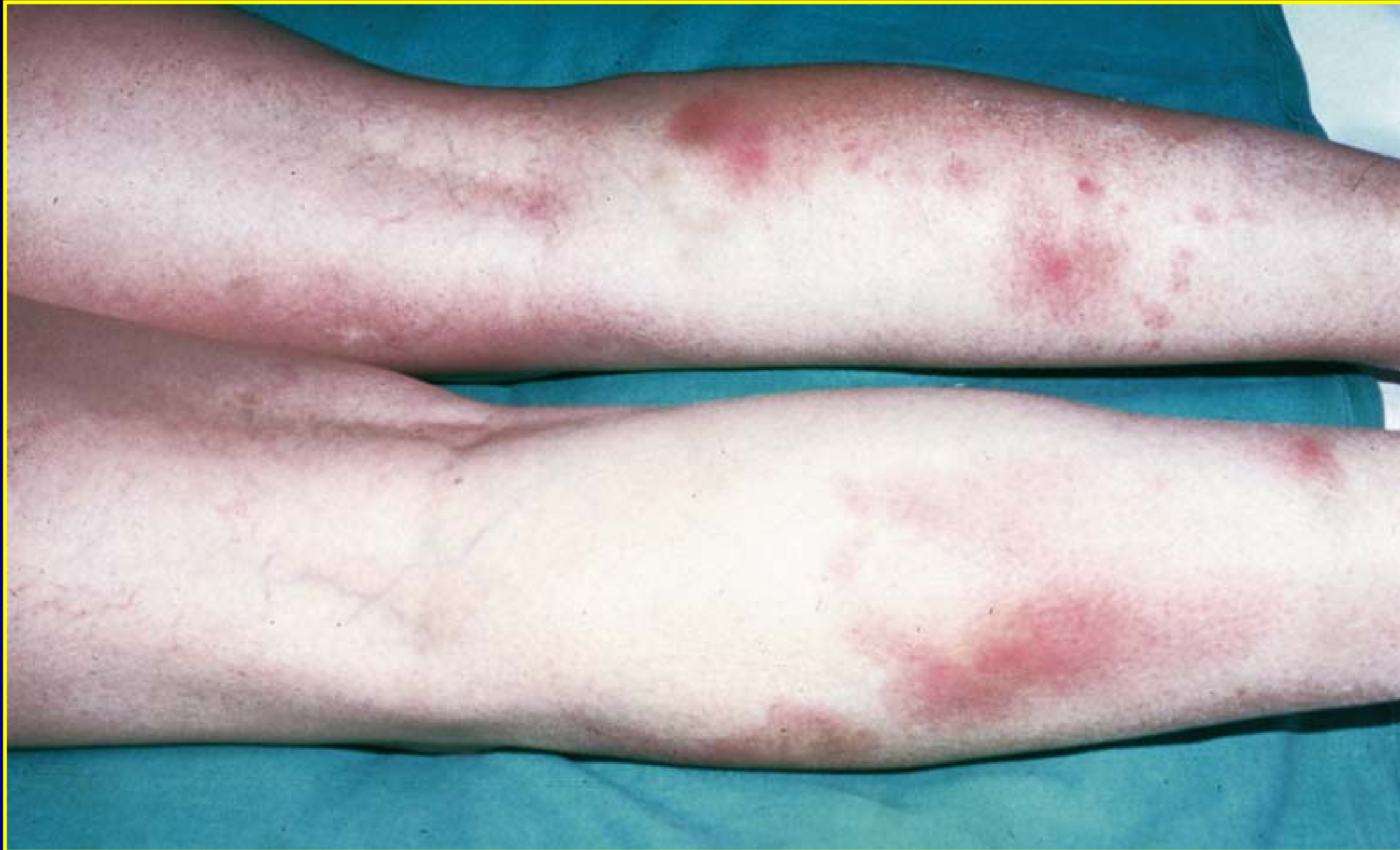
Courtesy of J-F Colombel, MD.

Complications Outside the Bowel: Arthritis



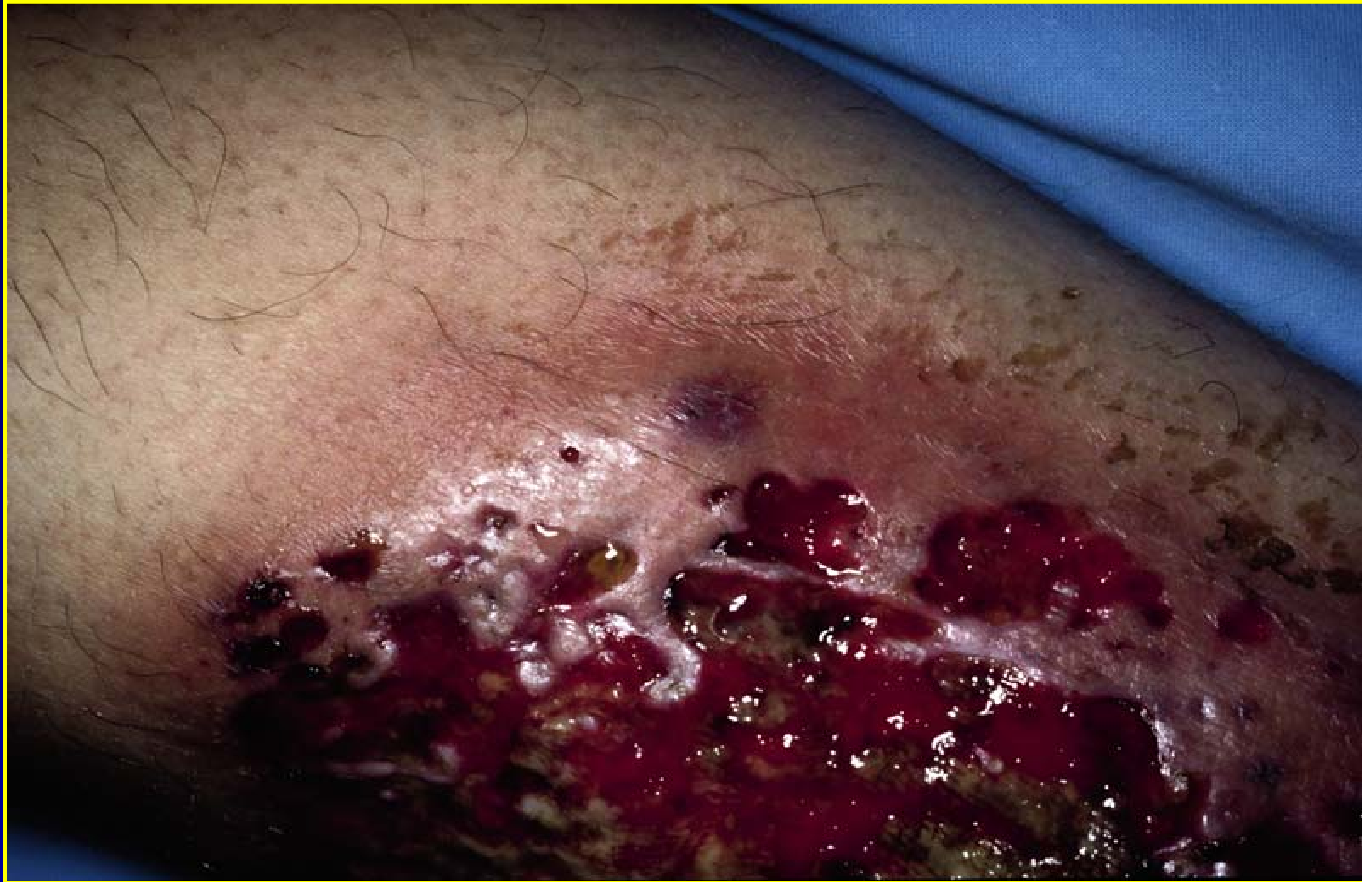


Erythema Nodosum in IBD



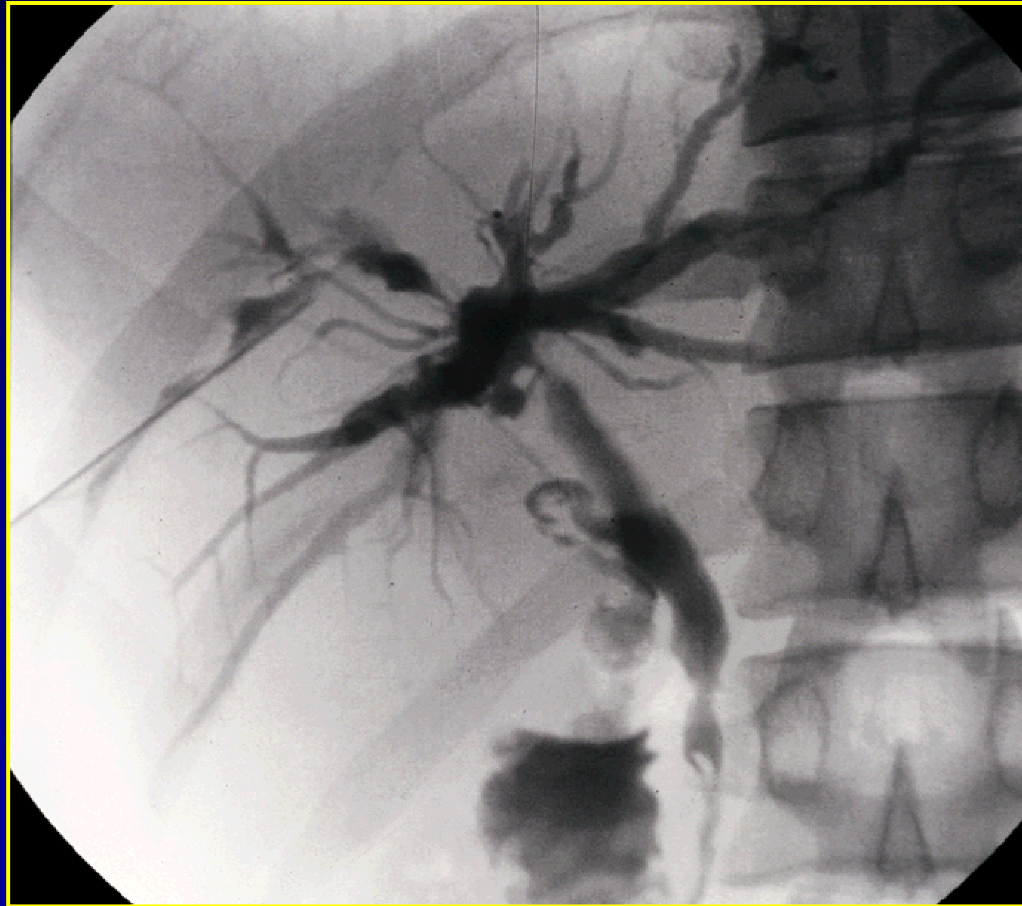
Courtesy of J-F Colombel, MD.

Pyoderma Gangrenosum in IBD



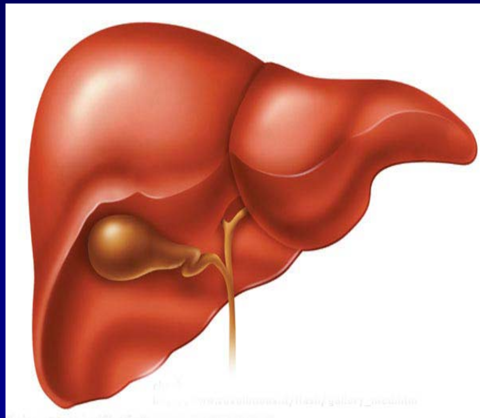
Courtesy of J-F Colombel, MD.

Sclerosing Cholangitis in IBD



Courtesy of J-F Colombel, MD.

IBD and the Liver

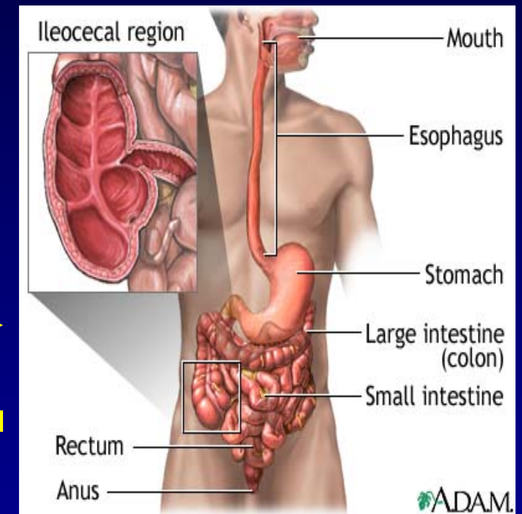


PSC

Medications

Gall Stones

Fatty Liver



IBD and PSC

- Up to 80% with PSC have UC
- About 5% with UC will have PSC
- Rarely associated with CD
- PSC-IBD may be a separate form of IBD

Why is this association important?

- Disease presentation
- Risk of Colon Cancer
- Colectomy Outcomes
- Transplant Outcomes

Disease presentation

- May not have symptoms (16%)* or abnormal colonoscopy
- May be associated with rectal sparing (50%)**
- Most patients have extensive involvement

*Escorsell A et al J Hepatol 1994,**Loftus EV et al. Gut 2005

Risk of Colon Cancer

UC Duration	10 Years	20 Years	25 years
UC Only	2%	5%	10%
UC + PSC	9%	31%	50%

Broome U et al. Hepatology 1995

What do you do?

- If you have PSC get checked for UC
- If you have UC begin surveillance immediately
- Consider medication for prevention

Chemoprevention

- Ursodeoxycholic acid
- Mesalamine
- Folic acid if taking sulfasalazine

Ursodeoxycholic acid and Colon Cancer*

- 59 patients with PSC and UC studied
- 69% had used ursodiol
- 26% of patients had dysplasia
- Odds of neoplasia development decreased by 84%
- Average Ursodiol dose 10mg/kg by mouth
- Criticized study

Tung; Ann of Int Med 2001

Ursodeoxycholic Acid and Colon Cancer*

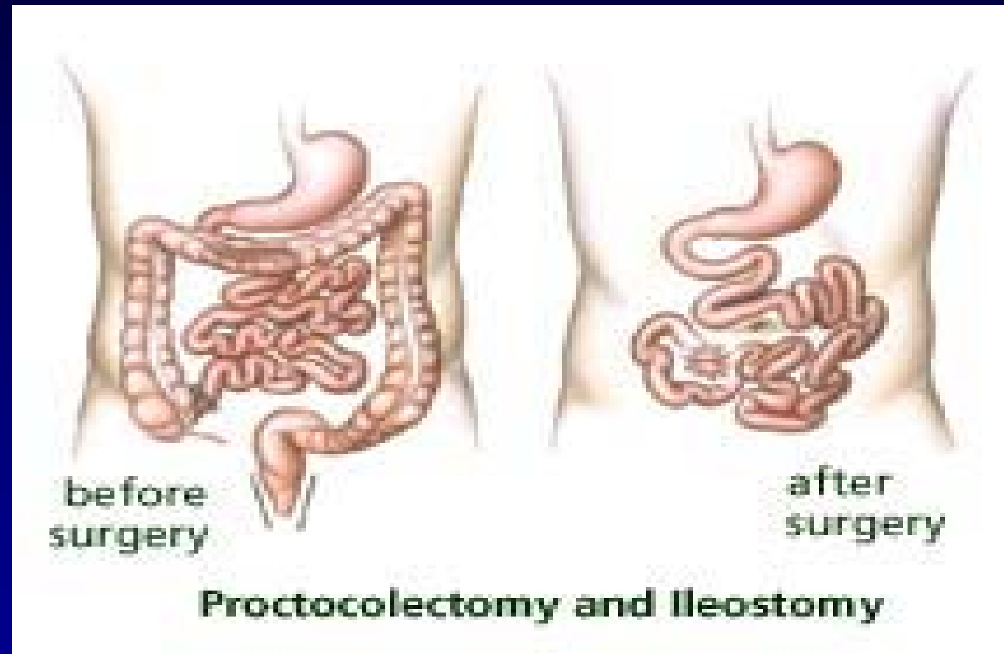
- 52 patients from a prior randomized trial
- Decreased risk of dysplasia and cancer by 74%
- Dose 13-15mg/kg/day
- Strong evidence

Pardi DS, Gastroenterol 2003

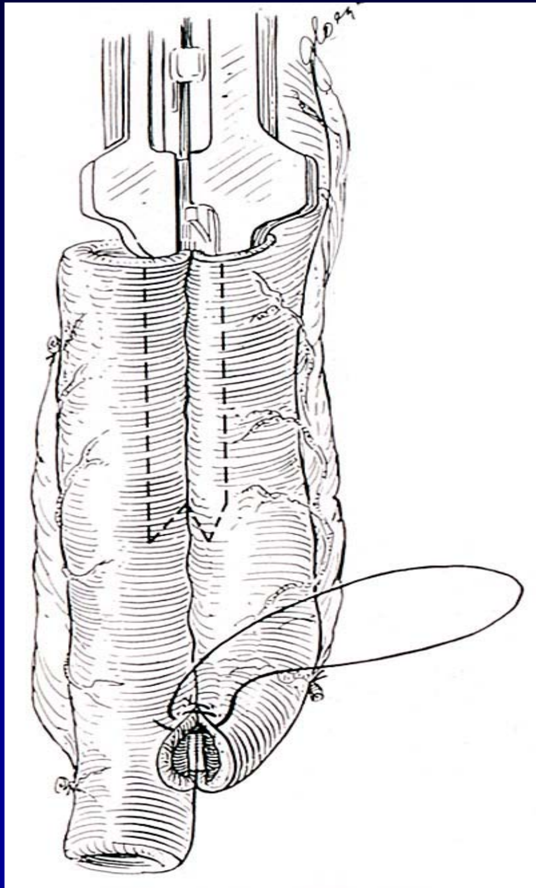
Our Practice

- UC alone: Mesalamine
- UC + PSC: Ursodiol + Mesalamine

Surgery for UC: Ileostomy

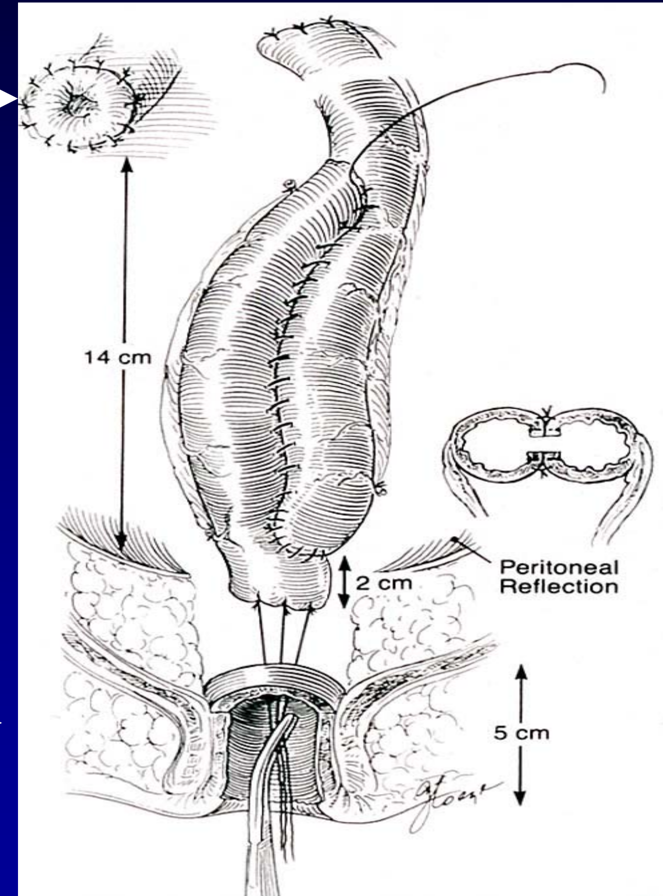


Ileal Pouch Construction



Temporary Ileostomy →
(Taken down at
second surgery)

Ileal Pouch pulled
down to anus and
attached to anal
verge (first surgery) →



Pouchitis and PSC

	Risk of Pouchitis		
Years After Surgery	1	5	10
UC	15.5%	36%	45.5%
UC + PSC	22%	61%	79%

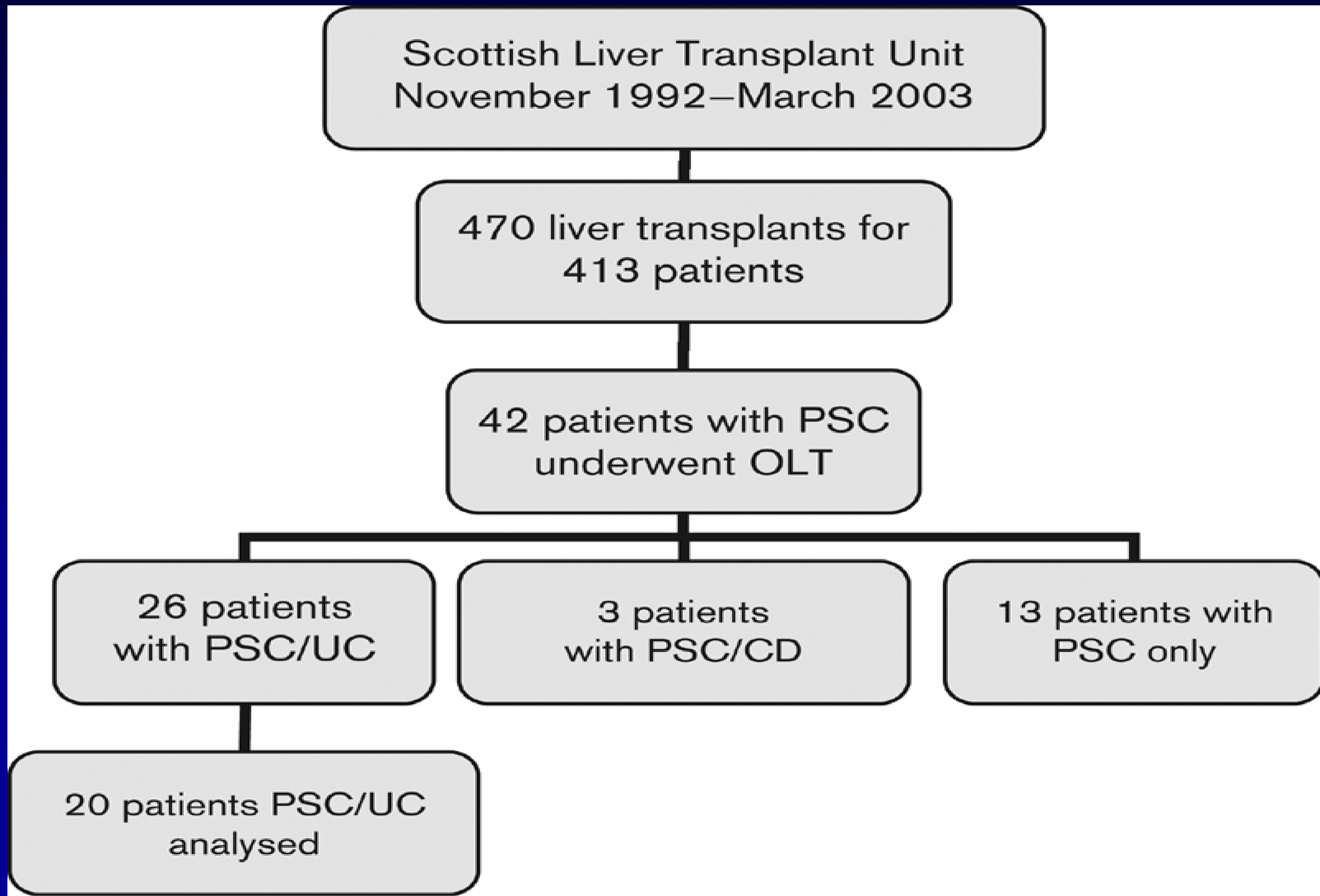
Penna C. Gut 1996

Surgery Outcomes

- Increased risk of acute and chronic pouchitis
- Ileoanal pouch is preferred surgery
- Ileostomy assocated with peristomal varices and bleeding

Transplant Outcomes

Gwo-Tzer Eur J Gastro&Hep 2006



Course of UC After Liver Transplant

- UC has a more aggressive course post-transplant despite immunosuppression
  - More Relapses
  - Greater need for corticosteroids
  - May have a higher rate of neoplasia

Gwo-Tzer et al Eur J Gastro&Hep 2006

Conclusions

- If you have PSC get checked for UC
- If UC found begin surveillance colonoscopy
- Find a physicans with expertise
- Prophylaxis with ursodeoxycholic acid
- Aggressive approach for treatment and cancer prevention
- GET CONNECTED!!

Resources for Patients

Crohn's & Colitis Foundation of America, Inc.

- Phone: 800-932-2423
- Website: http://www.ccfa.org

Pediatric Crohn's & Colitis Association, Inc.

- Phone: 617-489-5854
- Website: http://pcca.hypermart.net

Mayo Clinic IBD Team

- John Cangemi M.D.
- Michael F. Picco, M.D.,Ph.D.
- Donna Shelton A.R.N.P.

Mayo IBD Team

Division of Gastroenterology

Division of Colorectal Surgery
- Phillip Metzger, M.D.

Clinical Studies Unit

Mayo Clinic Resources

- Mayo IBD Group 904-953-2453
- On the Web “Mayo Clinic Jacksonville”
  - mayoclinic.org
  - mayoclinic.org/jacksonville/patientinfo
  - mayoc;linic.org/gi-jax