University of Colorado Hospital
CROHN'S & COLITIS CENTER

IBD and PSC
Integrated Medical and Surgical Care

Mark Gerich, MD
Assistant Professor of Medicine
Division of Gastroenterology
mark.gerich@ucdenver.edu

Jon Vogel, MD
Associate Professor of Surgery
Department of Surgery
jon.vogel@ucdenver.edu

www.uch.edu/ibd

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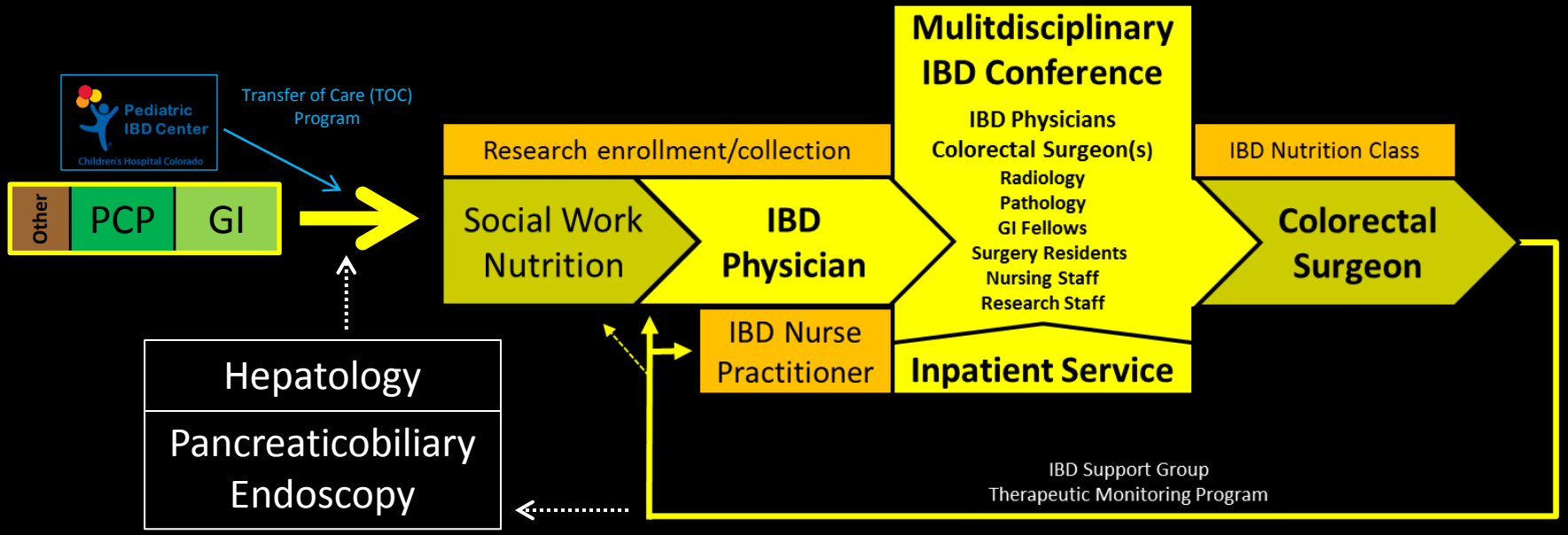


PSC-IBD
(PSC-associated IBD)

- Approximately ¾ of PSC patients have IBD

- PSC is more common in UC vs Crohn's

- PSC-IBD Characteristics:
  - Mild pancolitis
  - Rectal sparing
  - Very mild ileal inflammation ("backwash ileitis")

PSC-IBD
Management Issues

- Generally well-controlled
- Increased risk of colon dysplasia/cancer
- Up to one-third will have colectomy
- Pouchitis: 2/3 PSC vs 1/3 no PSC

PSC-IBD

Increased Risk of Colon Dysplasia/Cancer

- 5% Lifetime Risk of Colon Cancer in the General Population

Ulcerative Colitis	
10 years:	2%
20 years:	8%
30 years:	18%

PSC-IBD	
10 years:	10%
20 years:	33%
30 years:	40%

- Risk goes up soon after the diagnosis of coexisting PSC/IBD

→ Evaluate all patients with PSC for IBD
→ Start CRC screening immediately at diagnosis of PSC-IBD
→ Perform annual colonoscopy

Gut 1997;41:522-25
CGH 2011;9:52-56

PSC-IBD

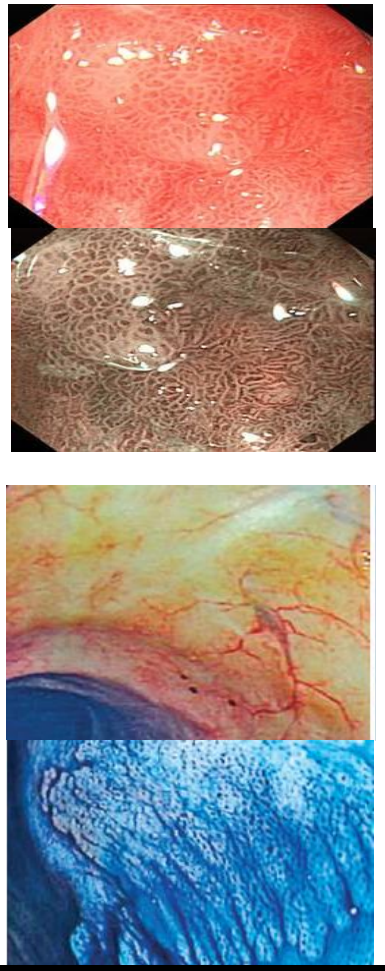
How to Reduce Colon Cancer Risk?

- Minimize inflammation
- No clearly effective medical prevention
  - Mixed results for ursodeoxycholic acid (UDCA)
- Annual colonoscopy (chromoendoscopy)

PSC-IBD

Methods of Colon Cancer Surveillance

- Narrow Band Imaging (NBI)
  - Blue light: hemoglobin absorption
  - Penetration of mucosa only
  - Highlights vessels
  - → No better than standard colonoscopy
- Chromoendoscopy
  - Spray blue dye to highlight abnormalities
  - Targeted biopsies, not random
  - Colon must be uninflamed and clean
  - → Better than standard/NBI

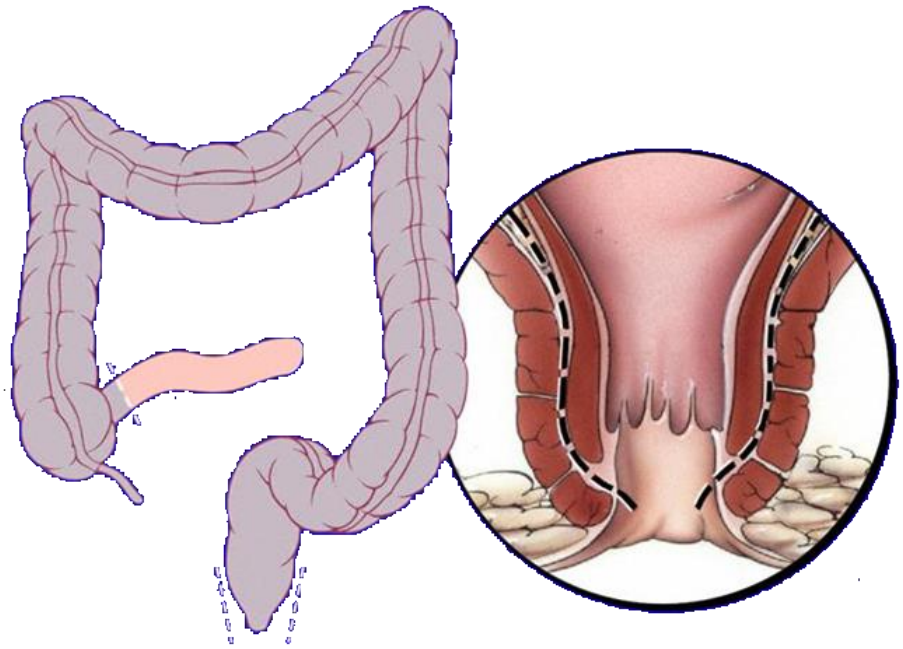


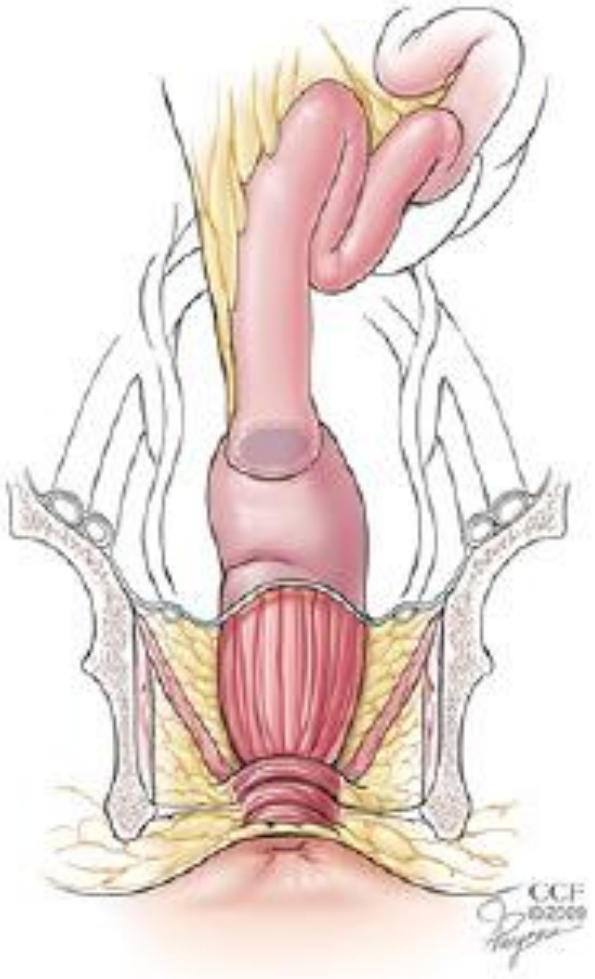
→ Chromoendoscopy is the emerging standard of care for colon cancer surveillance for PSC-IBD patients (and probably soon for all IBD patients)

Colorectal Surgery in PSC-IBD

- Why is colectomy performed?
- J-pouch or something less?
- If J-pouch, what does the PSC patient need to know?
- Is colectomy safe after a liver transplant?
- What effect will transplant have on colitis?

Total and Subtotal Colectomy

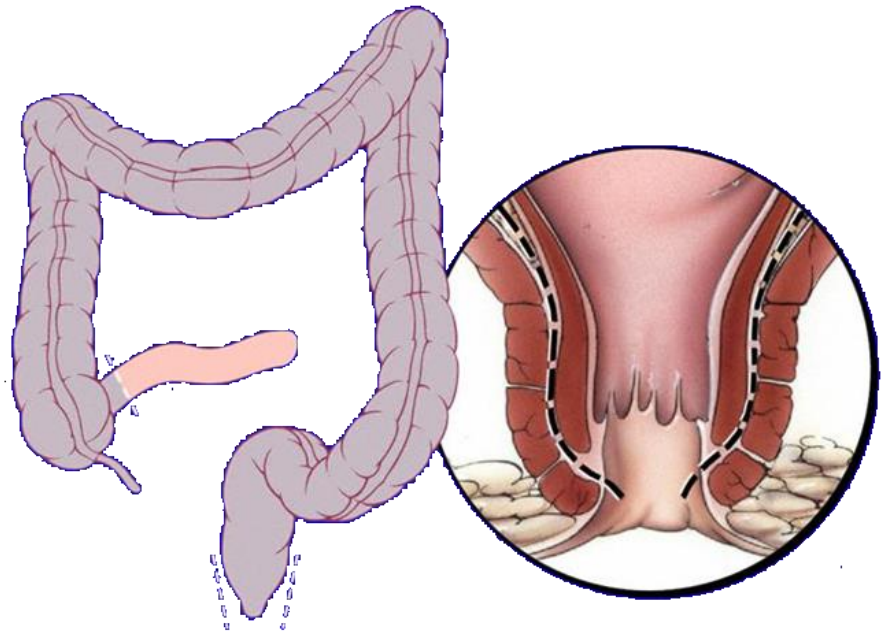




Rectal sparing in 52% PSC-UC compared to 6% in UC alone

--Loftus et al. IBD, 1997

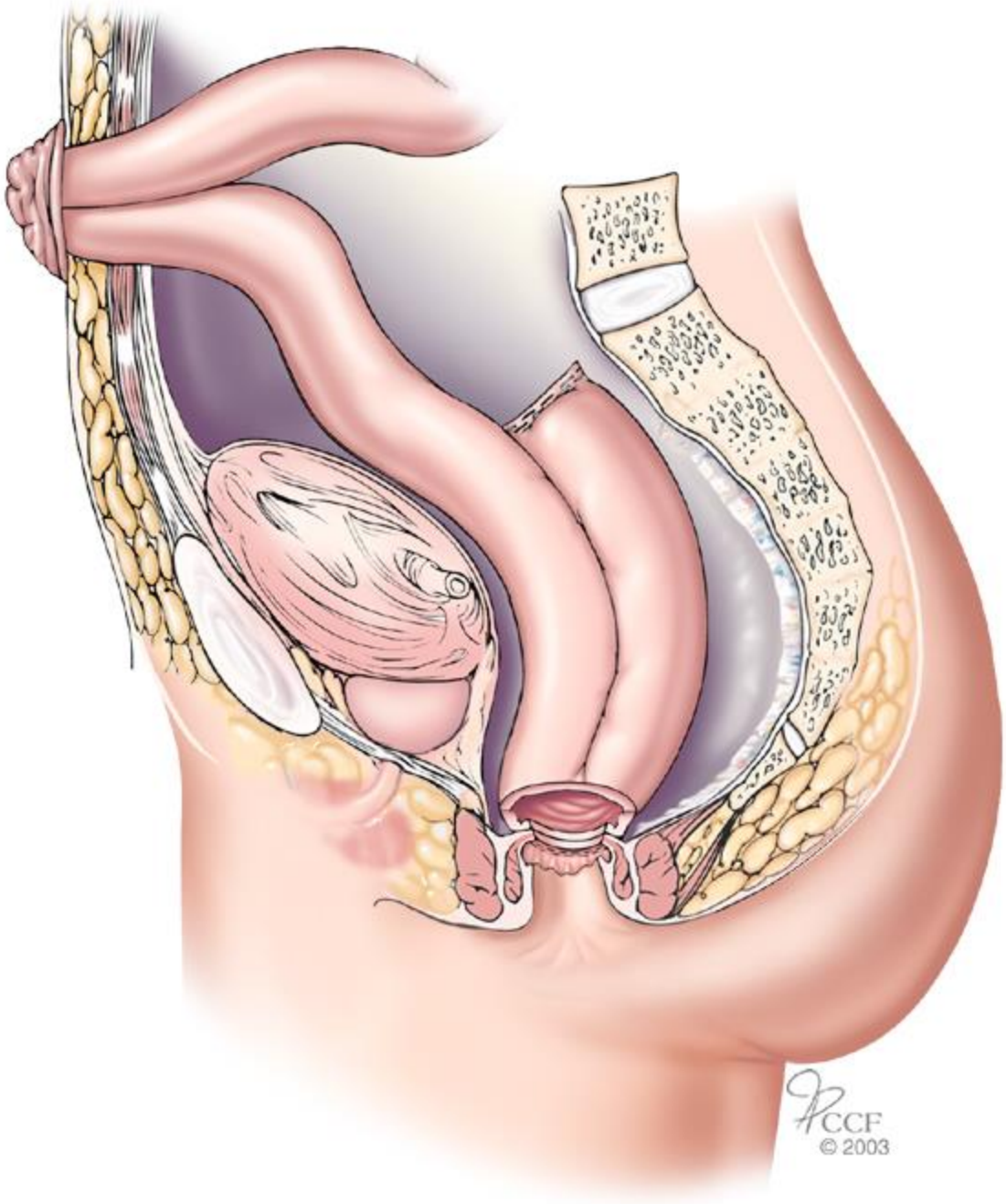
Total Colectomy (Proctocolectomy)



Indications

- **Significant co-morbidity**
- **Elderly, frail**
- **Marginal or poor sphincter strength**
- **Some rectal cancers**
- **Failed IPAA**
- **Morbid obesity**
- **Patient choice**

J-Pouch



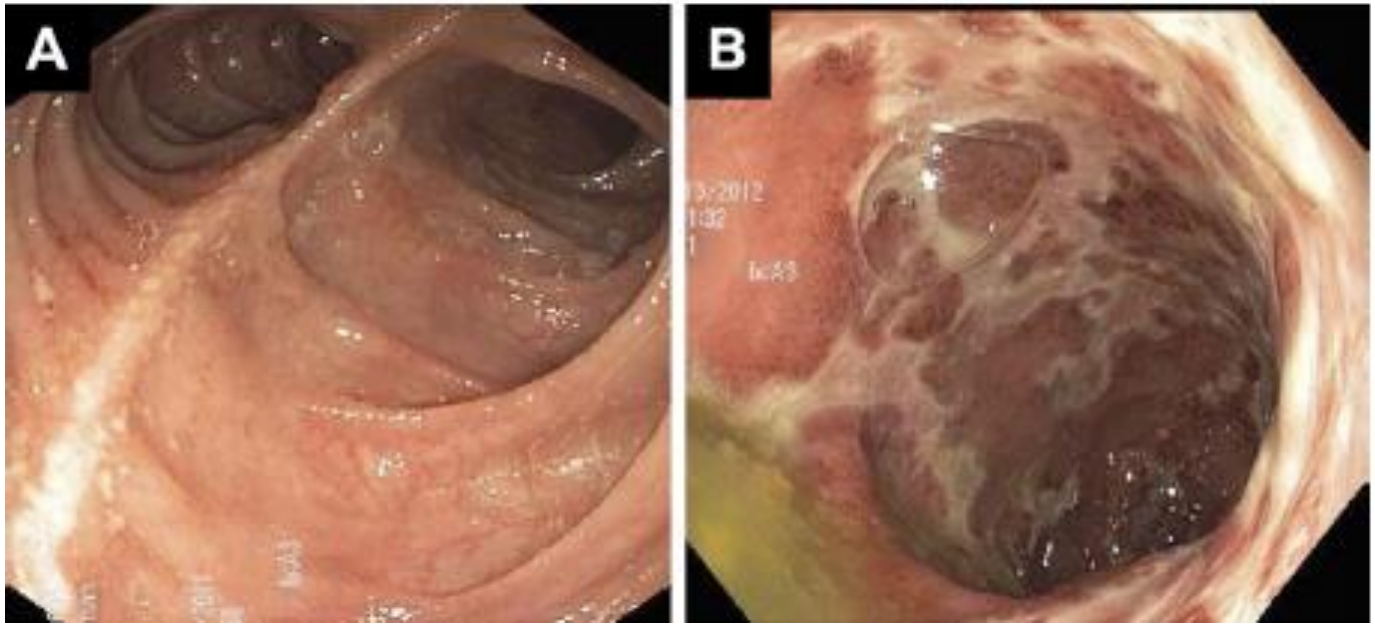
Ileal Pouch Outcomes (N=3703)

- **Early Morbidity**
  - **IPAA leak 5%, Pelvic sepsis 6%**
- **Late Morbidity**
  - **Failure 5%, SBO 13%, Pouchitis 34%,**
- **Function**
  - **BM: 5-7 per day, 1 at night**
  - **Pad use: 25%**
  - **Incontinence (never/rarely): 80%**
- **Female Infertility: 30-60%**
- **Female Sexual Dysfunction: 10-25%**

V. Fazio, Ann Surg 2013; JA Cornish, 2007; L. Beyer-Berjot, 2013; SG Rajaratnam, 2011

Pouchitis

Pouchitis occurs about twice as often in PSC-IBD patients compared to IBD patients



Shen B. CGH 2013;11:1538-1549

Ileal J-Pouch in PSC

- The 1-, 5-, 10- and 20-year risk of **acute pouchitis** for PSC-IPAA was 10%, 19%, 31% and 65% respectively, compared to 3%, 10%, 14% and 28% in UC-IPAA (p=0.03).

- More PSC-IPAA (36%) had poor **nocturnal pouch function** (vs 2% in UC-IPAA; p=0.0016).

- There were no differences in surgical complications, quality of life or sexual function between the 3 main groups.

→ PSC-IPAA suffer more acute pouchitis and have worse functional outcomes than UC-IPAA.

M. Pavlides, 2014, Oxford (UC-PSC 21, UC 79, 1983-2012)

IPAA after Liver Transplant for PSC

- We reviewed our multi-institutional experience performing proctocolectomy-IPAA for UC after Liver Transplant for PSC

- During a median follow-up of 52 months, complications have included transient dehydration (n = 6), chronic pouchitis (n = 2), recurrent PSC (n = 2), small bowel obstruction (n = 2), and pouch-anal anastomotic stricture (n = 1)

- Median 24-h stool frequency was 5, and fecal continence was reported as satisfactory by all patients

→ Proctocolectomy-IPAA can be performed safely after OLTX.

CS Choi, et al. J Gastrointest Surg. 2008 (1989-2006)

PSC-IBD
Liver Transplant Status and Colitis

- Cleveland Clinic, 1985-2011
- Liver transplant in 86, no liver transplant in 81
- In the no transplant group:
  - More UC flares
  - More often require colectomy (75 vs. 27%)
- Liver transplant independently decreases the risk for colectomy in UC-PSC (HR= 0.43)

U. Navaneethan, 2012

IBD Surgery in PSC: SUMMARY

- Colorectal Cancer/dysplasia
- Liver transplant appears to reduce the need for colectomy
- J-Pouch can be safely made after liver transplant
- Ileorectal anastomosis is an option
- Pouchitis is more common in PSC patients
- Screening for cancer must continue

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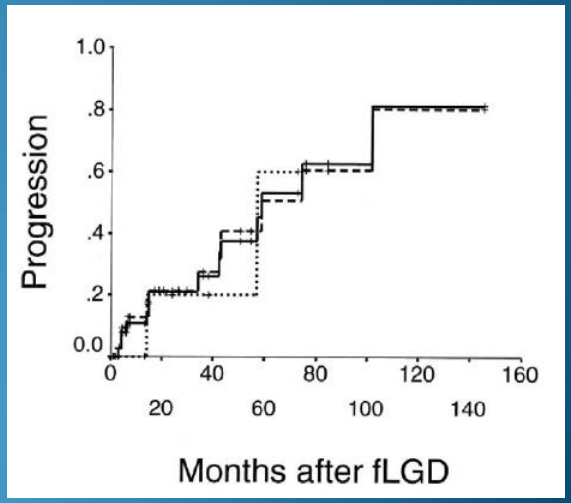
END

Low-Grade Dysplasia

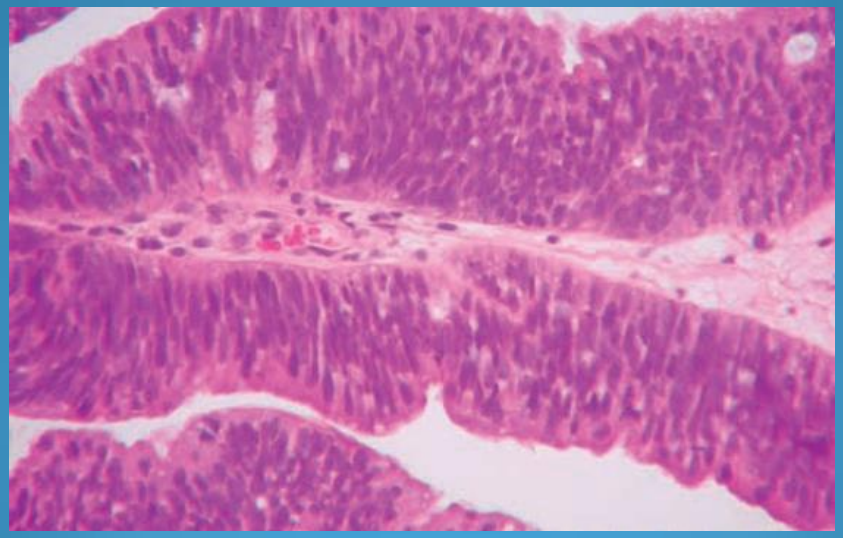
- Characterized by nuclei confined to basal half of the cell
- 30-54% risk for progression to HGD or CRC at 5 years
- 15-20% have CRC at immediate colectomy
- Multifocal LGD carries same risk of progression as unifocal
- May progress directly to CRC
  - 92% tubuloglandular carcinomas



Arch Pathol Lab Med 2010;134:876-95
Lancet 1994;343:71-74
Am J Surg Pathol 2006;30:1022-29
Gastroenterology 2004;126:1634-48
Gastroenterology 2003;125:1311–19

High-Grade Dysplasia

- Characterized by nuclei stratified haphazardly across basal & apical halves of the cell
- 32% risk for progression to CRC at some follow up period
- 42% have CRC at immediate colectomy



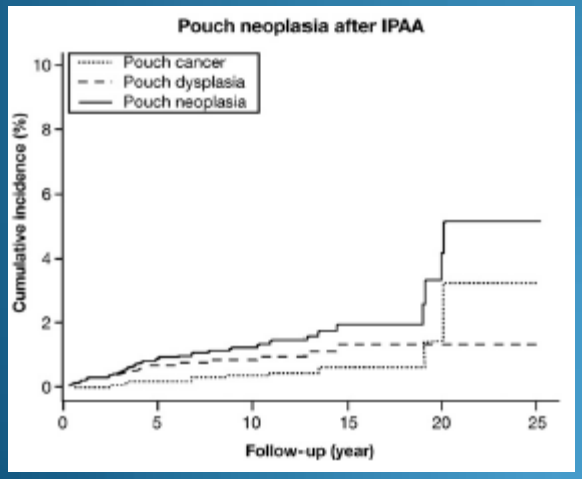
Arch Pathol Lab Med 2010;134:876-95
Lancet 1994;343:71-74

Ursodeoxycholic Acid

- Ann Intern Med. 2001;134:89-95
  - Decreased risk of dysplasia
    - aOR 0.14, p=0.005
    - Mean dose 10mg/kg
- Gastroenterology. 2003;124:889-93
  - Decreased risk of dysplasia
    - OR 0.26, p=0.034
- Aliment Pharmacol Ther. 2005;22:783-788
  - No change in risk of dysplasia, Improved overall mortality
    - Dysplasia - RR 0.59, p=0.17
    - Mortality – RR 0.44, p=0.02

Ileal Pouch Anal Anastamosis

- Is there a risk of cancer in the pouch or rectal cuff following IPAA?
  - Retrospective review, 3203 patients with IPAA for IBD
    - 38 (1.19%) patients with pouch neoplasia
      - 11 adenoca, 3 SCC, 1 lymphoma, 23 dysplasia



	All patients		Excluding rectal cancer/dysplasia[a]	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Male sex	1.4 (0.69–2.85)	1.16 (0.56–2.39)	1.63 (0.76–3.48)	1.39 (0.64–3.02)
Age at pouch construction	**1.03 (1.0–1.05)**	1.01 (0.98–1.04)	**1.03 (1.0–1.06)**	1.01 (0.97–1.04)
Duration of ulcerative colitis	**1.04 (1.01–1.08)**	1.01 (0.97–1.05)	**1.05 (1.01–1.08)**	1.02 (0.98–1.06)
Primary sclerosing cholangitis	1.06 (0.14–7.74)	0.41 (0.05–3.19)	1.31 (0.18–9.63)	0.54 (0.07–4.14)
Chronic pouchitis	0.73 (0.25–2.06)	0.69 (0.24–2.00)	0.81 (0.28–2.31)	0.75 (0.26–2.15)
Extensive colitis	1.26 (0.44–3.60)	1.53 (0.53–4.39)	1.70 (0.52–5.60)	1.84 (0.55–6.12)
Colectomy for cancer	**8.92 (3.13–25.38)**	**13.43 (3.96–45.53)**	**13.7 (4.15–45.18)**	**17.53 (4.51–8.17)**
Colectomy for dysplasia	**3.24 (1.59–6.58)**	**3.62 (1.59–8.23)**	**3.37 (1.58–7.21)**	**3.38 (1.43–7.98)**
Mucosectomy	1.23 (0.54–2.80)	0.78 (0.34–1.8)	1.19 (0.49–2.88)	0.75 (0.3–1.86)

Gastroenterology 2010;139:806–812