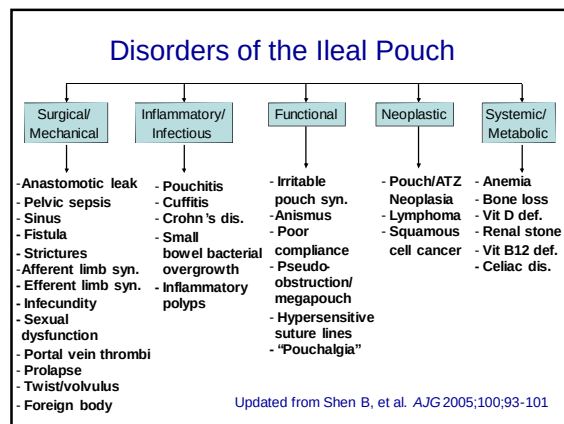
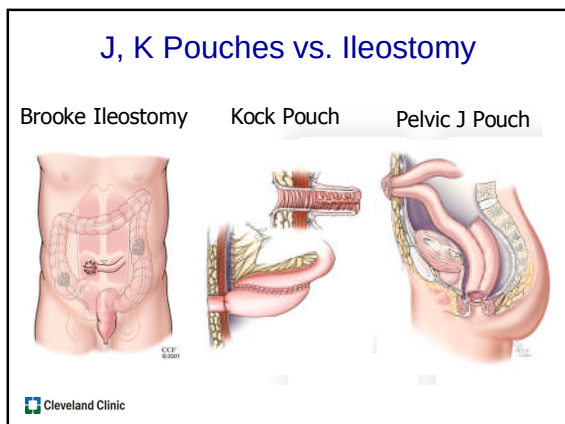
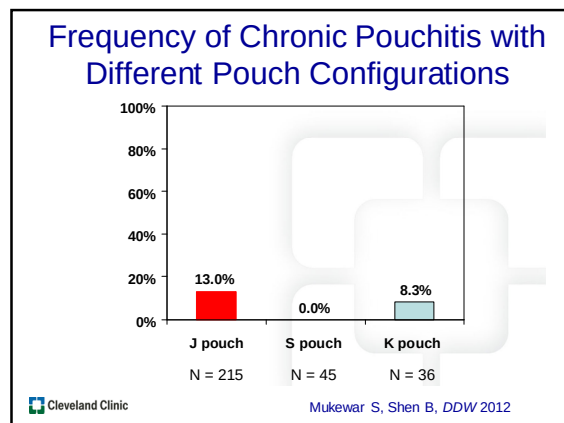
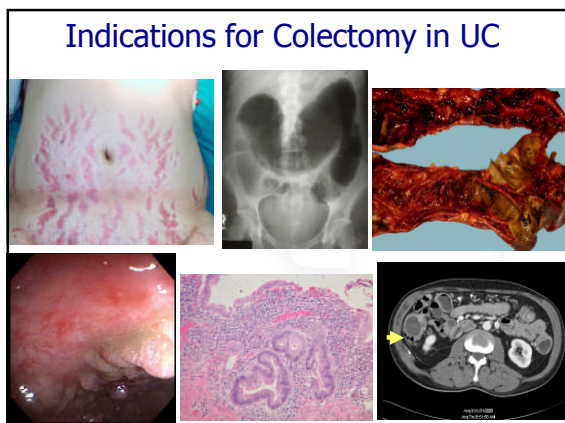
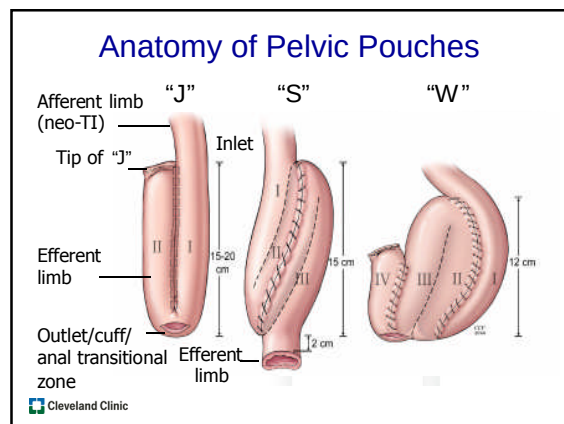
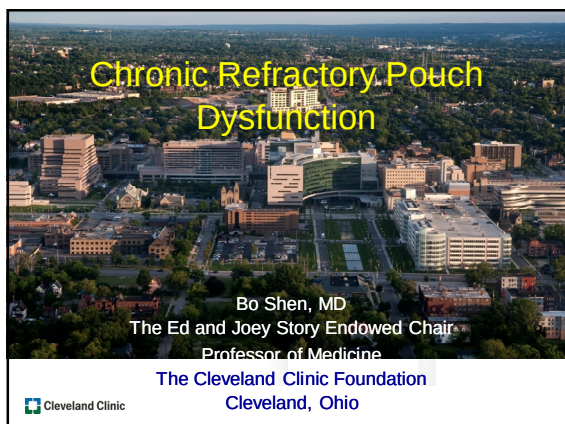
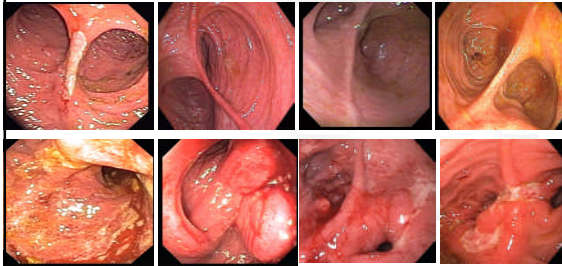


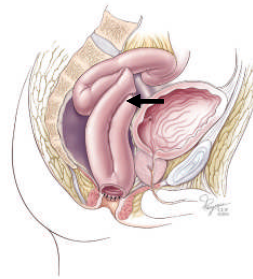


Owl's Eyes and Pouch Dysfunction



Cleveland Clinic

Afferent Limb Syndrome

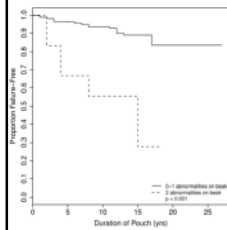


Shen B, Remzi FH, Fazio VW. *CGH* 2008;6:145-58

Cleveland Clinic



Endoscopic Predictors of Pouch Failure



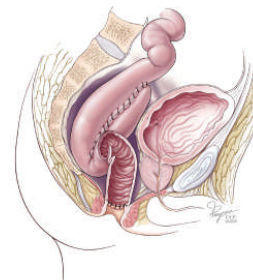
Factor	HR (95% CI)	p
Crohn's pouch	2.7 (1.2, 6.3)	0.018
Surgical complications	4.4 (1.7, 11.2)	0.002
Post-operative biologics	5.3 (2.5, 11.2)	<0.001
2 abnormalities of "Owl's beak"	3.6 (1.5, 8.7)	0.005
Cuff endoscopy score	1.5 (1.3, 1.7)	<0.001

N = 426

Cleveland Clinic

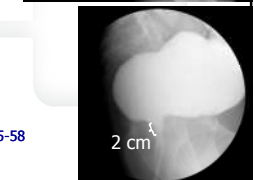
Alder K, Shen B. *IBDJ* 2013

Efferent Limb Syndrome

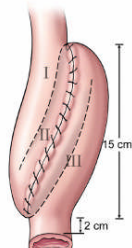


Shen B, Remzi FH, Fazio VW. *CGH* 2008;6:145-58

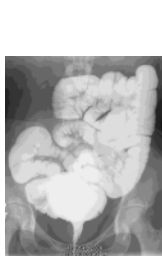
Cleveland Clinic



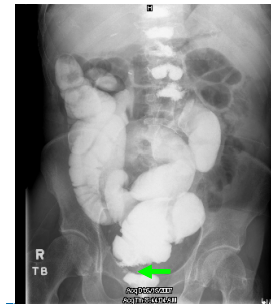
S pouch (no owl's eyes)



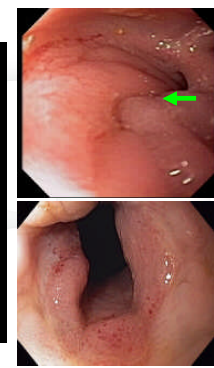
Cleveland Clinic

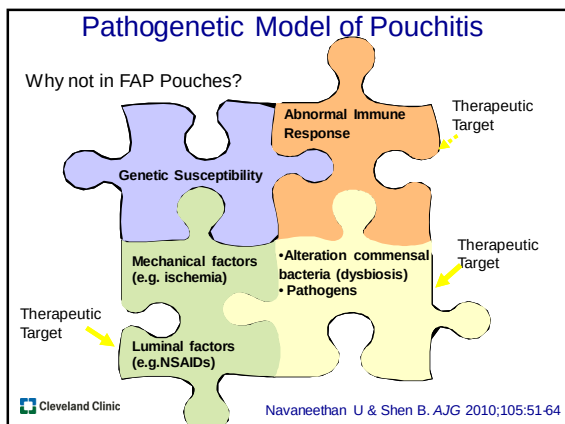
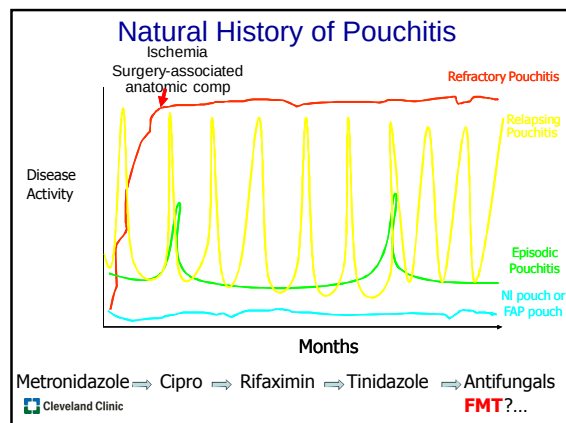
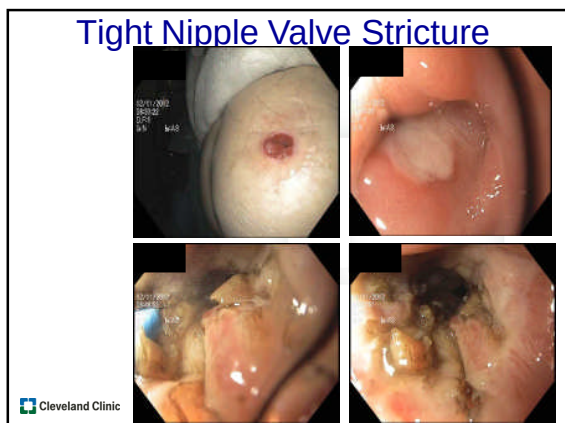
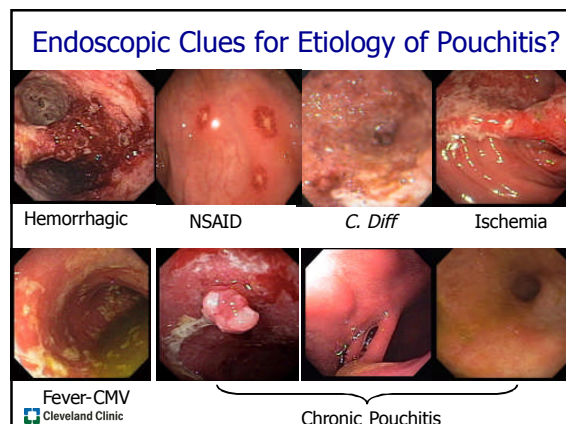
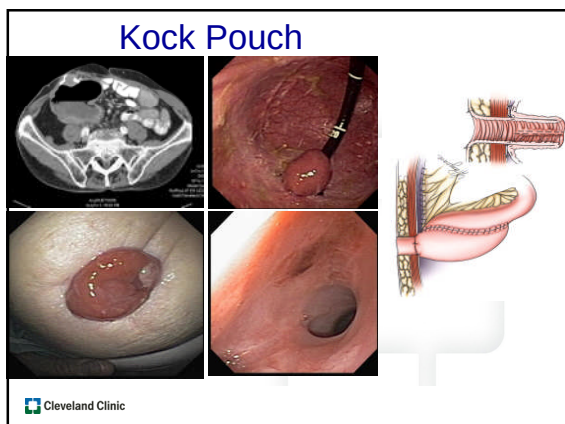


Twisted Pouch



Cleveland Clinic





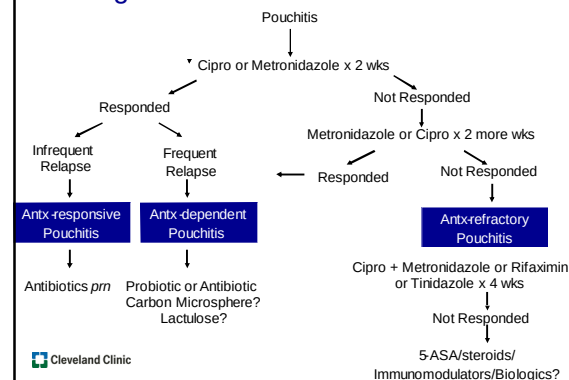
- ### Risk Factors for Pouchitis
- Extensive UC
 - Backwash ileitis
 - Primary sclerosing cholangitis
 - P-ANCA
 - IL-1ra, NOD2 polymorphisms
 - NOD2 gene polymorphisms
 - Precolectomy thrombocytosis
 - Non-smoker
 - NSAIDs
 - Arthralgia
 - Surgical techniques??
- Fazio VW, et al. Ann Surg 1995
Schmidt CM, et al. Ann Surg 1998
Lohmuller JL, et al. Ann Surg 1990
Fleshner P, et al. Gut 2003
Achkar JP, et al. CGH 2005
Shen B, et al. AJG 2005
Meier CB, et al. IBDJ 2005
Shen B, et al. CGH 2006
Fleshner P, et al. CGH 2007
Koltun W, et al. DCR 2011
Tyler A, et al. Gut 2012

RCT of Antibiotic Therapy in Pouchitis

Authors	N	Type of pouchitis	Agent	Days	Median Δ in PDAI score
Madden 1994	13	Chronic pouchitis	Metro 400 mg TID vs. placebo	7	N/A
Shen 2001	16	Acute pouchitis	Cipro 1 g/d vs. n Metro. 20 mg/kg/d	14	Cipro -6.7 Metro -5.9
Isaacs 2007	8	Acute or Chronic pouchitis	Rifaximin 1.2 g/d vs. placebo	28	-1.6 in study group

Cleveland Clinic

Management of “Conventional” Pouchitis



Cleveland Clinic

Open-labeled Trials of Antibiotics in Pouchitis

Study	N	Type of pouchitis	Drugs	Duration (days)	Median Δ in PDAI
Madiba 1994	47	acute p. antx dependent p. chr antx refractory p.	Metro 200 mg TID	30	Clin response in 77% acute p.
Shen 2008	51	Antibiotic dependent p.	Rifaximin 200 mg/day	90	-3
Shen 2007	16	Chronic antx refractory p.	Cipro 1 g/day + Tinidazole 15mg/kg/d	28	-7
Gionchetti 2008	18	Chronic antx refractory p.	Cipro 1 g/d + Rifaximin 2 g/d	15	-7
Abdelazraq 2005	8	Chronic antx refractory p.	Cipro 1 g/d + Rifaximin 2g/d	14	-12
Kombluth 2006	16	Chronic antx refractory p.	Rifaximin 0.6-0.8 g/d	21	Clin response in 81%
Mimura 2002	44	Refractory acute p.	Metro. 800-1000mg/d + Cipro 1 g/d	28	-9
Hurst 1996	52	Acute antx responsive p.	Metro. 750 mg/d or Cipro 1 g/d	7	Clin response in 94%

Cleveland Clinic

Idiopathic Pouchitis (dysbiosis-associated)

Cleveland Clinic

Probiotics in Primary or Secondary Prophylaxis of Pouchitis

Authors	Year	N	Design	Outcome
Gionchetti/Gastro	2000	40	RCT	Relapse 9 mo: 15% vs 100%
Gionchetti /Gastro	2003	40	RCT	2 (10%) in study group; 8 (40%) in placebo group had pouchitis at 12 mo
Mimura/Gut	2004	36	RCT	Relapse 9 mo: 6% vs 85%
Shen/APT	2005	31	Open-labeled	On VSL3 at 8 mo: 19%
McLaughlin/DDW	2008	13	Open-labeled	Remission 13%

Cleveland Clinic

Rationale for Antibiotic/Probiotic Therapy in Idiopathic Pouchitis

- “Shoot blindly”
- Target: dysbiosis
 - alteration in quality/quantity of commensal bacteria
- Consequences
 - Bacterial resistance
 - Opportunistic infection (*C. difficile*)

Cleveland Clinic

Fecal Coliform Culture in Pouchitis

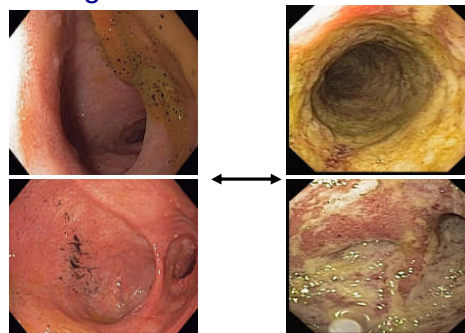
	Number Patients	Resistant	Sensitive + Treat
<i>E. Coli</i>	6	Ciprofloxacin (100%)	Co-amoxiclav (53%)
<i>Klebsiella</i>	1	Co-amoxiclav (40%)	Trimethoprim (13%)
Coliform, not classified	12	Cefixime (60%)	Colistin (33%)
<i>Pseudomonas</i>	1	Trimethoprim (73%)	
<i>Morganella</i>	1		

4-wk treatment with sensitive antibiotics (N =15):
 - Median 24-hr stool frequency: 14 → 9
 - Median PDAI symptom score: 4 → 0

Cleveland Clinic

McLaughlin SD. *CGH* 2009;7:545

Range of *C. difficile* Pouchitis



"Innocent?" superimposed "infectant"? or original culprit?

Cleveland Clinic

Secondary Pouchitis (with identifiable etiology/triggering factors)

- Pathogen-associated pouchitis
- NSAID-induced pouchitis
- Ischemic pouchitis
- Immune-mediated pouchitis

Cleveland Clinic

Campylobacter Pouchitis



Fever, malaise, dehydration

Rx: Erythromycin



Cleveland Clinic

Shen B, et al. *AJG* 2010;105:472-3

Clostridium difficile Infection in Pouch

Authors	Year	N	Prevalence	Outcome
Mann/ DCR	2003	1	-	Recovered
Shen/ DDS	2006	1	-	Recovered
Shen/ CGH	2008	115	18%	Risk factors: Male (OR=5.0)
Shen/NRGH	2009	1	-	Fatal
LI/IBDJ	2013	196	11% (PCR for toxin B)	Refractory/Recurrence to vancomycin



C. diff
pouchitis



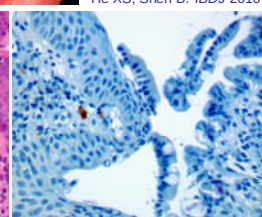
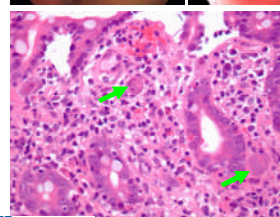
C. diff
enteritis

Cleveland Clinic

CMV Pouchitis

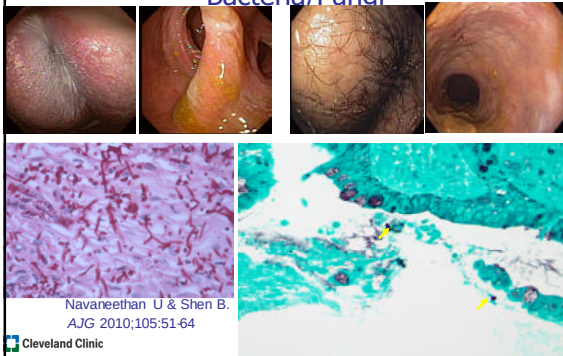


He XS, Shen B. *IBDJ* 2010

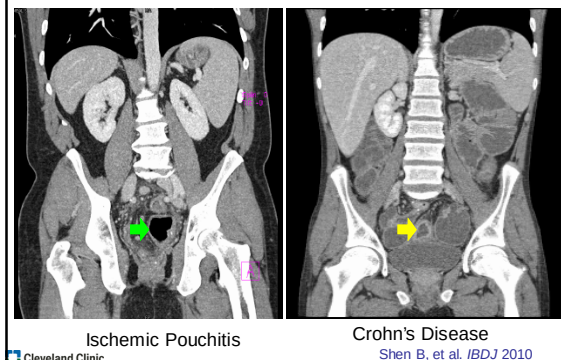


Cleveland Clinic

Candida: Part of Mucosal Associated Bacteria/Fungi



Imaging Features of Ischemic Pouchitis



Ischemic Pouchitis

Clues:

- Male
- "Difficult pouch" in operative note (the issue of "reach")
- Obese or excessive weight gain (>15% of baseline)
- Abdominal surgery (hernia repair, mesh)
- Portal vein thrombi
- Antibiotic refractory



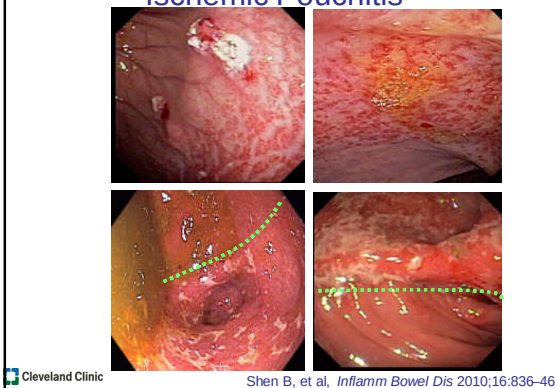
Shen B, et al, *Inflamm Bowel Dis* 2010;16:836-46

Implication of the Identification of Ischemic Pouchitis

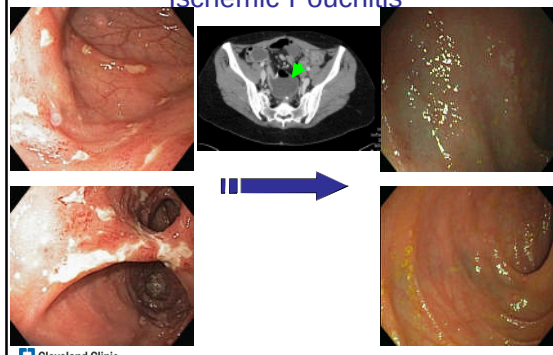
- Different from ischemic colitis or mesenteric ischemia
 - Necrosis/bowel infarction hardly occurs
 - Doppler or angiogram often negative
- Potential surgical treatment
 - Lysis of adhesion
 - Pouch revision or redo pouch (J → J; J → K)



Ischemic Pouchitis



Lysis of Adhesion in Treatment of Ischemic Pouchitis



Clinical Clues for Immune-mediated Pouchitis

- Pouchitis + enteritis
- Chronic antibiotic-refractory pouchitis
- Concurrent autoimmune disorders
- Serum autoantibodies



1-Year Budesonide in PSC-associated Pouchitis/Enteritis

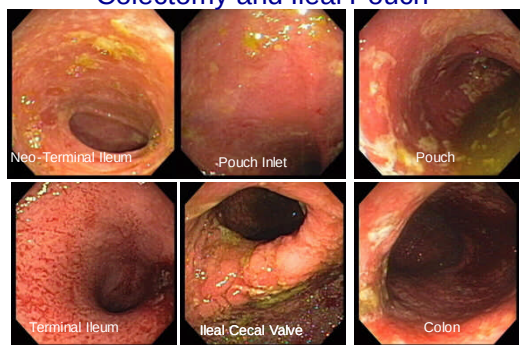
	Pre-	Post-	P
Afferent limb Endoscopy Score	2.3 ± 1.9	0.8 ± 1.0	0.001
Pouch Endoscopy Score	2.5 ± 2.2	0.7 ± 0.9	0.001

- N = 18
- Induction: 9mg/day 1 – 3 months
- Maintenance: 3mg/day
- No impact on LFTs



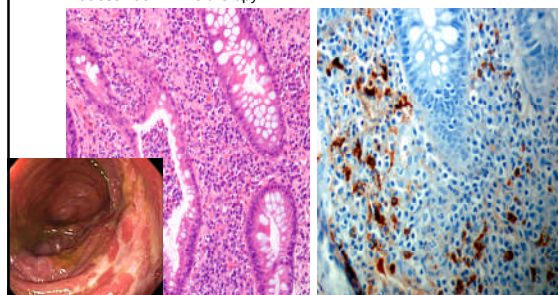
Navaneethan U, et al. JCC 2012;6:536-42

Enteritis in PSC + UC with or without Colectomy and Ileal Pouch



IgG4-associated Pouchitis

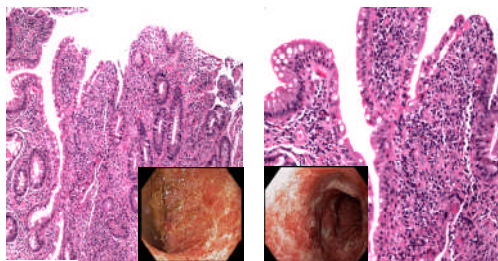
- 29% in refractory pouchitis
- Serum IgG4 may be normal
- Current autoimmune disorders are common
- Budesonide-1st line therapy



Navaneethan U, et al. JCC 2011;5:570-6

PSC-associated Pouchitis/Enteritis

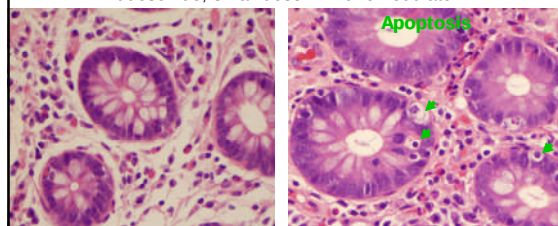
- Long segment of distal small bowel disease in addition to diffuse pouchitis
- Concurrent autoimmune disorders are common (31% vs. 6% in control)
- Budesonide-1st line therapy



Shen B. IBDJ 2011;17:1890-900

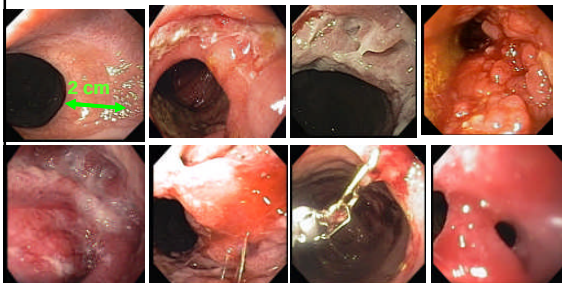
Autoimmune (GVHD-like) Pouchitis

- Chronic antibiotic-refractory pouchitis
- Concurrent autoimmune diseases
- Serum auto-antibodies
- Budesonide, small dose immunomodulator

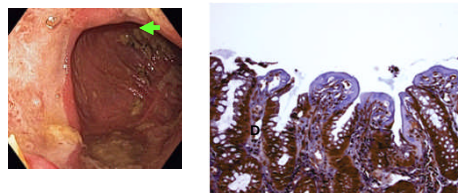


Jiang W, et al. DCR 2012;55:459-57

Cuffitis: A Residual UC?

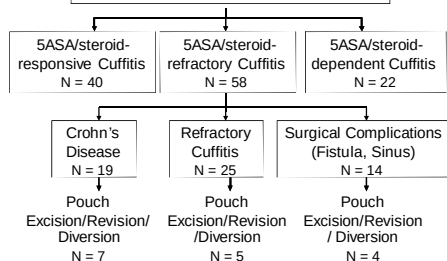


Ischemic/Collagenous Cuffitis



Shen B, et al. IBDJ 2010

Cuffitis Diagnosis at the 1st Visit*

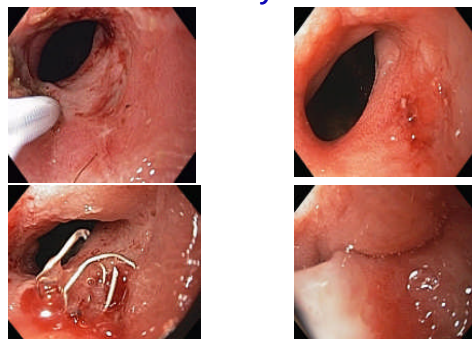


*Mean duration of IBD before colectomy = 7.4 ± 7.2 yrs

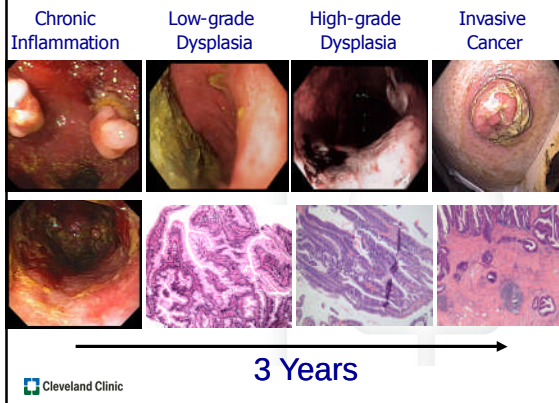
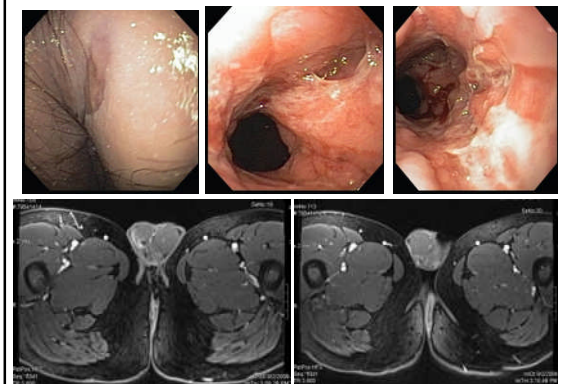
Mean duration of the pouch = 7.1 ± 5.3 yrs

Wu B, et al. IBDJ 2013

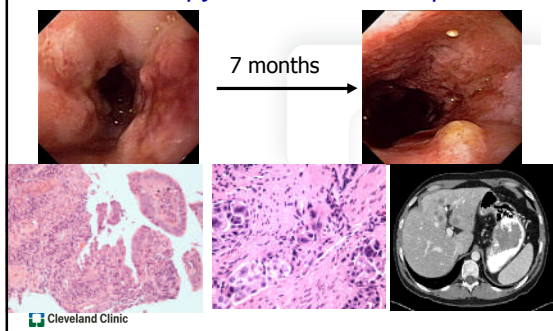
Lysis Adhesion in Treatment of "Refractory Cuffitis"



Refractory Cuffitis-A Sign of CD?



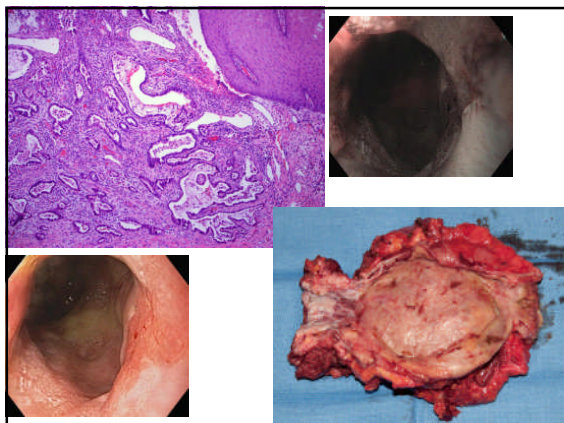
Pouch Cancer/Dysplasia: Is Surveillance Endoscopy Indicated & Adequate?



Cox Model for Risk Factors for Pouch Neoplasia

	Adjusted HR (95%CI)	P
Male gender	1.16 (0.56-2.39)	0.686
Age at pouch	1.01 (0.98-1.04)	0.586
Duration of UC	1.01 (0.97-1.05)	0.547
PSC	0.41 (0.05-3.19)	0.394
Chronic pouchitis	0.69 (0.24-2.00)	0.497
Extensive colitis	1.53 (0.53-4.39)	0.430
Colectomy for cancer	13.43 (3.96-45.53)	<0.0001
Colectomy for dysplasia	3.62 (1.59-8.23)	0.002
Mucosectomy	0.78 (0.34-1.8)	0.559

Kariv R, et al. *Gastroenterology* 2010;139:806-812.



Classification of Crohn's Disease of Pouch



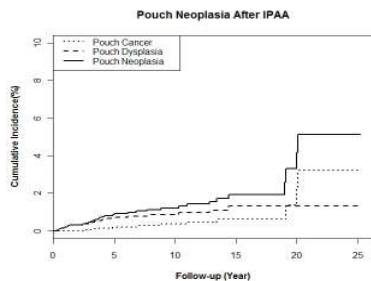
Inflammatory

Fibrostenotic

Fistulizing

Cleveland Clinic

Pouch Neoplasia: Cleveland Clinic Experience N=3203

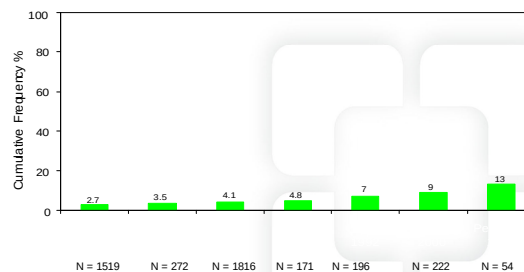


adenocarcinoma 11; lymphoma 1; SCC 3; dysplasia 23

Cleveland Clinic

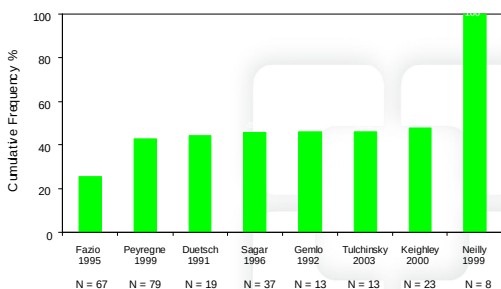
Kariv R, et al. *Gastroenterology* 2010;139:806-812.

Crohn's Disease in Patients with IPAA



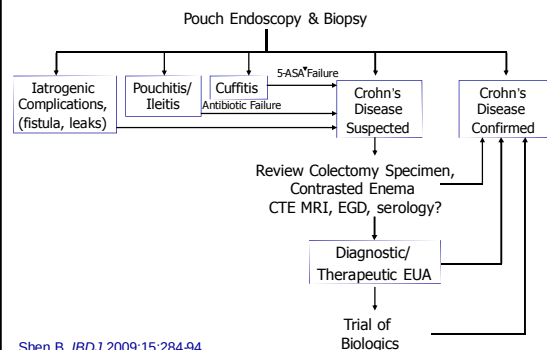
Cleveland Clinic

Pouch Failure in Patients with Crohn's Disease

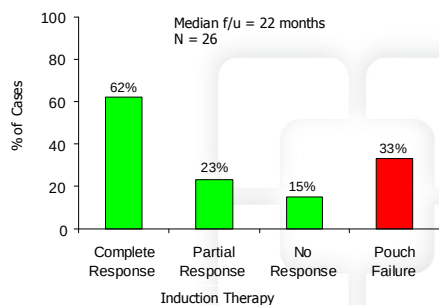


Cleveland Clinic

Diagnostic Algorithm for Crohn's Pouch

Shen B. *IBDJ* 2009;15:284-94

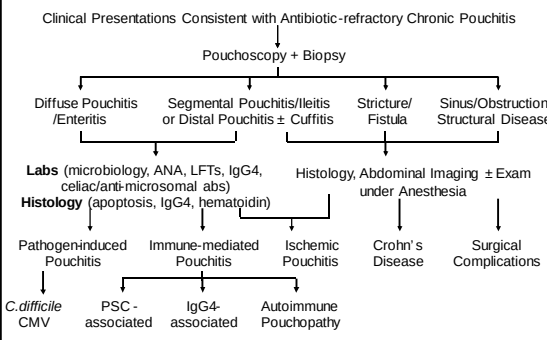
Open-Labelled Trial Infliximab in Fistulizing Crohn's Disease of the Pouch



Cleveland Clinic

Colombel JF, et al. *AJG* 2005

Diagnosis/Management of Pouch Disorders

Shen B. *CGH* 2013

Adalimumab for Crohn's Disease of Pouch

Factor	Short term	Long term
Clinical response (N=48)		
None (%)	14(29.2)	22(45.8)
Partial (%)	10(20.8)	10(20.8)
Complete (%)	24(50.0)	16(33.3)
Clinical response inflammatory or fibrostenotic disease (N=23)		
None (%)	7(30.4)	12(52.2)
Partial (%)	6(26.1)	4(17.4)
Complete (%)	10(43.5)	7(30.4)
Clinical response in fistulizing disease (N=25)		
None (%)	7(28.0)	10(40.0)
Partial (%)	4(16.0)	6(24.0)
Complete (%)	14(56.0)	9(36.0)
Mucosal healing (%)	20(41.7)	13(27.1)
Pouch failure (%)	NA	9(18.8)

Cleveland Clinic

Li Y, et al. *IBDJ* 2012;18:2232-9

Summary

- A number of patients with chronic refractory pouch dysfunction in fact have surgery-associated mechanical or structural disorders
- Pouchitis is disease spectrum with ranging etiopathogenetic pathways, disease course, and prognosis
- De novo* Crohn's disease can occur in pouch patients with a preoperative diagnosis of UC
- Emerging *C. difficile* infection is challenging
- Cuffitis can in patients with restorative colectomy with ileal pouches
- Cancer risk persists after colectomy
- Most pouch cancer occurs at the cuff area

Thank You!

