**J, S, K Pouches vs. Ileostomy**

Brooke Ileostomy  Kock Pouch  Pelvic J Pouch

**Anatomy of Pelvic Pouches**

Afferent limb (neo-T1)  Tip of “J”  Inlet  Efferent limb

Outlet/cuff  Efferent limb

Shen B. 2012
Disorders of the Ileal Pouch

**Surgical/ Mechanical**
- Anastomotic leaks
- Pelvic sepsis
- Pouch sinuses
- Pouch fistulae
- strictures
- Afferent limb syn.
- Efferent limb syn.
- Infecundity
- Sexual dysfunction
- Portal vein thrombi
- Pouch prolapse
- Foreign bodies

**Inflammatory/ Infectious**
- Pouchitis
- Crohn’s dis.
- Small bowel bacterial overgrowth
- Inflammatory polyps

**Functional**
- Irritable pouch syn.
- Anismus
- Poor compliance
- Pseudo-obstruction/ megapouch
- Hypersensitive suture lines
- “Pouchalgia”

**Neoplastic**
- Pouch/ATZ Neoplasia
- Lymphoma
- Squamous cell cancer

**Systemic/ Metabolic**
- Anemia
- Bone loss
- Vit D def.
- Renal stone
- B12 deficiency
- Celiac dis?

Pathogenetic Model

**Why not in FAP Pouches?**

**Abnormal Immune Response**
- Alteration commensal bacteria (dysbiosis)
- Pathogens

**Genetic Susceptibility**

**Mechanical factors (e.g. ischemia)**

**Luminal factors (e.g. NSAIDs)**

**Therapeutic Target**

Updated from Shen B, et al. AJG 2005

Navaneethan U & Shen B. AJG 2010;105:51-64
Histologic Evolution from Colonic Metaplasia to Pouchitis: Role of Fecal Stasis?

Endoscopic Clues for Etiology of Pouchitis?
Natural History of Pouchitis

- Ischemia
- Surgery-associated anatomic comp

Disease Activity

Months

- Metronidazole
- Cipro
- Rifaximin
- Tinidazole
- Antifungals

RCT of Antibiotic Therapy in Pouchitis

<table>
<thead>
<tr>
<th>Authors</th>
<th>N</th>
<th>Type of pouchitis</th>
<th>Agent</th>
<th>Days</th>
<th>Median Δ in PDAI score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Madden 1994</td>
<td>13</td>
<td>Chronic pouchitis</td>
<td>Metro 400 mg TID vs. placebo</td>
<td>7</td>
<td>N/A</td>
</tr>
<tr>
<td>Shen 2001</td>
<td>16</td>
<td>Acute pouchitis</td>
<td>Cipro 1 g/d vs. Met. 20 mg/kg/d</td>
<td>14</td>
<td>Cipro -6.7, Metro -5.9</td>
</tr>
<tr>
<td>Isaacs 2007</td>
<td>8</td>
<td>Acute or chronic pouchitis</td>
<td>Rifaximin 1.2 g/d vs. placebo</td>
<td>28</td>
<td>-1.6 in study group</td>
</tr>
</tbody>
</table>
## Open-labeled Trials of Antibiotics in Pouchitis

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Type of pouchitis</th>
<th>Drugs</th>
<th>Duration (days)</th>
<th>Median ( \Delta ) in PDAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shen 2008</td>
<td>51</td>
<td>Antibiotic dependent p.</td>
<td>Rifaximin 200 mg/day</td>
<td>90</td>
<td>-3</td>
</tr>
<tr>
<td>Shen 2007</td>
<td>16</td>
<td>Chronic antx refractory p.</td>
<td>Cipro 1 g/day + Tinidazole 15 mg/kg/d</td>
<td>28</td>
<td>-7</td>
</tr>
<tr>
<td>Gionchetti 2008</td>
<td>18</td>
<td>Chronic antx refractory p.</td>
<td>Cipro 1 g/d + Rifaximin 2 g/d</td>
<td>15</td>
<td>-7</td>
</tr>
<tr>
<td>Abdelrazaq 2005</td>
<td>8</td>
<td>Chronic antx refractory p.</td>
<td>Cipro 1 g/m/d + Rifaximin 2 g/d</td>
<td>14</td>
<td>-12</td>
</tr>
<tr>
<td>Kombluth 2006</td>
<td>16</td>
<td>Chronic antx refractory p.</td>
<td>Rifaximin 0.6-0.8 g/d</td>
<td>21</td>
<td>Clin response in 81%</td>
</tr>
<tr>
<td>Mimura 2002</td>
<td>44</td>
<td>Refractory acute p.</td>
<td>Metro. 800-1000 mg/d + Cipro 1 g/m/d</td>
<td>28</td>
<td>-9</td>
</tr>
<tr>
<td>Hurst 1996</td>
<td>52</td>
<td>Acute antx responsive p.</td>
<td>Metro. 750 mg/d or Cipro 1 g/d</td>
<td>7</td>
<td>Clin response in 94%</td>
</tr>
</tbody>
</table>

## Probiotics* in Primary or Secondary Prophylaxis of Pouchitis

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

*VSL#3
**primary prophylaxis
Management of “Conventional” Pouchitis

Pouchitis

Cipro or Metronidazole x 2 wks

Responded

Infrequent Relapse

Antx-responsive Pouchitis

Antibiotics prn

Frequent Relapse

Probiotic or Antibiotic
Carbon Microsphere?
Lactulose?

Antx-dependent Pouchitis

Not Responded

Metronidazole or Cipro x 2 more wks

Responded

Not Responded

Antx-refractory Pouchitis

Cipro + Metronidazole or Rifaximin or Tinidazole x 4 wks

Not Responded

5-ASA/steroids/Immunomodulators/Biologics?

Idiopathic Pouchitis (dysbiosis-associated)
Rationale of Current Antibiotic/Probiotic Therapy in Idiopathic Pouchitis

• “Shoot blindly”
• Target: dysbiosis (alteration in quality/quantility of commensal bacteria)

• Consequences
  – Bacterial resistance
  – Opportunistic infection (C. difficile)

Fecal Coliform Culture in Pouchitis

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

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

McLaughlin SD. CGH 2009;7:545
Secondary Pouchitis
(with identifiable etiological/triggering factors)

- Pathogen-associated pouchitis
- NSAID-Induced pouchitis
- Ischemic pouchitis
- Immune-mediate pouchitis
Clinical Clues for Pathogen-associated Pouchitis

- Fever, chills
- Malaise, weight loss
- High WBC

**Clostridium difficile** Infection in Pouch

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>N</th>
<th>Prevalence</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mann/DCR</td>
<td>2003</td>
<td>1</td>
<td>-</td>
<td>Recovered</td>
</tr>
<tr>
<td>Shen/DDS</td>
<td>2006</td>
<td>1</td>
<td>-</td>
<td>Recovered</td>
</tr>
<tr>
<td>Shen/CGH</td>
<td>2008</td>
<td>115</td>
<td>18%</td>
<td>Risk factors: Male (OR=5.0)</td>
</tr>
<tr>
<td>Shen/NRGH</td>
<td>2009</td>
<td>1</td>
<td>-</td>
<td>Fatal</td>
</tr>
<tr>
<td>Li/IBDJ</td>
<td>2013</td>
<td>196</td>
<td>11% (PCR for toxin B)</td>
<td>Refractory/Recurrence to vancomycin</td>
</tr>
</tbody>
</table>
Range of *C. difficile* Pouchitis

Lessons Learned on *C. difficile* Pouch

- Attention to male patients
- It can be deadly
- It can occur in symptomatic or asymptomatic patients with abnormal or normal pouchoscopy
  - Should all patients be treated?
- PCR is more sensitive than EIA
  - Over treat?
- Metronidazole is NOT the first line therapy
  - The majority of patients have been exposed to or were on the agent, at the time of diagnosis
- My approach: Vancomycin 1 gm/day x 2 – 4 wks.
  - Relapse or recurrence: Fidoxamicin, Fecal transplantation?
**Campylobacter Pouchitis**

Fever, malaise, dehydration

**Rx:** Erythromycin


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**CMV Pouchitis**

He XS, Shen B. *IBDJ* 2010
**Candida**: Part of Mucosal Associated Bacteria/Fungi

Navaneethan U & Shen B. 
AJG 2010;105:51-64

1-Year Budesonide in PSC-associated Pouchitis/Enteritis

<table>
<thead>
<tr>
<th></th>
<th>Pre-</th>
<th>Post-</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afferent Limb Endoscopy Core</td>
<td>2.3 ± 1.9</td>
<td>0.8 ± 1.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Pouch Endoscopy Score</td>
<td>2.5 ± 2.2</td>
<td>0.7 ± 0.9</td>
<td>0.001</td>
</tr>
</tbody>
</table>

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

Secondary Pouchitis
(with identifiable etiological/triggering factors)

- Pathogen-associated pouchitis
- NSAID-Induced pouchitis
- Ischemic pouchitis
- Immune-mediate pouchitis

Clinical Clues for Ischemic Pouchitis

- Male
- Obese or excessive weight gain (>15% of baseline)
- Abdominal surgery (hernia repair, mesh)
- Portal vein thromobi
- Antibiotic refractory

**Ischemic Pouchitis**


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**Imaging Features of Ischemic Pouchitis**

Ischemic Pouchitis

Crohn’s Disease

Shen B, et al. *IBDJ* 2010
Histologic Hallmark for Ischemic Pouchitis

Ischemic Colitis
Ischemic Pouchitis

Frequency of Chronic Antibiotic-refractory Pouchitis among J, S, and K Pouches

- J pouch: 13.0% (N = 215)
- S pouch: 0.0% (N = 45)
- K pouch: 8.3% (N = 36)

Mukewar S, Shen B, *DDW* 2012
Implication of Ischemic Pouchitis

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

Lysis of Adhesion in Treatment of Ischemic Pouchitis
Secondary Pouchitis
(with identifiable etiological/trIGGERING FACTORS)

- Pathogen-associated pouchitis
- NSAID-Induced pouchitis
- Ischemic pouchitis
- Immune-mediate pouchitis

Clinical Clues for Immune-mediated Pouchitis

- Pouchitis + enteritis
- Antibiotic-refractory
- Concurrent autoimmune disorders
- Serum autoantibodies
Enteritis in PSC + UC with or without Colectomy and Ileal Pouch

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
**IgG4-associated Pouchitis**

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

**Autoimmune (GVHD-like) Pouchitis**

- Mainly seen in chronic antibiotic-refractory pouchitis
- Concurrent autoimmune diseases
- Serum auto-antibodies
- Budesonide, small dose immunomodulator therapy

**Normal Pouch**

**Autoimmune Pouchitis**


**De novo Celiac Disease- Contributing Factor to Pouchitis?**

- 6 mo pre-colectomy
  - Negative Serology

- 3 mo gluten-free diet
  - Negative Serology

- 1 mo post ileostomy takedown
  - Positive Serology

**Shen L, et al. IBDJ 2009**

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**Work-up Algorithm for Secondary Pouchitis**

1. **Clinical Presentations Consistent with Antibiotic-refractory Chronic Pouchitis**
   - Pouchoscopy + Biopsy
   - **Diffuse Pouchitis /Enteritis**
   - **Segmental Pouchitis/ileitis or Distal Pouchitis ± Cuffitis**
   - **Stricture/ Fistula**
   - **Sinus/Obstruction/ Structural Disease**

2. **Labs** (microbiology, ANA, LFTs, IgG4, celiac/anti-microsomal abs)

3. **Histology** (apoptosis, IgG4, hematoidin)

4. **Pathogen-induced Pouchitis**
   - **C. difficile**
   - **CMV**

5. **Immune-mediated Pouchitis**
   - **PSC-associated**
   - **IgG4-associated**

6. **Ischemic Pouchitis**

7. **Autoimmune Pouchopathy**

8. **Histology, Abdominal Imaging ± Exam under Anesthesia**

9. **Crohn’s Disease**

10. **Surgical Complications**

**Shen B. CGH 2013**
Summary and Conclusions

• Pouchitis is disease spectrum with ranging etiology, risk factors, disease course and prognosis
• Commensal/pathogenic bacteria play the key role in disease initiation, development, and exacerbation in pouchitis
• In patients with constitutional symptoms, watch for pathogens
• Investigation of secondary causes of refractory pouchitis (PSC, concurrent autoimmune, ischemia)
• Prevention and management of C. difficile pouchitis increasingly become a challenge

“I Love My Pouch”
Thank You!