IBD and its mimics
+ BSG guidelines

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Pathological features of CIBD biopsies

- Diffuse chronic inflammation
- Active inflammation:
  - crypt abscesses
  - intra-epithelial polymorphs
- Crypt architectural distortion
- Crypt atrophy/shortening
- Goblet cell depletion
- Thickening of muscularis mucosae
- Surface irregularity
- Surface erosions
- Surface epithelial flattening
- Discontinuous inflammation
- Epithelioid cell granulomata
- Focal active inflammation
- Discontinuous crypt distortion
- Focal cryptitis
- Basal giant cells
- Submucosal inflammation
- Basal lymphoid aggregates
- Intralaminal polymorphs
- Increased basal lymphocytosis

Jenkins et al, 1997
The histopathological spectrum of CIBD

**Crohn’s Disease**
- Infective Colitis (bacterial)
- Infective Colitis (viral)
- Infective Colitis (others)
- Ischaemic/Radiation Colitis

**Ulcerative Colitis**
- Drugs
- Diverticular Colitis
- Diversion Colitis
- Lymphocytic / Collagenous Colitis
- HIV / GVHD Colitis
- Behcet’s Disease
- Miscellaneous - CGD, Lymphoma, pneumatosis, etc
From Jenkins et al, 1997
The BSG Inflammatory Bowel Disease Pathology Initiative
Is the mucosa inflamed?

- No
  - No histological features of IBD

- Yes
  - IBD favoured over other causes
  - IBD definite or very likely*

*In conjunction with the clinical picture
IBDU: IBD unclassified
A: Normal

B: Right colon, ↑ LP cells

C: Occasional branching

D: Irregular villiform outline

E: Crypt distortion

F: Crypt distortion, trans-LP inflammation

G: Basal plasmacytosis

H: Basal lymphoid aggregates
A: Cryptolytic granuloma
B: Paneth cell metaplasia
C: Distribution
D: Intra-biopsy variability
E: Upper LP cellularity
F: Diversion features
G: Collagenous colitis
H: Diverticular colitis
<table>
<thead>
<tr>
<th>Feature</th>
<th><strong>UC Pre-treatment</strong></th>
<th><strong>UC Post-treatment</strong></th>
<th><strong>CD Pre- and post-treatment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease distribution</td>
<td>Diffuse and continuous</td>
<td>Patchy, discontinuous or continuous</td>
<td>Patchy/segmental or continuous</td>
</tr>
<tr>
<td>Rectal involvement</td>
<td>Always (adults)</td>
<td>Variable</td>
<td>Occasional</td>
</tr>
<tr>
<td>Disease severity</td>
<td>Distal &gt; proximal</td>
<td>Patchy and variable</td>
<td>Patchy and variable</td>
</tr>
<tr>
<td>Ileal involvement</td>
<td>Occasional (distal 1–5 cm)</td>
<td>Occasional</td>
<td>Often (usually &gt;5–10 cm)</td>
</tr>
<tr>
<td>Disease location in colonic wall</td>
<td>Superficial (mucosal)</td>
<td>Superficial (mucosal)</td>
<td>Superficial or transmural</td>
</tr>
<tr>
<td>Transmural lymphoid aggregates</td>
<td>Rare, beneath ulcers only</td>
<td>Rare, beneath ulcers</td>
<td>Any location</td>
</tr>
<tr>
<td>Fissures</td>
<td>Rare, superficial (fulminant colitis)</td>
<td>Rare superficial (fulminant colitis)</td>
<td>Deep, any location</td>
</tr>
<tr>
<td>Sinuses and fistulas</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Perforation</td>
<td>Rare</td>
<td>Rare</td>
<td>Occasional</td>
</tr>
<tr>
<td>Granulomas</td>
<td>Most related to ruptured crypts</td>
<td>Most related to ruptured crypts</td>
<td>Not crypt related</td>
</tr>
</tbody>
</table>

From Odze, Mod Pathol 2015; 28: S30-S54
## Discontinuous changes in UC

<table>
<thead>
<tr>
<th>Circumstances</th>
<th>Feature</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>New or longstanding UC</td>
<td>Caecal patch</td>
<td>No adjacent disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Similar to distal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May also involve AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consider Crohn's</td>
</tr>
<tr>
<td>Rectal sparing</td>
<td></td>
<td>Consider Crohn's</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exclude local therapy</td>
</tr>
<tr>
<td>Appendiceal disease</td>
<td></td>
<td>Not uncommon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Seen only in resections</td>
</tr>
<tr>
<td>Fulminant UC</td>
<td>Can be segmental</td>
<td>Discontinuous</td>
</tr>
<tr>
<td>Longstanding UC</td>
<td>Discontinuous</td>
<td>Consider effect of therapy</td>
</tr>
<tr>
<td></td>
<td>Patchy inflammation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patchy crypt changes</td>
<td></td>
</tr>
</tbody>
</table>
What are the issues in CIBD pathology

- Can we differentiate infection from CIBD?
- What is indeterminate colitis?
- Ileal involvement in CIBD
- Are there hard diagnostic features for Crohn’s disease?
- What are the post-treatment changes in CIBD?
- Do appearances return to normal in CIBD?
- How should we report dysplasia in CIBD?
- What is new in the management of dysplasia in UC?
How do we differentiate infection from CIBD?

- crypt architectural distortion takes about 6 weeks to develop in CIBD
- diffuse crypt architectural distortion is usually CIBD, particularly ulcerative colitis, as is a villiform surface (rarely in chronic shigellosis and chronic amoebiasis)
- diffuse chronic inflammation is usually CIBD (occasionally seen infections)
- basal lymphoid aggregates is usually CIBD, both UC and CD
- mucin depletion – less helpful
- infection shows predominant acute inflammation with oedema but little or no chronic inflammation or crypt change (only in chronic shigellosis and amoebiasis)
Indeterminate colitis: the Price definitions

- 30/330 cases
- all colectomies/proctocolectomies
- most (21/30) showed features of fulminant disease (myocytolysis, telangiectasia, acute V-shaped clefts)
- some attributes of Crohn’s disease (fissures, TMI, focal mucosal inflammation) but no granulomas
- some attributes of ulcerative colitis (diffuse disease with rectal involvement (14/30))

Price, 1978
Indeterminate colitis

- pathologists do find it difficult to make this diagnosis
- GI pathologists don’t – in second opinion work, especially!
- criteria for the diagnosis are variable and that the literature on its significance is just a little ambiguous
- criteria for the diagnosis have changed with time: morphology and position of granulomas, skip lesions of UC
Why do we label UC as indeterminate or Crohn’s disease

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Fulminant (severe, toxic) colitis</td>
</tr>
<tr>
<td>2.</td>
<td>Insufficient clinical, radiologic, endoscopic, pathologic info</td>
</tr>
<tr>
<td>3.</td>
<td>Failure to utilize major diagnostic criteria of CD</td>
</tr>
<tr>
<td>4.</td>
<td>Failure to recognize unusual pathologic variants of UC and CD</td>
</tr>
<tr>
<td>5.</td>
<td>Failure to recognize non-IBD mimics and superimposed diseases</td>
</tr>
<tr>
<td>6.</td>
<td>Attempt to distinguish UC from CD in biopsies[^1]</td>
</tr>
<tr>
<td>7.</td>
<td>Attempt to change IBD diagnosis based on pouch or diversion-related complications</td>
</tr>
</tbody>
</table>

From Odze, Mod Pathol 2015; 28: S30-S54
Insufficient clinical, radiologic, endoscopic, pathologic information

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>1. Clinical</td>
<td>Family hx, PSC, type of symptoms/signs, serology, prior surgery, perianal disease</td>
</tr>
<tr>
<td>2. Radiological</td>
<td>Segmental vs diffuse, small intestinal involvement, strictures, fistulas, wall thickness</td>
</tr>
<tr>
<td>3. Endoscopic</td>
<td>Type/appearance of ulcers, distribution of disease, appearance of ileum</td>
</tr>
<tr>
<td>4. Pathological</td>
<td>Prior biopsies (and resections)</td>
</tr>
</tbody>
</table>

From Odze, Mod Pathol 2015; 28: S30-S54
<table>
<thead>
<tr>
<th><strong>UC with CD-like features</strong></th>
<th><strong>CD with UC-like features</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fulminant UC</td>
<td>Mucosal (non-mural) disease</td>
</tr>
<tr>
<td>Segmental disease (caecal/periappendiceal patch,</td>
<td>Rectal involvement only (~5–10%)</td>
</tr>
<tr>
<td>effects of healing and/or therapy)</td>
<td></td>
</tr>
<tr>
<td>Rectal sparing (children)</td>
<td>Diffuse colonic disease</td>
</tr>
<tr>
<td>Granulomas (crypt related, infection)</td>
<td></td>
</tr>
<tr>
<td>Ileum involvement (backwash, infection, drugs,</td>
<td></td>
</tr>
<tr>
<td>bowel prep)</td>
<td></td>
</tr>
<tr>
<td>UGI involvement (rare)</td>
<td></td>
</tr>
</tbody>
</table>

From Odze, Mod Pathol 2015; 28: S30-S54
Diseases that may result in changes in the type, pattern and severity of inflammation

- CMV
- Pseudomembranous colitis
- Ischaemia
- Radiation
- Drugs
- Microscopic colitis
- Other

From Odze, Mod Pathol 2015; 28: S30-S54
Backwash ileitis

- 10% of total colectomy specimens in ulcerative colitis show inflammation in the terminal ileum
- usually confined to the terminal 10 to 15 cms of the ileum
- macroscopically mucosa is diffusely reddened & granular with erosions and ulcers
- when mild, superficial, but deep ulceration and inflammatory polyp formation well described
- ileo-caecal valve usually dilated, allowing the contents of the colon to enter the small intestine
- continuity of inflammatory pathology between the proximal colon and the terminal ileum and the incompetent ileo-caecal valve
- backwash ileitis is not a primary enteritis but rather an effect upon ileal mucosa induced by colonic contents
Ileal involvement in CIBD: backwash ileitis vs Crohn’s disease

**Backwash ileitis**
- diffuse
- usually superficial
- only terminal 15 cms of ileum

**Crohn’s disease**
- patchy
- granulomas
- ? aphthoid ulcers, ? ulcer-associated cell lineage/pyloric metaplasia
Ileal involvement in CIBD: backwash ileitis vs Crohn’s disease

easier in resections:

fissuring ulcers

granulomas

transmural inflammation

connective tissue changes of CD
What are the post-treatment changes in CIBD?

- medically treated UC becomes patchy
- flat mucosa normal and inflammatory polyps inflamed
- there may be ‘rectal sparing’ in UC if treated with enemas
- UC mucosa can return to normal on treatment
- IV cyclosporin for fulminant UC can produce mimicry of dysplasia
- surgery, especially diversion

Cyclosporin associated dysplasia

almost normal flat mucosa
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Many of the iatrogenic diseases mimic IBD

- Ischaemic colitis
- Radiation colitis
- [Behçets’s disease]
- Drug-induced colitis
- Microscopic (lymphocytic/collagenous) colitis
- Infectious colitis
- Diversion colitis
- Pouchitis
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Ischaemic colitis

• especially with aortic surgery
• disease of elderly
• associated with aortic atheroma,
• may be total - infarction
• may be subtotal - mucosal disease with subsequent fibrosis
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Ischaemic colitis
Radiation colitis

- Follows therapeutic radiation e.g. for Hodgkin’s disease, carcinoma of cervix
- Acute disease: mucosal ulceration, diarrhoea
- Chronic disease: related to vascular occlusion, fibrosis, radiation fibroblasts
female patient presenting with intestinal obstruction
laparotomy: resection of strictured area
• radiation enteritis and colitis may present up to 40 years after previous radiotherapy (cervix, endometrium, bladder, prostate, etc)
• in chronic radiation pathology of the gut, the submucosa is the main target
• vessels, hyaline fibrosis, stellate/atypical fibroblasts
• mucosa may be relatively normal – be aware of this in biopsies
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Behcet’s disease

- Mucocutaneous ulceration: skin, genital tract, GIT
- Associated with venulitis

Chen, Shyu and Chao

Gastroenterology
129:407-775
Findings:

- flask-shaped deep ulcers of small intestine
- lymphocytic venulitis
- multiple oral aphthous ulcers
- iritis

Diagnosis: Behçet’s disease
Behçet’s disease in the intestines

- idiopathic multi-system syndrome characterised by orogenital ulceration and ocular manifestations
- disease of young adults and more severe in males
- high prevalence rates in the Mediterranean basin, especially Turkey
- pathologically a vasculitis, usually lymphocytic and venous
- 1-2% of patients will have small intestinal involvement
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**Drug-induced**
- NSAID-induced colitis
  - inhibit cyclo-oxygenase (COX-1 and COX-2)
  - small intestinal ulceration
  - less commonly, diffuse colitis
  - also may be seen in collagenous colitis
NSAIDs and the gut

- gastritis, duodenitis and peptic ulceration
- small and large intestinal ulceration and perforation
- eosinophilic enteritis
- diaphragm disease
- exacerbation/cause of appendicitis
- cause relapse (and ? cause) inflammatory bowel disease, especially ulcerative colitis
- cause diverticulitis in diverticular disease
- cause microscopic colitis (both lymphocytic and collagenous colitis)
<table>
<thead>
<tr>
<th>Pattern of injury</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal active colitis</td>
<td>Ipilimumab, NSAIDs, sodium phosphate</td>
</tr>
<tr>
<td>Chronic colitis</td>
<td>Mycophenolate, ipilimumab, TNF-inhibitors, NSAIDs, rituximab</td>
</tr>
<tr>
<td>Apoptosis excess</td>
<td>Ipilimumab, mycophenolate, antimitabolites, TNF-inhibitors, colchicine, taxane, NSAIDs, sodium phosphate enema</td>
</tr>
<tr>
<td>Dilated damaged crypts and apoptosis</td>
<td>Mycophenolate, sodium phosphate enema, 5-FU</td>
</tr>
<tr>
<td>Small intestinal villous atrophy (coeliac disease-like)</td>
<td>Olmesartan, mycophenolate, ipilimumab, colchicine, azathioprine, NSAIDs</td>
</tr>
<tr>
<td>Microscopic colitis</td>
<td>Olmesartan, ipilimumab, NSAIDs, lansoprazole, ranitidine, ticlopidine, simvastatin, paroxetine, carbamazepine, penicillin, flutamide, cyclo3 fort, sertraline</td>
</tr>
<tr>
<td>Increased mitoses</td>
<td>Colchicine, taxane</td>
</tr>
<tr>
<td>Erosions/ulcers</td>
<td>NSAIDs, KCl, kayexalate</td>
</tr>
<tr>
<td>Diaphragms/stenosis</td>
<td>NSAIDs</td>
</tr>
<tr>
<td>Ischaemic colitis</td>
<td>NSAIDs, kayexalate, cocaine, diuretics, sumatriptan, dopamine, methysergide, amphetamines, oestrogens, ergotamine, alostron, digitalis, pseudoephedrine, vasopressin, interferon</td>
</tr>
<tr>
<td>Pseudomembranous colitis</td>
<td>Antibiotics, proton pump inhibitors</td>
</tr>
<tr>
<td>Crystal deposition</td>
<td>Kayexalate, kalimate, sevelamer, cholestyramine, bisphosphonates</td>
</tr>
<tr>
<td>Strictures</td>
<td>KCL, pancreatic enzymes</td>
</tr>
<tr>
<td>Pseudomelanosis coli</td>
<td>Laxatives</td>
</tr>
<tr>
<td>Sigmoid diverticular perforation</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Hypereosinophilia</td>
<td>NSAIDs, oestrogen-progesterone drugs, plavix</td>
</tr>
<tr>
<td>Malakoplakia</td>
<td>Corticosteroids</td>
</tr>
<tr>
<td>Epithelial atypia</td>
<td>i.v. cyclosporin</td>
</tr>
</tbody>
</table>
NSAIDs and the gut: diaphragm disease

Lang et al, 1988
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Microscopic (lymphocytic/collagenous) colitis
- clinically watery diarrhoea
- no gross abnormality on endoscopy
- histologically, increased chronic inflammatory cells in lamina propria (microscopic colitis)
- may be increased sub-epithelial collagen
- may be increased intra-epithelial lymphocytes
- associated with NSAID use
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Microscopic Colitis and IBD

• collagenous colitis (CC): changes more common in proximal and transverse colon
• mixed inflammatory infiltrate: lymphocytes, plasma cells and eosinophils
• infiltration of crypt and surface epithelium by lymphocytes
• epithelial injury shown by mucin depletion and flattening of surface epithelium
• expansion of subepithelial collagen plate (>10µm)
• relative preservation of crypt architecture
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Microscopic Colitis and IBD

- lymphocytic colitis (LC) similar to collagenous colitis
- fewer eosinophils in inflammatory infiltrate
- infiltration of crypt and surface epithelium by lymphocytes
- epithelial injury shown by mucin depletion and flattening of surface epithelium
- no thickening of subepithelial collagen plate
- relative preservation of crypt architecture
Microscopic Colitis and IBD

- rarely CC and LC may cause difficulty in differentiation from either UC or CD
- some histological features of CC and LC may be seen in IBD, especially increased collagen
- some patients with IBD may present with histological features of CC and LC
- unsure whether conditions co-exist or CC/LC evolve into IBD
Microscopic Colitis and IBD

• retrospective analysis of some CC/LC patients has revealed abnormal endoscopic features compatible with IBD

• some CC/LC cases have histological features of IBD: cryptitis, crypt distortion, metaplasia, granulomas, multinucleated giant cells

• some CC patients with superficial ulceration have been exposed to NSAIDs
## IATROGENIC BOWEL DISEASE

### Microscopic Colitis and IBD

<table>
<thead>
<tr>
<th>Feature</th>
<th>Microscopic Colitis</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>‘Watery’ diarrhoea</td>
<td>Bloody diarrhoea</td>
</tr>
<tr>
<td>Endoscopic</td>
<td>Normal/erythema</td>
<td>Friability, erythema</td>
</tr>
<tr>
<td></td>
<td>Rare ulcers</td>
<td>Ulcers common</td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mononuclear</td>
<td>Stromal/intraepithelial</td>
<td>Stromal</td>
</tr>
<tr>
<td>Cryptitis</td>
<td>Rare/focal</td>
<td>Common, abundant</td>
</tr>
<tr>
<td>Ulceration</td>
<td>Rare/focal</td>
<td>Common, extensive</td>
</tr>
<tr>
<td>Paneth cells</td>
<td>Uncommon</td>
<td>Usually present</td>
</tr>
<tr>
<td>Basal PCs</td>
<td>Rare</td>
<td>Usually present</td>
</tr>
<tr>
<td>Basal lymph.agg</td>
<td>Rare</td>
<td>Usually present</td>
</tr>
<tr>
<td>Crypt distortion</td>
<td>Uncommon, focal</td>
<td>Usually present, multifocal/diffuse</td>
</tr>
<tr>
<td>Granulomas</td>
<td>Rare</td>
<td>Related to crypt rupture (UC)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Present in CD</td>
</tr>
</tbody>
</table>

Yantiss and Odze Histopathology  
2006; 48:116-132
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Infectious colitis

- multiple bacterial agents
- superficial half of crypts
- acute inflammation
- often resolve spontaneously (acute self-limiting colitis)
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How do we differentiate infection from CIBD?

• crypt architectural distortion takes about 6 weeks to develop in CIBD

• diffuse crypt architectural distortion is usually CIBD, particularly ulcerative colitis, as is a villiform surface (rarely in chronic shigellosis and chronic amoebiasis)

• diffuse chronic inflammation is usually CIBD (occasionally seen infections)

• basal lymphoid aggregates is usually CIBD, both UC and CD

• mucin depletion – less helpful

• infection shows predominant acute inflammation with oedema but little or no chronic inflammation or crypt change (only in chronic shigellosis and amoebiasis)
Crypt distortion and villiform change in UC
Infection vs CIBD

- don’t ever forget amoebiasis
- steroids or other immunosuppressants for systemic amoebiasis = disaster with very high mortality
- always look for amoebae in atypical CIBD
- ? routine PAS
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Infectious colitis

- specific form is pseudomembranous colitis
- associated with antibiotic usage
- caused by enterotoxin of *Clostridium difficile*
- may occur as part of cross-infection/epidemic
- treat with vancomycin
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Infectious colitis
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Diversion colitis

• disease of rectal stump after intermediate surgery for UC, colorectal carcinoma or diverticular disease
• chronic inflammation: lymphoid follicles, active chronic inflammation, possible granulomas
• beware overdiagnosis of Crohn’s disease
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Diversion Colitis

- chronic inflammatory condition that develops in bowel segments excluded from faecal stream
- develops months to years following surgery
- regresses 3-6/12 after re-establishment of faecal stream
- most asymptomatic: may complain of mucoid/bloody discharge, cramping or abdominal pain
- possibly related to deficiency of short chain fatty acids
Diversion proctocolitis

- diversion of the colon and rectum is undertaken for carcinoma, DD, CIBD and sundry other conditions
- the indication for diversion influences the pathology
- pathological changes:
  - chronic inflammation
  - lymphoid follicular hyperplasia
  - active inflammation
  - significant mimicry of CIBD
  - including granulomas
The defunctioned rectum in UC
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Diversion colitis
IATROGENIC BOWEL DISEASE

Diversion Colitis

- mucosal erythema, friability, nodularity, ulceration
- lymphoid hyperplasia: prominent lymphoid aggregates with germinal centres in mucosa and submucosa
- in these areas, crypts may be shortened or distorted
- superimposed cryptitis, crypt abscesses, aphthous ulcers, frank ulceration
- features of chronicity: Paneth cells, increased lymphoplasmacytic infiltration
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Diversion Colitis

• granulomas, fissuring ulcers, transmural inflammation may be found in patients with a prior history of UC or without any history
• raises possibility of CD
• when possible, obtain biopsy of segment to be diverted as a baseline
• in UC patients, lymphoid hyperplasia may be extremely prominent, as well as active features and ulceration
• may need a ‘test’ of faecal stream to decide whether IBD or diversion colitis
The defunctioned rectum in UC

- there is pronounced mimicry of CD in the defunctioned rectum in UC and extreme care is required before changing the CIBD type. 

  *Warren et al, 1993,
  *Goldstein et al, 1997*

- always review previous pathology (uninfluenced by previous surgery): the previous colorectal biopsies & colectomy
The pelvic ileal reservoir/ileal pouch
Restorative proctocolectomy with ileal reservoir
Ileal pouch-anal anastomosis

Parks AG, Nicholls RJ.
Proctocolectomy without ileostomy for ulcerative colitis.
The pelvic ileal reservoir/ileal pouch
Restorative proctocolectomy with ileal reservoir
Ileal pouch-anal anastomosis

Indications: Ulcerative colitis, FAP, necrotising enterocolitis, JP
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Pouchitis

• disease of ileo-anal reservoir formed after pan-proctocolectomy
• may be related to bacterial overgrowth
• may be recurrence of disease (UC)
• active chronic inflammation of small bowel mucosa, with crypt flattening and colonic metaplasia
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Pouchitis

• 50% of UC patients after IPAA will develop at least 1 episode of pouchitis in the 1st year
• may be acute (<4 weeks) or chronic (>4 weeks)
• may be intermittent (1 or 2 episodes), relapsing (>3 episodes), continuous or treatment-refractory
• pathological predictors of pouchitis:
  o superficial fissuring colonic ulcers
  o severe appendiceal inflammation
  o severe pancolitis
• 12% will require immunosuppressive therapy or surgical resection
• refractory pouchitis may resemble CD with pouch fistulas, stenosis, and anal fissures
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Pouchitis

- diagnosis depends on a combination of clinical, endoscopic and pathological features
- active inflammation in lamina propria and crypt epithelium +/- ulceration
- ‘chronic’ features such as architectural distortion, pyloric metaplasia, villous shortening and increased chronic inflammatory cells may represent an adaptive form of ‘colonic’ metaplasia
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Pouchitis

- features of treatment-refractory pouchitis may closely mimic CD
- proximal strictures, pouch stenosis/fistulas, anal fissures/fistulas and extracolonic disease may occur
- need to review original diagnosis
- occasionally CD patients will have inadvertent IPAA formation and in these it may be difficult to decide if pouchitis is a complication of the procedure or CD itself
- afferent limb ulcers were more common in CD than in UC
- data on granulomas unconfirmed
The mucosal pathology of the pouch

Three groups:

A: 40-50%: UC and FAP: no active inflammation: normal or mild chronic changes/villous abnormalities

B: 40%: mainly UC but occasional FAP: chronic changes but transient active inflammation

C: 10-15%: always UC: severe chronic active inflammation: chronic changes constant: (chronic relapsing) pouchitis
<table>
<thead>
<tr>
<th>Pouch dysfunction (clinical)</th>
<th>Pouch inflammation (pathological)</th>
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</thead>
<tbody>
<tr>
<td>Pouchitis (chronic relapsing)</td>
<td>Pouchitis (chronic relapsing)</td>
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<tr>
<td>Crohn’s disease</td>
<td>Crohn’s disease</td>
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<tr>
<td>Specific infection</td>
<td>Specific infection</td>
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<tr>
<td>Primary decreased compliance</td>
<td>Secondary pouchitis</td>
</tr>
<tr>
<td>Decreased compliance due to pelvic sepsis</td>
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<tr>
<td>Irritable pouch syndrome</td>
<td>Cuffitis</td>
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<tr>
<td>Cuffitis</td>
<td>Mucosal prolapse (anterior strip pouchitis)</td>
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<tr>
<td>Strictured anastomosis</td>
<td>Mucosal ischaemia</td>
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<td>Long efferent limb</td>
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<tr>
<td>Decreased pouch emptying</td>
<td>Prepouch ileitis</td>
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<td>Pelvic floor dysfunction</td>
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<tr>
<td>Pouch stricture</td>
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<td>Adhesions</td>
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<tr>
<td>Prepouch ileitis</td>
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</tbody>
</table>

*After Sandborn & Pardi, 2004*                                      *Warren & Shepherd, 1993*
Pouchitis

• better termed ‘chronic relapsing pouchitis’

• 10-20% but very variable (definitions)

• defined by clinical (diarrhoea/discharge, systemic symptoms, like UC), endoscopic and histopathological criteria

• not just chronic inflammation in the pouch – need active inflammation
Pouchitis – definition and assessment

• should not be merely histopathological

• clinical, endoscopic and pathological

• pouchitis disease assessment index (PDAI)
The pelvic ileal reservoir in the long term

pouch creation

↓

new colon-like milieu

↓

colonic metaplasia/colonisation

↓

UC aetiological factors

↓

long term pouchitis

↓

dysplasia & malignancy
Pouch versus cuff disease

• 42 year old male with 10 year history total ulcerative colitis, eventually unresponsive to medical treatment.
• restorative proctocolectomy with J pouch 2 years previously.
• 2 months pain, fever, diarrhoea from pouch x 14 per day and x 4 at night.
• pouchoscopy – normal pouch and biopsy revealed healthy villous pouch mucosa
• review – area of inflammation in ATZ/cuff.

ileal pouch
cuff
Pouch pathology: is this Crohn’s disease?

- granulomas, esp in lymphoid tissue
- ulcer-associated cell lineage

*MacNeill, Guindi & Riddell, 2004*  *Warren & Shepherd, 1993*
The pelvic ileal reservoir in the long term

pouch creation

new milieu

colonic metaplasia/colonisation

UC aetiological factors

long term pouchitis

dysplasia & malignancy
Surveillance of the pouch – current thoughts?

- FAP patients require surveillance
- the rectal cuff with cuffitis requires surveillance
- patients with type C pathology/pouchitis merit surveillance
- can we leave the others alone?
Pouch risk of neoplasia

<table>
<thead>
<tr>
<th>Yrs</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
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</thead>
<tbody>
<tr>
<td>%</td>
<td>0.9</td>
<td>1.3</td>
<td>1.9</td>
<td>4.2</td>
<td>5.1</td>
</tr>
</tbody>
</table>

The follow up of ileal pouch mucosa

All patients:
endoscopy & biopsy @ 1 year

Type A & B histology
- No pouchitis
  - Endoscopy & biopsy @ 10 yrs
Type C histology
- Type C histology
  - No dysplasia
    - Indefinite
  - Chronic relapsing pouchitis
    - Endoscopy & biopsy @ 2 yrs
  - No dysplasia
    - Repeat endoscopy & biopsy @ 3 months
- Dysplasia
  - LGD
    - Re-biopsy at 6 months
  - HGD, DALM or multifocal
    - Excise pouch

after McLeod et al, 2007
The follow up of ATZ/cuff

- begin follow-up examination 8-10 years after onset of ulcerative colitis
- follow patients every 2 years to 20 years, then yearly thereafter
- if dysplasia/cancer in colectomy specimen, follow patient annually

after McLeod et al, 2007
THANK YOU FOR YOUR ATTENTION
ANY QUESTIONS?