DEFINITIONS

- Microscopic colitis is a syndrome of unknown etiology characterized by otherwise idiopathic watery diarrhea with normal colonoscopic appearances, but histological evidence of colonic mucosal inflammation
- Synonym: watery diarrhea—colitis syndrome
MICROSCOPIC COLITIS

- Two histologic varieties
  - Lymphocytic colitis
  - Collagenous colitis
- Diarrhea due to decreased colonic water and electrolyte absorption
- Important cause of secretory diarrhea, especially in older patients
- Must biopsy normal-appearing colonic mucosa in patients with chronic diarrhea

PROPOSED ETIOLOGIES

- Infection
- Allergy
- Diet
- Immune mechanism/HLA-DQ linkage
- Drug-induced
  - NSAIDs
  - PPIs
  - SSRIs
- Altered collagen synthesis/degradation
PATHOLOGY:
Microscopic Colitis

- Gross appearance: normal or near normal; no ulcers, friability, exudates
- Mucosa: irregular, loosely attached cuboidal colonocytes; decreased goblet cells; increased intraepithelial lymphocytes
- Lamina propria: expanded cellular infiltrate; mild cryptitis; no crypt distortion

MICROSCOPIC COLITIS
PATHOPHYSIOLOGY OF DIARRHEA IN MC

• Colonic water absorption is inversely proportional to lamina propria cellularity, suggesting that inflammatory mediators reduce mucosal fluid and electrolyte absorption and increase stool weight.¹
• Sodium transport, barrier function altered.²
• Collagen table thickness does not correlate with stool weight.¹

¹Gastroenterology 1992;103:1790-6.
CLINICAL ASPECTS

- Lymphocytic colitis: F = M
- Collagenous colitis: F >> M
- Age of onset generally >40 yrs.
- Incidence: 10-15% of patients evaluated for chronic diarrhea at referral centers
- Onset of diarrhea typically insidious
- Diarrhea variable in severity, but usually continuous
- In 1/3, may be confused with IBS-D1

MICROSCOPIC COLITIS: Clinical Clues

- Older patients
- + Rheumatological disease; celiac disease
- Associated fecal incontinence
- Stool weight typically ~500 g, always <1000 g

ASSOCIATED CONDITIONS

- Arthritis
- Hypothyroidism
- Hyperthyroidism
- Diabetes mellitus
- Chronic hepatitis
- Primary biliary cirrhosis
- Drugs (PPIs, NSAIDs, chemotherapy, SSRIs)
- Atrophic gastritis
- Scleroderma
- Pulmonary fibrosis
- Adenomas
- Carcinoid tumors
- Histiocytic lymphoma
- Celiac disease
- Smoking
DIFFERENTIAL DIAGNOSIS OF WATERY DIARRHEA

- Microscopic colitis
- Laxative abuse
- Iatrogenic diarrhea
- Bile acid diarrhea
- CHO malabsorption
- Endocrine diarrhea
- Mast cell disease
- Chronic idiopathic secretory diarrhea
- Amyloidosis
- Diabetic neuropathy
- ? SB bacterial overgrowth
- ? Radiation enteritis
- ? Ischemia

STOOL ANALYSIS

- Usually watery diarrhea, but can vary
- Rectal bleeding, if present, due to hemorrhoids or anal fissure
- Can have fecal leukocytes; frank pus rare
- Fecal electrolytes indicate a secretory diarrhea (small osmotic gap)
- Steatorrhea not typical
EVALUATION

• Quantitative stool collection
  – Define secretory diarrhea
  – Exclude steatorrhea
• Colonoscopy with multiple biopsies from throughout the colon
  – Sigmoidoscopy may be sufficient
• Have biopsies reviewed by an experienced pathologist

TREATMENT

• Symptomatic therapy with antidiarrheals
• Anti-inflammatory therapy
  – Sulfasalazine, mesalamine, other 5-ASA drugs
  – Corticosteroids (prednisone, budesonide)
  – Immunosuppressive drugs (azathioprine)
• Bile acid binding resins
• Bismuth subsalicylate
ANTIDIARRHEAL DRUGS

- Stool weight tends to be moderate (300—600 g/24h)
- Incontinence is a major problem in many
- Diphenoxylate and loperamide helpful in some patients
- Codeine, morphine, or deodorized tincture of opium may be necessary
- Spontaneous remissions occur

5-AMINOSALICYLATES

- Mesalamine and similar agents used by analogy with classical inflammatory bowel disease
- No placebo controlled studies
- Open label study suggests improvement in 86% of patients with LC, 42% with CC\(^1\)
- No evidence of need for maintenance therapy

\(^1\)Am J Gastroenterol 2003;98:340—7
CORTICOSTEROIDS

- Paradoxically high doses of prednisone may be needed
- Incomplete response to prednisolone 50 mg daily for two weeks\(^1\)
- Budesonide 9 mg daily for 6 weeks superior to placebo\(^2\); meta-analysis of 3 studies yielded NNT of 2\(^3\)
- Relapse common

\(^1\)Scand J Gastroenterol 2003;38:606—10
\(^2\)Gastroenterology 2002;123:978—84
\(^3\)Am J Gastroenterol 2009;104:235-41

IMMUNOSUPPRESSIVE DRUGS

- Limited experience with azathioprine, 6-mercaptopurine, anti-TNF drugs
- May be useful in patients who are unresponsive to antidiarrheals, 5-amino-salicylates, or corticosteroids\(^1\)
- Low doses may be effective
- Mayo Clinic experience generally positive\(^2\)

\(^2\)Gastroenterology 2001;120:1483--4
BILE ACID BINDING DRUGS

- Bile acid malabsorption (BAM) may occur frequently in patients with microscopic colitis\textsuperscript{1,2}
- Cholestyramine or colestipol reduced diarrhea in 92\% of CC patients with BAM and in 67\% of CC patients without BAM\textsuperscript{2}
- ? Binding of something other than bile acid

\textsuperscript{1}Scand J Gastroenterol 2003;38:826—30
\textsuperscript{2}Gut 2000;46:170--5

BISMUTH SUBSALICYLATE

- Bismuth subsalicylate has both antibacterial and anti-inflammatory effects
- Open label trial of 8 x 262-mg tablets daily for 8 weeks showed response rate of 92\%\textsuperscript{1}
- Histological resolution in 75\%\textsuperscript{1}
- Randomized, blinded study showed similar results (abstract)\textsuperscript{2}

\textsuperscript{1}Gastroenterology 1998;114:29—36
\textsuperscript{2}Gastroenterology 1999;116:A880
PROGNOSIS

• Diarrhea can be controlled in most patients with microscopic colitis
• Variable course with remissions and relapses common
• Little evidence of progression to more classical forms of inflammatory bowel disease
• No evidence for development of neoplasia