Approach to the Patient with Chronic Diarrhea

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Diagnostic Approach to Chronic Diarrhea

- BLOODY – gross or occult
- Fatty
- Watery
Diarrhea with Blood → Colitis

- Infection
- IBD
- Ischemia
- Some drugs
  - NSAIDs
  - Isotretinoin
- SCAD – Segmental Colitis Associated with Diverticular Disease
- Radiation
- Diversion colitis

Infection Uncommon

Stool Culture
- *Salmonella*
- *Campylobacter*
- *Yersinia*
- *Aeromonas*
- *Plesiomonas*
- *C. difficile*

O + P
- Ameba
- Trichuris
Chronic Bloody Diarrhea: Work-up

- Colonoscopy/biopsy – mainstays of diagnosis
- Helpful to distinguish IBD vs. infection

Colonic Biopsy can Diagnose Specific Infections

- Pseudomembranes
  - C. difficile
  - STEC
- Viral Inclusions
  - CMV
  - HSV
- Parasites
  - Ameba
  - Shistosomiasis
- Tuberculosis
Abnormal Mucosa Transverse Colon

4 cm ulcer transverse colon

TB vs Crohn’s Disease

<table>
<thead>
<tr>
<th>Tuberculosis</th>
<th>Crohn’s</th>
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<tbody>
<tr>
<td>Ulcers Transverse</td>
<td>Linear</td>
</tr>
<tr>
<td>Sharp edge</td>
<td>Deep</td>
</tr>
<tr>
<td>Adjacent inflamed</td>
<td>Not inflamed</td>
</tr>
<tr>
<td>Aphthe rare</td>
<td>Common</td>
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<tr>
<td>IC valve destroyed</td>
<td>Not common</td>
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Diagnostic Approach to Chronic Diarrhea

- Bloody – gross or occult
- FATTY
- Watery

Case

A 67 year old woman comes for a second opinion for fecal incontinence and weight loss. This has been a problem for 2 years – she has had a colonoscopy with normal colonic biopsies, and anorectal manometry showing decreased anal resting sphincter pressure and decreased squeeze. Since this evaluation, she continues to have 2 large soft bowel movements daily, with fecal staining (especially when she plays pickle ball at the senior center). She has lost 10 pounds over the past year.
History cont’d

Social History
Widowed, husband died of pancreatic cancer

Family History
No GI cancers

Past Medical History
• Meds – none
• Surgery – Cholecystectomy 15 yrs prior
• Vaginal births (2 adult children)

Exam
• Thin woman
• Vital signs normal
• Skin – no rash
• Abdomen – normal, RUQ scar, no organomegaly, mass or tenderness
• Stool FOBT negative
### Initial Evaluation

**CBC**
- **Hct**: 38
- **MCV**: 90 (nl 81 – 98)
- **WBC**: 7,600, nl diff

**Normal Electrolytes**
- **Bilirubin**: 1.0
- **Albumin**: 4.0

### Our Patient

**Fecal fat** – 60 drops/hpf (normal <20)

**24 hr stool** – 618 gm
- **44 gm fat**

**Mucosal or pancreatic?**
- >9.5 gm fat/100 gm stool = pancreatic insufficiency likely
- **Hers 7 g/100 g fat**
Therapeutic Trial

Pancreatic enzymes
   Slightly better

CT abdomen
   Normal pancreas

Serology

Sprue serology positive

- IgA endomysial + tTG IgA
- SBBx = sprue
- Better on GFD
- Serology normalized
Steatorrhea – Clinical Clues

Dietary history – Intake compared to others
Weight loss
Stools – Not always diarrhea, may be bulky
Hard to flush
Oily droplets floating on toilet water (unhydrolyzed TG)

Steatorrhea – Vitamin Malabsorption

Fat soluble vitamins D A K E

Osteomalacia D
Night blindness A
Easy bruisability K
Vitamin E
Fecal Fat Analysis

Qualitative – Can be subjective
Variable lab personnel
Nl is less than 20 drops/hpf

Quantitative – 24 hr on 100 gm fat diet

Weight < 200 – 300 gm
Fat < 7 gm / 24 hr

Stool Fat Tests – Caveats

1. High carbohydrate diet – increases stool weight to 300 – 400 gms

2. Voluminous stools will raise fat excretion (up to 14 g/24 hour)

3. Correct for fat intake – low fat diets

4. False positives; Olestra, Brazil nuts
Steatorrhea

Mucosal
- CELIAC SPRUE
- CROHN’S
- Ileitis/
  ileal resection
- Short bowel
  syndrome

Luminal
- PANCREATIC
  INSUFFICIENCY
- Bile salt deficiency
- Bacterial overgrowth
- SIBO

Malabsorption – think about…

- Post gastric surgery or anti-reflux surgery – history
- Chronic mesenteric ischemia – history
- Drugs, including HAART – history
- Radiation – history
Malabsorption – think about…

- Parasites – stool tests
  - Giardia
  - Cryptosporidia
  - Cyclospora
  - Isospora belli

Next Steps in Evaluation

- Radiologic imaging – cross sectional
  CT Abdomen and pelvis and CT Enterography

- Capsule study

- Enteroscopy or DBE for biopsy
Uncommon Small Intestinal Diseases

- Collagenous sprue
- Whipple’s disease
- Eosinophilic enteritis
- Lymphoma
- Amyloid

Luminal – Pancreatic Insufficiency

- Direct function test: secretin test, research tool
- Indirect tests
  - Serum amylase/lipase
  - Serum trypsin
  - Fecal chymotrypsin
  - Fecal elastase

ALL HAVE POOR SENSITIVITY/SPECIFICITY
Fecal Elastase 1

- 6% of pancreatic enzymes
- Abnormal: < 200 μg/gram stool
- But abnormal in many other conditions
  - Celiac disease
  - IBD
  - IBS
  - HIV
  - Diabetes


Pancreatic Insufficiency

- Empiric trial of enzymes – reasonable
  - High dose – monitor wt gain or fecal fat
  - If respond, image pancreas

- Another option is to rule out mucosal disease first
Bile Acid Diarrhea

- Bile acids cause colonic salt and water secretion and increased colon motility

- Secondary bile acid malabsorption
  - Ileal resection or disease (Crohn’s)
    - < 100 cm – watery
    - > 100 cm – malabsorption

- Primary bile acid malabsorption? (misnomer)

Luminal – Small Intestinal Bacterial Overgrowth (SIBO)

- Structural causes
  - SI diverticulosis
  - Stricture
  - Surgical diversions

- Dysmotility
  - Scleroderma
  - Intestinal pseudo-obstruction

- Others?
  - Diabetes
  - IBS
  - Acid suppression
**SIBO Diagnosis**

- Clue: high folate, low $B_{12}$
  Bacteria produce/consume

- SB aspirate

- Breath tests – not great

- Therapeutic trial – probably best
  Antibiotics

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**Watery Diarrhea**

- If Not Bloody and

- Not fatty

- It’s WATERY . . .

All the rest
Watery Diarrhea - History

- Surgery – gall bladder, stomach, intestine
- Family history
  - Celiac
  - IBD
- Sexual history
  - Infections
  - HIV
- Travel History – Traveler’s diarrhea
  - High risk areas

Watery Diarrhea - History

- Medications – 7% of all drug side effects especially “new” ones
  - Antimicrobials
  - PPIs (lansoprazole)
  - NSAIDS, 5-ASAs
  - SSRIs
  - Psycholeptics
  - Allopurinol
  - Metformin
  - Angiotensin ARBs
Watery Diarrhea – Diet

- Alcohol
- Dairy
- Caffeine?
- Nutritional supplements, herbals, OTC drugs
- Fructose and sorbitol – osmotic diarrhea

Watery Diarrhea – Diabetes

- Visceral autonomic neuropathy
- Bacterial overgrowth
- Celiac disease
- Pancreatic insufficiency
- Unabsorbed CHO (Sugarless sweets)
Watery Diarrhea – Post Cholecystectomy Diarrhea

- Incidence 20%
- Can be delayed
- Rarely severe
- Rx – bile acid binders

Watery Diarrhea

Increased bile acid biosynthesis is associated with IBS – ID

Wong et al, Clin Gastroenterol Hepatol, 2012; 10:1009
Bile Acid Diarrhea (IBS – ID Patients)

Hepatic Bile Acid Synthesis
• Genetic variations in proteins involved in feedback regulation of bile synthesis
• Result
  • Increased bile acid secretion
  • Increased bile acid in colon
  • Increased secretion and transit → diarrhea
• May be why cholestyramine works
• Called 1° bile acid malabsorption

Watery Diarrhea – Initial Evaluation

• History + Exam

• Initial labs
  • CBC
  • Chemistries (total protein, albumin)
  • Thyroid tests
  • Celiac serology
  • ESR/CRP
  • Stool FOBT
Watery Diarrhea – Infections

Stool exam low yield

- Ameba
- Giardia
- Cryptosporidia
- Cyclospora
- Blastocystis hominis (?)
- Candida (?)
- Yersinia
- Salmonella
- Aeromonas
- Plesiomonas
- C. difficile (recurrent)

Watery Diarrhea – Mucosal Disease

- Colonoscopy + biopsy
  - Crohn’s
  - Microscopic colitis
  - Colon cancer
  - Large rectal villous adenoma
- Small bowel diseases – EGD + duodenal biopsy
  - Previously Mentioned
Chronic Diarrhea – Yield of Biopsy at Colonoscopy

Series vary: 10—20%

Most commonly:
- IBD
- Microscopic Colitis
- Pseudomelanosis coli
- Spirochetosis

Pseudomelanosis coli

- Surreptitious laxatives
- Factitious Diarrhea
Microscopic Colitis—Collagenous and Lymphocytic

Typically:
- Chronic watery diarrhea
- Colon bx diagnostic
- Other w/ u – negative

Histology: increased lamina propria lymphocytes, intraepithelial lymphocytes, increased collagen band in CC, not LC
Where to biopsy

Studies vary, usually left colon adequate

Right colon alone 10% in one series

Transverse colon highest yield in another

Probably Shouldn’t Biopsy
Normal Cecum

Cecal and rectal biopsy in 85 healthy adults

Cecal biopsies had increased microscopic inflammation, abnormal architecture and cryptitis compared to rectal biopsies

Paski et al, Amer J Gastroenterol 2007
When to Biopsy TI

Chronic diarrhea and Right lower quadrant pain are the best indications to biopsy normal TI

Still yield low 1 – 2 %

Watery Diarrhea

If work-up negative so far,

• Consider other stool tests
  • Fecal Fat
  • Laxative screen
  • Osmotic gap

• Consider small bowel evaluation
**Stool Osmotic Gap**

Normal 290 – 2 (Na+K)

- Secretory < 50
- Osmotic > 125
- Contamination > 375

Lab will not do test on solid stool, so can use to confirm diarrhea

**Secretory Diarrhea**

Continues with fast

- Hormonal:
  - ZE – Gastrin
  - VIP – VIP
  - Carcinoid – 5HIAA
  - Medullary Ca – Calcitonin
  - Thyroid

- Idiopathic secretory diarrhea
Idiopathic Secretory Diarrhea

Often sudden onset
Up to 20 pound weight loss, then stable
Lasts 2 years

1. Epidemic
   Contaminated food or water
   “Brainerd” Minnesota

2. Sporadic
   Travel to local lakes or other
   No one else sick

Previously healthy, likely infectious
Epidemic – Brainerd
Sporadic – travel, lakes, no one else sick
Abrupt onset,
20 lb wt loss then stable
Resolves over 2 yrs
Case – 63 y o Woman

6 months watery diarrhea
Onset after trip to Missouri
Large volume, 6 – 7/day even fasting
No abdominal pain
Prerenal azotemia twice
IV fluid dependent
20 lb wt loss, now stable
Sounds secretory

Normal w/u

Stool culture, O + P
Celiac antibodies
EGD + Bx
Colon + Bx
Abdominal CT scan
Her 24 HR Stool

980 gm – on a “good” day
12 gm fat (dragged by high volume)
Laxative screen normal
Na 119, K 17
Osmotic gap 290 –2 (119 + 17) = 3
 calculated is better than measured osms
Thus, secretory diarrhea

Secretory Diarrhea

- Infection – R/O’d
- Mucosal – R/O’d
- Factitious – R/O’d
- Hormonal?
Evaluation

- VIP – nl VIP
- ZE – nl gastrin off PPI, octreotide scan
- Carcinoid – nl 5HIAA
- Medullary Ca Thyroid – nl calcitonin

Gradual improvement over 3 mos

Dx: Sporadic Idiopathic secretory diarrhea
When I am stumped . . .  
I Take More History

- Diarrhea onset 
  - After Infectious gastroenteritis  
    PI – IBS  
  - After GI tract surgery  
    Post-cholecystectomy  
    Post anti reflux surgery  
  - Sugarless chewing gum  
    10 packs/day

- Family history 
  
  Example: Celiac disease in 65 yo 
  with sent for evaluation of recurrent *C. difficile*
When I am stumped . . . I May Order a Special Study

- A woman with protein losing enteropathy,
- Extensive evaluation negative except diffuse edema of small intestine
- ↑ eosinophils in duodenal bx

DBE → eosinophilic enteritis
When I am stumped . . .
Empiric Trials

- Cholestyramine
- Pancreatic enzymes
- Bile acid supplement
- Antibiotics
- Antimotility agents
- Tincture of opium

Dx of Obscure Diarrheas at Referral Center

Fecal incontinence
Functional, IBS
Iatrogenic – drugs, surgery, radiation

Surreptitious laxatives
Colon + bx
Microscopic colitis

Schiller, Sleisinger & Fordtran, GI & Liver Dis, 2002
Dx of Obscure Diarrheas at Referral Center – Cont’d

SB bacterial overgrowth
Panc insufficiency
CHO malabsorption

Hx + Therapeutic trial

Peptide secreting tumors
Chr idiop secre diarrhea

Assays + Scans

Schiller, Sleisinger & Fordtran, GI & Liver Dis, 2002

Summary

1. History, + stool characteristics & initial labs will guide w/u
2. Reasonable w/u will diagnose most
   Check Diet/meds
   Exclude infection
   Endoscopy and Biopsy
   – upper & lower
3. If normal further w/u to include therapeutic trials
4. Uncommon causes are uncommon