Approach to the Patient with Diarrhea

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Alarm Symptoms

- Weight loss
  “Beware the diet that works”

- Blood in stool

- Nocturnal diarrhea
Diagnostic Approach to Chronic Diarrhea

- Bloody
- Fatty
- Watery

Case

41 yo Ukrainian man, carpenter

11 days diarrhea, without blood or mucus,
Crampy abdominal pain, Fever,
No travel or exposures
Had had bloody diarrhea for several weeks 6 months prior
Recently quit smoking
Febrile, otherwise normal exam
Any thoughts?

- Next steps:
  - Culture stools?
  - IBD serology?
  - Sigmoidoscopy?

Stool Tests

Enteric Bacteria – negative

O + P negative

CT diffuse wall thickening; descending and sigmoid colon with mesenteric stranding

Next steps?
Flexible Sigmoidoscopy to Transverse Colon

Diffuse colitis, erosions
Yellow membranes

Given empiric Rx for *C. difficile*
Path – acute inflammation
  No changes of IBD
  No viral inclusion
  IHC + shell vial positive for CMV
  Serum CMV positive (IgM and IgG)

Course

*C. difficile* Rx d/c'd
HIV negative
Ganciclovir started, 2 wks IV
Slightly better after 10 days
Less fever
Eventually improved after 20 days in hospital
Several Weeks Later

Colonoscopy – Colitis from rectum to hepatic flexure

Bx – IBD, probably ulcerative colitis

Oral mesalamine

Prednisone + sulfasalazine added
Now has dx of IBD—pptd by CMV?

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
Colonoscopic Appearances

Infections – often patchy

Ulcerative Colitis – typical

Crohn’s – segmental

Ischemia – Rectal sparing
  Location, location, location
  Can be multifocal

Infectious Colitis
Grade I – II Ischemia

Ulcerative Colitis
Radiation Proctitis

Whipworm (Trichuris)
## Colorectal Biopsy

<table>
<thead>
<tr>
<th>IBD</th>
<th>Infection</th>
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</thead>
<tbody>
<tr>
<td>Abnl architecture</td>
<td>Normal</td>
</tr>
<tr>
<td>Acute &amp; Chronic</td>
<td>Acute</td>
</tr>
<tr>
<td>inflammation</td>
<td></td>
</tr>
<tr>
<td>Basal inflammation</td>
<td>none</td>
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</tbody>
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## Normal Colon

![Normal Colon Image](image)
Colonic Biopsy can Diagnose Specific Infections

- Pseudomembranes
- Viral Inclusions
- Parasites
- 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>
</tr>
</thead>
<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>Apthae rare</td>
<td>Not common</td>
</tr>
<tr>
<td>IC valve destroyed</td>
<td>Not common</td>
</tr>
</tbody>
</table>
Case # 2

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, normal mood and affect

Vital signs normal

Skin – no rash

Abdomen – normal, RUQ scar, no organomegaly, mass or tenderness

Questions

Does she have diarrhea?
  - Fecal incontinence vs. diarrhea?

Do you have any initial diagnostic ideas?

What are next steps in evaluation?
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
- 24 hr stool – 618 gm
  - 44 gm fat
Mucosal or pancreatic?
What is your differential diagnosis?
**Therapeutic Trial**

Pancreatic enzymes  
Slightly better

CT abdomen  
NL pancreas

Fat – 7 g/100g stool (<9.5)

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**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
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
5. Panc – biliary source clue
   > 9.5 gm fat/ 100 gm stool
Steatorrhea

Luminal
- Pancreatic Insufficiency
- Bile salt deficiency
- Bacterial overgrowth

Mucosal
- Celiac sprue
- Crohn’s

Luminal – Pancreatic Insufficiency

- Direct function test: secretin test, research tool

- Indirect tests
  - 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
Luminal – Bile Salt Deficiency

- Secondary
  - Cirrhosis, including PSC and PBC
  - Ileal disease or resection
    - < 100 cm – watery
    - > 100 cm – fatty
  - Bacterial Overgrowth

- Primary
  - Primary bile salt deficiency
  - Watery diarrhea
    - Under diagnosed?

Bile Acid Diarrhea

Bile acids cause colonic salt and water secretion

Secondary bile acid malabsorption
  - Ileal resection or disease (Crohn’s)
    - (< 100 cm)
Primary (Idiopathic) Bile Acid Malabsorption – Dx

- Se HCAT retention test – available in Europe
  - (selenium homocholic acid taurine)
  - Low retention (10–15%) is abnormal

- Elevated serum bile acids (not available)

- Compensatory elevated bile acid precursor (C4) due to loss (blood test)

- Secondary gain

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<sub>12</sub>
  Bacteria produce/consume
- SB aspirate
- Breath tests – not great
- Therapeutic trial – probably best

**Mucosal – Celiac Disease**

- Diarrhea
- Weight Loss
- Iron deficiency
- Infertility and recurrent fetal loss
- Microscopic colitis
- Abnormal liver enzymes
Celiac Diagnosis

- Antibody tests – On gluten
  - IgA tTG or EmA and Serum IgA (2–3% of sprue patients are IgA deficient)
  - tTG preferred
  - Not antigliadin ab (unless deaminated)
- Small bowel biopsy +
  - Response to therapy
- Genotype–HLADQ2, DQ8
  - Rules out if negative
  - Can use if mild sx, neg serology and borderline biopsy

Malabsorption – think about…

- Parasites
  - Giardia
  - Cryptosporidia
  - Cyclospora
- Post gastric surgery or anti-reflux surgery
- Chronic mesenteric ischemia
- Radiation
- Ileitis/resection
- Drugs, including HAART
Malabsorption – Uncommon Small Intestinal Diseases

- Causes
  - Collagenous sprue
  - Whipple's disease
  - Eosinophilic enteritis
  - Lymphoma
  - Amyloid

- Diagnosis
  - Radiologic imaging
  - Capsule study
  - Enteroscopy or DBE for biopsy

Watery Diarrhea

- If Not Bloody and

- Not Steatorrhea,

- It's Watery . . .

All the rest
Watery Diarrhea – Medical History

- Diabetes, other diseases
- 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
Watery Diarrhea – Diet

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

Alcohol

- Chronic ETOH → diarrhea?
- Multiple possible mechanisms
  - Motility
  - Mucosal damage
  - Flora
  - Immune
- Literature not strong, none recent

Bode, Best Practice 2003, Rajendiam, Dig Dis 2005
How Much Alcohol is Too Much?

- More than 1 gm/kg → induces diarrhea

- 70 gm – 70 kg person
  - 3 glasses wine
  - 1 drink (hard liquor)

- Wouldn’t take much

Watery Diarrhea – Diabetes

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

- Incidence 20%
- Can be delayed
- Rarely severe
- Low bile acid absorption in TI at night
- Rx – bile acid binders

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 culture low yield

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

Watery Diarrhea – Mucosal Disease

- Colon
  - Crohn’s
  - Microscopic colitis
  - Colon cancer

- Small bowel diseases
- Previously Mentioned
Watery Diarrhea – Evaluation

• Colonoscopy + biopsy
  • Crohn’s
  • Microscopic colitis
  • Colon cancer
• EGD + duodenal biopsy

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
Lymphocytic Colitis

Colonoscopy – Microscopic Colitis

Mild abnormalities in 1/3
- Erythema
- Friable
- Ulcers
- Mucosal lacerations on insufflation

Smith J Am Coll Surg 2007
Collagenous Colitis – Tears

Where to biopsy

Studies vary, usually left colon adequate

Right colon alone 10% in one series

Transverse colon highest yield in another
Chronic Diarrhea – Yield of Biopsy at Colonoscopy

Series vary: 10—20%

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

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
**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

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**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

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
- Iatrogenic – R/O’d
- Hormonal?

Evaluation

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

Gradual improvement over 3 mos

Dx: Sporadic Idiopathic secretory diarrhea

Idiopathic Secretory Diarrhea

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
Watery Diarrhea—uncommon...

- Hyperthyroidism
- Addison’s disease
- Lymphoma
- Mastocytosis
- Rectal villous adenoma
- Chronic mesenteric ischemia

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
When I am stumped . . .
I Take More History

- Family history

Example: Celiac disease in 65 yo sent for evaluation of recurrent *C. difficile*

When I am stumped . . . I May
Redo an Important Study

- Pancreatic insufficiency – a woman with steatorrhea and poor response to enzymes, had a normal CT + EUS

- A repeat CT showed pancreatic atrophy
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
- ? Slight ↑ eosinophils in duodenal bx

DBE → eosinophilic enteritis
When I am stumped . . .

Empiric Trials

- Cholestyramine
- Pancreatic enzymes
- Antibiotics
- Antimotility agents

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 → Assays + Scans
Chr idiop secr diarrhea

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

Therapeutic Trials

• Unexplained steatorrhea – pancreatic enzymes
• Unexplained idiopathic
  Bile acid resins
• Opiates helpful in some
  Opium tincture 2 – 20 drops QID
• Others
  Octreotide
  Clonidine
  Probiotics
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