



A 23-Year-Old Man with Bloody Diarrhea and Fever – Chapter 29

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Based upon: [LABORATORY MEDICINE CASEBOOK](#).

An introduction to clinical reasoning

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History and Presentation

- A 23-year-old man brought to the ER with complaints of bloody, mucoid diarrhea, fever and general weakness of 10 days duration. Patient attributed symptoms to food poisoning from an undercooked hamburger
- After 5 days patient was seen by GP and antibiotics prescribed
- No improvement over the next five days. Patient brought to the ER.
- Physical Exam
 - Alert, ill-appearing male
 - BP: 120/90
 - HR: 118 bpm; RR: 20
 - Rest of exam unremarkable
 - Abdomen: soft and non-tender; bowel sounds heard
 - No splenomegaly
 - Rectal exam: normal sphincter tone, no tenderness; no masses
 - Fresh blood present on examining glove

What's your differential?

- **Cramping, abdominal pains, bleeding and changed bowel habits**
 - **Cancer:**
 - **Inflammatory bowel disease:**
 - **Ulcerative colitis** – Inflammatory diarrhea, fever, and abdominal pain – large intestine ONLY
 - **Crohn's disease** – Small intestine, but may extend into large intestine, as well
 - Bacterial Enteric pathogens
 - **Compylobacter jejuni** – Causes patchy destruction of the mucosa and inflammatory diarrhea, fever and abdominal pain
 - **Shigella** – One of principal causes of dysentery
 - **Entamoeba histolytica, Clostridium difficile** also can cause inflammatory colitis
 - **Non-inflammatory bowel disease:**
 - **Irritable bowel syndrome**
 - **E. coli infection** – Secretory, non-inflammatory diarrhea cause by entero-toxigenic toxins
 - Viral infections
 - **A malabsorption syndrome:**
 - **Celiac sprue** – Malabsorption injury to villous epithelial cells from gluten -

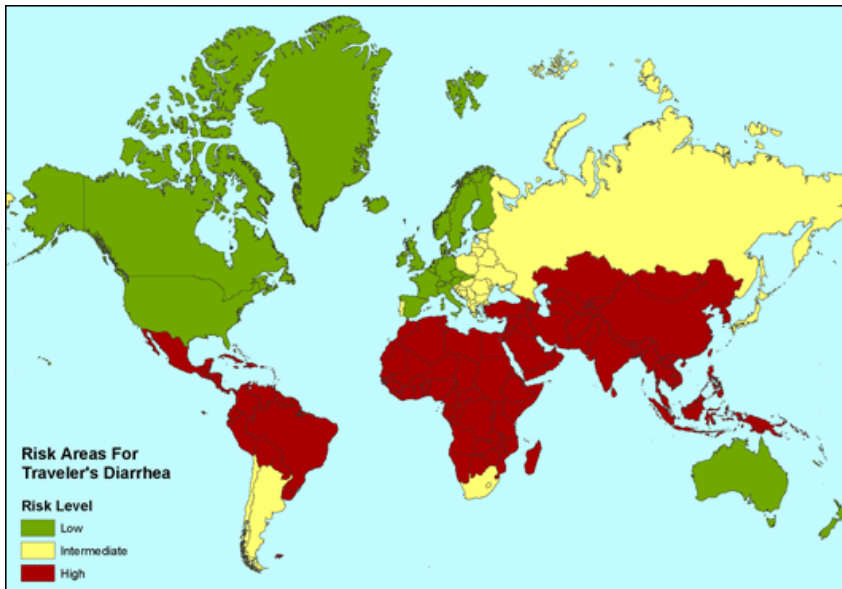
[Shigellosis]

- Shigellae
 - Gram-negative, nonmotile, facultatively anaerobic, non-spore-forming rods.
 - Differentiate from E.coli on the basis of pathogenicity, physiology (failure to ferment lactose or decarboxylate lysine) and serology.
- Endemic in *developing* countries where sanitation is poor.
- Infection → fecal-oral contamination. An early symptom, diarrhea due to enterotoxins may occur as the organisms pass through the small intestine.
- The hallmarks of shigellosis are bacterial invasion of the colonic epithelium and inflammatory colitis.

Enterotoxigenic *Escherichia coli*

- ETEC → bacterial diarrheal illness.
 - Leading cause of travelers' diarrhea and a major cause of diarrheal disease in underdeveloped nations, especially among children.
 - Food or water contaminated with animal or human feces. Significant, but self-limiting and rarely life-threatening illness.
 - The toxins and the diseases that ETEC causes are not related to *E. coli* O157:H7.

How about Traveler's Diarrhea?



Bacterial Enteric Pathogens

- Most common cause of TD. (85%) of TD cases, parasites about 10%, and viruses 5%.
- ***Enterotoxigenic Escherichia coli (ETEC)***
 - Most common cause of TD worldwide is ETEC.
 - Large inoculum necessary
 - Breakdown of sanitation.
 - Watery diarrhea/cramps. Fever +/- Ingestion of a large of this organism is necessary to produce disease.
- ***Enteroaggregative E. coli (EAEC)***
- Increasingly recognized as a cause of TD (up to 25%) of cases.
- ***Campylobacter jejuni***
- Common cause of diarrhea in developed countries but is many times more prevalent in developing countries.
 - Travel to Asia a higher risk in most studies. *Campylobacter* infections may be associated with bloody diarrhea as well as fever.
- ***Salmonella spp.***
 - Infrequent cause of TD worldwide.
- ***Shigella spp.***
 - The low infectious dose of this organism makes it one of the more commonly reported bacteria associated with TD.
 - *Shigella* may cause a bloody diarrhea with constitutional symptoms and fever.
- ***Vibrio spp.***

Inflammatory Bowel Disease

- Exact cause - unknown
 - Related to protective immune cells that are present in the lining of the intestines.
 - These normally turn on and off to fight harmful substances like bacteria and viruses that pass through intestines.
 - In IBD an initial trigger: infection, something taken in from the diet or the surrounding environment → activates immune system. It fails to turn off

HEMATOLOGY

	Patient	Normal
WBC	11.28 X 10³/uL	(3.3-11.0)
Neut	69 %	(44-88)
Band	22 %	(0-10)
Lymph	4%	(12-43)
Mono	3%	(2-11)
Eos	1%	(0-5)
Baso	1%	(0-2)
RBC	4.76 X 10 ⁶ /uL	(3.9-5.0)
Hgb	14.1 g/dL	(12.6-17.0)
HCT	43.1 %	(37.2-50.4)
MCV	90.4 fL	(80.5-102.1)
MCH	29.6 pg	(27.0-35.0)
MCHC	32.8 g/dL	(30.7-36.7)
Plts	280 thousands/uL	(130-400)

Shift to the Left



Band cell

- Includes:
 - Unilobed and two lobed nucleus predominate
- Seen in:
 - Acute infection
 - Metaboloc acidosis
 - Necrosis: myocardial infarct. malignant tumors
- Blood disease:
 - hemolytic crises,
 - severe blood loss
 - chronic granulocytic leukemia,

CHEMISTRY

Test	Patient	Normal
Glucose	100 mg/dL	(65-110)
Creatinine	1.4 mg/dL	(0.7-1.4)
BUN	7 mg/dL	(7-24)
Uric Acid	6.2 mg/dL	(3.0-8.5)
Cholesterol	151 mg/dL	(150-240)
Calcium	8.6 mg/dL	(8.5-10.5)
Protein	6.2 g/dL	(6-8)
Albumin	3.4 g/dL	(3.7-5.0)
LDH	176	(100-225)
Alk. Phos.	77 U/L	(30-120)
AST	12 U/L	(0-55)
Amylase	24 U/L	(23-85)
GGTP	15 U/L	(0-50)
Bilirubin/Bil. Direct	0.7 mg/dL/(.15 mg/dL)	(0.0-1.5)/(.02-18)

Urinalysis

Test	Patient	Normal
Sp. Gravity	1.028	(1.010-1.055)
pH	6	(5.0-7.5)
Protein	Neg	(Neg)
Glucose	Neg	(Neg)
Ketone	Trace	(Neg)
Occult blood	Neg	(Neg)
Color	Yellow	(Yellow)
Clarity	Clear	(Clear)
WBC	0/HPF	(0-5)
RBC	0/HPF	(0-2)
Bacteria	Neg	(Neg)
Urobilinogen	Neg	(neg)

Additional Studies:

Test	Patient	Normal
Stool Leukocytes	12 WBC/HPF (↑Neut)	(<5)
Blood Hemocult	Positive	(Neg)
Ova and parasites	Negative	(Neg)
Culture and Sensitivity for common enteric pathogens and campylobacteria	Pending	(Neg)
Clostridium Difficile	Pending	(Neg)

Significance of stool examination

- > 5 PMNs/HPF in the stool → inflammatory process
- Viruses - MOST COMMON causes of non-inflammatory diarrhea
- *E. coli* produces toxins → diarrhea but it is a non-inflammatory diarrhea. Leukocytes are typically absent
- Typical inflammatory causes of diarrhea include:
 - *Shigella* – dysentery and bloody diarrhea
 - *Campylobacter jejuni* – patchy destruction of mucosa in the small and large intestines – inflam. Diarrhea, fever and abdominal pain
 - *Yersinia enterocolitica* – similar clinical picture

Additional Studies:

Electrolytes

Test	Patient	Normal
Na+	136 mEq/L	(134-143)
K+	3.5 mEq/L	(3.5-4.9)
Cl-	95 mEq/L	(95-108)
CO ²	32 mEq/L	(21-32)

Other

Test	Patient	Normal
Erythrocyte Sedimentation Rate (ESR)	20 mm/hr	(0-15)
Blood Culture	PENDING	(Neg)

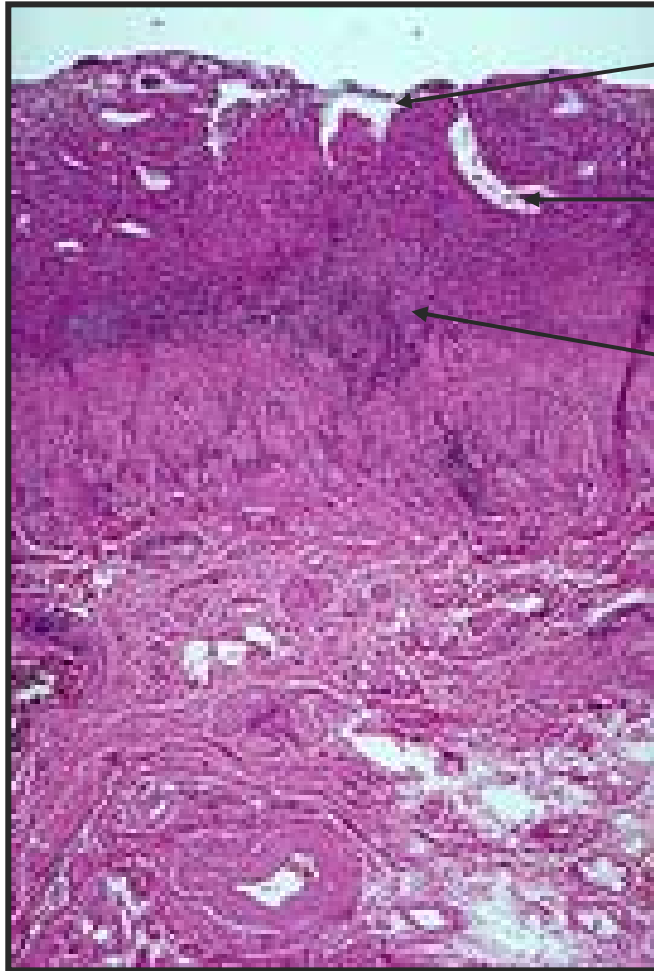
Diarrhea

- Base-losing acidosis (Metabolic acidosis)
 - Direct loss of HCO_3^- from the lumen of the small intestine results in acidosis
 - Normally HCO_3^- is secreted and reabsorbed in the small intestine
 - Prolonged diarrhea (ulcerative colitis or severe dysentery) prevents reabsorption and may → to a significant loss of HCO_3^- in the feces.
 - **Compensations:**
 - Hyperventilation
 - Renal excretion of the H^+ ions combined with the urinary buffers, (HPO_4^- , or NH_3). HCO_3^- is regenerated in the plasma.
 - Intracellular and bone buffering. H^+ ions can enter cells and be taken up by the cell and the bone buffers (eg, proteins, phosphate, bone carbonate).

Clinical Course

- Patient was admitted to the hospital and started on IV fluids.
- Colonoscopy was performed obtaining multiple biopsies of the rectum, the sigmoid, and the descending colon
- Patient was begun on specific treatment

Colonic Biopsy – H&E x12



Ulceration

Crypt Abscess

Inflammatory
infiltration of
lamina propria

Tubular glands
distorted, decrease
in the number of
goblet cells,
widened
muscularis mucosa

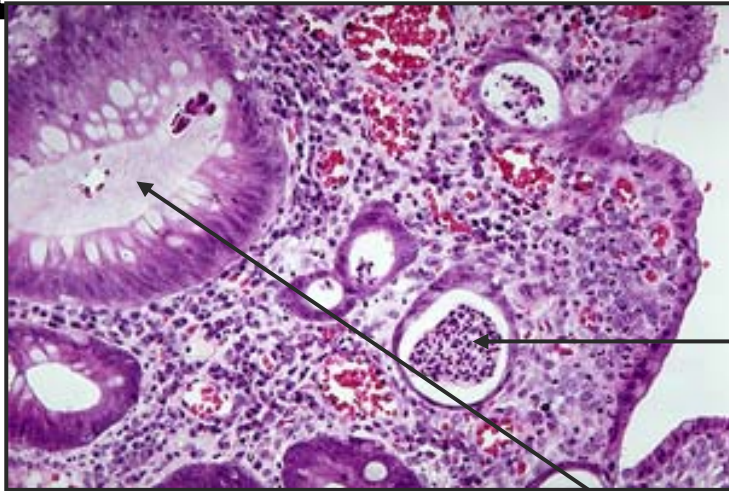
PATIENT



NORMAL

Ulcerative Colitis – H&E x50

Patient



Normal



- Crypts
 - pattern distorted
 - Crypt abscesses
 - Neutrophilic infiltration
- Goblet cell depletion

[Symptoms of Ulcerative Colitis]

- abdominal pain
- bloody diarrhea
- fatigue
- weight loss
- loss of appetite
- rectal bleeding
- loss of body fluids and nutrients
- 1/2 patients have mild symptoms, the other half have major symptoms
- 5% will develop colon cancer

Gross appearance – Ulcerative colitis



Ulcer

- Gross appearance of active ulcerative colitis
- Multiple areas of ulceration on the mucosal surface
- Intact mucosa between ulcers is markedly hemorrhagic and appears granular

Ulcerative colitis

- Usually occurs in the rectum and lower part of the colon.
- Rarely affects the small intestine except for the terminal ileum.
- Inflammation and sores in the lining of the large intestine → Inflammatory Bowel Disease
- Inflammation causes colon empty frequently i.e. diarrhea
- Differential may be difficult – Crohn's disease (usually small intestine) vs. Ulcerative colitis (colon)
- Principal age 15-30, no gender preference

Differential Dx. of Ulcerative Colitis

- Viral
 - Cytomegalovirus
 - Herpes
- Bacterial
 - Salmonella species
 - Shigella species
 - Yersinia enterocolitica
 - Vibrio parahaemolyticus
 - Aeromonas hydrophila
 - Neisseria gonorrhoeae
 - Chlamydia trachomatis
 - Syphilis
 - Staphylococcus aureus
 - Escherichia coli
- Protozoan
 - Amebiasis
 - Balantidiasis
 - Schistosomiasis
- Fungal
 - Histoplasmosis
 - Candidiasis
- Other
 - Clostridium difficile *Radiation colitis*
 - Crohn's colitis*
 - Medication/drugs*
 - Enemas
 - Laxatives
 - Local nonsteroidal anti-inflammatory drugs
 - Sulfasalazine
 - Penicillamine
 - Gold
 - Methyldopa
 - Eosinophilic gastroenteritis*
 - Behçet's syndrome*
 - Colitis in graft-versus-host disease*

Grading Clinical Severity of Ulcerative Colitis

■ Severe (15%):

- Diarrhea >6x/day
- Blood in stools
- Fever
- HR >90/min
- Anemia
- Hypoalbuminemia
- ↑ ESR
- Weight loss severe

■ Medical therapy is often ineffective
colectomy often required

■ Moderate

- Diarrhea <6x>4x/day
- Small amt of blood
- ↔ Low grade fever
- No tachycardia
- Mild anemia
- ↔ESR

■ Medical therapy often effective

■ Prognosis: Repeated attacks probable risk of fulminant colitis

■ Mild:

- Diarrhea >4x/day
- No Fever
- No tachycardia
- No Anemia
- No weight loss
- No hypoalbuminemia

Treatments of Ulcerative Colitis

- Typical treatments
 - Anti-inflammatory drugs
 - Corticosteroids
 - Intravenous ACTH
 - Surgery
- This patient received mesolamine (anti-inflammatory) and ACTH

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[Hematology review]

- Why were the PMNs even higher after treatment
- Answer: Glucocorticoids cause leukocytosis by causing the bone marrow to release PMNs into circulation

Typical lab findings – Ulcerative colitis

- **Anemia**) – Not present in this patient
- **Thrombocytosis** (ie, platelet count >350,000/mcL) – Not initially
- **Elevated sedimentation rate** (variable reference ranges, usually 0-33 mm/h)
- **Elevated C-reactive protein** (ie, >100 mcg/L): Both of these findings correlate with disease activity.
- **Hypoalbuminemia** (ie, albumin <3.5 g/dL)
- **Hypokalemia** (ie, potassium <3.5 mEq/L)
- **Hypomagnesemia** (ie, magnesium <1.5 mg/dL)
- **Elevated alkaline phosphatase**: More than 125 U/L suggests primary sclerosing cholangitis (usually >3 times the upper limit of the reference range).

- **BLUE - Present in this patient**

Ulcerative colitis versus Crohn's colitis

<i>Feature</i>	<i>Ulcerative colitis</i>	<i>Crohn's colitis</i>
<i>Clinical features</i>		
Rectal bleeding	Very common - 90%	Uncommon: may be occult
Diarrhea	Early, frequent, small stools	Less prevalent or absent
Abdominal pain	Predefecatory, urgency	Colicky, postprandial
Fever	Uncommon if uncomplicated	Frequent
Palpable mass	Rare	Frequent, right lower quadrant
Recurrence after resection	Rare	Frequent
Clinical course	Relapses/remissions 65% Chronic/continuous 20-30% Acute/fulminating 5-8%	Usually slowly progressive; fulminant
<i>Endoscopic features</i>		
Proctosigmoidoscopy	Diffuse pinpoint ulcerations, continuous lesions	Discrete aphthoid ulcerations, patchy lesions
<i>Radiologic features</i>		
Rectal involvement	Invariable	Infrequent
Distribution	Continuous	Segmental, discontinuous
Mucosa	Fine ulcerations	"Cobblestones"
Strictures	Rare	Frequent
Fistulas	Rare	Frequent
<i>Histologic features</i>		
Distribution	Mucosal	Transmural
Cellular infiltrate	Polymorphs	Lymphocytes
Glands	Mucin depletion <ul style="list-style-type: none"> • Gland destruction • Crypt abscesses 	Gland preservation
<i>Special features</i>		
	None	Granulomas, aphthoid ulcers, histiocyte-lined fissures

[Case Summary]

- Final Diagnosis:
 - Ulcerative colitis
- Future Considerations:
 - Management
 - Pharmacologic
 - Surgery
 - Risk of colon cancer – the earlier the onset; the higher the risk

[ALL DONE

]

Differential

- Possibilities that might account for this scenario?
 - **Irritable bowel syndrome** –
Characterized by cramping, abdominal pains and changed bowel habits