Infectious Diarrhea

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Outline

- Introduction
- Epidemiology
- Pathophysiology
- Specific Pathogens and Treatment
- Clinical evaluation and diagnostic approach
Introduction

- Diarrhea: increased liquidity (or decreased consistency) of stools and increased stool frequency (≥3 stools/day)
  - Normal state: ~10L fluid enter duodenum/day
    - All but 1L absorbed by the small intestine
    - Colon absorbs remaining fluid
    - Only ~100mL lost in stool
Acute vs Persistent Diarrhea

- **Acute**
  - <2wks of symptoms
  - Usually self-limited
  - Often accompanied by symptoms of N/V or abdominal cramps
  - Two diarrheal syndromes: inflammatory diarrhea or noninflammatory diarrhea
  - Four main categories:
    - Bacterial
    - Viral
    - Parasitic
      - Protozoal
      - Helminths
    - Noninfectious
  - Usually infectious

- **Persistent**
  - >2wks of symptoms
  - “Chronic” = >4wks
  - Can be due to
    - Increased intestinal secretion
      - Ex: carcinoid, VIPomas
    - Malabsorptive/osmotic diarrhea
      - Ex: bacterial overgrowth, pancreatic insufficiency, mucosal abnormalities, lactose intolerance
    - Inflammatory bowel diseases
    - Inflammatory conditions
      - Radiation enteritis
      - Microscopic colitis
      - Malignancy
    - Altered motility
      - Ex: IBS
    - Parasites
      - *Giardia*
      - *Cryptosporidium*
Episodes of Diarrhea

- **Acute diarrhea**: Presence of three or more loose, watery stools within 24-hours
- **Dysentery**: Bloody diarrhea, visible blood and mucous present
- **Persistent diarrhea**: Episodes of diarrhea lasting more than 14 days
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Epidemiology

• Diarrheal disease is the leading cause of childhood death worldwide
  – CDC and WHO, 2012
    • 810,000 children <5yo perish from diarrhea per year
      – 11% of 7.6mi deaths of children under 5yo
      – Translates into 2,200 children dying every day as a result of diarrheal diseases
      – Mostly developing countries

• 3rd most common syndrome seen in general practice in the US
  – Foodborne Diseases Active Surveillance Network (FoodNet), 2013
    • Identified 19,056 cases of Cx-confirmed bacterial and laboratory-confirmed parasitic infection
    • 4200 hospitalizations
    • 80 deaths among 48 million residents of 10 states (= 15% of the US population)
    • Most frequent infections caused by *Salmonella* (39%)
    • 2nd most frequent by *Campylobacter* (35%)
# Food Safety Progress Report for 2013

<table>
<thead>
<tr>
<th>Disease Agents</th>
<th>Percentage change in 2013 compared with 2006–2008</th>
<th>2013 rate per 100,000 Population</th>
<th>2020 target rate per 100,000 Population</th>
<th>CDC estimates that...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campylobacter</td>
<td>13% increase</td>
<td>13.82</td>
<td>8.5</td>
<td>For every Campylobacter case reported, there are 30 cases not diagnosed</td>
</tr>
<tr>
<td>Escherichia coli O157</td>
<td>No change</td>
<td>1.15</td>
<td>0.6</td>
<td>For every E. coli O157 case reported, there are 26 cases not diagnosed</td>
</tr>
<tr>
<td>Listeria</td>
<td>No change</td>
<td>0.26</td>
<td>0.2</td>
<td>For every Listeria case reported, there are 2 cases not diagnosed</td>
</tr>
<tr>
<td>Salmonella</td>
<td>No change</td>
<td>15.19</td>
<td>11.4</td>
<td>For every Salmonella case reported, there are 29 cases not diagnosed</td>
</tr>
<tr>
<td>Vibrio</td>
<td>75% increase</td>
<td>0.51</td>
<td>0.2</td>
<td>For every Vibrio parahaemolyticus case reported, there are 142 cases not diagnosed</td>
</tr>
<tr>
<td>Yersinia</td>
<td>No change</td>
<td>0.36</td>
<td>0.3</td>
<td>For every Yersinia case reported, there are 123 cases not diagnosed</td>
</tr>
</tbody>
</table>

For more information, see [http://www.cdc.gov/foodnet/](http://www.cdc.gov/foodnet/)

Preliminary FoodNet 2013 Data
Outline

- Introduction
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- Pathophysiology
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- Clinical evaluation and diagnostic approach
Pathophysiology

• **Infectious diarrhea**
  – Groups of organisms (whether bacterial, viral, parasitic, or protozoal)
    • Noninflammatory group
    • Inflammatory group
      – Non-invasive group
      – Invasive group

• **Cause 2 diarrheal syndromes**
  – **Noninflammatory diarrhea** (diarrhea without fever or blood)
    • Caused by *enterotoxin-producing organisms or viruses*
      – Adhere to the mucosa → disrupt the absorptive and/or secretory processes of the enterocyte → diarrhea
  – **Inflammatory diarrhea** (diarrhea with fever and blood)
    • Caused by *cytotoxin-producing, noninvasive bacteria*
      – Adhere to the mucosa → activate cytokines → stimulate intestinal mucosa to release inflammatory mediators
    • OR, caused by *invasive organisms* (*which can also produce cytotoxins*)
      – Invade the intestinal mucosa → induce acute inflammatory reaction → activates cytokines → release inflammatory mediators
Host Factors

• Host factors
  – Age
  – Personal hygiene (fecal-oral)
  – Gastric acidity, physical barriers (protective barriers, low inoculums)
  – Intestinal motility (expel the pathogens)
  – Enteric microflora
  – Specific immunity: phagocytes, B-cell, T-cell
  – Intestinal receptor
Enteropathogens
Causative Agents in Diarrhea

**Bacteria**
- *Vibrio cholerae O1*
- *V cholerae O139*
- *V parahaemolyticus*
- *Escherichia coli*
- *Plesiomonas*
- *Aeromonas*
- *Bacteroides fragilis*
- *Campylobacter jejuni*
- *C. coli*
- *C upsaliensis*
- *nontyphoidal Salmonella*
- *Clostridium difficile*
- *Yersinia enterocolitica*
- *Y pseudotuberculosis*
- *Shigella species*

**Viruses**
- *Rotavirus*
- *Norovirus (Calicivirus)*
- *Adenovirus (serot.40/41)*
- *Astrovirus*
- *Cytomegalovirus*
- *Coronaviruses*

**Parasites**

**Protozoan**
- *Microsporida*
  - *Encephalitozoon bieneusi*
  - *Enterocytozoon intestinalis*
  - *Giardia intestinalis*
  - *Cryptosporidium hominis*
  - *Entamoeba histolytica*
  - *Isospora belli*
  - *Cyclospora cayetanensis*
  - *Dientamoebafragilis*
  - *Blastocystis hominis*

**Helminths**
- *Strongyloides stercoralis*
- *Angiostrongylus costaricensis*
- *Schistosoma mansoni, S japonicum*
- *Capillaria philippinensis*
Campylobacter Infection

- Small gram negative bacteria
- Species: *jejuni* and *coli*
  - Two most common sp. involved in human disease
    - Usually from eating raw or undercooked poultry, drinking infected raw milk, or ingesting any food contaminated
  - Brief febrile prodrome
  - Watery, bloody, 10-14BM/d
  - Complications: reactive arthritis and Guillain-Barré syndrome
  - **Dx** established by stool Cx
  - **Treatment**: often resistant to FQ
    - Macrolide 1st line therapy in US

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"Campylobacter Infection"
E Coli Infection

- Enteropathogenic *E Coli* (EPEC) – diarrheal outbreaks in neonatal nurseries
- Enteroinvasive *E Coli* (EIEC) – illness similar to Shigella infection
- Enterotoxigenic *E Coli* (ETEC) – common traveler’s diarrhea
- Enteroaggregative *E Coli* (EAEC) – common traveler’s diarrhea
- Enterohemorrhagic *E Coli* (EHEC) – causes hemorrhagic colitis
  - = Shiga-toxin-producing *E Coli* (STEC)
  - Associated with Hemolytic Uremic Syndrome
  - Most infectious in US due to O157:H7 strain
    - Low-dose pathogen (<100 organisms needed for infection)
- **Dx** established by stool Cx
- **Treatment** is supportive
  - Avoid antimotility agents
  - Abx not needed
Shigella Infection

- Illness characterized with fever, abdominal cramping, small-volume, mucoid, bloody diarrhea
- Usually develops several days after exposure
- In US: disease develops mostly in children (daycare centers)
- In developing countries: areas of overcrowding and poor sanitation
- Low-dose pathogen (only a few organisms needed to cause disease)
- Dx established by stool Cx

**Treatment**
- Self-limited in most patients
- However, recommended for all patients to decrease transmission risk
- Empiric Abx therapy with fluoroquinolone 5d
- Oral rehydration is usually sufficient
Salmonella Infection

- **Typhoid fever**
  - *Salmonella typhi* and *Salmonella paratyphi*
  - Rarely occurs in US

- **Nontyphoidal salmonellae**
  - Frequent causes of gastroenteritis in US
  - Animal reservoirs: poultry and eggs → foodborne outbreaks
  - Children who handle pet reptiles (turtles, snakes, lizards, and iguanas)

- N/V/D and cramping abdominal pain 8-72hrs after exposure

- 5% patients develop invasive disease and extraintestinal manifestations (bacteremia, endovascular endocarditis, osteomyelitis)
  - Greatest risk: infants <1yo and elderly
  - Predilection for aortic plaque, other endovascular foci (ex: bone prostheses)

- **Dx** established by stool Cx (sample can take up to 72hrs positive)
Salmonella Infection (cont’d)

- **Treatment (not required for healthy persons)**
  - PO fluoroquinolones
  - Immunocompetent <2yo and >50yo
  - Immunocompetent of any age with severe infection requiring hospitalization
  - Immunocompetent of any age with known or suspected atherosclerotic plaques and endovascular or bone prostheses
  - Immunocompromised of any age

- **Length of treatment**
  - Immunocompetent: 7-10d (possibility of bacteremia)
  - Immunocompromised: minimum of 2wks
    - May need 4-6wks of treatment bc of high incidence of relapse
    - Asymptomatic shedding of Salmonellae occurs in stool for several wks
      - Thus, f/u stool Cx are not recommended for most immunocompetent pts

- **Infected food handlers (Typhoid Mary) and healthcare workers should remain home until asymptomatic**
  - Negative stool Cx are required for these individuals
Viral Gastroenteritis

- **Rotavirus** most serious cause in infants/young children, then Adenovirus and Astrovirus
- **Norovirus** affects all age groups
  - Most common cause of pathogen-induced gastroenteritis → epidemic outbreaks
  - Fecal-oral route → culprit in most food outbreaks
  - Low-dose pathogen (10-100 organisms required to cause infxn)
  - Highly contagious
- **Abrupt onset of V/D**
  - Vomiting usually predominant symptom
  - Frequently associated with fever, abdominal discomfort, and headache
  - Typically begin within 24hrs after exposure
- **Dx usually presumptive and based on clinic findings**
  - Stool Cx are negative for bacteria
  - Can make Dx with PCR if needed
- **Treatment**
  - No specific antiviral treatment needed
  - Immunity is short-lived and reinfection occurs
Giardiasis

- Two most common infectious causes of chronic diarrhea are parasites (Giardia and Cryptosporidium)
- Caused by *Giardia lamblia*
  - Exists in two forms
    - Infectious cyst that lives in the environment
    - Trophozoite that attaches to the small bowel
- Most infections occur in children (ex: daycare centers)
  - Waterborne transmission is major cause of epidemic spread
  - Cyst can live in lakes, streams, municipal water supplies
  - Relatively resistant to chlorination
- <50% infected pts develop symptoms
  - Generally acute and self-limited
  - Foul-smelling fatty stools
  - Abdominal cramps and nausea
  - Often last 2-4wks
  - Up to 1/3 pts will develop chronic infxn
- Malabsorption may occur and result in significant weight loss
  - Protracted illness and weight loss helps distinguish it from other causes of gastroenteritis
  - Lactose deficiency is very common and can persist for months after acute infxn and may be confused with disease relapse or failure of Abx therapy
- Dx established by ova and parasites in stool
  - Several stool samples needed bc the organism is excreted only intermittently
  - Immune assays of stool: 90% sensitive, 95% specific
- Treatment for symptomatic pts; asymptomatic pts indicated for children
  - Decreases spread of infection to others
  - Decreases risk of reinfection
  - Flagyl 5d most often used
Cryptosporidiosis

- Infection spread from person-person, or from contaminated water source
  - Drinking water, swimming pools, water parks
  - Organisms resistant to chlorine disinfectants
  - Not effectively removed by many water filters
- Immunocompetent pts: diarrhea, malaise, anorexia, crampy abdominal pain
  - Can last up to 2wks
- Immunocompromised pts: prolonged diarrhea lasting >1mo
  - Often associated with weight loss and wasting
  - Biliary disease, including acalculous cholecystitis and sclerosing cholangitis
    - May develop in those with HIV/concomitant crypto infxn
    - Chronic cryptosporidiosis associated with decreased survival
- Dx: Routine stool ova and parasites does not detect Cryptosporidium spores
  - Microbiology should perform acid-fast stains
  - Enzyme-linked immunosorbent assays of stool using monoclonal Abs against oocytes → sensitive and specific
- Treatment depends on immune status of host
  - Immunocompetent: no specific therapy needed; self-limited
    - If ssx persist >wks: nitazoxanide can be tried → hastens ssx resolution and clear oocysts from the stool
  - Immunocompromised: respond poorly to nitazoxanide, paromomycin, Bactrim, and Flagyl
    - Initiate HAART to induce immune reconstitution critical to control cysts
**Clostridium difficile Infection**

- Inflammatory condition of colon caused by ingestion of spore-forming anaerobic, gram-positive bacillus
  - Inflammatory response 2/2 toxin-inducing cytokines (toxins A and B)
  - Common cause acute care hospital-acquired diarrhea and 15-30% of all cases of Abx-associated diarrhea
  - Ubiquitous in general environment
  - Hospitals are major reservoirs
    - Spores can survive for months on hospital surfaces
    - Typical hospital-cleaning products do not have sporicidal activity

- Risk factors
  - Disruption of predominantly anaerobic intestinal flora by Abx
    - Weeks to months after antibiotic exposure
    - Almost all classes of Abx have been associated
      - Including fluoroquinolones
  - Increased hospitalization
  - Proximity to an infected roommate
  - Elderly and Immunocompromised
  - Additional risk factors: disruption of intestinal mucosa due to chemotherapy, decreased gastric acidity by PPI and H2 blockers, repeated enemas, prolonged nasogastric tube insertion and gastrointestinal surgery

- Virulent strains → increased incidence of infection in last 8yrs
  - Strains: BI, NAP1, toxinotype III, ribotype 027
  - Recent epidemic BI/NAP1 isolates have found to hyperproduce toxins A and B in vitro

- Clinical features
  - Mild disease: frequent watery stools, abdominal cramping
  - Colitis: fever, leukocytosis, cramps, fecal leukocytes
    - Documented by colonoscopy or CT
  - Severe disease: paralytic ileus with cessation of diarrhea and development of toxic megacolon; multi-organ failure/sepsis
**C difficile Treatment**

- Before 2000: Flagyl and Vancomycin were considered to have comparable efficacy and relapse rates
  - Given higher cost of PO Vanc and theoretical concern about development of VRE enterococci after exposure to enteral Vancomycin → Flagyl generally preferred 1st agent for pts with mild or moderate C Difficile infxn
  - Newer evidence suggests that Vancomycin may be more effective than Flagyl
    - Most important with severe disease
- About 20% will relapse after initial tx → function of ecologic derangement of colon flora and not resistance to either of these agents
  - 45% have single recurrence
  - 50% experience two or more repeat episodes
- Limited data exists on alternative agents
  - Ex: IV immune globulin, probiotics such as *Saccharomyces boulardii* and *Lactobacillus rhamnosus*, rifaximin, nitazoxanide and tolevamer
### C difficile Treatment (cont’d)

<table>
<thead>
<tr>
<th>Mild</th>
<th>Severe/Normal Bowel Function</th>
<th>Severe/Ileus</th>
<th>First Recurrence</th>
<th>Subsequent Recurrence (≥2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Flagyl 500mg PO TID for 10-14d</td>
<td>• Vancomycin 125mg enterally QID for 10-14d</td>
<td>• Vancomycin 125mg enterally QID for 10-14d plus IV Flagyl</td>
<td>• Treatment with the same drug used to treat the 1st episode is recommended</td>
<td>• Vancomycin** 125mg enterally QID for 10-14d, followed by pulse dose over 4-6wks</td>
</tr>
<tr>
<td>• Vancomycin* PO 125mg QID for 10-14d</td>
<td>• Patients with severe infection who do not respond to medical treatment might require emergent colectomy</td>
<td>• Patient with severe infection who do not respond to medical treatment might require emergent colectomy</td>
<td></td>
<td>• Sequential Vanc followed by Rifaximin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Concomitant Vanc with Rifampin (resistance already described)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• IV immune globulin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• Infuse donor stool</td>
</tr>
</tbody>
</table>

Vancomycin (effective in enteral form only)

*Vancomycin is typically reserved for pts with severe disease, those who cannot tolerate or fail to respond to Flagyl, and pregnant patients (in whom Flagyl is contraindicated)

**Vancomycin alone rather than with Flagyl, in part because of the adverse effects (ex: peripheral neuropathy) resulting from long-term exposure to Flagyl
Fecal Instillation

- Fecal instillation: donor specimens of stool to restore bacterial homeostasis → fecal microbiota transplantation (FMT)
  - Design
    - 20pts (median age 64.5yrs, range 11-89yo)
    - At least 3 episodes of mild-moderate *C difficile* infxn and failure of 6-8wk taper with Vanc
    - Or, at least 2 episodes of severe *C difficile* requiring hospitalization
    - Healthy volunteers (unrelated) screened as potential donors → FMT capsules generated, stored at -112F
    - Patients received 15 capsules on 2 consecutive days
    - Followed for 6mo
  - Results: resolution of diarrhea in 14pts (70%; 95%CI, 47-85%)
    - Single capsule FMT
    - All 6 nonresponders were retreated (lower pretx health scores)
      - 4 resolution of diarrhea
      - $=90\%$ (95%, 68-98%) rate of clinical resolution of diarrhea (18/20)

Conclusion:
1. FMT has shown to be effective in treating relapsing or refractory *C difficile*
2. Need larger studies to confirm these results and evaluate long-term safety/effectiveness
Outline

• Introduction
• Epidemiology
• Pathophysiology
• Specific Pathogens and Treatment
• Clinical evaluation
  – Guidelines
  – Laboratory evaluation
  – Management
Guidelines

• “Guidelines on Acute Infectious Diarrhea in Adults” (1997)
  – Practice Parameters Committee of the American College of Gastroenterology

• “Practice Guidelines for the Management of Infectious Diarrhea” (2001)
  – Infectious Disease Society of America
  – Currently being updated
Patient Evaluation

• Per ACG

  1. Medical evaluation should occur for a subset of patient with more severe illness

  2. The clinical and epidemiologic history is central to the patient medical evaluation and management
Admission for Acute Diarrhea

• Initial goal
  – Identify those with “severe illness”
    • Profuse watery diarrhea with dehydration
      – Definition = “dry mucous membranes, decreased urination, and
tachycardia, skin tenting, etc”
    • Dysentery, passage of many small volume stools containing
      blood and mucus
    • Fever (temp ≥ 101.3F)
    • Passage of ≥ 6 unformed stools/24h or a duration of illness >48h
    • Diarrhea with severe abdominal pain in patient >50yo
    • Diarrhea in elderly (≥ 70yo) or immunocompromised state
Historical Clues

- Careful history will provide clues to the causative agent
  - Travel history
  - Recent hospitalizations
  - Underlying medical illnesses
  - Sexual history
  - Exposure to daycare
  - Ingestion of unsafe foods
  - Ingestion of untreated fresh water
  - Exposure to animals
  - Sick contacts
  - Recent antibiotics
  - Foodborne or waterborne outbreaks of diarrhea
# Epidemiologic Clues

<table>
<thead>
<tr>
<th>Vehicle</th>
<th>Classic Pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water (including foods washed in such water)</td>
<td>Vibrio cholerae, Norwalk agent, Giardia organisms, Cryptosporidium organisms</td>
</tr>
<tr>
<td>Food</td>
<td></td>
</tr>
<tr>
<td>Poultry</td>
<td>Salmonella, Campylobacter, Shigella spp.</td>
</tr>
<tr>
<td>Beef</td>
<td>Enterohemorrhagic E Coli, Taenia saginata</td>
</tr>
<tr>
<td>Pork</td>
<td>Tapeworm</td>
</tr>
<tr>
<td>Seafood/shellfish (including raw sushi and gefilte fish)</td>
<td>Vibrio cholerae, V. parahaemolyticus, V vulnificus; Salmonella spp.; tapeworm, Anisakis</td>
</tr>
<tr>
<td>Cheese</td>
<td>Listeria spp.</td>
</tr>
<tr>
<td>Eggs</td>
<td>Salmonella spp.</td>
</tr>
<tr>
<td>Mayonnaise-containing food and cream</td>
<td>Staphylococcus and Clostridium; Salmonella</td>
</tr>
<tr>
<td>Pies</td>
<td>Salmonella, Campylobacter, Cryptosporidium and Giardia spp.</td>
</tr>
<tr>
<td>Animal-to-person (pets and livestock)</td>
<td>Most enteric bacteria, viruses, and parasites</td>
</tr>
<tr>
<td>Person-to-person (including sexual contact)</td>
<td>Shigella, Campylobacter, Cryptosporidium, and Giardia spp.; viruses; Clostridium difficile</td>
</tr>
<tr>
<td>Daycare center</td>
<td>Clostridium difficile</td>
</tr>
<tr>
<td>Hospital, Abx, or chemotherapy</td>
<td>Giardia and Cryptosporidium spp.</td>
</tr>
<tr>
<td>Swimming pool</td>
<td>E Coli of various types; Salmonella, Shigella, Campylobacter, Giardia, and Cryptosporidium spp., Entamoeba histolytica</td>
</tr>
</tbody>
</table>
Empiric Therapy

- Per ACG
  - In patients with fever (≥101.3°F) plus either leukocytes-, lactoferrin-, or hemoccult- positive stools or in patients with acute dysentery or in patient with moderate and severe traveler’s diarrhea, antimicrobial therapy may be given empirically.
Laboratory Evaluation

- Per ACG
  - The fecal leukocyte, lactoferrin, or hemoccult blood test is a useful screening test in patients with moderate-severe acute infectious diarrhea because they support the use of empiric therapy in the febrile patient and when negative may eliminate the need for stool Cx in some cases of diarrhea.

  - A stool Cx should be obtained in a patient with one of the following: severe diarrhea; temperature ≥101.3F; passage of bloody stools; stools contain leukocytes, lactoferrin, or hemoccult blood; or the patient with persistent diarrhea has not been treated with Abx agents empirically.

  - Patients with diarrhea lasting 2-4wks without systemic symptoms may be studied for cause of illness or may be treated empirically with anti-Giardia therapy.

  - Patient not treated with empiric antiparasitic therapy should be studied for parasitic causes of diarrhea if they have persistent diarrhea; diarrhea has followed travel to Russia/Nepal/mountainous regions; they have been exposed to infants attending day care centers; diarrhea has occurred in a homosexual male or a patient with AIDS; diarrhea is part of a community waterborne outbreak.
Fecal Leukocytes

- Studies have suggested that stool Cx are unlikely to grow organisms in absence of fecal leukocytes
  - May be used to decide which stool samples should be sent for bacterial Cx
  - Supports the Dx of bacterial cause
- Limitations
  - Smear performed on fresh specimen
    - Collected in a cup and not on a swab or diaper
  - Requires careful evaluation by skilled microscopist
  - Not specific for infectious disorder
    - Other inflammatory conditions can yield positive result
  - Sensitivity is 60%
Fecal Lactoferrin

• Latex agglutination assay developed because of the limitation of fecal leukocyte testing
  – Byproduct of WBCs
    • Glycoprotein expressed by activated neutrophils
  – More precise and less vulnerable to variations in stool processing
  – More sensitive than fecal leukocyte testing

• Cons
  – Will be elevated in any inflammatory process
  – Not specific for infectious diarrhea
  – Costly ($3.75 per test, for kit)
  – False-positive with breastfed infants
Stool Culture

• May aid in determining pathogen
• Helps focus Abx therapy in those with high-likelihood of enteric pathogen
• Guidelines advocate culturing those with fever, dysentery, severe diarrhea and stools that contain leukocytes

Limitations

– Yield from stool Cx is low
  • FoodNet (1997) surveyed 264 clinical laboratories
    – Reported processing 233,212 stools for *Salmonella* and *Shigella*
    – Of those: 2,069 Salmonella isolations (0.9% yield) and 1,272 Shigella isolations (0.6%)
    – Campylobacter 1.4%, E Coli 0.3%

– Expensive (between $900-1200 per positive result)

– Necessary?
  • Most cases of infectious diarrhea resolve in <3d

– Careful specimen collection crucial
  • Stool specimens left at room temperature may result in false-negatives

– Only processed for common pathogens (*Shigella, Salmonella, Campylobacter*) will have to ask the laboratory for other appropriate testing should other enteric pathogens be suspected (ex: *Yersinia, Vibrio, E Coli 0157:H7*)
Stool Ova and Parasite

• In acute diarrhea: routine examination is not cost effective
  – Most parasitic infections have chronic presentations

• When?
  – If high pretest probability (ex: travel to endemic country, exposure to infants, HIV + diarrhea)

• At least 3 stool specimens are needed
  – Accommodates for sporadic passage of O&P in stool
C Difficile Stool Tests

• Dx requires lab identification of toxin in sample

• When?
  – In those with recent/remote
    • Abx usage
    • Hospitalization
    • Closed-community living arrangement (ex: nursing home)
    • Recent chemotherapy exposure
# C Difficile Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Detects</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxin assay</td>
<td>Primarily toxin B</td>
<td>Standard; highly sensitive and specific</td>
<td>Requires tissue Cx facility; labor intensive; results take 24-48hrs</td>
</tr>
<tr>
<td>Toxin enzyme immunoassay</td>
<td>Toxin A or A&amp;B</td>
<td>Fast (2-6hrs); easy to perform; high specificity</td>
<td>Not as sensitive as the cytotoxin assay</td>
</tr>
<tr>
<td>Glutamate dehydrogenase enzyme immunoassay</td>
<td>Bacterial enzyme (glutamate dehydrogenase)</td>
<td>Fast (&lt;1hr); inexpensive; easy to perform; very sensitive</td>
<td>Poor specificity; toxin testing required to verify Dx</td>
</tr>
<tr>
<td>Culture</td>
<td>Toxigenic and nontoxigenic C difficile</td>
<td>Most sensitive; allows strain typing in epidemics</td>
<td>Requires anaerobic Cx; labor intensive; not specific for toxin-producing bacteria; results take 2-5d</td>
</tr>
<tr>
<td>Batched real-time (RT) PCR</td>
<td>tcdB (toxin)</td>
<td>Good sensitivity and specificity</td>
<td>Labor intensive; typically run in batches (1 daily); expensive; not yet commercially available</td>
</tr>
<tr>
<td>On-demand real-time (RT) PCR</td>
<td>tcdB (toxin), tcdC deletion and binary toxin (outbreak strain)</td>
<td>Rapid (&lt;1hr); requires less than 2min of preparation; highly sensitive and specific</td>
<td>Expensive; not yet commercially available</td>
</tr>
</tbody>
</table>
Other Stool Studies

- **Quantitative stool collection for weight**
  - Useful to document quantity of stool and whether steatorrhea is present
  - 48-72hr stool collection
  - >250g/24h = presence of diarrhea
    - Stool weight >1000-1500g/24h suggests a secretory process
    - Less useful study
  - Patient should eat three moderately high-fat meals/day while collecting specimen
  - Avoid Olestra (increases fecal fat measurements)

- **Quantitative fecal fat**
  - >14g/d specific for disorder of fat digestion and absorption
  - 7-14g/d nonspecific phenomenon from any diarrheal illness

- **Stool laxative screen**
  - Helpful in suspected laxative abuse
  - Check stool magnesium, phosphate, and sulfate levels
  - Phenolphthalein: bright red color after alkalinization of stool
  - Bisacodyl: detected in urine
**IDSA: “3-day Rule”**

- One approach to reducing testing of specimens
- Patients with diarrhea that develops after 3d of hospitalization have VERY LITTLE yield when Cx for standard bacterial pathogens
  - Not submitting for routine stool Cx → saves $$
    - These specimens account for 15-20% of all submitted
    - 1996: estimates show this could have saved $20-73mi
  - Conversely, may yield *C. difficile* in 15-20% of cases

Clin Inf Dis 1996 “Effective use of the clinical microbiology laboratory for Dx diarrheal diseases”
JAMA 1990 “Inappropriate testing for diarrheal disease in the hospital”
Endoscopy

- Not usually needed in Dx of acute diarrhea
- However, F/S may be useful in pts with
  - Signs of proctitis: tenesmus, rectal pain, rectal discharge
  - Moderate-severe illness suspected of *C Difficile*-induced diarrhea
    - Presence of pseudomembranes highly suggestive
  - Assistance in distinguishing other causes of bloody diarrhea (ex: IBS, ischemic colitis) from those with infectious causes
Management

• Per ACG
  – Fluid and Electrolytes
    • In all patients with diarrhea requiring medical evaluation, fluid and electrolyte therapy and alteration of the diet should be part of the management
  – Nonspecific Therapy
    • When nonspecific therapy is desired, loperamide is the drug of choice for most cases of diarrhea
    • Bismuth subsalicylate is the preferred agent when vomiting is the important clinical manifestation of enteric infection
    • Loperamide is the recommended treatment for immunocompromised patients with diarrhea of uncertain etiology; bismuth should not be used in these patients
  – Antimicrobial Therapy
    • Specific antimicrobial therapy is given when a treatable pathogen is identified in stool samples submitted to the lab
    • Antimicrobial Therapy is currently not recommended for patients with diarrhea due to *E Coli O157:57* and other Shigatoxin-producing *E Coli*
Evaluation of acute diarrhea

Initial assessment
Evaluate for: dehydration, duration, and inflammation (fever, blood in stool)

Symptomatic therapy (hydration, alteration of diet)

Severe illness - hypovolemia, bloody stools, fever, ≥6 unformed stools per 24 hours, duration >1 week, severe abdominal pain, elderly (age ≥65 years), or immunocompromised

- Yes
  - Test for fecal leukocytes
  - Routine stool culture
  - Consider nonroutine stool culture or ova and parasites in select situations (see text)
  - Consider C. difficile if recent antibiotic therapy

- No
  - Illness continues
  - Illness resolves

Inflammatory
(eg, Campylobacter, Shigella, Salmonella, Entero-hemorrhagic E. coli, C. difficile)

- Consider empiric antibiotic therapy while awaiting culture results in the following groups: patients with fever or bloody diarrhea; patients with >8 stools per day, dehydration, symptoms >one week, immunocompromised, if hospitalization considered.

- Consider specific therapy once pathogen identified (see text for indications, type of treatment)

Noninflammatory
(eg, Norwalk, Rotavirus, C. perfringens, S. aureus, B. cereus, Giardia, drugs, occasionally IBD)

- Continue symptomatic therapy
- Further evaluation if symptoms persist
References

• Articles

• Books

• Photos

• Website
  – www.uptodate.com
  – www.CDC.com
  – http://www.cdc.gov/foodnet/