

Endocarditis, including Prophylaxis

ACOI Board Review 2019

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“No Disclosures”

UPRIGHT

L
DH



Infective Endocarditis

- Persistent bacteremia (blood cultures drawn >12 hrs apart) w/ organisms that tend to be associated w/ endovascular infections e.g. *S. aureus*, *Strep. viridans*, HACEK group
- “At-risk” underlying heart disease, including IVDA

HACEK Group

- Haemophilus spp. (not H. influenzae)
- New name: Aggregatibacter spp. Old name: Actinobacillus spp.
- Cardiobacterium spp.
- Eikenella spp.
- Kingella spp.

Modified Duke Criteria for Endocarditis*

- **Major clinical criteria:**
 - Persistently + blood culture for “typical” organisms
 - + echocardiogram, including partial dehiscence of prosthetic valve, myocardial abscess
 - Evidence of endocardial damage e.g., new valvular regurgitation
 - Serological or + culture for *Coxiella burnetti*

*these criteria may not apply to IVDA's

Modified Duke Criteria for Endocarditis*

- **Minor clinical criteria:**
 - Predisposing condition (valvular heart dx, IVDA)
 - Fever
 - Vascular phenomena (embolic events)
 - Immunologic phenomena (Roth spots, glomerulonephritis, Osler nodes)
 - + blood cultures not meeting strict major criteria

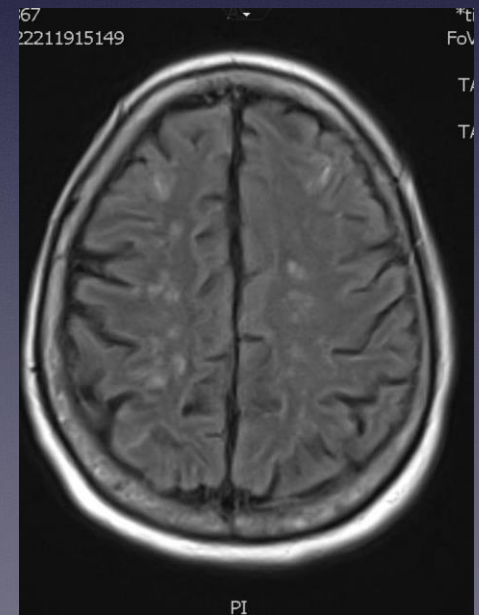
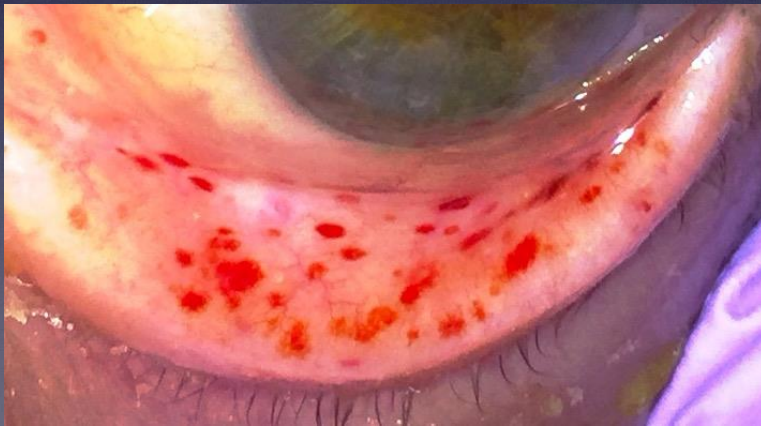
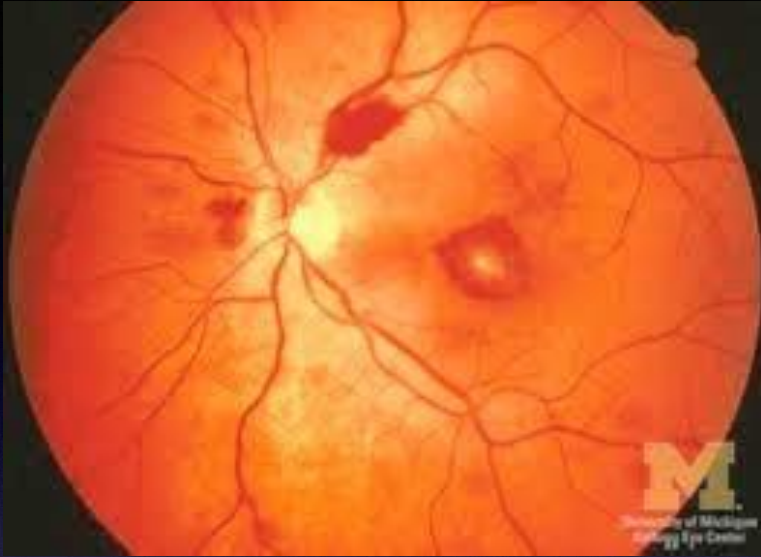
*Durak et al. Am J Med 1994; 96:200 (added echocardiograms to criteria)
Li et al. CID 2000;30:633

Modified Duke Criteria for Endocarditis

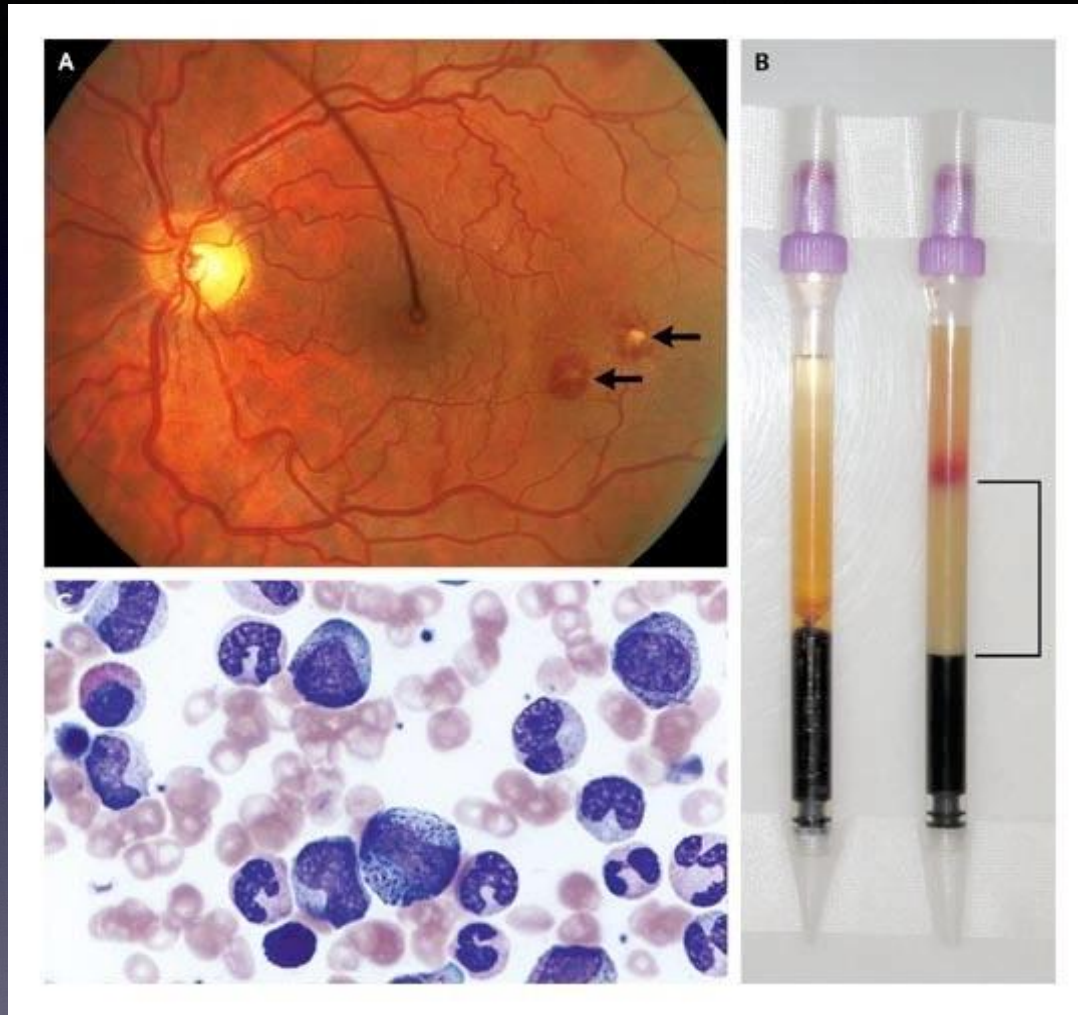
- Definite Endocarditis:
 - + histology
 - + Gram stain or cultures from surgery or at autopsy
 - Two major clinical criteria
 - One major + 3 minor criteria
 - Five minor criteria
- Possible Endocarditis
 - One major + one or two minor clinical criteria
 - Three minor clinical criteria

“Soft” signs / “peripheral stigmata” of I. E.

- Unexplained fever, weight loss, anemia of chronic disease, elevated ESR
- Roth spots
- Conjunctival, mucosal hemorrhages
- Splinter hemorrhages
- Osler nodes (tender; immune complexes; pads of fingers and toes)
- Janeway lesions (non-tender; embolic; culture positive; palms and soles)
- Microscopic hematuria
- Splenomegaly



Roth Spots

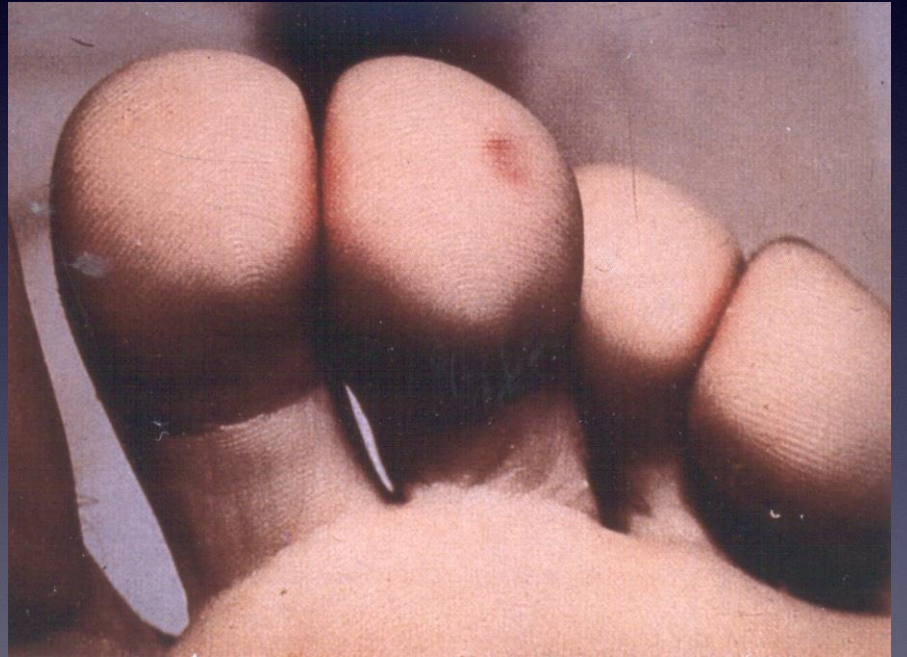


Varga Z, Pavlu J. N Engl J Med 2005;353:1041-1041.



The NEW ENGLAND
JOURNAL of MEDICINE





“Pearls”

- Multifocal “pneumonia” in an IVDA w/ positive blood cultures (usually *S. aureus*) is “right-sided” endocarditis
- *Strep. bovis/gallolyticus (pasteurianu)* bacteremia/endocarditis is highly associated w/ GI malignancy
- A + blood culture for any of the “HACEK group of organisms is endocarditis until proven otherwise
- Most common organism (acute dx) : *S. aureus*
Reason: (prior) medical care

“Pearls”

- Indications for early surgery in left-sided endocarditis:
 - Most agreed upon - CHF from native-valve dysfunction [large vegetations, invasive dx beyond cusps/leaflets (NEJM June 28, 2012)]
 - Mobile vegetations > 10 mm
 - Failure of medical tx, major embolic events, prosthetic valves, certain organisms (fungal, pseudomonas (?), Coxiella, MDR)

Culture Negative Endocarditis

- Prior antibiotics
- Slow growing, fastidious organisms
 - NVS (nutritionally variant streptococci), now reclassified as 4 species of *Abiotrophia*
 - HACEK grp
 - *Brucella*, *Coxiella* (Q fever) spp., fungal (*Aspergillus* spp.)

Prophylaxis

Wilson et al. Prevention
of Infective Endocarditis.
Circulation. May 8, 2007

Conditions for which Prophylaxis w/ Dental Procedures Recommended

- Prosthetic valve (or prosthetic material used in valve repair)
- **Prior endocarditis**
- Congenital heart dx
 - Unrepaired cyanotic CHD
 - Completely repaired congenital heart defect w/ prosthetic material or device - for 6 mo following procedure
 - Repaired CHD w/residual defects at, or adjacent to, site of prosthetic patch
- Cardiac transplant recipients w/ valvulopathy
- NOT MVP

Procedures for which Prophylaxis Recommended

- All dental procedures that involve manipulation of gingival tissue or the periapical region of teeth, or perforation of the oral mucosa
(Routine anesthetic injections through non-infected tissue do not require prophylaxis)
- Invasive procedures of the respiratory tract that involve incision or biopsy (T&A), including incision via bronchoscopy, or to treat an established infection (drainage of abscess/empyema)
- Note: routine GI endoscopy no longer included

Prophylaxis for Dental and Respiratory Tract Procedures (target is the “viridans” strep)

- **ALL: 1 dose only, w/in 1 hr prior to procedure**
- Amoxicillin 2 gms p.o. w/in 1 hr prior to procedure
 - If unable to take p.o.:
 - ampicillin 2gm (IM or IV)
 - or.....cefazolin 1 gm (IM or IV)
 - or.....ceftriaxone 1 gm (IM or IV)
 - If allergy:
 - cephalexin 2 gms p.o. (unless anaphylaxis to PCN)
 - azithromycin/clarithromycin 500 mgs p.o.
 - or.....clindamycin 600mg p.o. (IM or IV)
 - or.....cefazolin/ceftriaxone IM or IV (unless anaphylaxis to PCN)

Infections of the GI Tract

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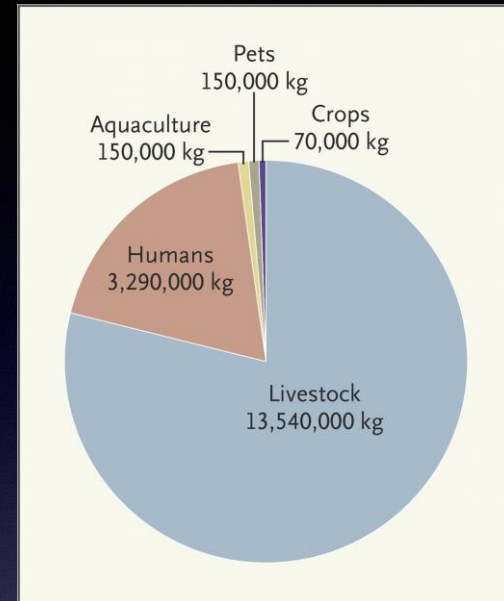
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Foodborne illness

- At least:
 - 48 million cases/yr in U.S.
 - 128,000 hospitalizations
 - 3000 deaths
 - No pathogens identified in most cases
 - leafy green vegetables most common source, (including recent outbreaks of E. coli O157:H7 in Canada and U.S.)
 - Prevention: food irradiation



in the U.S.



Hollis A, Ahmed Z. N Engl J Med 2013; 369:2474-2476.



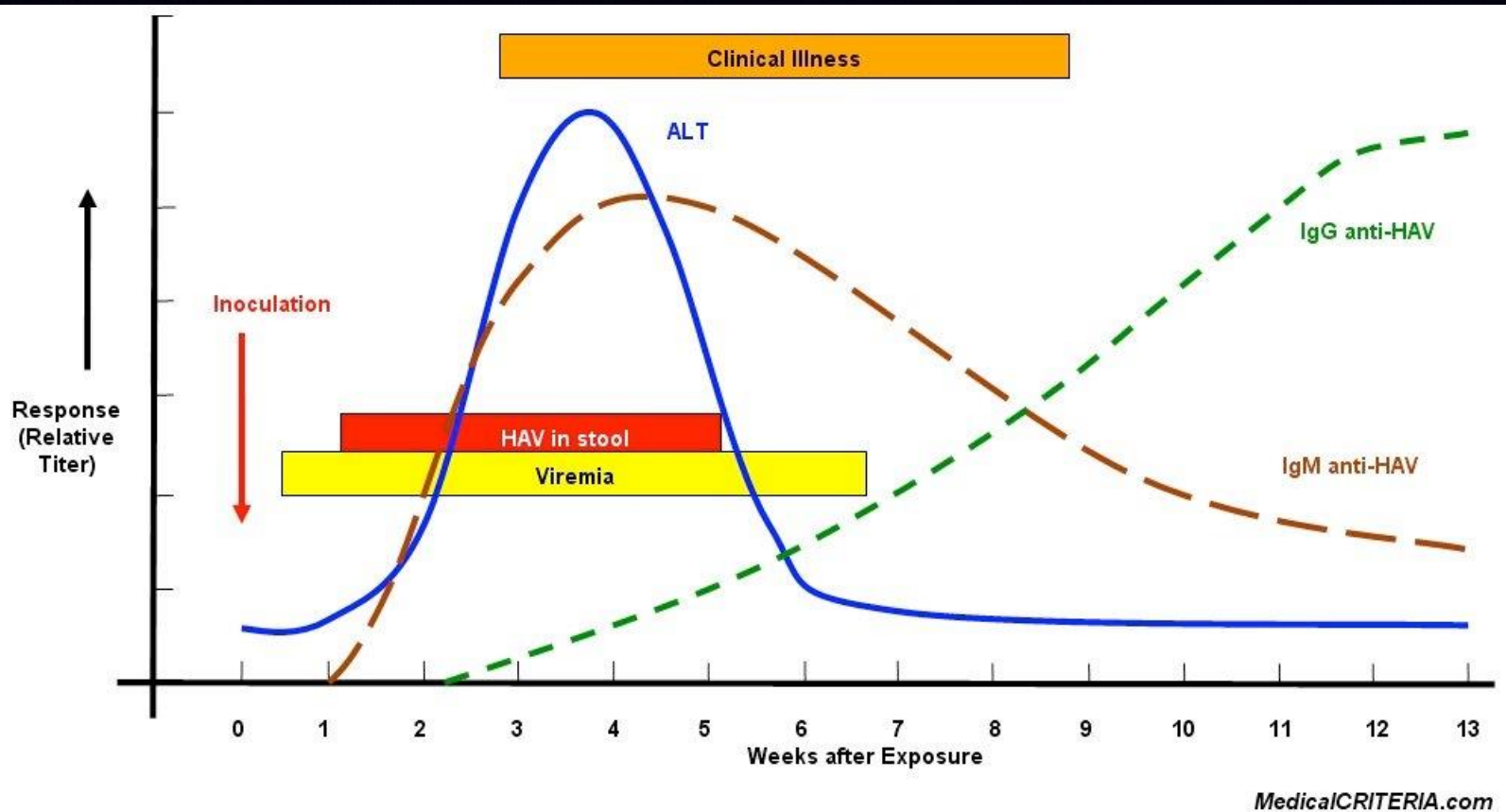
Hepatitis A

- RNA virus spread by fecal/oral transmission (e.g., food handlers), including contaminated food/water
- Traditionally, greatest risk for U.S. citizens: international travel (1/2 of cases)
- Incubation period: ~30days (range 15 - 49 days)
- Dx: IgM anti-HAV ab
- Contagiousness: from incubation period until 1 week after jaundice appears
- Tx: supportive, including hydration

Hepatitis A

- **New** - recent and ongoing outbreak prevalent in:
 - MSM
 - homeless
 - drug abusers (not necessarily intravenous)
- “point-source” [fomites; person-to-person (hygiene?)]
- more severe illness than usually described
- higher mortality than usually described
- Prevention: vaccine
 - Passive immunization w/ immune globulin w/in 2 weeks of exposure, though efficacy unclear

Hepatitis A

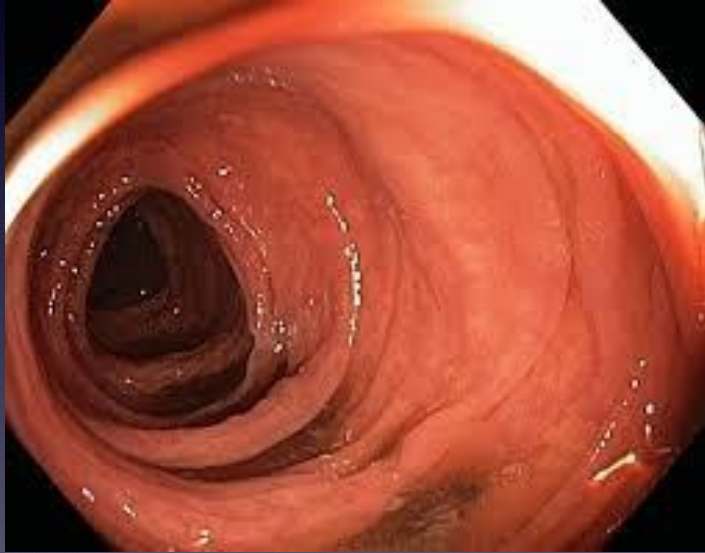


Hepatitis E

- Most common cause of acute hepatitis/ jaundice in the world
- 20,000,000 infections annually
 - 3.4 million cases of acute hepatitis; 70,000 deaths
 - 21% of adults in U.S. are seropositive
- 4 genotypes; 2 very different epidemiologic patterns of disease
- best known for association w/ **fulminant hepatitis / death in pregnancy**

Clostridium difficile

- Both nosocomial and “community-associated” diarrhea
- 3 toxins:
 - A (presence of anti-toxin A ab in pt may be protective)
 - B - essential for virulence. Anti-toxin B abs protect against recurrence
Cytopathic effect of toxin B (“Gold standard”); [Dx: multiple other tests now available, including PCR]
 - Binary - unclear significance
- Colonization may protect against infection due to either immunity or non-toxin producing strains
- NAP1/027 strain may cause more severe dx due to deletion of gene controlling toxin production



C. difficile

- Acquisition of C. diff spores
 - Prior or current hospitalization
 - Exposure to infant carriers or infected adults
 - HCW use of alcohol-based agents rather than soap and water
- Older age
- Antibiotics (particularly quinolones, clindamycin, 3rd and 4th generation cephalosporins)
- Feeding tubes, GI surgery, kidney disease
- Chemotherapy, organ transplant
- PPI's, NSAIDs
- Inability to generate antibodies to toxins
- trehalose (a sugar used as a food additive)? - believed to support the growth of C. diff

- Dx: (challenging) if PCR alone - high false + rate
- Tx:
 - p.o. metronidazole only for mild illness and no longer “preferred” for first line rx
 - p.o. vancomycin for more severe disease (may also be better than metronidazole for mild dx)
 - Fidaxomicin (Dificid®) \$\$\$\$ (decreases relapse rate in non-NAP1/027 strains)
- Life threatening:
 - I.V. metronidazole + p.o. vancomycin at higher dose
 - Vancomycin via cecostomy tube or retention enema
 - Colectomy

- Relapse: optimal approach not clear (Note: 20 - 35% risk of 1 relapse; if this occurs, ~60% risk of additional relapses)
 - Fidaxomicin (Dificid[®]) \$\$\$\$ (for NAP1-negative strains)
 - Repeat original rx?; longer courses?; tapering doses?
 - Saccharomyces boulardii lyo (Floristor[®])? or other probiotics (Note: DO NOT use this or other probiotics if pt is on chemotx)
 - Rifaximin (Xifaxan[®]); Nitazoxanide (Alinia[®])
 - IVIG
 - Fecal transplant - optimal route?
 - Monoclonal antitoxin ab, e.g. Bezlotoxumab, when added to conventional tx, may decrease relapse rate somewhat (Wilcox et al. NEJM 2017)
 - Tigecycline (Tygacil[®])

Noroviruses

“Winter Vomiting Disease”

- 2/3 of all food-borne illnesses; water sources as well. Often affect **cruise ships**, ECFs
- Majority of (presumptive) viral gastroenteritis outbreaks in adults; extremely high attack rate, w/ secondary transmission as high as 90%
- 10^6 - 5×10^9 viral particles/gm of stool
- Infectious dose: 18 - 1000 particles
- Person to person spread; contaminated food, water, environmental surfaces, vomitus
- Viral shedding may precede illness and continues after recovery
- 1/3 of infected persons may be asymptomatic

Noroviruses

- Virus persists on environmental surfaces; alcohol-based sanitizers may be sub-optimal
- Acute onset N/V, non-bloody diarrhea, lasting 12-72 hrs
- Fever (50%), myalgia, headache
- 12 - 48 hr incubation
- Dx: clinical, PCR
- Multiple strains - no cross protection; new pandemic strains every 2 - 4 years
- No long term immunity, though some individuals may be genetically resistant to at least some strains

S. aureus (Preformed Toxin)

- Severe vomiting w/in 4 - 6 hrs; minimal diarrhea
- Fever uncommon
- Egg products, cream, mayonnaise (potato salad)
- Foods w/ high salt/protein content, including pork, particularly ham
- (Preformed) toxin is heat stable; cooking does not prevent illness
- Tx: supportive

Bacillus cereus (Preformed Toxin)

- Short and long incubation syndromes
- Short incubation (1 - 6 hrs); ~ S. aureus:
 - ingestion of preformed toxin (heat stable)
 - profuse vomiting; minimal diarrhea
 - fever uncommon
 - commonly from fried rice
- Tx: supportive

Traveler's Diarrhea

- Usually enterotoxigenic E. coli
- Contaminated food or water
- 12 hr to several days incubation
- diarrhea predominates
- Prophylaxis:
 - Pepto-bismol[®]
 - rifaximin
- Tx: rifaximin or.....
 - quinolones (Mexico); macrolides (Asia)

Vibrio cholerae

- Contaminated water/poor sanitation
- Following an earthquake, huge outbreak in Haiti, imported by U.N. relief workers. Catastrophic outbreak, contributing to huge, ongoing humanitarian crisis in Yemen
- Massive amounts of painless, odorless diarrhea - “rice-water” stools
- Toxin mediated
- No fever
- Tx: hydration/electrolytes; doxycycline, azithromycin, quinolones

Listeria monocytogenes

- Gram + rod
- 24 hr incubation w/ fever, headache, abdominal pain and diarrhea
- For Boards, -> meningoencephalitis in immunocompromised patients, including extremes of age, cell-mediated immunodeficiencies, pregnancy, HIV
- Unpasteurized/contaminated dairy products; raw milk
- Hot dogs, deli meats, Mexican - style cheeses, cantaloupes, avocados
- Grows well at low temperatures - “leftovers”
- Tx: supportive for GI illness, though some give abs to prevent CNS dx in high risk pts

E. coli 0157:H7 (Shiga toxin)

(and other, toxin-producing similar strains)

- Undercooked hamburger; apple cider, raw milk, sprouts, Romaine lettuce, visitors to dairy or “petting” farms (New: flour!)
- 3 - 4 day incubation period
- Bloody diarrhea (> 90% of cases) w/ severe abdominal pain
- Usually no fever
- TTP in adults; T.T.P.-H.U.S. in 10% of infected children < 10 y.o.
- Tx: controversial whether abs make things worse; therefore, supportive - NO ABS - especially QUINOLONES, NO anti-motility agents

Shigella

- Fecal - oral transmission
- Often acquired outside the U.S., e.g. cruise ships
- High attack rate w/ secondary person-to-person spread common [due to low # organisms (<200) necessary to cause dx]
- Bloody, mucousy stools; fever, cramps, tenesmus
- If bacteremic -> think HIV

Shigella

- Usually self limited - no need to treat
- Current recommendations are to treat only immunocompromized or those ill enough to require hospitalization (CDC.gov/shigella)
- Tx: ceftriaxone or azithro if kids; azithro or quinolones if adults (historically - ampicillin, not amoxicillin)

Typhoid Fever - *Salmonella typhi*

- Following international travel, particularly India, Southeast Asia, sub-Saharan Africa
- ~220,000 deaths in 2014
- High fever, hepatosplenomegaly
- Relative bradycardia/leukopenia
- Fecal leukocytes sometimes emphasized as mononuclear
- Constipation common, though diarrhea also seen; bowel perforation w/ high mortality

Salmonella typhi

- “Rose spots”
 - macular rash from which *S. typhi* can be isolated
- Tx:
 - azithromycin
 - quinolones
 - 3rd gen. cephalosporins
- Prevention: avoiding fecal contamination of food/water supply, vaccine (note: humans are the only reservoir for this organism)





A British Concentration Camp in South Africa; 1902

Salmonella non-typhi

- 94,000,000 cases/yr (80,000,000 foodborne)
- 155,000 deaths
- Highest incidence in east/Southeast Asia
- 70% of food-borne outbreaks; *S. typhimurium*, *S. enteritidis* most common in U.S.
- 8-12 hr to 2 day incubation period common
- Headache/nausea/muscle pain
- Diarrhea, chills/fever, abdominal pain

Salmonella non-typhi

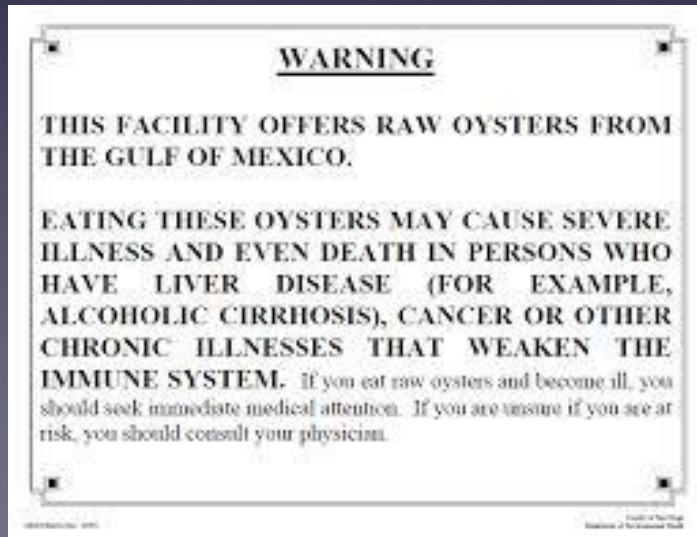
- (Pooled) eggs, poultry (including baby chicks at Easter), peanut butter; numerous other foods
- Reptiles, including turtles and iguanas
- No blood (sometimes) distinguishes from shigella
- Usually treat only if bacteremic (if young, consider HIV) or....high risk of becoming so, w/ prosthetic valve or aortic aneurysm
- If multiple blood cultures + for *S. choleraesuis* or *S. typhimurium*, think endovascular infection (e.g. infected aneurysm), especially in the elderly
- Tx: quinolones; 3rd gen. cephalosporins; azithromycin



- reported in 35 states as of 3/17/18
- (outbreak investigation ended 5/18)

Vibrio vulnificus

- Ingestion of **raw oysters**, other filter-feeding mollusks, during warmer months, w/in past 7 days by pts w/ **cirrhosis**, other immunocompromised conditions
- GI illness w/ bacteremia, overwhelming sepsis
- Distinctive bullous skin lesions





Vibrio vulnificus

- With liver disease/hemochromatosis:
 - 80 x more likely to become ill
 - 200 x more likely to die
 - 60% mortality
- 1% of seafood-related illnesses, 80-90% of seafood-related deaths (~50 deaths/yr in U.S.)
- Found in salt water, in warmer months, where water temps > 22 C
- Tx: doxycycline/gentamicin/3rd generation cephalosporins; surgery

Campylobacter jejuni

- Poultry, international travel [the latest: puppies]
- Pseudoappendicitis; colitis, fever, bloody diarrhea; these pts may appear quite ill
- If bacteremic, think HIV
- Corkscrew or spiral shaped organisms on gm stain of stool
- Often precedes Gullain-Barre' syndrome
- Recently linked to immunoproliferative small bowel disease (alpha chain disease), a small intestinal MALT (lymphoma)
- Tx: macrolides

Yersinia enterocolitica

- From pork, including chitterlings
- Grows well at low temperatures - “leftovers”
- Mesenteric adenitis, pseudoappendicitis
- Protracted courses of diarrhea
- Also assoc. w/ sepsis from blood transfusion
 - Explosive diarrhea
 - > 50% mortality following rapid onset septic shock
 - Rx: TMX-SMP/doxycycline/quinolones
- Reactive arthritis if HLA-B27
- Tx of diarrhea: supportive

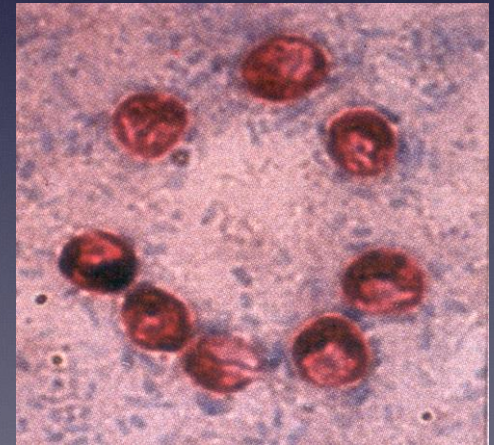
Giardiasis

- Travel to Russia; camping in the Rockies (drinking from fresh water streams)
- Chronic, watery diarrhea, malabsorption, bloating, flatulence
- No fever, no eosinophilia, no fecal leukocytes
- Common source outbreaks from day care centers (human-human spread)
- Prolonged disease w/ IgA deficiency
- Dx: antigen detection
- Tx:
 - metronidazole
 - quinacrine; nitrazoxanide (Alinia®)



Cryptosporidium

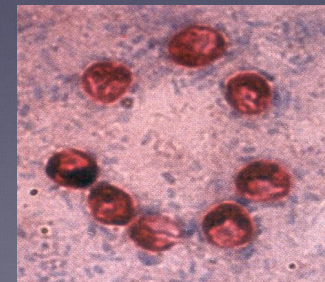
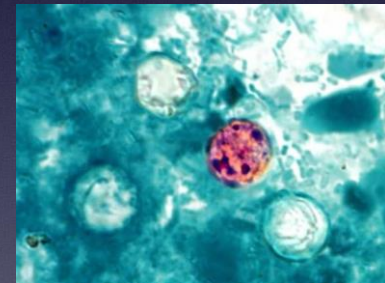
- Travel to Russia, day care centers, swimming pools; animal contact, esp. if animal has diarrhea
- Continuous/prolonged watery diarrhea w/ cramping in HIV+ patients w/ low CD4. Prolonged cases of diarrhea in immunocompetent hosts as well
- 3 - 6 microns in diameter
- No established effective treatment in HIV (other than treating the HIV itself)
- In immunocompetent: nitrazoxanide[®])



as seen on acid-fast stain

Cyclospora cayatanensis

- Imported raspberries (Guatemala), other fresh produce (basil, mesclun lettuce) grown in tropical/sub-tropical climates
- Stagnant water; travel to Nepal, Peru, Caribbean; increased during the rainy seasons
- ~7 day incubation
- Acid-fast (“big cryptosporidium”); 7.5 - 10 microns in diameter
- Tx: trimethoprim-sulfa



Amebiasis

Entamoeba histolytica (vs. E. dispar)

- Isoenzymes (“zymodemes”) determine invasiveness
- Colitis, tenesmus, bloody diarrhea in patient from tropical Africa, Asia, Latin America
- “flask shaped” colonic ulcers
- Liver abscess: “anchovy paste”
solitary right lobe
- Tx:
 - of abscess component - metronidazole
 - of intestinal component - paromomycin, diloxanide

Ciguatera Poisoning

- Tropical fish: barracuda, snapper, amberjack, grouper
- Onset: 1 to 12 hrs
- Pruritis; circumoral and extremity paresthesias
- Sensation of loose or painful teeth
- Painful intercourse
- Sensation of temperature reversal; “shock-like” sensation when touching metal
- Rx: mannitol, amitriptyline (Elavil[®])

Botulism

- N/V, diarrhea, dry mouth, followed by **descending paralysis** w/in 18-36 hrs
- Bilateral cranial nerve palsies w/ early ptosis and/or double vision
- dysphagia
- home canned foods, fermented fish; skin popping “black tar” heroin
- GI complaints 6-24 hrs after ingestion, followed by acute liver and renal failure

Trichinosis

- *T. spiralis*
- Diarrhea followed by myalgia, periorbital edema
- Eosinophilia
- Undercooked pork, wild game
- Rx: Albendazole + prednisone



	Onset (hrs)	Preformed toxin?	Fever?	? Vomiting predominant
<i>S. aureus</i>	1 - 6	yes	no	yes
<i>C. perfringens</i>	8 - 16	no	no	no
<i>E. coli</i>	12	no	+/-	no
<i>V. cholerae</i>	12	no	dehydration	no
<i>B. cereus</i>				
a.	1 - 6	yes	no	yes
b.	8 - 24	no	no	no

	Fever	Bloody?	Bacteremia?	Ab's effective?
Shigella	yes	yes	yes	yes
Salmonella (non-typhi)	yes	no	no	no
V. parahemolyticus	yes	yes	no	maybe
E. coli	yes	no	no	no
E. coli 0157:H7	usually not	yes	no	Contraindicated ??
Campylobacter	yes	yes	+/-	yes
Yersinia	yes	yes	yes	no

Blackburn's Rule # 2



Blackburn's Rule # 2

There has never been an outbreak of food poisoning from beer and french fries!!

Added References:

- Gupta SB et al. Antibodies to Toxin B Are Protective against *Clostridium difficile* Infection Recurrence. CID 2016; 63:730-734
- McDonald LC et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). CID 2018;xx:1-48
- Shane AL et al. 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea. CID 2017;65:1963-1973