- Other
  - **Antibiotic Associated Diarrhea: 1° *Saccharomyces boulardii*,** 2° *Lactobacillus acidophilus, Lactobacillus bulgaricus, Enterococcus* fecium SF68, *Bifidobacterium longum, Lactobacillus* GG
  - Hospitalized Diarrhea: C.diff, meds esp abx, fast rate hypertonic tube feedings, elixir meds w/ sugar alcohols, intestinal ischemia, fecal impaction
  - Obscure Diarrhea: fecal incontinence, functional diarrhea, IBS, surreptitious laxatives, microscopic colitis, bacterial overgrowth, pancreatic exocrine insufficiency, idiopathic diarrhea, eosinophilic gastroenteritis
  - HIV Diarrhea
    - High CD4 Gastroenterocolitis (always check Cx, Guaiac, WBC, O&P, Acid Fast Stain, C.diff toxin and if +WBC/Blood then do Colonoscopy w/ Bx for pathology and pathogen culture)
      - Infection: Ordinary Bugs esp Salmonella, Shigella, Campylobacter, C. diff, TB (these infections are more virulent, chronic and harder to Tx compared to in non-HIV pts)
      - HAART: PPI but especially Nelfinavir & Ritonavir
    - Low CD4 Gastroenterocolitis
      - Parasites (most common type of pathogen) esp Cryptosporidium, Microspora, Isospora, Cylcospora
      - Viral esp CMV (second most common CMV infection, consider if stool studies are continually negative but pt still has diarrhea), HIV aka "AIDS Enteropathy" (if all is negative)
      - Fungal esp Histo
      - Tumor esp Lymphoma & Kaposi
      - Bacteria
        - MAC
          - Other: elevated LFTs, typically occurs at the duodenum
          - Dx: endoscopy shows yellow mucosal nodules with "frosted" mucosa,
          - Bx: staining, Cx
          - Tx: difficult to eradicate requiring multiple abx (amikacin, ethambutol, rifampin, clarithromycin, cipro)
        - TB
          - Mech: ingestion followed by penetration into 1° TI/cecum (uniquely affects the entire ICV on both sides resulting in valve incompetence) and then in descending order ascending colon/jejunum, duodenum, stomach, esophagus, sigmoid colon → circumferential and perpendicular (not parallel unlike in Crohn's) ulcers AND/OR hypertrophic mass from scarring/fibrosis (often looking like cancer) along w/ enlarged mesenteric LAD (DDx *Yersinia enterolitica* can cause the same findings)
          - S/S: chronic ab pain, RLQ ab mass, weight loss, D/C, bleeding
          - Complication: stenosis w/ obstruction, perforation (esp during Tx), hemorrhage, fistula, serosal tubercles w/ ascites and peritoneal involvement
          - Tx: TB Abx ± Surgery
  - Traveler's Diarrhea
    - Epidemiology
      - Incidence: when person from industrialized country is traveling to…
        - High Risk: 45% (Central/South America, South Asia, Africa)
        - Mod Risk: 15% (Caribbean, North Asia, Middle East, Mediterranean, Eastern Europe)
        - Low Risk: 5% (Western Europe, Canada, Australia, South Africa)
    - RFs
      - destination (highest if to developing areas), national origin (highest if from industrialized areas), eating/hygiene habits (ingestion of fecal contaminated food/water), length of stay, age (toddlers and young adults), living w/ locals, immunosuppressed, pregnancy, hypochlorhydria
    - Mechanism
      - contaminated food/beverages
    - DDx
      - Acute (10% >1wk)
        - Watery (85%): ETEC 50%, EAEC 15%, Rotavirus 5%
        - Invasive (15%): Campylobacter 10%, Shigella 10%, Salmonella, Invasive E.coli
        - NB organisms are only identified in 80% of cases nevertheless it is believed that nearly all cases are 2/2 an infection b/c they respond to antibacterials
        - NB 15% of cases have multiple infections
      - Chronic (5% >1mo)
        - persistent chronic infections w/ bacteria or parasites (Yersinia, TB, Aeromonas, Plesiomonas, Giardia, Ameba, Crypto, Cyclo)
        - antibiotic associated diarrhea or even C.Diff
        - tropical sprue
        - unmasked chronic dz

        - SIBO
        - Secondary disacchardase deficiency
        - post-infectious IBS (refer)
    - Websites
        - WHO: www.apps.who.int/tools/geoserver/www/ith/index.html
        - CDC: www.wwwnc.cdc.gov/travel/destinations/list.aspx
    - Px
        - 1st Dietary Discretion
            - avoid high risk foods: uncooked vegetables, meat, seafood, ice, tap water, unpasteurized dairy products, street vendor food
            - anything cooked/boiled and is still hot >60C, dry, high sugar, peeled fruit is safe
        - 2nd Prophylaxis
            - Indication: pt has previous bouts of traveler's diarrhea, significant medical comorbidities, IBD, immunosuppressed, important trip w/ tight agenda and thus not able to tolerate even the shortest of illnesses
            - **1° Rifaximin** 220mg PO w/ each meal TID (very effective ~75% and minimal SEs but some question whether it covers all invasive bacteria)
            - **2° Bismuth Subsalicylate** (Pepto-Bismol) 262mg 2 tabs PO w/ each meal and at bedtime (not as effective ~65% and minimal SEs)
                - Mech: forms complexes w/ mucus coating ulcers, some antibacterial/antisecretory/anti-inflammatory properties
                - SEs: turns stool black (colonic bacteria convert subcitrate/subsalicylate to black sulfide), salicylate toxicity if CKD
            - **3° Cipro** 750mg PO QD or **Levaquin** 500mg PO QD (most effective ~80% but more SEs, resistance is emerging, r/o C.diff)
            - Not Doxy/Bactrim b/c significant resistance
            - Probiotics (*S. boulardi and Lactobacillus GG*) can help some
        - CDC Website for Vaccines (ETEC/Cholera are currently available in Europe/Canada but not in US)
    - Tx (give and tell to take if diarrhea develops)
        - **Watery: Fluid/Electrolyte Replacement + Antimotility Agents + Rifaximin/FQ** (if on Px use a different agent)
        - **Dysentery: " " + Azithromycin** 1000mg x1
        - **If not any better then Tx for Giardia and if not any better then stools studies & EGD/colonoscopy**

- Definition
    - subjective loose stool
    - objective increased output ≥200g/d (nl: 160g/d) and/or frequency ≥3x/d (nl: whatever is normal for pt?)
- Mechanism
    - water moves across intestinal mucosa by passive osmotic forces generated by electrolyte/nutrient absorption and in diarrhea there is incomplete reabsorption of water due to either (1 = secretory) disordered electrolyte transport specifically decreased absorption of electrolytes or increased secretion of electrolytes or (2 = osmotic) presence of an osmotically active agent
    - NB in reality causes of diarrhea are rarely pure secretory or osmotic rather they are caused by multiple mechanisms collectively regulated by the PINE Regulatory System (Paracrine, Immune, Neural, Endocrine) which affects permeability, transport, motility, metabolism
- Approach
    - NB Rule out other stuff
        - Fecal Impaction which causes encoporesis
        - Fecal Incontinence which naturally occurs with loose stools but if pts have firm stools with increased Hz or volume then consider incontinence
    - Acute: <2wks (usually a few days, if mild, immunocompetent and no alarming Sx then just symptomatic treatment and otherwise do work-up)
        - **Infection (most common)**
        - **Drugs**
        - **Food-Allergy**
        - **Food-Poisoning**
        - **New Onset Chronic Diarrhea**
    - Persistent: 2-4wks
    - Chronic: >4wks
        - **Watery**
            - **Osmotic**
            - **Secretory**
            - **Motor**
        - **Fatty (can present as watery if mild)**
            - **Malabsorption**

        - **Maldigestion**
    - **Inflammatory (can present as watery if mild)**
- H&P and Work-Up
    - Duration: Acute vs Chronic
    - Qualities: nocturnal diarrhea indicates something organic is going on, diarrhea with meals or fasting, Low Individual BM Volume but High Hz w/ Pain suggests LI pathology vs High Individual BM Volume but Low Hz w/o Pain suggest SI pathology
    - Associations: daycare, travel, unusual pets at home, farm/zoo, water parks, unusual/unsafe restaurants/foods like raw meat, unpasteurized milk, shellfish, etc, sick contacts, new meds, etc
    - Meds: PPI use b/c gastric acid is decreased
    - Aggravating Factors: diet, stress, etc vs Mitigating Factors: diet, OTC meds, Rx meds, etc
    - PEx: dehydrated, sphincter tone, etc
    - Labs: CBC (infection, anemia), CMP (hypokalemia, metabolic acidosis, ARF, hypomagnesemia), Spot Stool Collection (WBC w/ Wright's Stain or Lactoferrin/Calprotectin/PMN-Elastase Assay, C&S (only do if WBC +, checks for Campylobacter, Salmonella, Shigella other bacteria not routinely sought therefore if clinical suspicion is high then tell micro department to check for other bacteria, ? sometimes sporadic shedding of Salmonella can occur), O&P, Giardia Ag, Crypto Ag, Rotavirus Ag, Norovirus Ag, Ameba Serology, C.diff Toxin, FOBT), 24,48,72hr Stool Collection (weight, Osm, lytes, fat, pH) do this while pt is eating regular diet, keeping diary of volume and what is going in, keep specimens cold, do not use anti-motility agents, KUB in toxic pts
    - Endoscopy: Flex Sig or if +HIV then Colonoscopy b/c CMV and lymphoma often occurs primarily in the proximal colon, endoscopic aspirate/biopsy esp helpful for Giardia, Crypto/Micro/Isosporidia, MAC, CMV
- Management (refer to medication section)

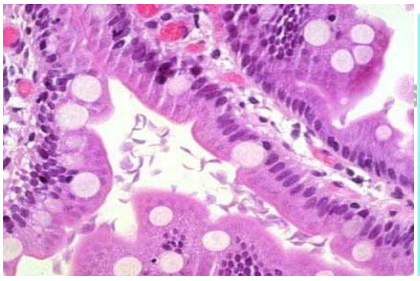
Acute Diarrhea

- **New Onset Chronic Diarrhea** (refer)
    - Sometimes it is difficult to differentiate dysentery (infectious inflammatory diarrhea) from ulcerative colitis
- **Drugs** (almost every drug can cause diarrhea therefore inquire about any new drugs, also if a chronic drug has high r/o causing diarrhea and it is not essential then discontinue)
    - antibiotics associated diarrhea
        - Epidemiology
            - Incidence: 2-5% of abx treatments
            - Most Common Abx: Ampicillin, Augmentin, Cefexime, FQ, Bactrim
        - Mechanism
            - (1) flora disturbance results in alterations in bacterial fermentation of non-absorbed carbs and deconjugation of bile salts
            - (2) erythromycin stimulates motilin receptors
            - (3) drug allergy
            - (4) superinfection: 1° *C. difficile* (only 10% of AAD, refer) 2° *C. perfringes* type A, *Staphylococcus aureus, Salmonella enteric, Klebsiella oxytoca*
        - Tx
            - Stop antibiotic
            - Probiotic: *Saccharomyces boulardii* and *Lactobacillus rhamnosus GG*
    - antacids (containing Mg)
    - antiarrhythmics (esp quinidine)
    - antihypertensives (esp BB)
    - anti-inflammatories (esp NSAIDs, gold, 5-ASA, colchicine)
    - chemo (most)
    - antivirals (HARRT)
    - acid reducers (PPI, H2B)
    - vitamin/mineral/herbals
    - caffeine ("Starbuck's diarrhea")
- **Food Allergies** (refer)
- **Food Poisoning** (bacteria that contaminates food and when allowed to rest at room temp toxins are formed which are subsequently ingested by person and causes Sx characterized by N/V/cramping ab pain occasionally followed by watery D occurring 1-6hrs after ingestion and lasting <1-2d)
    - ***Staphylococcus aureus*** (**high sugar custards/creams**, high salt deli meats)
    - ***Bacillus cereus*** (**reheated fried rice**, vanilla sauce, cream, meatballs, boiled beef, barbecued chicken)
    - ***Clostridium perfringens*** (**meat/gravy** that is not cooked high enough to kill spores then the meat is allowed to cool slowly allowing for spore germination and then the meat is reheated but not high enough to kill organisms and then eaten, NB "enteritis necroticans" is the term for a severe cases resulting from ingestion of poorly cooked pork causing bowel necrosis and perforation) *botulinism* (improper canning in adults vs honey in infants (refer))
    - *Listeria monocytogenes* (raw vegetables/fruits (cantolope, celery, sprouts), cole slaw, shrimp, deli meats, unpasteurized dairy products, NB complications: meningoencephalitis, endocarditis, etc w/ high mortality in pregnant women)
    - *Ciguatera* (fish including snapper, grouper, etc, consume dinoflagellates which create a toxin the becomes stored in the fish's muscle (does not affect the fish and the fish does not taste bad not appear spoiled), the toxin is heat/frozen

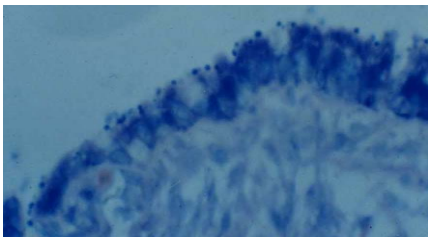
resistant, when the fish is eaten it causes early GI Sx and later CNS Sx including paresthesia, blurred vision, palsies, autonomic dysfxn)
    - *Scombroid* (occurs after ingesting improperly refrigerated fish esp tuna, mackerel, etc which allows bacteria to decarboxylate histidine into histamine (hence often misdiagnosed as a fish "allergy") resulting in flushing, warmth, erythema, pruritus, palpitations hence no real GI Sx)
- **Infection**
    - General
        - early inflammatory diarrheas begin as a watery diarrhea so still consider in DDx
        - if no fever >103, not prolonged course aka >3d, no recent travel to high risk areas, no significant comorbidities, no tenesmus, no bloody diarrhea, no dehydration then no w/u is needed just rehydrate
        - only 10% of acute infectious diarrhea actually benefit from abx and these include…
            - any community acquired diarrhea w/ ≥4BM/d, ≥3d and ≥1 of the following: ab pain, fever, vomiting, myalgia, headache = FQ x1-10d
            - stool defined EIEC, *V. cholera, C. diff,* some *Salmonella, E. histolytica, Giardia*
            - stool defined prolonged cases of *Campylobacter, Salmonella, Aeromonas, Plesiomonas*
            - traveler's diarrhea
    - **Watery/Non-Inflammatory** Diarrhea: Noninvasive Bacteria but produce **Enterotoxins and/or Adherence Proteins** which impair absorption/secretion in **SI** → large volume watery D, no fever, cramping ab pain if any, N/V, + RBC but NOT Bloody, NO WBC, Duration: self-limited, Dx: b/c self-limited not needed, Tx: b/c self-limited not needed
        - Virus (75% of watery diarrhea cases)
            - *Calicivirus aka Norovirus aka Norwalk Agent* (most common one in children)
                - Types: based on site of outbreak (Norwalk Virus aka Norovirus in Norwalk, Ohio, Hawaii, Montgomery, Sapporo, et al)
                - Epidemiology: cruise ships, children fecal oral route in daycare centers, adults eating shellfish or nursing home, epidemics occur in families, camps, hospital
                - S/S: incubation period x1d, stereotypic F→N/V→D x3d, fecal excretion x3wks therefore contagious during this period of time
                - Px: none and there is no protective immunity!!!
            - *Rotavirus* (most common one in children)
                - Epidemiology: winter season, young children where adults are generally asymptomatic, fecal oral route
                - S/S: similar to calicivirus
                - Dx: immunoassays of stool Ag (rarely ordered), electron microscopy of duodenal Bx (rarely ordered)
                - Px: vaccine (NB old vaccine caused intussusception), protective immunity develops after infection, breast feeding is protective
            - *Enteric Adenovirus Serotype 40/41*
                - Epidemiology: children & AIDS pts otherwise adults are asymptomatic
                - S/S: incubation 8-10d, diarrhea x1-2wks
                - Predictable Sequence: F→V→D, Duration: 4-6d, Season: all year round, Pt: infants, Reinfection: uncommon b/c immunity develops
            - *Astrovirus*
                - Epidemiology: children
            - *Torovirus*
                - Epidemiology: children
            - HIV: CMV, HSV, HIV
        - Bacteria
            - *Escherichia coli*
                - General: Normal GI Flora Species (causes non GI dz) vs Non-GI Flora Species (causes GI dz)
                - Watery Diarrhea Pathogenic Types (4 cause watery diarrhea vs 2 cause dysentery)
                    - Entero-Toxigenic (ETEC)
                        - Epidemiology: contaminated foods, most common cause of adult bacterial traveler's diarrhea, cruise ships, children in developing countries
                        - Mechanism: heat labile toxin (↑cAMP) and heat stable toxin (↑cGMP) → increased intestinal secretion
                    - Entero-Pathogenic (EPEC)
                        - Epidemiology: infant nursery outbreaks
                        - Mechanism: attaches and effaces mucosa
                    - Entero-Aggregative (EAEC)
                        - Epidemiology: HIV pts
                        - Mechanism: bind mucosa in a "stack of bricks" pattern
                    - Diffusely Adhering (DAEC)
                        - Epidemiology: children

        - Mechanism: bind mucosa in a diffuse pattern
        - Tx: 1 Cipro 500mg PO BID 2 Bactrim
- *Vibrio cholera* (most studied enteric pathogen)
    - Epidemiology: currently in the 7th pandemic w/ the El Tor and 0139 Bengal strain which started in 1961 including Africa (most cases), Asia, Middle East, South America, sporadic cases occur along the Gulf Coast, among US travelers to endemic areas only 41 cases have been reported in the last 50yrs
    - Acquisition: contaminated food/water, person-to-person is not common, large inoculums is needed, humans are the only host which are harbored in the gallbladder (hence "cholera" which is Greek for bile)
    - Mech: comma shaped GNR w/ a single flagellum → secretes the cholera enterotoxin → increases cAMP → increased intestinal secretion
    - S/S: wide range from an asymptomatic carrier state (ratio of asymp to symp is 400:1) →→→ fulminant (>1L/hr) rice water diarrhea (clear w/ flecks of mucus) w/ death w/in 3hrs of onset
    - Dx: Bx (nl), Cx (?), Serology (convalescent titers after infection)
    - Px: no vaccine
    - Tx: aggressive PO/IV rehydration, replete K/bicarb which are particularly low, abx (1 tetracycline 500mg PO Q6hrs x3d, 2 FQ, Doxy), before these measures there was ~2/3 mortality not it is 1%

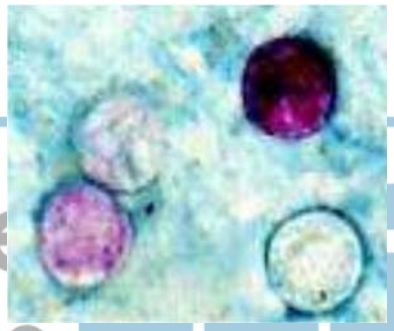
- **Parasite-Protozoa** (unicellular, cyst (the form that transmits) to trophozoite (the form that grows, feeds, divides, etc), replicate in host, size of RBCs, multiply w/in humans via asexual binary fission, - eosinophilia)
    - *Giardia lamblia/duodenalis/intestinalis aka "Giardiasis"*
        - Epidemiology: fecal contaminated food/water, adult who drinks well water or recently camped and drank stream water, swimming in fresh water, contact w/ a person who has giardiasis hence person-to-person transmission, child in daycare who are exposed to stool, anal intercourse, **Ig deficiency (VERY IMPORTANT cause of severe chronic giardiasis),** 1° Traveler's D (parasite), very infectious, additional reservoir in dogs/cats,
        - Mechanism: ingest cysts → convert to trophozoite in the presence of stomach acid → trophozoite adheres to duodenum and damages microvilli eventually causing atrophy and thus malabsorption → cysts form again as they are exposed to pancreatic alkali and bile salts and are released into stool
        - S/S: asymptomatic or steatorrhea but also anorexia, cramps, bloating, flatulence, dyspepsia, sulfuric belching b/c of malabsorption
        - Complications: lactase deficiency (hence don't assume reinfection or inadequate eradication rather test w/ HBT)
        - Dx: O&P (50% sens), Duodenal Aspiration or String Test (80% sens), Duodenal Bx (85% sens), Stool Ag ELISA (90% sens and 100% spec)
        - Tx: Metronidazole or Tinidazole



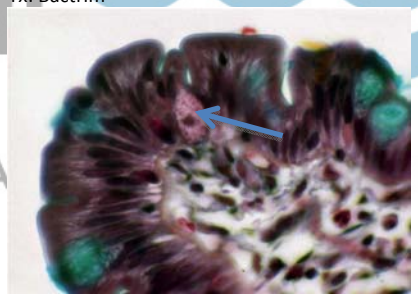

    - *Cryptosporidium parvum aka hominis aka "Cryptosporidiosis"*
        - Epidemiology: fresh produce (lettuce), chlorinated swimming pool water (Dallas 2008, Milwaukee 1993, resistant to chemical disinfectants and water purification), unpasteurized milk, animals, person-to-person contact, daycare centers, travelers, very infectious
        - Mechanism: ingest cyst → sporozoa form in the presence of bile salts → sporozoa attach to small intestine and stimulate elongation of the microvilli → microvilli fuse around the sporozoa creating a vacuole → sporozoa turn into merozoites → merozoites form eggs which are shed into feces
        - S/S: self limited diarrhea (immunocompetent) → severe chronic diarrhea (immunocompromised)
        - Complications: AIDS cholangiopathy, respiratory Sx, pancreatitis
        - Dx: Stool Acid Fast Stain (not sensitive), Stool ELISA Ag (more sensitive)
        - Tx: Nitozoxamide



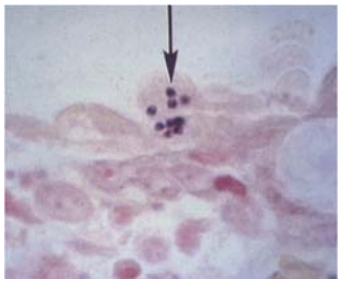
- *Cyclospora cayatenensis*
  - Similar to *Cryptosporidium* except
    - Epidemiology: fecal contaminated water and food (Gautemalan raspberries, Missouri/Thailand Basil, Pennsylvania Snow Peas)
    - Mechanism: requires development outside of human before becoming infectious
    - Complications: cholecystitis
    - Bx: "really big crypto"
    - S/S: diarrhea is more chronic lasting 4-6wks
    - Tx: Bactrim



- *Isospora belli*
  - Similar to *Cylospora* except
    - Epidemiology: tropics
    - Mechanism: more invasive
    - Tx: Bactrim



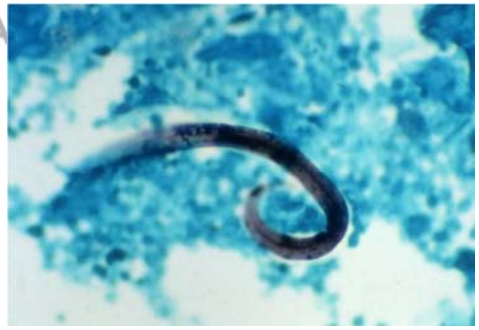
- *Microspora aka Enterocytozoon bieneusi/intestinalis*
  - Similar to *Cyclospora* except
    - Epidemiology: AIDS and s/p organ transplantation
    - Complications: disseminate to the kidney, prostate, upper respiratory tract, gallbladder
    - Tx: Thalidomide or Albendazole



- *Blastocystitis hominis*

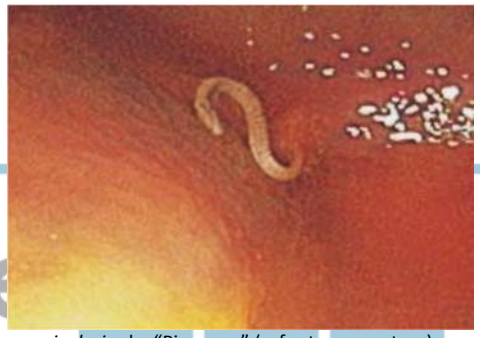
- **Pathogenicity has been debated** as most pts are asymptomatic but now it is believed to that some pts get IBS-type Sx that seem to resolved w/ Tx / Iodoquinol or Metronidazole

- **Parasite-Helminth aka Worms:** multicellular, egg to larva to worm, size from mm to meters, can survive for decades in humans so even a remote history of foreign travel, emigration and exotic diet is important, replicate outside host via various sexual ways, most are asymptomatic but can cause severe dz in certain circumstances, some pass w/ BM and terrify pts, some believe that helminth exposure is protective against diseases that damage b/c of excessive immune reactions (eg. IBD), + eosinophilia, Tx: various weird dugs but they all work by paralyzing the worm so that it releases and clears out of the GI tract
  - Nematodes (Roundworms)
    - *Ascaris lumbricoides aka "Ascariasis"*
      - Epidemiology: world-wide developing countries, 25% of the world's population are carriers!!!
      - Mechanism: fecal contaminated vegetables → eggs hatch in duodenum releasing larvae which penetrate the intestine → enter mesenteric veins → larva migrate through liver through heart to lungs → larvae break through alveoli and ascend airway → swallowed and enter small intestine and then mature → eggs are formed and released into stool
      - S/S (no diarrhea): most asymptomatic → when there is heavy worm burden you develop complications: lungs (pneumonia), intestine (obstruction), biliary tree (worms enter the pancreaticobiliary tree causing obstructive cholangitis, cholecystitis, pancreatitis)
      - Dx: Visual (endoscopy, toilet), Stool O&P
      - Tx: Albendazole
    - *Strongyloides stercoralis* aka Strongyloidiasis
      - Epidemiology: tropical areas esp southeastern USA, auto-infection occurs often resulting in subclinical infection for decades
      - Mechanism: larvae in soil penetrates skin at feet (serpiginous urticarial rash) → larvae migrates and enters veins → larvae travel thru heart to lungs → larvae break through alveoli and ascend airway (Loeffler's Syndrome: coughing, wheezing, eosinophilia) → swallowed and enter small intestine (nausea, ab pain, blood loss, right sided eosinophilic colitis) → larvae are released into stool → eggs are formed outside the human
      - S/S: most asymptomatic → when the immune system is suppressed **(often post transplant)** strongyloides that has been dormant for several years can remerge systemically called **"hyperinfection syndrome" w/ sepsis and severe lung/GI dz therefore screen all pre-transplant patients**
      - Complications: sepsis (as the larva penetrates the intestine it carries with it bacteria), larva infection in various organs (brain, lungs)
      - Dx: Serum Ab, Stool O&P
      - Tx: Ivermectin AND Antibiotics b/c pts often get super-bacterial infections for some reason

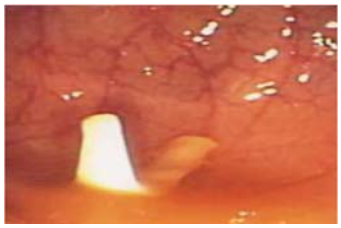


    - *Paracapillaria philippinensis*
      - Mechanism: eggs found in bird droppings enter fresh-water → fish swallow eggs → ingest raw fish → thousands of worms form in intestine
      - S/S: severe sprue like diarrhea and protein loosing enteropathy that progresses to death from heart failure and sepsis w/in 2mo
      - Dx: Stool O&P
      - Tx: Albendazole
    - *Necator americanus, Ancylostoma duodenale, Ancylostoma caninum* aka Hookworms
      - Epidemiology: 750 million are infected worldwide
      - Mechanism: larva in fecal contaminated soil penetrates skin ("cutaneous larva migrans") → larva reaches veins through heart to lungs → larva

penetrate alveoli and migrate up airway → larva are swallowed entering into intestine and damage mucosa → eggs form and are released into feces
        - S/S: larva secrete an anticoagulant and damage mucosa resulting in blood loss and significant IDA
        - Dx: Endoscopy (visualize larva), Stool O&P
        - Tx: Albendazole
    - *Trichuris trichura* aka "Whipworm"
        - Epidemiology: 800 million people worldwide harbor infection, temperate/tropic regions esp southeastern USA, retarded children who play in soil
        - Mechanism: ingest eggs → larva form in intestine → larva travel to cecum → eggs reform and are released into feces
        - S/S: most asymptomatic but if heavy infestation then Sx of diarrhea, bleeding, growth retardation
        - Complications: **rectal prolapse** and anemia
        - Dx: stool O&P
        - Tx: Mebendazole or Albendazole



    - *Enterobius vermicularis* aka "Pinworm" (refer to anorectum)
    - *Anisakis simplex* and *Pseudoterranova decipiens* aka "Anisakidosis"
        - Mechanism: marine mammal ingests the larva → eggs form in intestine and pass into stool → crustaceans ingests larva → saltwater fish ingest crustacean and larva enters fish muscle → humans raw fish → larva in human intestine creates an allergic reaction
        - S/S: severe ab pain, N/V, hematemesis
        - Complications: anaphylaxis
        - Dx: finding worm on endoscopy
        - Tx: none needed b/c infection is transient as this worm cannot survive in human
- Cestodes (Tapeworms)
    - *Echinococcus granulosus/multicoularis* (refer to liver notes)
    - *Diphylobothrium latum*
        - Epidemiology: Europe/Russia/Alaska
        - Mechanism: fleas eat larva → freshwater fish eat fleas → larva travels into fish muscle → humans ingest raw freshwater fish → worm in GI tract absorbs VitB12 but is otherwise not invasive
        - S/S: **VitB12 deficiency otherwise no GI Sx**
        - Dx: Stool O&P, Visualization (by pt in stool or doctor during endoscopy, NB largest human parasite reaching up to 40ft in length)
        - Tx: Praziquantel or Albendazole
    - *Taenia solium/saginata* aka "Cystercisosis"
        - Epidemiology: *T. solium* (pork) vs *T. saginata* (beef), world-wide distribution
        - Mechanism: pigs/cows graze on field fertilized w/ human feces contaminated w/ eggs → animals ingest eggs → worm develops in intestine and penetrates entering into vasculature → worms invade muscle, CNS, eye, heart → humans ingest raw meat → worm stays in intestine → eggs form and are released into stool
        - S/S: most are asymptomatic but some have ab pain and loss of appetite
        - Complication: pancreaticobiliary obstruction or if human ingests eggs directly (like the animals) then the worms that form can also invade the human body
        - Dx: stool O&P, serology
        - Tx: Praziquantel or Albendazole



- *Hymenolepis nana/diminuta*
  - Epidemiology: person-to-person, world-wide distribution
  - Mechanism: ingest infected insects → eggs release oncospheres which invade lymphatic and turn into larva → larva rupture back into intestinal lumen and turn into worms → eggs are released into stool → insects eats eggs in stool
  - S/S: most are asymptomatic but some have anorexia, ab pain, diarrhea
  - Dx: Stool O&P
  - Tx: Praziquantel
- Trematodes (Flatworms aka Flukes)
  - GI Flukes
    - *Fasciolopsis buski, Heterophyes spp., Echinostoma* spp.
      - Epidemiology: Asia, Africa, Middle East
      - Mechanism: ingest freshwater plants infected w/ worms → worms in small intestine → eggs form and are released into stool → eggs ingested by snails and turn into worms → worms infect freshwater plants
      - S/S: usually asymptomatic
      - Dx: stool O&P
      - Tx: Praziquantel
  - Liver Flukes (refer)

- **<u>Dysentery/Inflammatory</u>:** Invasive Bacteria Attacks Mucosa via **Cytotoxins and/or Invasive Proteins** which damage epithelium in **<u>TI/LI</u>** → small volume D, NO N/V, +RBC +/- Bloody, +WBC, Mucus/Purulent, lower quadrant pain w/ tenesmus, Fever, Duration: variable, Dx: need to, Tx: Bactrim/Cipro generally covers most except Campylobacter/Amebiasis (NB may prolong Salmonella and is contraindicated in O157:H7), NB the following is in order of incidence (except C.diff)
  - NB Proctitis can be seen w/ Shigella, HSV, Gonorrhea, Syphilis, Chlamydia
  - Virus (uncommon in immunocompetent pts)
    - CMV: pancolitis
    - HSV: distal colitis
  - Bacteria
    - *Clostridium difficile* Infection (CDI)
      - Epidemiology
        - RFs: antimicrobial exposure, chemotherapy esp MTX use, immunosuppressed, older age, healthcare setting, medical comorbidity
          - Abx
            - **1° Clindamycin**
            - 2° Ceph/Amp/FQ
            - 3° Bactrim/Macrolides
            - NB vancomycin and metronidazole can cause CDI!!!
          - New Important RFs
            - PPIs (unclear b/c spores are already resistant to acid)
            - IBD (start w/ vanc, try not to use steroids or escalate immunosuppressive therapy when they are infected)
            - Pts who are not able to produce IgA/G to Toxin A (pt will more likely become infected rather than just colonized)
            - Pregnancy
          - NB newborns are resistant to C.diff b/c they lack the receptors that toxins bind but they have high asymptomatic colonization rates b/c they have not yet developed a stable flora to prevent colonization as opposed to adults
        - C.diff was an obscure bacteria until 1978 when the link b/t C.diff and AAD was made and now since 2000…
          - (1) increasing incidence (25% of in-pt diarrhea)
          - (2) increasing mortality (10%)
          - (3) increasing recurrence (10%)

- (4) increasing occurring in low risk populations
- (5) new hypervirulent strain (B1/NAP1/027)
    - Why bad?
        - (1) mutation of *tcdD* gene (normally it regulates expression of *tcdA/B* gene) → unregulated production of Toxin A/B
        - (2) produces a new Binary Toxin CDT that is not made by other strains
        - (3) it is 100% resistant to FQ (other strains are 40% resistant)
        - (4) increased spore formation

- Mechanism
    - Oral ingestion of C.diff or its spores from stool contaminated fomites (highly infectious w/ only 2 organisms needed to establish infection) →
    - **Asymptomatic Colonization** (2% of healthy adults and 15% of inpts treated w/ abx) →
    - Shift in flora profile →
    - **Abx Associated Diarrhea** – AAD (looks like non-specific colitis, ~2d incubation period) = Watery Diarrhea →
        - Toxins A/B made by gene *tcdA/B* are released into colonic lumen, bind receptor, internalized by colonocytes and destroys the cell aka cytotoxic
    - **Pseudomembranous Colitis** – PMC (looks like colitis but w/ small 2-10mm white/grey/yellow plaques representing sloughed off cells and inflammatory exudates separated by intervening normal mucosa) = Dysentery →
    - **Toxic Megacolon** = hemorrhagic colitis (this stage is heralded by actually improvement in diarrhea while the pt clinically looks sicker, if PMC is not Tx then mucosal damage becomes so bad that the colon dilates to >6cm on KUB, becomes atonic and perforates) → Sepsis/Death
    - Can C.diff cause enteritis???
- Dx
    - Labs
        - leukemoid reaction
        - hypoalbuminemia
        - AKI
    - Endoscopy
        - 20% of CDI has only proximal colon involvement hence flex-sig may miss infection
        - Early dz will just show non-specific colitis
    - Two Part Screen
        - **GDH (Glutamate DeHydrogenase) Ag w/ Enzyme Immunoassay (EIA) and then confirm with PCR = Colonized Carrier**
        - **Toxin A Production w/ Enzyme Immunoassay (EIA) = Active CDI**
            - NB Culture Cytotoxicity Assay (more sens/spec but takes long time, expensive, technically difficult, etc therefore not performed much anymore)
        - Algorithm
            - GHD+ and Toxin+ = Toxigenic-A CDI = Tx
            - GHD- and Toxin- = No CDI therefore look for other causes of diarrhea
            - GHD+ and Toxin- = Two Possibilities
                - Non-Toxigenic CDI = Carrier therefore look for other causes of diarrhea
                - Toxigenic-B CDI = Check for Toxin-B Production using PCR
            - GHD- and Toxin+ = Repeat Test
    - NB tests should be performed only on symptomatic pts w/ unformed stool
    - NB if all negative then order second and if negative and still highly suspicious then flex sig
    - NB follow up stool analysis of stool toxin levels is not recommended
    - NB pts after symptomatic CDI are carriers for about 6wks nevertheless once a pt has had symptomatic infection you consider them lifelong carriers
    - NB refrigerate sample if not tested immediately b/c toxin can denature at RT
- Tx (Px and Tx of asymptomatic carriers is not recommended as it has not been shown to reduce incidence)

- If pt is not responding after 3d of Tx then escalate but don't recheck toxin
- **Mild (WBC<15k, Cr<1.5, adult)**
  - General: contact isolation, correct hand hygiene w/ soap/water b/c spores are resistant to alcohol, d/c antimotility agents, stop abx or switch to less offending agent (eg. bactrim, aminoglycosides, erythromycin, et al)
  - Flagyl 250mg QID or 500mg QID PO x10-14d
    - The way flagyl works is that it is absorbed in the SI and when the LI is inflamed serum leaks bringing flagyl with it, very little actually is not absorbed and makes it way to the colon directly hence IV is equivalent to PO
    - Resistance is increasing such that some go ahead and Tx all initial cases w/ vanc
- **Mod (WBC >15k, Cr>1.5, young/elderly/pregnant)**
  - Vanc 125-500mg PO QID x10-14d
    - Unclear exact dose
    - second line so as to decrease r/o VRE
    - more expensive than flagyl
    - unlike flagyl not effective when given IV
    - can be give down NGT
    - liquid or capsules
    - PO is preferred but Enema is possible (500mg in 100mL on NS, via Foley, clamp for 1hr, do Q6hrs)
- **Severe/Fulminant**
  - Flagyl 500mg PO TID + Vanc 500mg PO QID x14d
  - IVIG (400mg/kg IV 2-3x w/ 3wk intervals) to bind toxins (b/c the reason for recurrence is the inability for certain pts to make Ab to toxins thus give IVIG collected from other pts)
  - Subtotal Colectomy w/ Ileostomy
    - Should you continue abx afterwards? Unclear some do Vanc PO for SI and Vanc enema for rectal stump
- **Recurrence** (can occur as early as 3-5d after last Tx, some get post-infectious IBS, resistance to flagyl or vanc is uncommon, some think that spores take haven in diverticula)
  - 1st Recurrence (20% risk) = Tx like first episode
  - 2nd Recurrence (45% risk) = Vanc Taper 125mg PO QID x10d, BID x7d, Qd x7d, Q2D x8d, Q3d x15d
    - Other: 125mg PO QID x10d then 125mg PO QD x1d then off for four days and do this x5
    - Other: 125mg PO QD x14d then Rifaximin x14d
    - NB never use flagyl after first recurrence b/c likely not effective and repetitive use has SEs
  - 3rd Recurrence (60% risk) = various approaches (most say now stool transplant)
    - Antibiotics
      - Old: rifaximin, nitazoxanide, tigecyclin
      - New: fidaxomicin (Dificid) 200mg PO BID x10-14d (2011 NEJM showed non-inferiority and lower recurrence rate when compared to vanc)
    - Probiotics
      - PO *Saccharomyces boulardii* (Florastor) and *Lactobacillus* GG (Culturelle 1 tab PO BID)
      - "fecal transplant" aka colonic flora reconstitution via NJT or retention enema = >90% effective!!!
      - Give non-toxigenic strains of *C.diff*?
    - Immunity
      - Passive IVIG (unclear if helpful as studies are poor)
      - Active Vaccine (in development)
    - Resin Binders (unclear if helpful as studies are poor and there is some evidence that they bind abx and thus may be harmful)
      - Cholestyramine

        - Tolevamer
        - Colestipol
- *Campylobacter spp.* (most common, 2.5 million cases/yr)
    - Species: C. *jejuni* (normal pt), *C. fetus* (immunocompromised pt), *C. cinaedi/fennelliae* (homosexual pt), *C. coli, C. hyointestinalis, C. upsaliensis*
    - Epidemiology: normal GI flora in various animals (poultry, cow, sheep, pig etc) hence acquired when one ingests undercooked meats (60% of raw chicken juices), highly infectious requiring only 500 bacteria
    - S/S: 1-10d incubation period, prodrome (coryza, headache, malaise), biphasic dysentery w/ a brief period of improvement in the middle, constitutional Sx (HA, myalgia, backache, malaise, anorexia, vomiting), lasts x1-2wks, 25% relapse rate
    - Complications: **Guillan-Barre Syndrome**, pancreatitis, cholecystitis, HUS, bacteremia, meningitis, reactive arthritis, **Immunoproliferative Small Intestinal Disease (IPSID)*****
    - No asymptomatic chronic carriers
    - Tx: abx has no effect on course of illness except if started very early (1° Erythromycin 250mg PO BID x5d 2° Cipro (emerging resistance))
- *Salmonella spp* = "Salmonellosis" (second most common, 1.5 million cases/yr) vs "Typhoid Fever"
    - Nomenclature: GNR w/ Two Species
        - *S. enterica* (6 subspecies, only the first causes disease in warm-blooded animals while the other 5 cause dz in only cold-blooded animals)
            - *S. enterica entirica* (I) (1454 serotypes)
                - Non-Typhoid Serotypes (NTS): Enteritides, Typhimurium (most common ones)
                - Typhoid Serotypes (TS): Typhii, Paratyphi (most common ones)
            - *S. enterica salamae* (II)
            - *S. enterica arizonae* (III)
            - *S. enterica diarizonae* (IV)
            - *S. enterica houtenae* (V)
            - *S. enterica indica* (VI)
        - *S. bongori* (no subspecies)
    - Epidemiology
        - Salmonellosis
            - Incidence
                - 93,000,000 illnesses/yr and 155,000 deaths/yr across the world w/ most cases occuring in 3rd world countries
                - in the US there are 42,000 illnesses/yr (likely underreported, some estimate 1.4million illnesses/yr) and 400 deaths/yr making it the 2nd most common cause of dysentery in the US
            - Pattern: ½ of cases occur in the setting of large outbreaks
                - cantaloupe-1991 400 cases
                - alfalfa sprouts-1996 135 cases
                - dry cereal-1998 209 cases
                - orange juice-1999 207 cases
                - mangoes-1999 78 cases
                - peanut butter-2008 529 cases
                - chicken eggs-2010 1939 cases
                - papayas-2011 106 cases
                - tuna-2012 258 cases
        - Typhoid Fever
            - 22,000,000 illnesses/yr and 200,000 deaths/yr across the world w/ nearly all cases occurring in 3rd world countries (high risk: southcentral and southeast Asia vs medium risk: Africa, Latin America, Middle East) w/ only 400 illnesses/yr in the US (most cases were attributed to recent travel from high risk countries or immigrants)
    - Mechanism
        - NTS
            - Reservoir
                - Domestic Animals (ingestion of uncooked meat or fecal contaminated food/drink): poultry, pigs, cows, buffalo, sheep

- Pets (ingestion of fecal contaminated food/drink): esp reptiles/turtles (90% are carriers) but also dogs, cats, guinea pigs, hamsters, birds, mice
- Unique RFs
  - Hemolytic Anemia (eg. SCD, Malaria, Bartonella)
    - blockage of reticuloendothelial system by macrophages that have ingested breakdown products of RBCs are unable to phagocytose salmonellae in the blood leading to high rate of extra GI infections
  - Schistosomiasis
  - Ulcerative Colitis
- Mechanism: ingestion of salmonella w/ 6-12hr incubation → salmonella induces intestinal epithelial cells to phagocytize them and once inside salmonella alters cytoskeletal architecture, membrane fxn, signal transduction, et al allowing for intracellular survival → an inflammatory response is then mediated against salmonella which allows for the bacterium to undergo lymphatic/hematologic spread to other organs

- TS
  - Mechanism: ingestion of food/drink contaminated w/ human feces laden w/ TS w/ incubation period of 7-14d → salmonella penetrates TI thru a paracellular route (no damage during this process unlike NTS) and enters bloodstream w/ bacteria sequestering within macrophages in reticuloendothelial system (liver, spleen, BM) and multiply and are shed back into blood

- S/S
  - NTS
    - Enterocolitis (75%)
      - 1° ileum and 2° colon
      - N/V, "pea soup" D, F/C/myalgia/arthralgia/HA
      - 6hr-2d incubation period
      - lasts 3d-2wks w/ avg 3wks
      - Complications: hemorrhage and toxic megacolon
    - Bacteremia (5%)
      - Occurs when pt has RFs noted above
      - esp w/ *S. enterica entirica* serotypes: choleraesuis and heidelber
      - Complications
        - Hematologic: sepsis, endocarditis, mycotic aneurysm
        - Localized: osteomyelitis, arthritis, meningitis, cholecystitis, pneumonia focal abscess
    - Death (<1%)
    - Chronic Asymptomatic Carrier in GB (0.1-1%) NB Tx is not effective
  - TS (a systemic infection)
    - Systemic: fever-bradycardia (Faget's Sign), malaise, myalgia, headache
    - GI: Ab Pain and Diarrhea
    - Derm: Rose's Spots (blanching erythematous 2-4mm papules on ab/chest)
    - GB = Cholecystitis
    - CNS = AMS, Meningoencephalitis, GBS, Seizures
    - Heart = Pancarditis
    - Lungs = Pneumonia
    - Kidney = Pyelonephritis, GN
    - Heme = DIC, HSM
    - Bone = Osteomyelitis
    - Chronic Carrier Rate (1-4%)
      - signified by +stool Cx >1yr
      - cause for local endemics
      - RFs (older age, female gender, extremes of age, gallbladder dz)

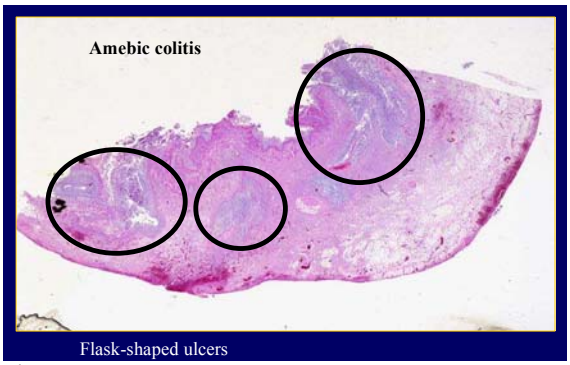
        - Tx susceptible abx for x1mo but reappearance can occur in 85% of pts therefore consider cholecystectomy if gallstones as they may be the sanctuary
        - ? increased r/o carcinoma of the gallbladder
    - Dx
        - Colonoscopy (hyperemia, granularity, friability, ulcerations)
        - Histology (ulceration, hemorrhage, crypt abscesses, edema, shortened crypts, PMNs in lamina propria)
        - Cx (blood, stool, urine, BM et al, stool is only 35% sensitive b/c of intermittent shedding)
        - Serology (value is unclear)
        - NB it is required that a + Dx be reported to county health department
    - Tx
        - Prevention
            - General: proper hygiene, proper food cooking, irradiate food products
            - NB no vaccine available for NTS but there is one for TS (give if travelling to 3rd world country)
            - NB after convalescence asymptomatic pts continue to excrete Salmonella bacilli into stool intermittently for ~5wks
        - Treatment
            - Tx is not uniformly recommended b/c
                - Abx fails to alter the rate of clinic recovery of gastroenterocolitis based on a meta-analysis of 12 trials w/ 778 pts b/t pts Tx and those on placebo
                - Abx increases the frequency and duration of chronic carrier state b/c abx Tx alters bowel flora which would encourages clearance
            - Indications for Tx
                - Severe Sx (BM >10/d, high fever, need for hospitalization) = 1° FQ, 2° 3rd Ceph, Amoxicillin, Bactrim x10-14d (5% of serotypes demonstrate resistance to one of these antibiotics)
                - Pt who is at higher risk of developing Extra-GI Salmonellosis (RFs above + CV stuff (valve dz, prosthetic valve, grafts, aneurysm) + <1yo/>50yo) OR Pt has developed Extra-GI Salmonellosis = 1° Chloramphenicol 50mg/kg/d divided QID IV, Ampicillin 1g IV Q6hrs, 2° Cefotaxime 2g IV Q6hrs, Ciprofloxacin 750mg IV BID x10d-6wks depending on infection location
            - Typhoid Fever
                - Tx is indicated for all infections w/ Ciprofloxacin
                - Glucocorticoids for severe infections

- *Shigella dysenteri* (most severe, least common), *flexneri, boydii, sonnei* (least severe, most common) = "Shigellosis" (third most common, ½ million cases/yr)
    - Epidemiology: occurs as epidemics in wars (Peloponnesian War, American Civil War, WWI), endemic in tropical countries, small inoculum needed b/c it can survive in acid stomach, most common transmission is person-to-person
    - Mechanism: various toxins → destroys mucosa
    - S/S: "bacillary dysentery", can take a chronic course up to weeks w/ relapses looking like UC, chronic carrier rate is low and only lasts 3-4mos but when present pts can get recurrent illnesses
    - Dx: no serology just stool Cx
    - Complications: mengismus/seizures (important in children), toxic megacolon, appendicitis, erythema nodosum, HUS, leukemoid reaction, myocarditis, pneumonitis, reactive arthritis
    - Tx: no abx if mild (but most never even see the doctor therefore if you see then Tx) only if mod/severe w/ Cipro 500mg PO BID x3d, high resistance to Amp/Bactrim (they used to be the preferred agents), NB abx must absorbed to reach the organism therefore you cannot use for example rifaximin or an IV abx
- *Yersinia enterolitica* O:8,5,27 (fourth most common, 100k/yr)
    - Epidemiology: chitterlings (hog intestine), pet feces, undercooked pork, unpasteurized milk products

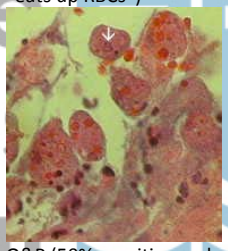
- Mechanism: 1° Peyer's patches at TI 2° colon
- S/S: <5yo (enterocolitis) vs >5yo (mesenteric adenitis, ileitis looking like appendicitis, aphthous ulcers in TI) NB Sx can be chronic making you think of IBD
- Complications: Erythema Nodosum, pharyngitis, glomerulonephritis, pancarditis, reactive arthritis, sepsis, thyroiditis, pneumonia, septic arthritis
- Deadly in cirrhotics and pts w/ iron overload
- Dx: blood serology
- Tx: abx do not alter the course of illness except if severe then use either Cipro 500mg PO BID, Tetracycline 500mg PO QID, Bactrim 160/800mg PO BID

- *Escherichia coli* (fifth most common, 100k/yr)
  - Dysentery Pathogenic Types (4 cause watery diarrhea vs 2 cause dysentery)
    - Entero-Invasive (EIEC)
    - Entero-Hemorrhagic (EHEC) (refer to hemostasis notes)
      - HUS: F + Microangiopathic Hemolytic Anemia + Thrombocytopenia + AKI/Hematuria/Proteinuria
- Other (non cholera) *Vibrio* spp
  - Mechanism: create various toxins leading various types of Sx
  - Types: *V. parahemolyticus* (eating raw oysters from any coast across the world), *V. vulnificus* (open skin exposure to warm salt water, especially deadly to pts w/ liver dz), *V. mimicus, V. hollisae, V. furnissii, V. fluvialis, V. metschnikovii,* et al
  - S/S: watery diarrhea to dysentery
  - Complications: cellulitis, otitis, pneumonia, cholangitis, sepsis
  - Tx: 1° tetracycline 500mg PO QID 2° Chloramphenicol, Pen-G if severe or multiple comorbidities otherwise conservative Tx
- *Aeromonas spp.*
  - Epidemiology: ubiquitous across the world, untreated brackish well/spring water, summer time, very high carrier rate questioning pathogenicity
  - Mechanism: GNR → various cytotoxins
  - S/S: watery diarrhea (can become chronic) to dysentery BUT also skin infections, bacteremia, multiorgan infections esp in immunocompromised pts
  - Tx: Bactrim/FQ/Tetracycline if complicated/chronic case
- *Plesiomonas shigelloides*
  - Epidemiology: raw oyster
  - S/S: watery diarrhea to dysentery
- *Lysteria monocytogenes*
  - Epidemiology: unpasteurized cheese, hot dogs, deli meat
  - S/S: meningitis, flu-like illness, diarrhea
  - NB very dangerous in pregnant women or immunosuppressed pts

- Parasite
  - *Entamoeba* aka "Amoebiasis"
    - Species
      - Pathogenic: *E. histolytica, Dientamoeba fragilis* (originally thought to be non-pathogenic but now it is believed that it may causes mild GI Sx)
      - Non-Pathogenic: *E. dispar, E. polecki, E. hartmanni, E. coli, Iodemoeba buetschlii*
    - Epidemiology: world-wide but highest concentration in Central/South America, Africa, India, 90% of pts are colonized but asymptomatic vs 10% symptomatic GI Dz (of these a minority develop extra-GI Dz), in the US those at highest risk are male homosexuals, institutionalized persons, young/old, immunosuppressed, pregnant
    - Mechanism: cyst in feces contaminates food/water → ingest contaminated food/water → gastric acid and pancreatic enzymes stimulates cyst to release trophozoite in the SI → trophozoite invades right colon (only 10% of pts, 2/2 toxins but also on the degree of host inflammatory response i.e. greater response = greater damage, range [mucosal thickening → punctate shallow **flask shaped** ulcers (b/c invasion is halted at muscularis hence it then spreads laterally) → necrosis causing dysentery → ± spread to the liver or other organs causing complications (below) → cysts reform and are excreted into feces



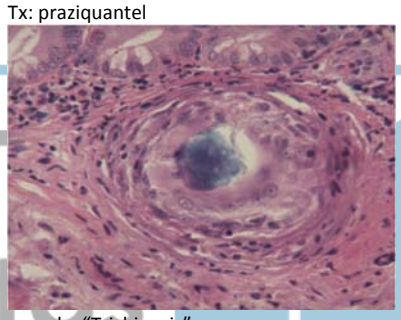
- S/S: very gradual dysentery unlike other infectious causes
- Complications (can occur up to years after GI infection and only 10% of pts report a h/o GI Sx)
  - intestinal amoebiasis: toxic megacolon, fistulas, ameboma (formation of granulation tissue are around ameba resulting in obstruction))
  - hepatic amoebiasis: liver abscess (most common) w/ anchovy paste pus, generally don't aspirate unless Tx is failing or the abscess is very large and at risk of rupture, only 20% of aspirates are + for trophozoites
  - extraintestinal amoebiasis: any –itis (peritonitis, pleuritis, pericarditis) or abscess (brain)
- Dx
  - Colonoscopy (not flex sig b/c right sided infection, Bx will show trophozoites, "dirty necrosis", inflammation AND erythrophagocytosis aka trophozoite "eats up RBCs")



  - O&P (50% sensitive and specificity, therefore ordered to rule out other stuff)
  - Serum Serology and Stool ELISA Antigen (90% sensitive and 85% specificity, which is also important b/c O&P cannot distinguish b/t pathogenic and non-pathogenic types: *E. dispar* and *E. hartmanii*)
- Tx (Tx even asymptomatic carriers (90% of infections!!!) b/c 10% will develop Sx and/or complications)
  - Luminal Amebicides: Paromomycin or Tinidazole
  - Tissue Amebicides: Metronidazole or Iodoquinal (no need to Tx if carrier only)

- *Schistosoma* spp aka "Schistosomiasis"
  - Epidemiology: World-Wide, 200million affected
  - Mechanism: larvae in fresh water penetrates skin causing a pruritic papule then migrates thru veins to specific venous systems laying eggs in surrounding tissue causing unique syndromes and then the eggs are excreted into urine/feces where snails take them up and release them again
  - S/S: Non-specific Acute Schistosomiasis aka Katayama Fever (2/2 brisk immune response to eggs resulting in F, HA, ab pain, myalgia/arthralgia, dry cough, D, LAD, HSM, urticaria) followed by Specific Acute/Chronic GI/GU Syndromes dependent on exact species (NB chronic dz is 2/2 granulomatous reaction to deposited eggs resulting in Symmer's pipe stem fibrosis of vessels)
    - IMV (*S. interclatum/mekongi*) S/S: acute (dysentery, ab pain, HSM, etc) vs chronic (portal HTN, polyps, strictures, varices)
    - SMV (*S. mansoni/japonicum*) S/S: acute (ab pain) vs chronic (portal HTN)
    - Bladder Veins (*S. hematobium*) S/S: acute (dysuria, hematuria) vs chronic (obstructive uropathy, bladder carcinoma, polyps)
    - NB eggs have been known to lodge in other organs: lungs, brain, etc

- Complications
  - worms often ingest enteric bacteria and carry them through out the body serving as reservoirs for recurrent bacteremia (esp Salmonella)
  - IC from the worms can lodge in the kidney causing membranoproliferative glomerulonephritis
- Dx: stool/urine O&P, serology, biopsies (granuloma w/ dead organism in the middle), serum circulating cathodic/anodic antigens (CCA/CAA)
- Tx: praziquantel



- *Trichinella* spp. aka "Trichinosis"
  - Epidemiology: world-wide, becoming rare in the US but recently there have been outbreaks in the US 2/2 cougar jerky, black bear meat, horse meat
  - Mechanism: ingest larva present in raw meat (esp pork) → larva invades intestine and develop into worms → worms enter circulatory system and invade 1° striated muscle and 2° CNS
  - S/S: most asymptomatic but if heavy worm burden then two symptomatic phases: enteral (colitis w/ F, N/V, ab pain, D) and parenteral (F, myalgia, periorbital edema, dysphagia, headache, paresthesia)
  - Complications: myositis, neuritis, vasculitis = death
  - Dx: stool and intestinal Bx are unreliable therefore the only way to make a diagnosis is with a muscle biopsy and with serology
  - Tx: Albendazole + Glucocorticoids

Chronic Diarrhea

- Watery (for any body fluid the number of cations (mainly Na, K) = number of anions (mainly Cl, HCO3, NB in increased motility some usually absorbed anions are not absorbed like SCFAs), Stool Osmotic Gap = Measured Stool Osmolality (nl 290 mOsm/kg) – Calculated Stool Osmolality (2(Na+K) mOsm/kg) NB x2 to include Cl and HCO3)
  - NB use the calculated osm not the measured osm b/c the latter is altered by bacterial degradation of carbohydrates as the stool sits at room temperature
  - NB stool osm >400 or <200 suggests contamination w/ specimen or urine, respectively
  - *Osmotic* (Large Gap >125 mOsm/kg in theory any # >0 but >125 signifies a true osmotic process = presence of an unmeasured osm, low volume <1L/d, nocturnal/fasting diarrhea uncommon) = anything that is poorly absorbed and osmotically active = water is drawn into lumen
    - Poorly Absorbed Substances
      - **Osmotic Laxatives (refer)**
    - Poorly Absorbed Electrolytes (just measure these specific ions to see if high eg Mg >200mEq/L)
      - **Ion Containing Antacids** (PO_4^{3-}, SO_4^{2-}, Mg^{2+}) are transported across mucosa by mechanisms that are saturated at relatively low [ion]
    - Poorly Absorbed Fat/Protein (rarely causes an osmotic diarrhea and also very rare)
    - Poorly Absorbed Carbs (pts also complain of bloating/gas, you can check stool pH, carbs fermented in colon results in drop in pH 2/2 fatty acid production, a pH <6 suggests excess carbs but a pH >6 does not rule out b/c could be mild carb malabsorption or gut flora could be reduced 2/2 abx, you can also check for "reducing

substances" which are any sugars than have an aldehyde/ketone (eg. lactose, fructose, galactose, pentose but NOT sucrose or lactulose)

- Congenital Disaccharidase Deficiency
  - **Lactase Deficiency aka Lactose Intolerance**
    - Types
      - Acquired Lactase Deficiency: genetically programmed reduction in lactase synthesis via SNP 13910 bases upstream from the LPH gene (CC = normal loss of gene expression vs TT = abnormal persistence of gene expression but even then it is only few in number hence the reversible states)
      - Congenital Lactase Deficiency: never had the enzyme even at birth
      - Reversible Lactase Deficiency: had tolerance but then had intestinal injury resulting in temporary loss of lactase from CD, infectious gastroenteritis, etc
      - NB some pts have milk protein allergy and not lactose intolerance
    - Mechanism
      - lactose cannot be broken down due to a deficiency on the brush border disaccharidase (lactase) thus allowing lactose to exert an osmotic effect (explosive diarrhea) and be fermented by colonic bacteria (pyruvate, lactate, SCFA, H2/CO2/CH4 gas) also bloating, flatulence, borborygmi, cramping
    - Epidemiology
      - the normal variant is to NOT have lactase activity during adulthood thus the mutation is to have lactase activity which is seen in North European Whites, Punjab/Delhi Indians and African Hima/Tutsi/Fulani Tribes, all other people around the world are generally lactose intolerant, **therefore is a person who is supposed to have persistence based on ethnicity comes in with lactose intolerance one must suspect a reversible cause such as CD!!!**
      - various teleologic theories specifically protection of milk for baby
    - Dx
      - empiric lactose free diet
      - check for reducing substances in stool
      - **Lactose Hydrogen Breath Test (LHBT)**
        - Mech: a fraction of intestinal H2 that escapes consumption is absorbed into blood and 100% of it is cleared thru the lungs therefore the rate of H2 exhalation = rate of absorption = rate of production
        - Pre: lactose free diet for >3d, fasting ON, no smoking/drinking/sleeping/exercising during study, if pt has elevated baseline H2 >3ppm then reschedule
        - Test: breath samples are taken at baseline and Q30min x5hrs after given 25g of lactulose in 250mL of water
        - +: H2 >20ppm or CH4 >10ppm or H2+CH4 >15ppm from baseline (presence of Sx during test is also very helpful)
        - NB early peaks suggests rapid transit, SIBO or oral cavity bacterial degradation
        - NB remember methane producers (refer to SIBO)
    - Tx: restriction, enzyme replacement w/ Lactaid but only partially works, if young take Ca/VitD and follow development of osteoporosis, remind pts that it will worsen with age
  - **Other: Sucrase, Isomaltase, Trehalase Deficiency**
    - _____ Hydrogen Breath Test (_HBT) similar is to LHBT
- **Sugar Alcohols** (Sorbitol/Mannitol) used as artificial sweeteners in sodas, chewing gum, candy, etc
- **High Fructose Corn Syrup** (easily overwhelms absorption and b/c of the its presence in many modern industrialized foods like soft drinks it is very common, switch to diet)
- **Any Malabsorption/Maldigestion (below)**

- *Secretory* (Small Gap <50 mOsm/kg in theory 0 = increase in a measured osm, high volume >1L/d, nocturnal/fasting diarrhea common) always exclude infection first then exclude structural disease = drive the epithelium to secrete water and electrolytes
  - **Luminal Secretagogues** which disrupt intestinal transport
    - **Infection w/ Non-Invasive Pathogens**

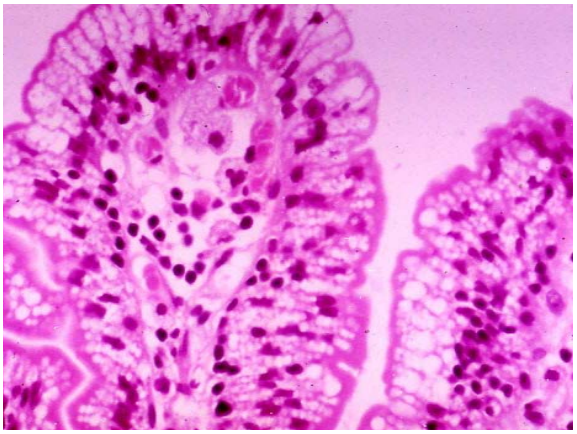
        - Viruses: Adenovirus
        - Parasites: *Giardia lamblia*, *Cyclospora cayetaresis, Cryptosporidium parvum*
    - **Bile Salt Excess**
        - Mechanism
            - Bile acids enter colon and inhibit water absorption
        - Etiology
            - postcholecystectomy (gallbladder serves as a reservoir for bile salts at night when they are not needed, when the gallbladder is removed bile salts enter SI during night, the large volume of bile acids overwhelms TI absorption and enters the colon, 80% get loos stools vs 10% get significant diarrhea vs 10% nothing, female > male, occurs w.in days-weeks of chole)
            - <100cm ileal resection/dz which disrupts enterohepatic circulation and thus bile acids are not absorbed and go into colon and stimulate secretion by acting as detergents on the epithelium increasing permeability
            - Over time everyone naturally loses some of their ability to absorb bile acids as well
            - Ileitis: CD, Radiation, IBS
            - Ileal Bypass
            - Idiopathic
        - Dx: fecal BA but empiric Tx is the best test
        - Tx: bile acid resins
    - **Stimulant Laxatives** (check for presence using chromatographic methods)
    - **Long Chain Fatty Acids**
- **Circulating Secretagogues** (Tx: octreotide) which disrupt intestinal transport by altering intracellular messengers like cAMP/cGMP/Ca and synthesis/localization/degradation of transport proteins)
    - Endocrine: serotonin (Carcinoid), gastrin (Gastrinoma), glucagon (Glucagonoma), VIP (VIPoma), calcitonin (Medullary Carcinoma of Thyroid), thyroid (Hyperthyroidism), low corticosteroids (Addisons)
    - Neurologic: Substance P, Ach
    - Inflammatory: Histamine, Cytokines, Mastocytosis
    - Meds: erythromycin
- **Other**
    - **Cancer**
        - Lymphoma (obstruct lymphatics)
        - Rectal Villous Adenoma (secrete large amounts of K rich gelatinous fluid)
    - **Congenital Absence of Sugar Transporters (glucose, galactose)**
    - **Congenital Absence of Ion Transporters**
        - **Congenital Chloriderrhea**: congenital absence of chloride-bicarbonate exchanger in ileum/colon resulting in accumulation of chloride in lumen obligating retention of cations and thus water in lumen, Tx: reduce chloride load by (1) limiting oral Cl intake specifically ?, (2) decreasing GI Cl secretion by inhibiting gastric chloride secretion with PPI, (3) stimulating Cl absorption by enhancing short-chain fatty acid absorption with butyrate
        - **Congenital Sodium Diarrhea**
    - Idiopathic (protracted but self-limited course lasting <2yrs)
        - Epidemic Secretory Diarrhea (affects a group of people, first described in Brainerd, Minnesota hence often called Brainerd's Diarrhea, believed to be 2/2 infection but no agent found)
        - Sporadic Secretory Diarrhea (only affects one person)
        - Chronic Idiopathic Secretory Diarrhea (first described by Schiller/Fordtran/Little in 1992, abrupt onset but self-limited lasting on average 17mo)

- Neuromuscular
    - **Neuro Dysregulation**: enteric NS is messed up and alters the fluid/electrolyte absorption b/c the contact time between luminal contents and mucosa is increased aka "Intestinal Hurry or Rapid Transit" not allowing for proper absorption or mixing or decreased aka "Slow Transit" resulting in bacterial overgrowth
        - Intestinal Hurry
            - Vagotomy (done for PUD surgery)
            - Gastric Bypass (done for Bariatric surgery)
            - Celiac Plexus Neurolysis
            - Diabetic Diarrhea (~5% of diabetes)
                - T1DM w/ autonomic neuropathy w/ rapid gastric emptying and rapid intestinal transit causing impaired mixing of food w/ secretions and decreasing contact time of food w/ mucosal surface for absorption, can alternate w/ constipation
                - medications (acarbose/metformin)

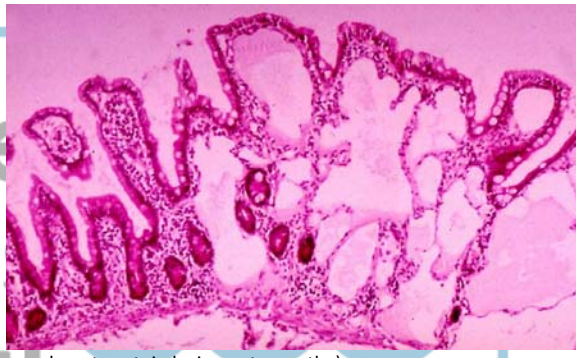
        - foods (sugar alcohols)
        - other associated dz (celiac disease, pancreatic exocrine insufficiency, SIBO)
        - other autonomic problems (rectal incontinence)
    - IBS
    - Post-Prandial Diarrhea
    - NB "Dumping Syndrome" S/S: flushing, hypoTN, diarrhea, post-prandial hypoglycemia, Cause: unregulated gastric emptying, osmotic shifts, rapid release of peptide hormones, Tx: modified diet, antidiarrheals, Octreotide
- Slow Transit
    - Scleroderma

- Inflammatory (ask about blood/pus, FOBT, Fecal WBC, Fecal Lactoferrin/Calprotectin (enzymes found in WBCs, more expensive but easy to check, fast, no need for fresh stool), SBFT/CT (strictures, ulcers, fissures, fistulas, et al), Endoscopy w/Bx sigmoid if no HIV while colonoscopy if HIV/old/sick, pain on PEx)
    - **General SI Mucosal Inflammatory Damage** (refer to intestine notes)
        - Infection
        - Ischemia
        - IBD
        - Radiation
    - **Infections w/ Invasive Pathogens**
        - Bacteria: EHEC, *Clostridium difficile,* TB, *Yersinia, Aeromonas, Plesiomonas*
        - Viruses: CMV, HSV, MAC
        - Parasites: Giardia, Cryptosporidia, Cyclospora, *Entamoeba histolytica "Amebiasis", Trichuris trichura* "Whipworm", Schistosomiasis
- Fatty (S/S: depend on nutrient malabsorbed but pts usually experience weight loss and vitamin deficiency and steatorrhea w/ foul smelling, oily, stool w/ food particles, NB floating is a misconception and likely 2/2 air in stool) Two Types: malabsorption/maldigestion, type of osmotic diarrhea)
    - 1st Qualitative Fecal Fat (have pt eat a high fat diet (100g/d) and then take a sample of stool and stain w/ Sudan III Stain after hydrolysis w/ glacial acetic acid and heat and + if >100 globules (>4mm in diameter) per HPF
        - NB conditions in which fecal fat excretion is increased: high fiber, solid fat, neonate (low levels of enzymes), non-absorbable fats eg. Olestra
        - NB qualitative test does not really correlate well w/ quantitative test
    - 2nd Quantitative Fecal Fat (have pt eat a high fat diet (100g/d) and then collect a 72hr amount of stool and the quantify amount of fat w/ van de Kamer method w/ <7g/d being normal while >14g/d or >10% intake is true fat malabsorption
        - NB a quantitative spot test called the acid steatocrit test seems to correlate well w/ the van de Kamer method
        - NB other fat malabsorption tests: ^{14}C-triolein breath test, beta-carotene photometric test
        - NB carb malabsorption tests (hydrogen breath tests, pH, anthrone method) and protein malabsorption tests (fecal nitrogen content, ^{14}C-octanoic acid ^{13}C-egg white breath test)
    - 3rd D-Xylose Test (determine if its malabsorption vs maldigestion w/ D-xylose Test as D-xylose does not require digestion as it can be absorbed directly and excreted unchanged into urine (give 25g of D-xylose and if 5hr urine xylose excretion is >5g or 1hr spot serum level is >20mg/dL then maldigestion and if <5 and <20 then malabsorption)
        - NB one can also check water soluble albumin/iron/folate/VitB12 for water soluble absorption fxn and fat soluble cholesterol/carotene/PTT/Ca for fat soluble absorption fxn as, like D-xylose, their absorption is independent of digestion as they can be absorbed directly
        - NB conditions in which D-xylose test is falsely positive: delayed gastric emptying, myxedema, vomiting, ascites, renal insufficiency, dehydrated
    - 4th Malabsorption (SI Bx) vs Maldigestion (pancreatic exocrine test (refer), empiric Tx below, NB TGL remain intact therefore stool is not that loose b/c TGL have little effect on colonic electrolyte absorption unlike FFA)
    - General
        - **Fat Transporter Defect**
            - Pancreatic Insufficiency (refer below, specific congenital enzyme deficiencies)
            - BA Deficiency (refer below)
            - Defective Mixing 2/2 Gastric/Intestinal Dysmotility (refer below)
            - Impaired Absorption (refer below)
            - Impaired Intracellular Ability to Form Chylomicrons (Abetalipoproteinemia, Familial Hypobetalipoproteinemia, Chylomicron Retention Disease aka Anderson's Disease, Cholesteryl Ester Storage Disease aka Wolman's Disease)
                - **Abetalipoproteinemia**
                    - Mechanism: AR defect in Microsomal Triglyceride transfer Protein (MTP) such that apoB cannot be made and thus lipoproteins that contain apoB specifically chylomicrons cannot be made resulting in accumulation of fat in enterocytes instead of going into lymphatics
                    - S/S: steatorrhea seen in children, interesting features include circulating acanthocytes (RBCs with spiny projections), retinitis pigmentosa, and neurologic deficits including cerebellar and spinal tract abnormalities
                    - Dx: **biopsy showing visible lipid vacuoles in enterocytes w/ oil red O stain**, yellowish mucosa on endoscopy

- Tx: low-fat diet supplemented w/ medium chain triglycerides and fat soluble vitamins



- Impaired Lymphatic Transport of Chylomicrons (Primary Intestinal Lymphangiectasia aka Milroy's Syndrome resulting in malformation of lymphatic system, Obstruction of Lymphatic Vessels 2/2 solid organ mets, lymphoma, Whipple's, TB, Sarcoid, CHF, RP fibrosis, trauma) = Lymphangiectasia aka Dilated Lacteals



- **Protein Transporter Defect** (always rule out protein losing enteropathy)
  - Pancreatic Insufficiency (refer below, specific congenital enzyme deficiencies)
  - Defective Mixing 2/2 Gastric/Intestinal Dysmotility (refer below)
  - Impaired Absorption (refer below, specific enzyme/transporter deficiencies eg. Hartnup's Disorder, Cystinuria, Lysinuric Protein Intolerance, Isolated Lysinuria, Iminoglycinuria, Blue Diaper Syndrome, Methionine Malabsorption Syndrome aka Oasthouse Syndrome, Lowe Oculocerebral Syndrome)
- **Carb Transporter Defect**
  - Pancreatic Insufficiency (refer below, specific congenital enzyme deficiencies)
  - Defective Mixing 2/2 Gastric/Intestinal Dysmotility (refer below)
  - Impaired Absorption (refer below, specific enzyme/transporter deficiencies eg. Congenital Lactase Deficiency, Sucrase Deficiency, Trehalase Deficiency)

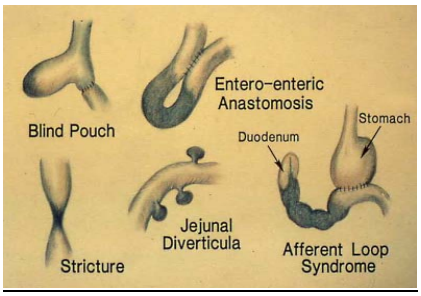
- *Malabsorption*
  - **Specific Enzyme/Transport Deficiencies** (rare)
  - **General SI Mucosal Absorptive Damage** (refer to intestine notes)
  - **Short Bowel Syndrome (SBS) aka Intestinal Failure**
    - Def: insufficient intestinal SA for adequate absorption of nutrients/fluids to sustain life in the absence of nutritional support
    - Reasons for SI resection: ischemia, Crohn's resection, radiation, SB tumors, bypass surgery, volvulus, strangulated hernia, prolonged obstruction
    - Mechanism
    - Complication (always remember recurrent dz)
      - GI
        - Diarrhea
          - (1) if <100cm of TI is resected then there is moderate bile acid malabsorption but the liver is able to keep up synthesis therefore there is normal digestion of fat but now a lot of bile salts enter the colon = bile salt diarrhea VS if >100cm of TI is resected then there is severe bile acid malabsorption and the liver is unable to keep up synthesis resulting in steatorrhea
          - (2) decreased SA

- (3) increased intestinal transit resulting in inadequate mixing, decreased contact w/ intestinal surface, etc
- (4) increased secretions
- (5) osmotic stimulation of water secretion by unabsorbed nutrients

        - VitB12 Deficiency
        - SIBO (2/2 loss of ICV)
        - PUD (2/2 hypergastrinemia which is only temporary)
    - Hepatobiliary
        - Cholelithiasis (2/2 GB stasis, loss of bile acid in stool and altered composition)
        - TPN Liver Dz (refer)
    - Kidney
        - Calcium Oxalate Nephrolithiasis (fat malabsorption → fat binds calcium → calcium cannot bind oxalate → oxalate is hyperabsorbed → oxalate is excreted into the urine where it binds calcium creating stones, Tx: restrict dietary oxalate and if hyperoxaluria continues then give calcium citrate)
        - Metabolic Bone Dz
        - CKD (unclear why)
    - CNS
        - Confusion (2/2 electrolyte changes, hyperammonemia 2/2 citrulline deficiency, D-lactic acidosis (high refined carb intake → not absorbed so enters colon → *Bacteroides* ferment creating SCFAs and L-lactate → drop in pH promotes growth of *Bifidobacterium, Lactobacillus, Eubacterium* which uniquely make D-lactate → confusion w/ Wernicke's like changes, Dx: AGMA w/ nl L-lactacte but + D-lactate >0.5mmol/L, Tx: correct AGMA, only eat complex carbs, ?abx Tx))
        - Memory Deficits
    - ID
        - TPN Line Complications
- Tx
    - General (nl SI is 760cm)
        - nutrition management depends on many factors: amount/location of SI lost, adaptation of the remaining SI, presence of colon/ICV, remaining active dz
        - General Rule: resection <50% of SI is well tolerated, 50-75% symptomatic, >75% life-threatening, worse if less colon and/or no ICV
        - Why is the colon important? carbohydrate salvage, water/electrolyte absorption, colonic brake
        - Why is the ICV important? it slows down SI transit and prevents entry of colon bacteria into SI decreasing r/o SIBO which if present worsens nutrient absorption
    - Approach
        - <u>(I) Early Post Operative Period: TPN, anti-diarrheals, elemental diet to promote intestinal adaptation but cautious PO diet, PPIs b/c of temporary hypergastrinemia!!!</u>
        - <u>(II) <1-2yrs: adaptation is beginning, increase enteral feeds and modify w/ high MCT and low fat/lactose, supplement minerals/vitamins, wean TPN</u>
            - Predictors of NOT being able to wean off TPN
                - **Intact Colon but <80cm of SI**
                - **No Colon and <115cm of SI**
                - **Active residual disease**
                - **Plasma Citrulline <300 (AA made by SI therefore plasma levels correlates w/ SI mass)**
        - <u>(III) >1-2yrs: adaptation has maximized therefore if still diarrhea than consider nighttime NG feedings prn and TPN prn</u>
    - **Intestinal Adaptation:** luminal nutrients (fiber, SCFA, glutamine) and pancreaticobiliary secretions → increased hormones (GH, GLP-2, VEGF, CCK, gastrin, Insulin, neurotensin) → structural changes (increased SA via taller villi and deeper crypts via increased enterocyte number), functional changes (increased brush border enzymes and increased intestinal transit time), microbiota changes (increase in colonic flora that can metabolize complex carbohydrates) → increased absorption
        - colonic salvage of unabsorbed carbs via SCFA and calcium (refer to physiology notes)
        - more pronounced in ileum than jejunum
        - bowel does NOT convert to other types of bowel (eg. jejunum does not turn into ileum by say acquiring bile acid transporters) it is just able to absorb general nutrients better

        - takes 1-2yrs to fully develop
        - younger pt, early enteral feeding, more ileum, good blood flow, few comorbid conditions = better adaptive changes
        - research is looking into ways in giving hormones (L-Glutamine, Growth Hormone, GLP-2, EGF) to promote adaptation
    - Diet
        - NPO w/ TPN x5d → Enteral Tube Feeds x5d (start when post-op ileus has resolved and pt is HDS and anastomosis has healed, give slow continuous feeds w/ elemental diet then frequent feeds w/ polymeric diet, use MCTs (Lipisorb) to supplement fat b/c they don't require bile salt and micelle formation for absorption and are absorbed by colon) → Oral Diet (small frequent meals, low oxalate diet, oral rehydration solutions, high calorie diet, lactose free)
            - If steatorrhea then low fat diet (remember that fat is energy rich so pt will being taking in less calories) or give only diet w/ only medium chain triglycerides (MCTs) b/c they do not require micellar solubilization and can be absorbed by the colon
            - If colon is present then start diet high in complex carbs (starch, fibers, etc) b/c they pass undigested into colon where colonic bacteria ferment complex carbs into SCFAs (butyrate, acetate, proprionate)
    - Follow
        - Assess weight, volume status, electrolytes, ostomy output and correct w/ goal UOP >1L/d (follow both serum/fecal/urinary levels)
        - Assess Ca/Zn/Fe/Mg/Selenium frequently b/c steatorrhea causes low levels
    - Meds
        - For 6mo the pt is in a hypergastrin state resulting in increased gastric secretions that results in diarrhea therefore give IV PPI initially b/c absorption of PO PPI is impaired or just give high dose
        - Anti-motility agents after nl post-op ileus resolves to increase intestinal transit
        - Bile-Acid Binders or Replacers depending on the anatomy (if limited resection (<100cm) then binders b/c absorption is impaired but not completely gone therefore the liver is able to compensate thus bile acids are constantly in the colon causing diarrhea vs if extensive resection (>100cm) then replacers b/c absorption is completely gone resulting in eventual complete loss of bile acid pool leading to steatorrhea)
        - Prenatal Multivitamin
        - Vit-ADEK (oral is generally fine, colonic flora make VitK so not usually needed)
        - VitB12 (you need >60cm TI resection for VitB12 malabsorption to occur)
        - Remember that in general meds are going to be poorly absorbed and that higher doses may be needed
    - Surgery
        - Intestinal Lengthening Procedures
            - Bianchi Procedure
            - STEP Procedure
        - Intestinal, Intestinal+Liver or Multivessel Transplantation
            - Indicated in SBS pts who (1) are TPN-dependent and have TPN-liver dz, (2) have frequent episodes of severe dehydration, (3) had an episode of fungemia, (4) had an episode of septic shock, (5) have two major vessel thrombosis
            - Very expensive
            - Many post-transplant complications

- **Small Intestinal Bacterial Overgrowth (SIBO)**
    - RFs
        - Hypochlorhydria (gastrectomy, atrophic gastritis, vagotomy, use of PPI/H2B/AA, etc)
            - Acid kills and suppresses growth of most bacteria that enter from the oropharynx
        - Dys/hypomotility (DM, scleroderma, amyloidosis, hypothyroidism, radiation enteritis, CIPO, meds (opiates, anticholinergics))
            - MMC and the strong arborad propulsive forces rid the SI of bacteria
        - Anatomic Problems (stricture, diverticulosis, entero-colonic/enteric fistulas, loss of or incompetent ICV, blind loops eg afferent loop syndrome of BII)
            - One continuous open lumen w/ a valve prevents stagnation and reflux



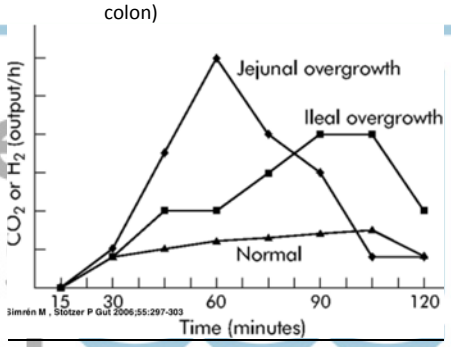
- Host Defense Problems (loss of mucus, immunodeficiencies)
  - IgA and Paneth cell products (eg. defensins) neutralize bacteria
- **Epidemiologic Observation**
  - **35% of low BMI but otherwise healthy/asymptomaic elderly people w/o any known RFs (likely subtle motility abnormalities) above have SIBO → w/ SIBO Tx pts subsequently gained weight (very important to know!!!)**
  - **Chronic Pancreatitis**
  - **Renal Dz**
  - **Liver Dz**

- S/S
  - **Maldigestion & Malabsorption: Diarrhea, Unique Fat Soluble Vitamin Deficiency (except VitK), Protein Loosing Enteropathy**
    - Why? (1) bacteria deconjugate bile acids in the SI thus no micelles form and bile acids move into colon and stimulate secretion, (2) bacterial proteases damage brush border disaccharidases/enterokinases and epithelial tight junctions
    - Why? bacteria produce VitK
  - **Megaloblastic Anemia**
    - Why? (1) bacteria separate IF from VitB12 and then consume VitB12 (most consistent abnormality) and (2) bacteria produce folate
  - **Gas Production: Bloating, Distension, Flatulence (probably the most common Sx)**
    - Why? bacteria ferment carbs and create gas
- Associations (it is unclear if SIBO is the cause, a consequence or simply an epiphenomon effect)
  - **IBS:** Pimental, et al in early 2000 noted abnl breath tests in a large percentage of IBS pts and subsequently observed significant improvements in IBS related Sx following normalization of breath tests w/ neomycin, nevertheless this link is controversial as the diagnostic criteria varied b/t studies, Sx improvement did always correlate w/ normalization of breath tests and it could be that any Sx improvement could reflect Tx on colonic bacteria only
  - **NASH:** there is a well established statistical link but the cause for the association is unclear (some suggest that altered SI permeability allows for increased endotoxin absorption)

- Dx
  - Clinical Picture that responds to empiric treatment ± non-invasive diagnostic test
  - "Gold" Standard: Bacterial Counts
    - Jejunal Luminal Aspiration and Mucosal Brushings
    - + if $>10^5$ CFU/mL OR $>10^3$ CFU/mL w/ increasing % of colonic GNC anaerobes as opposed to oropharyngeal GPC aerobes
    - Problems: misses distal SIBO, expensive, technically challenging in preventing contamination, proper collection technique is not well defined, most bacteria are not culturable!!!
    - NB Bx are generally normal but may show non-specific nor sensitive villous atrophy and intraepithelial lymphocytes on LM and vacuolization of microvillus and mitochondrial swelling on EM
  - Non-Invasive Tests
    - Types
      - *Fermentation*
        - Administer carbohydrate substrate (eg. glucose, lactulose, $^{13/14}$C-Xylose) → fermented by bacteria into SCFA, lactic acid and gases (H_2, CO_2, CH_4) → measure products (gas in breath, SCFA in jejunal aspirates, a 4-Hydroxyphenylacetic Acid in urine, etc)
      - *Bile Acid Deconjugation*
        - Administer exogenous bile acid conjugated to a marker substance (eg. ursodeoxycholic acid + p-aminobenzoic

acid (UDCA+PABA) → deconjugated by bacteria → measure PABA in urine

- Most Common: **Glucose Hydrogen Breath Test**
  - Prep: no bowel prep for >4wks, 48hr low fiber diet, 24hr diet w/ carb, 12hr ON fast, no smoking/exercise = false –, no abx x2wks
  - Design: rinse mouth out w/ antiseptic, ingest 50mg of glucose, measure baseline gas level then Q15min x2hrs, + if H_2 or CH_4 is >20/32ppm if baseline was <10/>10ppm at 2hrs)
  - Mech: normally glucose is completely absorbed but w/ SIBO some of it is fermented by bacteria forming gas, 1/5 of this gas exhaled
  - Problems
    - rapid transit → false + vs slow transit or gastroparesis → false –
    - methanogenic/sulfide-reducing bacteria which convert H_2 into CH_4 and H_2S → false – (10% of pts)
    - pts who have carb malabsorption (eg. CD, chronic pancreatitis) have more sugar available for fermentation → false +
  - NB lactulose has been used but not anymore, it is normally not absorbed but enters colon causing gas production unlike glucose which is entirely absorbed, therefore you will see two peaks in SIBO (one reflecting SIBO and the other reflecting lactulose in the colon)



- Tx
  - **Correct Underlying Cause**
    - Stop antisecretory meds to fix hypochlorhydria
    - Surgery to fix anatomy
    - Prokinetics to fix dysmotility (eg. Low Dose Octreotide 50mcg SC QD to stimulate motor activity)
  - **Nutritional Changes**
    - Nutritional Supplement
    - Fat Vitamin Replacement
    - FODMAP Diet
  - **Change Microbiota**
    - Antibiotics w/ activity against GN Anaerobes
      - Eg. metronidazole, amoxicillin, fluoroquinolones, tetracyclines/doxycyline, rifaximin, neomycin, trimethoprim-sulfamethoxazole
      - Choice (no evidence favoring one over another), Dose, Duration (7-14d) has not been standardized
      - assess for clinical response or breath test
      - recurrence is high ~44% at 9mo in one study esp if the underlying cause is not addressed → rotate abx w/ x2wk free period to prevent resistance and SEs
      - always discuss r/o C.diff infection
    - Prebiotics (controversial)
    - Probiotic (controversial)

- *Maldigestion*
  - **Pancreatic Insufficiency (refer to pancreatic notes)**
  - **Bile Salt Deficiency**
    - Mechanism
      - Can't absorb fat

        - NB unabsorbed FAs bind the portion of dietary calcium which normally binds dietary oxalate (causing excretion of oxalate) allowing oxalate to be absorbed and filtered by kidney causing calcium oxalate stones
    - Etiology
        - liver dz, cholestasis, inborn errors of BA synthesis, CCK deficiency, etc which has causes decreased BA entering the GI tract
        - bacterial overgrowth which deconjugates salts into acids rendering them useless for fat digestion
        - acidity from ZES or pancreatic insufficiency precipitates out bile acids
        - >100cm loss of TI (resection or dz) or congenital defects in Na-BA constransporter eventually results in decreased bile acid pool b/c the liver cannot keep up and make more BA (the liver can if <100cm)
        - Bound to cholestyramine
        - idiopathic bile acid malabsorption (adult onset)
    - Dx: (rarely done rather just empiric Tx)
    - Tx: bile acid replacement or medium chain triglycerides w/ a low fat diet
- **Gastric Disorders**
    - gastric surgery → (1) stomach is connected to the jejunum not the duodenum resulting inadequate mixing of chyme with enzymes/bile, (2) gastric emptying of chyme might precede arrival of enzymes/bile, (3) lack of gastric lipase, (4) loss of gastric acid leading to SIBO → maldigestion
    - gastrinoma → excess acid inactivates pancreatic enzymes