Nausea & Vomiting

Reflex Arc w/ Etiologies

- Afferent
  - Chemicals (stimulate the Area Postrema aka Vomiting Trigger Zone (VTZ) (Floor of the Fourth Ventricle outside of the BBB) which sense these chemicals in blood (typically results in morning N/V on an empty stomach with emission of mucoid material aka swallowed saliva or gastric secretions))
    - Drugs (most common)
      - Chemo
        - occurs in three phases: (1) anticipatory, (2) 2/2 direct stimulation of chemoreceptor trigger zone of brainstem, occurs w/in 24hrs of tx usually 1-2hrs, immediately after chemo, mediated by serotonin, etc and (3) after 24hrs of Tx, less intense but longer duration than acute, 3-7d after chemo, mediated by dopamine, substance P, etc,
        - most common chemo: cisplatin, dacarbizine, nitrogen mustards
        - Anticipatory: benzo + phenothiazines + dexamethason
        - Acute: 5-HT3 antagonists + dexamethasone
        - Delayed: benzo + metoclopramide + dexamethasone
        - NB radiation can also cause N/V
      - Analgesics: aspirin, NSAIDs, opiates (CHRONIC OPIATE USE CAUSES SIGNIFICANT NAUSEA AND DURING WITHDRAWAL THEFEFORE TAPER OFF)
      - CV: digoxin, antiarrhythmics, antihypertensives, diuretics
      - Hormones
      - Antimicrobials
    - Toxin: ethanol, nicotine
    - Endo: HyperCa, HypoNa, DM esp w/ DKA, Hypo/HyperPTH, Addison's, Uremia, Hyper VitA, Porphyria, Pregnancy
  - GI
    - **Any Type of Infection**
    - **Atypical GERD (surprisingly common)**
    - **Obstruction (always rule out)**
    - **Gastric Dysmotilities (eg. gastroparesis)**
    - **Mucosal Inflammation (eg. gastroenteritis)**
    - **Peritoneal Irritation**
    - **Malignancy**
    - **Pharyngeal Stimulation aka Gagging**
  - Non-GI: **Ovarian/Testicular Torsion "getting hit in the balls", Any Systemic Illness, Ischemic Heart Disease, Intense Pain, Post-Op**
  - Functional: **Functional Dyspepsia**
- CNS (Nucleus Tractus Solitarious 5-HT3, D2, M1, NK1 and Emetic Center CB1 therefore inhibition decreases N/V except for CB1)
  - **Migraine Headaches**
  - **Seizure Disorder**
  - **Psychiatric: Psychogenic, Anxiety, Eating Disorders, Pain**
  - **Increased Intracranial Pressure 2/2 Lesion, Hydrocephalus, Inflammation, Hemorrhage etc**
  - **Labyrinthine Disorders**
    - **Otitis Media**
    - **Motion Sickness**
    - **Labyrinthitis**
    - **Menier's Dz**
    - **Chronic Vestibular Dysfunction**
      - Consider in normal GES for suspected gastroparesis
      - Dx: Nystagmus, Romberg Test, Modified Fukuda Exam (march in place, eyes closed, hands covering ears so as eliminate priopioception, visual, auditory sensory input forcing the pt to use vestibular fxn to maintain balance, if >90° turn to Right or Left w/in 60sec then there is + vestibular dysfxn)
      - Tx: antihistamine (transdermal scopolamine or meclizine), benzo (diazepam)
  - **Functional Vomiting**
    - Rome II Committee on Functional GI Disorder Criteria: ≥ 1 episodes of vomiting for ≥3 days in the ≥3 months in the past year
    - Diagnosis of exclusion (especially exclude neurologic disorders, chronic partial bowel obstruction, gastric emptying disorders, eating disorders w/ self-induced vomiting) but usually there are underlying psychiatric conditions, antiemetic medications are not usually effective
    - NB 2% of normal population vomit 1x/mo
    - Often have to do gastric motility studies
  - **Cannabis Vomiting Syndrome**
    - Just like CVS in terms that it is cyclic (but can be chronic) but there is a clear precipitant (cannabis)

        - after long term exposure there is a paradoxic pro-nausea effect as THC accumulates and binds cerebral fat in addition THC also has direct effects on the GI tract promoting nausea
        - often pts take multiple hot water showers/baths b/c lessens nausea (this is not seen in CVS)
        - most pts have improved Sx after stopping for one week
        - TCAs are not helpful unlike in CVS
    - **Cyclic Vomiting Syndrome (CVS)**
        - Mechanism
            - unclear but some interesting theories like chronic cannabis abuse and mutation w/ mitochondrial DNA
        - Comorbidities
            - Migraine Headaches (part of the Migraine Diathesis Spectrum each with different predominant features, VERY IMPORTANT CORRELATION)
            - IBS
            - Motion Sickness
            - Seizure Disorder
            - MJ use (aside from the syndrome above)
        - Dx (3mo w/in the last 6mo)
            - Stereotypical episodes of vomiting regarding onset (acute) and duration (<1wk, avg 2d)
            - ≥3 discrete episodes in the past year (avg 12 episodes/yr, often begins at night or when awakening, less common during summer)
            - Absence of N/V in b/t episodes
            - No other causes of N/V (DOE) especially exclude neurologic disorders, chronic partial bowel obstruction, gastric emptying disorders
        - Pt
            - Becoming much more common than previously thought
            - first described in children but can affect any age group 6mo to 73yr but median age of onset is 6yo
            - Personality: competitive, perfectionist, high achieving, aggressive, strong willed, moralistic, enthusiastic, and especially anxious
            - Vicious cycle: the more anxious the pts get about an episode the more episodes they get
        - Pattern (Four Phases) (very stereotypical for each pt)
            - Interepisodic: pt is perfectly normal
            - Prodromal: pt develops ab pain, N, lethargy, anorexia, and pallor but is able to take PO meds to abort) Triggers: infection, stress, pregnancy, inadequate sleep/diet, menses, any emotional state (holidays, birthdays, family conflicts, etc)
            - Emetic: intense incapacitating retching/N/V, <2d, 24 N/V per episode, b/c of the vomiting prolapsed gastropathy or Mallory-Weiss tears often occur, 50% have ab pain, headaches, photo/phonophobia, tachycardia, HTN, diaphoresis, mild loose stools, low grade fever, leukocytosis (hence pts undergo extensive work-ups), inability to think clearly, irritable/abusive/demanding behavior, pts often crave water to drink and then subsequently vomit so called "guzzle-and-vomit" so as to dilute irritants in their vomitus
            - Recovery: symptoms remits but not quite back to normal as pt regains appetite and strength
        - Tx
            - Treatment (goal is to have pts sleep it off)
                - Ativan 1mg IV Scheduled Q4hrs unless sleeping
                - Dilaudid 4mg IV Scheduled Q6hrs unless sleeping
                - Phenergan 25mg IV Scheduled Q6hrs unless sleeping
                - Zofran 8mg IV Scheduled Q6hrs unless sleeping
                - IVF and Correct Electrolytes
                - Dark Uninterrupted Room
            - Px
                - Identify and Eliminate Triggers
                - Migraine Prophylaxis
                - H2B: Cyproheptadine
                - TCA: Amitryptiline 100mg PO Qhs
                - Antiemetics are generally not helpful

- Efferent
    - 1st cerebral cortex activates resulting in nausea
    - 2nd diaphragm/intercostal contractions w/ closure of glottis resulting in retching (Phrenic Nerve)
    - 3rd diaphragm/ab muscle contractions w/ LES relaxation and retrograde peristalsis resulting in vomiting (Vagus Nerve) (soft palate raises to block nasopharynx, respiration drive inhibited, glottis closes to prevent aspiration)
    - NB sometimes hypersalivation, arrhythmias, passage of gas, passage of stool
- DDx
    - **Regurgitation/Rumination**
        - not just seen in 3-6mo old infants but also in adults

        - effortless and non-forceful (no nausea or vomiting) retrograde flow of esophageal contents back into mouth (regurgitation) followed by re-chewing and then re-swallowing (rumination) or spitting out
        - usually occurs 1-2hrs after eating
        - belch reflex that has adapted unconsciously overtime
        - 2/2 relaxation of diaphragm
        - "food tastes the same going up as it did going down"
        - not distressful to the pt but can cause under-nutrition
        - confirm with manometry (R waves) and 24-hr pH testing
        - association with eating disorders
        - exclude Zenker's
        - Complications: esophagitis (rare)
        - Tx: reassurance, diaphragmatic breathing techniques (relax diaphragm before after meals, taught by a behavioral psychologist), consider upper GI pro-kinetics, SSRI (mirtazapine)
- Characterize
    - Acute <1wk vs Chronic >1wk
    - Bilious vs Non-Bilious (NB)
    - Bloody/Hematemesis vs Non-Bloody (NB)
    - Feculent vs Non-Feculent (NF)
    - Digested vs Undigested Food
    - Projective vs Non-Projectile
- Work-Up
    - Labs (beta-hCG)
    - GI Lab (Esophageal/Gastric Manometry)
    - EGD
- Complications
    - Tx Stomach/Esophageal Injury (esophagitis, Mallory-Weiss Tears, Boerhaaves, facial purpura, dental carries)
    - Glottic Spasm w/ Transient Asphyxia
    - Aspiration Pneumonia
    - Fluid/Electrolyte/Metabolic Disturbance (dehydration, hypochloremic metabolic alkalosis, hypokalemia, hyponatremia, hemoconcentration)
    - Under Nutrition
- Treatment
    - Correct Complications
    - OTC: VitB6, Ginger, Accu-Puncture/Pressure/Stimulation Wrist Bands
    - NGT Decompression
    - Frequent Small Bland Liquid Meals then Distal Enteral Feeding thru J-tube then Parenteral Nutrition
    - Prokinetics & Antiemetics (refer)

Functional Disease

- Epidemiology
    - Prevalence: 10-20% of population (only GERD is more common), 25-50% of out-pt GI visits
    - Seen in young adults but Sx often date back to childhood
    - F>M
    - World-Wide
    - term coined in 1940s
- Functional Diseases (28 Syndromes based on Rome III Criteria, no organic process)
    - Esophagus
        - **Functional Heartburn**
        - **Functional Chest Pain**
        - **Functional Dysphagia**
        - **Globus**
    - Stomach
        - **Functional Dyspepsia** (constellation of vague foregut symptoms (1° nausea) which are divided into "Post-Prandial Distress Syndrome" – PDS (80%, early satiety w/ post-prandial fullness) vs "Epigastric Pain Syndrome" – EPS (20%, epigastric pain/burning)
        - **Belching Disorders (Aerophagia)**
        - **Functional N/V (CVS)**
        - **Rumination Disorder**
    - Intestine
        - **Irritable Bowel Syndrome**
        - **Functional Constipation**
        - **Functional Diarrhea**
        - **Functional Ab Pain**
        - **Functional Bloating** (too much gas or decreased space b/c of muscular abdomen)
            - Types

- Bloating (subject sensation of increased ab pressure W/O increase in ab girth)
- Distension (subject sensation of increased ab pressure W/ increase in ab girth)

- Mechanism
  - Normal Intestinal Gas Volume: 200mL w/ Sx of bloating when >400mL, Normal Anal Passage Gas Volume: 450-1500mL/d w/ passage of 10-20x/d
  - 5 main (N_2, O_2, CO_2, H_2, CH_4) and several trace gases
    - In-put
      - Aerophagia (for every volume of food you swallow you swallow 1.5x times the volume in air!!!)
      - Neutralization of bicarb releases CO_2
      - Bacterial fermentation of sugars releasing H_2, CO_2 and CH_4 (odorless) and protein releasing H_2S and CH_4S (unpleasant odor)
      - Diffusion from blood
    - Out-put
      - Belching/eructation
      - Farting/flatulence
      - Bacterial consumption
      - Diffusion into blood
  - Etiology
    - Constipation (not so much increased gas but stool)
    - Malabsorption (eg. Celiac dz, etc)
    - Dysmotility including Obstruction
    - Pregnancy
    - Ascites
    - Adiposity
    - FODMAP Foods, Gas Producing Fibers
    - Microbiom Dysbiosis or Distinct Infection (eg. Giardia)
    - Alteration in Visceral Sensitivity (normal amount of gas but it causes more pain)
    - Holding onto gas for social reasons (normal amount of gas production but pt is not expelling it so it collects)
    - Muscular Ab Wall (pt is unable to provide compliance with increased food causing pain)
    - Paradoxic Musculature (normally when gas accumulates in the GI tract there should be compensatory diaphragmatic relaxation, costal expansion and contraction of upper ab wall, in pts with bloating there is the opposite effect)
  - Dx
    - check a KUB when there bloating at it's worst to actually confirm that they have gas in their abdomen vs stool
    - breath tests
  - Tx
    - Rule out underlying problem
    - Lifestyle Changes
      - avoid air swallowing (eat slowly, chew and don't swallow food whole, don't chew gum)
      - FODMAP diet
    - Meds
      - Enzyme Replacement: galactosidase (Bean-O, doesn't work), lactase (Phazyme?)
      - Detergent: Simethicon to help release trapped gas
      - Mask Smell: peppermint oil, activated charcoal underwear
      - Laxatives (avoid gas producing fibers and osmotic laxatives)
      - Probiotics (esp *Bifidobacterium infantis* 35624 (VSL#3 includes it)) and antibiotics
      - Visceral Modifying Agents
      - Other: kiwifruit extract, iberogast (STW5)

- Biliary
  - **Sphincter of Oddi Dysfunction**
  - **Functional GB Disorder**
- Anorectal
  - **Functional Fecal Incontinence**
  - **Functional Anorectal Pain (Levator Ani Syndrome and Proctalgia Fugax)**
  - **Functional Defecation Disorders (Dyssynergia)**

Irritable Bowl Syndrome

- Definition: Rome Criteria (recurrent ab pain (usually LLQ, poor localized, waxes/wanes, worse w/ eating, worse w/ emotional stressors) for ≥3d/mo in the last 3mo w/ ≥2 of the following)
    - (1) pain is relieved with defecation
    - (2) pain onset was associated w/ a change in stool frequency (increase or decrease)
    - (3) pain onset was associated w/ a change in stool form (looser or harder)
    - NB other S/S
        - GI: passage of mucus, bloating, distension, dyspepsia, GERD, et al
        - Extra-GI: migraines, backache, insomnia, fatigue, pelvic pain, dyspareunia, FM, et al
    - NB NO organic/alarming/nocturnal S/S (also pts should not be old)
    - NB NO structural/biochemical abnormalities
    - NB usually not steady and progressive
- Classification (NB pts can change from one form to another)
    - Diarrhea Predominant (IBS-D)
    - Constipation Predominant (IBS-C)
    - Mixed (IBS-M) or Alternating (IBS-A)
    - Undefined (IBS-U)
- RFs
    - 10-20% develop after bacterial OR viral gastroenteritis so called "Post Infectious IBS" w/ RFs (female, younger age, long duration of illness, psychosocial stressors) usually IBS-D, early Tx of infection appears to not influence rates of IBS
    - Affluent upbringing
    - Estrogen use
    - Food intolerance
    - Poor quality of life
    - FHx
    - Underlying psych conditions, a childhood which taught that attention is received better w/ reporting an illness than emotional distress, h/o abuse, ineffective coping skills and poor social network
    - Surgery for hysterectomy/abortion/stillbirth, etc
    - h/o narcotic use
- Mechanism (abnormal brain-gut axis physiology)
    - Hypersensitivity: pts are hypersensitive to normal repetitive stimuli in the GI tract like bloating, reflux, etc due to amplification in the limbic system (this explains why stress/anxiety enhances perception of pain while hypnosis/relaxation decreases perception of pain, eg. pts have a lower tolerance for rectal distension w/ a balloon compared to normal pts, pts tends to also have somatic hypersensitivity)
        - NB Gut (5-HT3) → ENS (Ach via Vagus) → CNS (Ant Cingulate Gyrus / Thalamus) NB hence 5-HT3 antagonist, Eg. alosetron (Lotronex) for IBS-D
    - Dysmotility: there are subtle changes in motility (eg. change in high amplitude propagated contractions (HAPCs), gastrocolic reflex, exaggerated motor response to meals, CCK, cholinergics, distension, gas
        - NB CNS → ENS (Ach via Vagus) → Enterochromaffin Cells / Interstitial Cells of Cajal (5-HT4) → Gut (Ach/SP3 = proximal constriction – VIP/NO = distal relaxation) NB you can't just give Ach b/c you need coordinated constriction/relaxation hence 5-HT4 agonists, Eg. tegaserod (Zelnorm) for IBS-C
    - Low Grade Inflammation: there are subtle changes in inflammatory cells in the bowel wall (eg. increased mast cells in muscularis, lymphocytes in myenteric plexus, etc) suggesting that balance b/t commensal enteric bacteria and host immune system is skewed (eg. post-infectious IBS)
        - Post-infectious IBS
            - **Occurs 3-6mo later, diarrhea predominant, 20% of IBS pts, 50% get better at 5yrs, can be after viral/bacterial infection**
            - **RFs: women, longer illness, younger age, use of abx**
    - Abnormal Flora or SIBO
    - Abnormal Gas Propulsion/Expulsion
    - Genetic Predisposition
    - Chronic Stressed State (eg. stress → increased CRF → increased ACTH → increased colonic motility) *** new concept ***
- Complications
    - Ischemic Colitis (unclear)
    - Celiac Dz (unclear)
    - Often pts undergo unnecessary surgeries (ex-lap, chole, appy, TAH) and b/c of this many IBS may eventually develop surgical complications
    - Poor QOL & Increased Health Care Costs
- Dx
    - PEx: no autonomic features, multiple unnecessary surgical scars, "stethoscope sign", "closed eyes sign" where a functional pt winces w/ eyes closed during palpation while an organic pt usually keeps eyes open in tearful anticipation of palpation
    - Always assess Alarm Sx: >50yo, Bleeding, FHx (IBD, GI Cancer), Night Time Sx, Acute Sx, Vomiting, Travel Hx, Fever
    - Always Rule Out: Celiac Dz w/ Serology, Inflammatory Process w/ CRP
        - **Celiac Disease or just Gluten Intolerance or Insensitivity**

        - **Chronic Pancreatitis**
        - **Microscopic Colitis**
        - **Atypical Crohn's**
        - **Lactose Intolerance**
        - **SIBO (try antibiotics) or just Altered Bowel Flora (try probiotics)**
        - **Idiopathic Adult Onset Bile Malabsorption**
        - **Food Allergy**
        - **Mesenteric Ischemia**
- Tx (very high placebo affect therefore hard to study drugs, symptom directed rather than disease modification)
    - Reassurance: I believe your Sx, you are not alone, this is not a psychologic problem (yours Sx are not in your head) but sometimes seeing a psychologists can help with issues like anxiety/stress which can exacerbate IBS
    - Education: this will be a lifelong problem, the focus will be on your Sx as there are no dz modifying agents, our goals should be realistic, avoid ED visits b/c they will often do unnecessary testing, you will not die from this, 10% develop an organic disease at 15yrs, establish relationship w/ PCP
    - 1st General Diet Changes
        - **High Fiber**
        - **Low Fat**
        - **Food Allergy Testing and Avoidance**
        - **Low FODMAP** (these carbs are poorly absorbed (stay in the lumen), osmotically active (keep water in lumen) and fermentable (creating gas, less rapid the longer the chain length) = ab distension = if visceral hypersensitivity then symptoms)
    - 2nd General Medication Trials based on Sx
        - CAM (refer)
        - Pre/Pro/Antibiotics: **1° *Bifidobacterium infantis* 35624 (Aligne) and B*ifidobacterium regularis* DN-173-010 (Activa)**, 2° *Lactobacillus casei (Danactive), Lactobacillus* GG, *Lactobacillus plantarum, Lactobacillus acidophilus,* VSL#3
        - Other (refer)
        - Anti-Diarrheals (refer)
        - Anti-Spasmodics (refer)
        - Proikinetics (refer)
        - Neuro-Modulators (refer) (NB TCAs are especially good for IBS-D b/c of the anticholinergic effects)
        - NO NSAIDs or Opiates (b/c of addiction and impaired motility leading to increased pain)
    - 3rd Behavioral Therapy
        - Psychotherapy
        - Hypnotherapy
        - Cognitive Behavioral Therapy
    - 4th Investigational Medications
        - Carbon-Based Absorbents (AST-120): for IBS-D, theory is that they absorb substances believed to be implicated in the pathogenesis
        - Pain Specialist

Ab Pain

- **General Ab Pain** (description w/ ultimate CONCLUSION: Acute Surgical Ab vs Non)
    - **Onset/Duration**: Acute vs Chronic
    - **Severity:** there are conditions which may mask abdominal pain: steroid use, diabetes, paraplegic, narcotics, etc
    - **Location:** quadrant/midline, radiation
    - **Aggravating-Alleviating Factors**: prandial, type of food, BM, position, stress, meds
    - **Associated Symptoms**: constitutional Sx, other GI Sx, GU Sx
    - **Quality**
        - **Colicky**: any viscera (renal-minutes, intestine-hours, biliary-days) vs Non
        - **Referred:** occurs when two visceral fibers that send nociceptive information from different parts of body converge onto one neuron in the spinal cord resulting in cross-over and the sensation of pain at either or both parts of the body
        - **Visceral** (midline, dull poorly localized cramping/burning/gnawing, secondary autonomic effects (N/V, diaphoresis), pt often moves around, follow unmyelinated C fibers (viscera) along autonomic NS, NT (Substance P and Calcitonin Gene Related Peptide), respond to mechanical (stretch, distension, torsion, forceful contractions BUT NOT cutting, tearing, crushing, etc) and chemical stimuli (any substance that is released during inflammation/ischemia, heat, radiation, etc)
            - Epigastric: UGI (anything supplied by CA: stomach, duodenum, hepotiliary, pancreas)
            - Periumbilical: MGI (anything supplied by SMA: jejunum, ileum, appendix, right colon)
            - Lower Ab: LGI (anything supplied by IMA: left colon, kidneys, ob/gyn)
        - **Somatic** (quadrant, sharp very localized stabbing, no secondary autonomic effects, pt is often very still, follow myelinated A-delta (peritoneum/muscle/skin), severe TTP w/ rebound w/ involuntary guarding aka rigidity, pain when shaking bed or having pt take a deep breath))
            - RUQ: Liver/Gallbladder esp –itis, Duodenum esp PUD, Lung esp PNA, Kidney esp Pyelo
            - LUQ: Spleen esp abscess, Esophagus/Stomach esp PUD, Pancreas esp –itis, Heart, Lung, Kidney

- RLQ: Colon esp Appendicitis, Ob/Gyn esp PID, Testicle esp –itis
- LLQ: Colon esp Diverticulitis, Ob/Gyn, Testicle

- Unusual Causes of Ab Pain
  - **Upper: Pulmonary** (PNA, PE), **Cardiac** (MI, pericarditis)
  - **Lower: Ob/Gyn** (Ectopic Pregnancy, PID w/ Tubulo Ovarian Abscess, Ovarian Torsion, Endometriosis, Ovarian Cancer)
    - NB remember that during pregnancy ab organs are displaced
  - **Other: Renal** (Pyelonephritis, Nephrolithiasis), **Vascular** (Aneurysm, Vasculitis)
  - **Derm/MS**
    - **Ab Wall Pain**
      - Etiology
        - (1) Radicular Pain of T7-12 w/ the most common being the anterior cutaneous nerve which runs along posterior ab wall and then takes a 90 degree turn passing thru a fibrous ring along the lateral border of the rectus abdominus muscle but anywhere on the wall is possible
          - Causes: idiopathic, scar entrapment from surgery, zoster, Spigelian hernias (gaps along rectal sheath allow for hernias), incisional hernias, trauma, hematomas, etc
        - (2) Ab Wall Lesions
          - Causes: strained muscles w/ an area of induration/hematoma, costal conchondritis, etc
      - Dx
        - Sharply localized pain to one finger tip, worse w/ traction on spot and anything that activates the ab wall (sneezing, laughing, walking, standing, etc)
        - "Hover Sign" (the pt will keep his/her hand near site as you do the exam and aggressively guard the area once you palpate near site)
        - "Carnett's Test" (tensing ab wall by flexing chin and partially sitting up exacerbates pain, visceral pain will improve b/c the flexed ab wall will form a barrier b/t hand and viscera)
        - Trigger point injection (27G needle, mix 5cc of 0.5% long acting Marcaine + 4cc 1% short acting Lidocaine + 1cc 40mg/dL Kenalog, 4 quadrant injection using all 10cc at spot, when needle hits spot pain should be elicited, there is small r/o allergy, hematoma, infection)
      - Tx
        - NSAID (Celebrex), Muscle Relaxer (Norflex), Nerve Modulator (Lyrica)
        - Voltaren Patch
        - Trigger Point Injection (above)
          - consider initial numbing agent to make dx and then have pt come back and do steroids for long term Tx
        - pain doctor for more definitive injection treatment w/ alcohol
    - **Shingles**
    - **Radiculitis**
  - **Overlooked Primary GI problems**
    - **Functional**
      - S/S: ab pain not well localized nor related to function, pain is more severe than that seen in IBS and thus is harder to Tx than IBS
      - Rome II Criteria >6mo of (1) continuous ab pain, (2) no relationship of pain w/ physiologic events, (3) loss of daily functioning, (4) no malingering and (5) DOE esp r/o certain disorders which often present as chronic obscure ab pain
    - **Internal Hernias from Adhesions**
    - **Food Allergy**
    - **Chronic Pancreatitis**
    - **Mesenteric Ischemia**
    - **Gallbladder Sludge, Chronic Cholecystitis, etc**
  - **Metabolic**
    - **Addison's Disease**
    - **DKA**
    - **Uremia**
    - **Hypercalcemia**
  - **Heme**
    - **Sickle Cell Crisis**
    - **Acute Porphyria**
  - **Toxin**
    - **Heavy Metal Poisoning (lead, arsenic)**
    - **Narcotic Bowel Syndrome**

        - Chronic ab pain that persists despite escalating opiates and worsens when opiates are tapered
        - Tx: start PEG, TCA/SSRI, Ativan 1mg PO Q6hrs and 1mg PO Q2hrs prn, Clonidine 0.1mg PO Q6hrs and then start opiate taper
- **Genetic**
    - **Fabry's Disease**
        - Rare X-linked deficiency of alpha-galactosidase resulting in sphingolipid deposition in various organs (in GI causes impaired motility with crampy post-prandial abdominal pain w/ diarrhea)
    - **Angioedema**
        - Types
            - (1) Mast Cell Mediated: 2/2 latex/foods, rapid onset (sec-min), short lasting (1-2d), + urticaria/pruritus, Tx: epi, antihistamines, steroids (NB stain Bx samples for Mast Cells)
            - (2) Bradykinin Mediated: 2/2 drugs (ACE-I, aspirin, etc), slow onset (wks-yrs), long lasting (2-4d), - urticaria/pruritus, Tx: C1-inhibtor concentrate, ?FFP, epi
            - (3) Hereditary Angioedema
                - Mech: mutation of C1-inhibitor resulting in increased bradykinin
                    - NB +FHx but 30% are sporadic mutations
                - S/S: recurrent episodes of non-painful/pruritic/erythematous angioedema in extremities, GI tracts (severe ab pain, N/V), oropharnyx (asphyxiation) and mucocutaenous jxns of lips/eyes/genitalia
                    - NB some attacks occur with minor trauma/stress
                    - NB last 1-3d
                    - NB begins during adolescence
                    - NB increased Hz of other autoimmune dz esp glomerulonephritis
                - Dx: check C3/4
                - Px: 17alpha-alkylated androgens like danazol and antifibrinolytics agents like epsilon aminocaproic acid
                - Tx: C1-inhibitor concentrate,?FFP, epi
                    - NB steroids/antihistamines are not helpful
- **Familial Mediterranean Fever (FMF)**
    - Epidemiology: Armenian, Turkish, Jewish (esp Sephardic not Ashkenazic/Mizrachi), Arab, Greek, Italian descent
    - Genetics
        - MEditerranean FeVer (**MEFV**) Gene
            - Locus: 16p13 w/ 10 exons
            - Transcript: 3.7kb, expressed predominantly in the myeloid lineage cells (eg. PMNs, Eosinophils, Macrophages, et al) and synovial fibroblasts (interestingly it is found in adenocarcinoma of the colon/prostate!!!)
        - **Pyrin/Marenostrin** Protein
            - Size: 781 residues
            - Action: deactivates the immune system by regulating transcription of a complex of proteins involved in inflammation called the "inflammasome"
        - FMF Genetics
            - 90% of mutations are located at one of five sites w/in exon 2/10 w/ Met694Val being the most severe
            - carrier rate varies in population studied but is highest at 1/6 in North African Sephardic Jews
            - It was originally believed to follow a purely AR pattern but this is not entirely correct as there are reports of pts w/ clinical FMF w/ only one mutation or no mutations at all and many pts have two mutations but no clinical FMF
    - Pathophysiology
        - the trigger for attacks is unclear but several lines of evidence suggest that the neutrophil is the effector of the inflammatory response at serosal surfaces, a mutated pyrin lowers the activation threshold for neutrophils such that any surrounding inflammatory preturbation triggers an overwhelming cascade of inflammation, the details though are still unclear
    - S/S
        - Syndrome: recurrent paroxysmal episodes of abrupt onset serosal/synovial inflammation lasting hrs to a few days resolving spontaneously accompanied by significant fever
        - General
            - first attack usually occurs during childhood (65% b/f 10yo, 90% b/f 20yo)
            - Pt is normal b/t attacks (a period ranging from weeks to months)

- stereotypic prodrome often exist in 50% of pts (lasting <24hrs, usually described as an "unpleasant sensation")
- some common precipitants: exercise, cold, emotional stress, menstruation

▪ S/S
- Serosal Inflammation
  - **Peritoneum → Peritonitis** (95%, focal to generalized, w/ peritoneal signs and ileus, resembles an "acute surgical abdomen" such that many pts have a h/o multiple exploratory laparotomies and unnecessary appendectomies, multiple episodes can be complicated by adhesions w/ subsequent SBO and infertility)
  - **Pleura → Pleuritis** (50%, generally unilateral w/ a small exudative effusion)
- Synovial Inflammation
  - **Synovium → Arthritis** (75%, mono-oligo-articular, usually in descending order knee→ankle→hip→elbow, can uniquely occur independent of other Sx and be more of a chronic Sx lasting weeks to months, sterile inflammatory effusion, multiple episodes can be complicated by joint damage)
- Other Inflammation (rare)
  - **Erysipelas**
  - **Protracted Febrile Myalgia**
  - **Pericarditis**
  - **Orchitis**
  - **Meningitis**
  - **Myalgia**
  - **Vasculitis**

▪ Complications (cause of most morbidity and mortality)
- **Secondary Amyloidosis (AA)**
  - Overall ~50% of FMF developed AA b/f the use of colchicine which has dramatically reduced the incidence
  - Some unfortunate pts (Type 2 FMF) develop amyloidosis as their presenting Sx
  - Risk varies w/ population (75% North African Jews to 2% Armenia)
  - Pts usually had early onset FMF
  - accumulation of the APR – Serum Associated Amyloid (SAA) – forming insoluble β-pleated sheets in organs (**1° kidney,** 2° spleen, liver, GI) producing progressive organ dysfunction (proteinuria → nephrotic syndrome → ESRD ~2-12yrs)
  - more commonly occurs w/ the Met694Val mutation
  - Dx: (refer)

o Dx
▪ Clinical Algorithm (Sx, Ethnicity, Age, Consanguinity)
▪ Genetic Testing (targeted mutation analysis: Glu148Gln, Met694Val, Met694Ile, Val726Ala, Met680Ile, Glu148Gln vs full sequence analysis of exon 2 and 10 which hold most of the known mutations)
▪ Labs (elevated APRs, neutrophil predominant leukocytosis)
▪ Response to Colchicine

o Tx:
▪ Two Goals: (1) prevention of acute attacks and (2) prevention of complications
▪ Several treatments had been investigated including antimicrobials, glucorcorticoids, salicylates, anthistamines either prophylactically or during attacks but with little effect → landmark studies in the 1970s demonstrated the effectives of **colchicine** in prevention of attacks and development of amyloidosis
- Mechanism: suppresses neutrophil recruitment and activation at sites of serosal inflammation (interferes w/ intracellular proteins involved in chemotaxis and phagocytosis hence its use in gout)
- begin at 1.2mg PO BID (TID-QID dosing for non-responsive pts or those w/ proteinuria)
- if pt demonstrates freedom of attacks dose can be reduced to QD but will always be lifelong
- if pt is experiencing a prodrome then take an additional tablet to abort or attenuate attack (if full blown attack then Tx w/ NSAIDs)
- SEs: nausea/diarrhea, BM suppression, neuropathy/myopathy, male gonadal toxicity, TEN (at these doses SEs are uncommon and if occur can be managed by decreasing dose)

- Class C Drug but some studies report its safety in pregnancy
- Follow-Up: yearly assessment of inflammation w/ APRs, kidney function w/ BMP and UA, amyloidosis w/ SAA levels, genetic testing of all first degree relatives
- How do you approach FMF pts unresponsive to colchicine?
  - determine compliance and investigate for evidence of secondary gain
  - confirm the accuracy of dx (other rare hereditary autoinflammatory disorders that do not respond to colchicine exist eg PFAPA Syndrome, PAPA Syndrome, HyperImmunoglobulinemia D and periodic fever Syndrome (HIDS),TNF Associated Periodic Syndrome, ELA2- Related Neutropenia, Blau Syndrome)
  - if true non-responder then consider other strategies: IV colchicine, interferon-alpha, infliximab, anakinra

Women & Pregnancy

Non-Pregnant
- Functional Dz
- Autoimmune Dz
- Structural Differences (shorted esophagus, presence of reproductive system, low hanging transverse colon)
- Constipation
- Fecal Incontinence
- Chronic Pelvic Pain Disorder: non cyclic pelvic pain for >6mo 2/2 IBS, interstitial cystitis, endometriosis (serosal surface, 1° rectum, pain correlates w/ depth of invasion, estrogen dependent, can cause various other Sx)

Endoscopy in Pregnancy
- Perform during 2nd trimester if possible
- Position pt in left lateral decubitus or left pelvic tilt to avoid compression on IVC/Aorta
- Consider fetal heart monitoring
- No grounding pad w/ uterus in between
- Sedation
  - Class-B: propofol, meperidine
  - Class-C: fentanyl
  - Class-D (risk): benzos

Pregnant
- **1st/2nd Trimester = 1-12wks/13-26wks (usually non-liver stuff EXCEPT <u>acute viral hepatitis, gallstones and HG</u> & less serious compared to problems later in pregnancy)**
  - **Acute Viral Hepatitis**
  - **Cholelithiasis**
  - **Hyperemesis Gravidarum**
    - RFs: younger women, first pregnancy, social stressors esp when the pregnancy is unwanted, multiple gestation, underlying psych hx, migraine headaches, motion sickness, mother w/ HG
    - Mechanism: unclear w/ several theories including hormone changes (likely higher beta-hCG), abnormal gastric motility, specific vitamin deficiencies
    - S/S: most (~100% of pregnancies) women have N/V occurring b/t 5-20wks gestation w/ peak at 10th week but when it becomes intractable leading to electrolyte/hydration disturbances, ketonuria, weight loss and exclusion of other causes then it is called HG (2% of pregnancies) = decreased BW in baby w/ no harm to mother
    - Labs
      - Vomiting Type Labs BUT ALSO
      - Increased Ca 2/2 hyperPTH
      - Increased AT (AST>ALT, <200)
      - Increased AP (<2xULN)
      - Increased TB (<4)
    - Tx
      - 1st: General
        - Supportive care w/ small frequent dry starchy and high protein foods (eg. crackers) and cold/clear/carbonated liquids (eg. Ginger Ale) to IVF
        - Ginger (250mg PO Q6hrs)
        - VitB6 (25mg PO Q8hrs)
      - 2nd: Ant-Histamine
        - 1° doxylamine-Unisom (25mg PO Q8hrs) NB Diclectin (VitB6 and Doxylamine)
        - 2° dimenhydrinate-Dramamine (100mg PO Q4hrs), diphenhydramine-Benadryl (50mg PO Q8hrs), meclizine-Antivert (25mg PO Q4hrs)
      - 3rd: Anti-Emetics

        - Class-B: ondansetron, metoclopramide
        - Class-C: promethazine, prochlorperazine, domperidone
    - 4th: Steroids
        - methylprednisolone-Solumedrol (16g IV/PO Q6hrs x3d then taper over 2wks) NB use before 10wks of gestation is associated w/ 4x increased r/o cleft lip
- **GERD**
    - 30-80% of pregnancies, worse the later the gestational age but stops just after delivery, reduced LES mediated by progesterone, increased ab pressure from enlarged uterus, ineffective gastric motility, etc
    - Tx: avoid Mg containing AA and sodium bicarbonate b/c induces contractions, H2B and PPIs are safe Class-B EXCEPT OMEPRAZOLE which is a class-C agent but in general avoid meds if possible
- **PUD** (PUD actually improves during pregnancy b/c of the cytoprotective effects of progresterone)
- **IBD** (refer)
- **Constipation** (all laxatives are fine except Mg based and Castor Oil b/c induces contractions, PEG seems to be laxative of choice)
- **Appendicitis** (increased risk, difficult to Dx clinically b/c the uterus displaces the appendix to different positions)
- **Diarrhea**
    - always rule out infection b/c can be more serious than in non-pregnant women
    - dehydration can cause decreased placental blood flow
    - common bacteria (Campylobacter, Shigella, Listeria, Malaria, Amebiasis, Giardia)
        - Campylobacter and Listeria are the worst b/c can cause spontaneous abortion, premature labor, neonatal sepsis, death
    - Only use pregnancy approved abx (ampicillin and erythromycin)

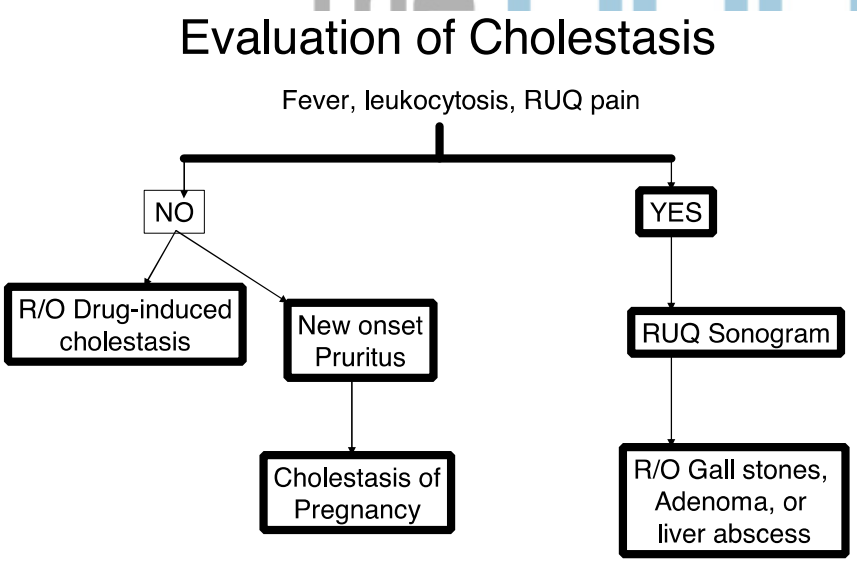
- **2nd/3rd Trimester = 27-39wks (usually liver stuff & more serious compared to problems early in pregnancy, remember that pregnancy could be a red herring such that a non-pregnant cause for liver injury could be present (intrahepatic cholestasis is the most common UNIQUE liver disorder of pregnancy BUT viral hepatitis is the most common OVERALL liver disorder in pregnancy) the other non-specific causes of liver injury can occur during any trimester of pregnancy)**
    - **Intrahepatic Cholestasis of Pregnancy (ICP)**
        - RFs: winter, Chilean-25% and Scandanavian-3% descent (very uncommon in US), +FHx, prior personal Hx
        - Mech: AD mutation of bile salt transporters (MDR3, SXR, etc) on hepatocyte which become saturated with high estrogen levels → intrahepatic cholestasis → increased serum bile acid
        - S/S
            - Mother
                - nocturnal pruritus of palms/soles
                - increased r/o gallstones
                - steatorrhea from bile salt depletion
            - Baby (% if untreated)
                - 50% premature w/ low BW
                - 40% VitK deficiency results in hemorrhage during delivery!!!
                - 10% die
        - Labs
            - Increased AP BUT GGT is normal or only mildly elevated (unlike other cholestatic conditions)
            - Increased AT (<1000)
            - Increased TB (<5)
        - Dx
            - elevated serum Total Bile Acid (TBA) (usually 100x ULN w/ nl 0-10mmol/L) and liver Bx (cholestatic changes but rarely needed)
        - Tx
            - 1° URSO, 2° bile-acid resin binders
            - temporary steroids for acute Sx
            - main Tx is delivery (esp if TBA >40) w/ Sx improving w/in 24hrs but abnl LFTs will persist for months but if Sx do not improve after delivery then consider a secondary Dx
            - give VitK before delivery
            - recurrence during pregnancy (60%) and if pt goes on estrogen OCP use therefore counsel pts
    - **Pre-Eclampsia & Eclampsia**
        - RFs: CKD, chronic HTN w/ 1/3 developing pre-eclampsia, paternal FHx, multiple gestation, nulliparity, advanced maternal age, DM, black, prior personal Hx
        - Mechanism: unknown
        - S/S
            - Heart: HTN (normally BP falls mid 2nd trimester and then rises back to nl afterwards)
            - Kidney: AKI w/ proteinuria
            - Neuro: HA w/ blurred vision → hyperactive DTRs → seizures → coma (if present then called eclampsia, can occur before/during/after labor)
            - Heme: DIC
            - Liver: ranges from mildly abnl LFTs to liver failure
                - Complications

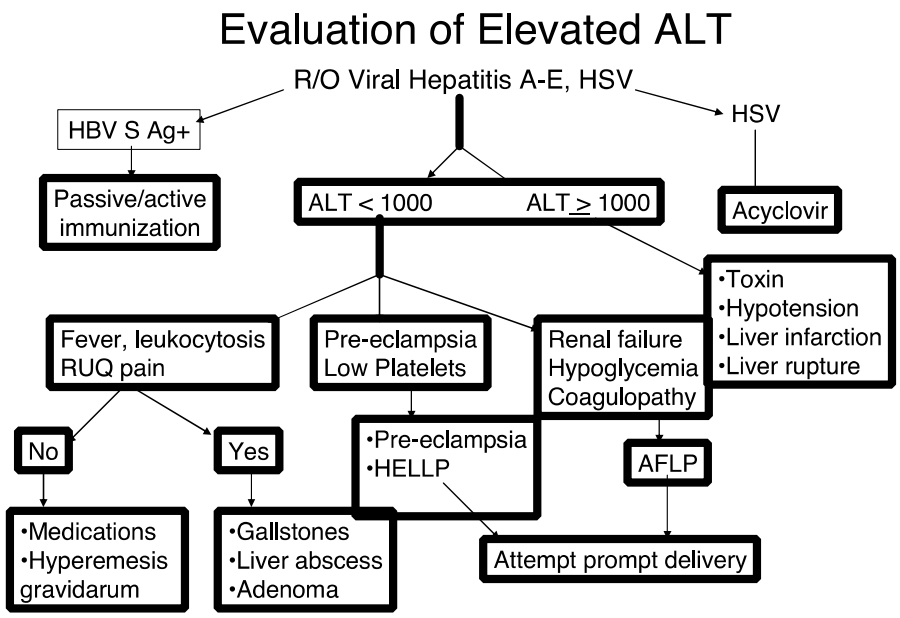
        - HELLP = Hemolytic anemia, Elevated LFTs, Low Platelets
            - can be seen in pregnancies even w/o pre-eclampsia or be the first presenting Sx
            - 75% pre-partum vs 25% post-partum
            - can worsen first 48hrs after delivery
            - similar LFTs as just pre-eclampsia
            - more ab pain, N/V, sudden weight gain
        - Hepatic Infarction or Rupture w/ Subcapsular Hematoma
            - Sudden ab pain, spiking fevers, worsening anemia, shock if rupture
            - Significant worsening in LFTs w/ AT ~5000
            - Up to 75% mortality for both mother and baby
    - Labs
        - Increased AT (<500)
        - Increased TB (<3)
    - Tx
        - If term then immediately induce labor b/c delivery is the definitive Tx but if preterm then…
            - Bedrest
            - Steroids to promote lung maturity if <34wks
            - Antihypertensives
            - MgSO4 for seizure prophylaxis
            - Correct coagulopathy
            - Watch for hepatic complications
        - Recurrence during next pregnancy (15%)
- **Acute Fatty Liver of Pregnancy (AFLP)**
    - RFs: prior personal Hx (20%), very rare in US
    - Mech: fetus (parents are heterozygous) has AR mutation for mitochondrial long chain hydroxyacyl-CoA dehydrogenase (LCHAD) or carnitine palmyitoyltransferase resulting in accumulation of long FA in fetus and during 3rd trimester spill over into mother's circulation causing microvesicular fatty liver disease
    - S/S
        - Can manifest 3rd-trimester all the way to post-partum
        - Can be associated w/ pre-eclampsia
        - N/V, ab pain, anorexia
        - Overall variable Sx but at extreme can result in fulminant liver failure w/ MOF
        - DIC w/ intrahepatic hemorrhage and hepatic rupture
        - nephrogenic DI is uniquely common
        - used to be very high fetal mortality now much better early recognition
    - Labs
        - Increased AT (<1000, AST>ALT)
        - Increased TB (<10)
        - Leukocytosis
        - Hypoglycemia
        - AKI
        - Coagulopathy
    - Dx
        - clinical but liver Bx if needed (microvesicular fatty infiltration w/ some inflammation) to differentiate from pre-eclampsia
        - genetic testing on mother
    - Tx
        - delivery of baby w/ recover typically afterwards however some women still need transplant after delivery
        - if baby survives then must be on a frequent diet low in fat but rich in medium chain FAs to prevent hypoglycemia/hypotonia/encephalopathy, etc
        - recurrence during next pregnancy 75%
- **Infection**
    - **HAV, HEV** (high r/o fulminate liver failure if pregnant therefore pts should avoid traveling to endemic areas), **HBV, HCV** (no ribavirin), **HSV**
    - **Schistosomiasis** (progesterone promotes aggressive abscess formation)
- **Cholelithiasis**
    - Increased risk compared to general population 2/2 increased GB cholesterol secretion, female gender, increased fasting GB volume, reduced GB emptying
    - Develop during 2nd-3rd trimester of pregnancy but only 1% become symptomatic
- **Vascular**
    - **Budd Chiari Syndrome** (very important)
    - **Splenic Artery Aneurysm**

- LFTs should remain normal during pregnancy except

Increased	Decreased
▪ AP (<2-4x ULN) in 3rd trimester (not pre-partum, 1st or 2nd trimester) and post-partum b/c it is made by the placenta ▪ Alpha Fetoprotein ▪ A1AT ▪ Ceruloplasmin ▪ Coagulation Factors ▪ Cholesterol	▪ Albumin b/c of hemodilution ▪ Ferritin ▪ Globulin ▪ GGT

  - NB abnormal AT, GGT, PT, TB is NEVER normal and should be investigated
- False Stigmata of Chronic Liver Disease (pregnant women does not actually have chronic liver dz)
  - **Spiders and Palmar Erythema** 2/2 high estrogen state
  - **Small Uncomplicated Upper Esophageal Varices** 2/2 increased blood flow thru azygous system 2/2 increased plasma volume
- Female pt's with underlying chronic liver dz
  - Most pts are actually infertile therefore uncommon
  - If they do get pregnant there is an increased r/o maternal complications and prematurity w/ still birth AND some liver complications may worsen esp AIH (flares can occur post-partum due to the quick loss of the immunotolerant state during pregnancy therefore continue steroids/azathioprine esp during delivery), PBC (continue URSO), Hepatic Masses (Adenomas and Hemangiomas therefore monitor w/ US) therefore counsel pts
  - b/c pregnant women naturally develop small varices if a women w/ portal HTN from cirrhosis gets pregnant then the r/o of developing significant varices is much higher w/ a 25% r/o bleeding during 2nd/3rd trimester and during labor therefore some recommend screening EGD during early 2nd trimester w/ prophylactic banding and remember to NEVER use vasopressin during Tx of acute variceal bleed b/c can cause uterine contractions





Vascular Dz

- General
  - Vasculature
    - Source
      - Celiac: esophagus/stomach/duodenum/pancreas/liver
      - SMA: SI, ascending/transverse colon
      - IMA: descending colon and sigmoid
      - Internal Iliac Branch: rectum
    - NB there is actually little anastomosis (only Arc of Riolan, Marginal Artery of Drummond, Central Anastomic Artery) between SMA/IMA and IMA/Iliac hence watershed areas of injury at splenic flexure (point of Griffith) and sigmoid (point of Sudeck)
    - NB the esophagus/stomach/duodenum/rectum rarely become ischemic as they are supplied by multiple blood vessels with rich collaterals
- Categories
  - **Ischemic Colitis** (most common)
    - Pattern: can range from transient asymptomatic reversible colopathy w/ submucosal hemorrhage/edema (50% of cases) → colitis w/ classic linear longitudinal ulcers (50% of cases) → chronic colitis w/ strictures/ulcers/abscesses/psuedopolyps OR fulminant colitis (very rare)
      - NB often confused w/ IBD
    - Etiology **(usually low perfusion not vessel occlusion but it can occur)**
      - Why is the colon more susceptible to low perfusion and not the intestine? low blood flow and decrease in blood flow during periods of functional activity
      - **Idiopathic** (most common, unlike in mesenteric ischemia where a cause is almost always found)
      - **Systemic Hypoperfusion**
        - Shock (triggers splanchnic constriction and pts are often given vasopressors which also clamp down on the gut)
        - Marathon Runners
        - Aortic/Colonic Surgical Complications
        - s/p Colonoscopy & Barium Enema
        - Meds that Decrease Splanchnic Perfusion
          - 5-HT1 Agonists (triptans) vs 5-HT3 Antagonists (alosetron-Lotronex)
          - Laxatives (sorbitol, MgCitrate and NaPO4, bisacodyl, glycerin enemas)
          - Sympathomimetics (cocaine and pseudoephedrine)
          - NSAIDs (decrease in vasodilating PG and increase in vasoconstrictive LT)
          - Chemo (alkaloids, taxanes)
          - Other (anticholinergics, furosemide, estrogens, digoxin, kayexalate)
      - **Obstructing Colon Lesion**
        - Classic Pt: elderly women w/ COPD and IBS who has an partially obstructing lesion (chronic constipation +/- fecal impaction, cancer, diverticulitis, volvulus, stricture, Hirchsprung's)

        - Mechanism: obstruction → increased intracolonic pressure → decreased blood flow → ischemic segment that is proximal to AND separated from precipitating lesion
    - S/S **(not very acute/sick)**
        - R sided: sudden cramping mild-moderate LLQ pain
        - L sided: bloody diarrhea, urgency
    - Dx
        - TOC Colonoscopy (submucosal hemorrhagic/edematous nodules which is equivalent BE thumbprints, be careful to avoid perforation, occasionally you will see a "colon single strip sign" which is a single lie of erythema w/ erosionis/ulceration along the longitudinal axis, rectum is spared and watershed areas most affected as explained above)
        - Bx (iron laden macrophages and submucosal fibrosis, remember that many biopsies for inflammation come back as mild ischemia)
        - Imaging (thumbprinting representing submucosal hemorrhage/edema resolves w/in a few days or turns into colitis
        - NB usually do not do an angiogram (b/c by the time of presentation colon blood flow has already returned to normal in most cases) unless there are continued alarms symptoms: very severe pain, peritoneal signs, Sx for >2wks, isolated right sided dz b/c it may be due to SMA dz, recurrent sepsis/dz
    - Tx
        - If not alarm Sx then just observe, treat underlying cause, give abx/IVF and rest bowel as CI usually resolves on its own w/in 2-3d (Sx) and wks-mos (colonoscopy findings), if distended colon consider rectal tube
        - f/u colonoscopy 4-8wks after to r/o stricture which occur 20% of pts but if they occur they usually resolve in 12-24mos w/o Tx
        - 20/40% mortality / need for surgery if right sided CI vs 5/10% if non-right sided dz
- **Mesenteric Ischemia** (less common)
    - Pattern: double hit w/ first hit being the embolus/thrombus followed by mesenteric vasoconstriction aka **Non Occlusive Mesenteric Ischemia (NOMI)** that can persist after the SMAE/SMAT/SMVT has been corrected and can be reversed w/ papaverine but remember that NOMI can also occur after a non-GI CV event (MI, shock, dialysis), Dx w/ angiography which diffuse narrowing/irregularity of branches
    - Etiology **(usually vessel occlusion not low perfusion)**
        - **SMA Embolism – SMAE** (50%, embolus usually from LA/V lodges at points of narrowing usually distal to origin of branches, always acute)
        - **NOMI** (30%)
        - **SMA Thrombosis – SMAT** (10%, atherosclerotic dz 1-2cm distal from origin of SMA, can be acute w/ no collaterals and/or chronic w/ collaterals, and if chronic plaque and pt has acute pain then doubt whether it is the cause)
        - **SMV Thrombosis – SMVT** (10%, any hypercoagulable state, any portal HTN state, any adjacent inflammation, pregnancy, blunt abdominal trauma, post op, splenomegaly/splenectomy, sepsis, etc infarction is rare, can be acute or chronic, location depends on cause, if chronic then just like portal HTN Sx, if acute then presents like AMI)
        - **Focal Segmental Ischemia – FSI** (rare, non-life threatening short segment ischemia b/c of adequate collaterals, 2/2 emboli, vasculitis, bliunt trauma, radiation therapy, can present as acute enteritis or chronic stricturing enteritis complicated by obstruction and SIBO, Tx is just resection of the segment)
    - Acute (completely occlusive process)
        - NB Presentation, management, outcome, etc is highly variable depending on cause, acuity/duration (acute vs chronic), type of vessel involved (arterial vs venous), location/degree of injury (diffuse vs focal), presence of collateral blood flow, etc
        - S/S **(very acute/sick w/ high mortality of 50%, much higher if infarction has already occurred)**
            - Pts are severely ill w/ sudden onset severe ab pain that is out of proportion to PEx (SMV is less striking, NOMI is overshadowed by the underlying systemic condition that caused it and often ab pain is absent)
            - Bleeding uncommon but if present then signifies infarction or right colon involvement
            - AMS in the elderly
            - most important predictor of survival is whether infarction has occurred (pre-infarction 20% survival vs post-infarction 70% survival)
        - Dx
            - TOC Imaging: Standard CT to rule out other causes of pain then CTA/V or MRA/V then Selective Mesenteric Angiography
                - CT Findings: early ischemia looks normal therefore cannot rule out MI occasionally you will see distension, wall thickening, abnl wall enhancement, fluid, lack of enhancement of arteries w/ timed IV contrast, arterial emboli and venous thrombosis while later on you will see pneumatosis, mesenteric venous & portal gas
                - KUB: normal early on then ileus, thumbprinting, air-fluid levels later on and then pneumatosis and vascular gas much later on

        - Duplex US: not perfect b/c (1) only the proximal portions of vessels can be studied, (2) occlusions can be seen in asymptomatic pts, (3) blood thru SMA is variable, (4) NOMI cannot be diagnosed
    - Labs: leukocytosis, AGMA, high PO4, D-lactate, amylase, AlkPhos, hyperK, hyperPO4, LDH
    - Laparoscopy: can be falsely normal as blood is shunted to serosa making it appear normal and when air is insufflated into ab cavity SMA pressure is compromised therefore don't do for diagnostic purposes
- Tx
    - General hemodynamic resuscitation w/ IVF but NOT vasopressors
    - Bowel Rest
    - BS Abx (amp/gent/MNZ) b/c the bacteria in the gut are at high r/o leaking into peritoneum and/or blood stream
    - Serial PEx to r/o perforation
    - NGT/Rectal Tube decompression
    - Correct underlying problem
    - If vasospasm then papAvarine (phosphodiesterase inhibitor that results in splanchnic vasodilator) infused directly into SMA via angiography catheter into SMA placed by IR, 30-60mg/hr (1mg/mL), run it before surgery, during surgery, and after surgery until pt clinically resolved and angiography normal
    - Consider IA Thrombolytics (must be done w/in 12hrs)
    - Consider Vascular Surgery (embolectomy, thrombectomy, vessel reconstruction, angioplasty, bowel resection, etc)
        - If small amount of bowel affected then resection w/ anastomosis but if extensive with questionable areas of viability then resect clearly necrotic regions only and perform a 2nd look 12-24hrs later
    - There is evidence that blocking the RAA System with ACE-I protects bowel from ischemia
    - Anticoagulants (very controversial, consider in MVT)

- Chronic (partially occlusive process, usually 2/2 SMAT)
    - S/S of "Intestinal Angina"
        - as food enters stomach blood is shunted to the stomach away from SI resulting in ischemia and post-prandial ab pain beginning 30min after eating and subsiding slowly after 1-3hrs, sometimes the thought of food can cause pain, b/c this pain is associated w/ eating pts often get "sitophobia" and over time as they avoid eating they begin to lose weight loss, as the dz gets worse the pain becomes constant
    - Dx
        - Purely a clinical Dx b/c most imaging below is unreliable and the only good test is GI tonometry which is rarely available
        - CTA/MRA and if abnormal then Mesenteric Angiography may show limitation in flow but not diagnostic b/c many people have limitations in flow w/o Sx
        - Plain films or BE may show calcification but otherwise normal
        - Endoscopy w/ Bx is not helpful
        - NB Doppler US is a bad test b/c it looks at the proximal 1cm of vessels
        - NB rarely you will see antral ulcers, gastroparesis, acalculous cholecystitis
    - Tx
        - Angioplasty vs Surgical Revascularization

- Other
    - **Celiac Axis Compression Syndrome, Median Arcuate Ligament Syndrome, Dunbar Syndrome**
        - Epidemiology: young thin females
        - Mech: originally believed that pain was 2/2 chronic mesenteric ischemia from the MAL (unites diaphragmatic crura passing over aorta) compressing the celiac trunk however the SMA provides ample collateral blood flow therefore the new theory is that pain is 2/2 compression of the celiac ganglion itself nonetheless very controversial b/c a lot people have compression on arteriography but don't have Sx and release of the compression does not always alleviate Sx
        - S/S: triad of ab pain, weight loss and bruit
        - Dx: often a DOE, pts often have an extensive work-up and surgeries, Duplex US and angiography can reveal changes in dynamic blood flow
        - Tx: (only effective in select pts) w/ division of the MAL, gangliectomy, arterial reconstruction

Food Allergy & Eosinophilic Disorders

- Classification
    - Food Aversion
        - Presence of Toxin (eg. histamine in scombroid fish poisoning)
        - No Presence of Toxin

- Food Intolerance
  - Enzyme Deficiency (eg. lactose Intolerance)
  - Pharmacologic (eg. tyramine in aged cheeses)
- Food Allergy

Food Allergy

- Epidemiology
  - 5% of infants (milk, egg white, peanut) vs 2% of adults (shellfish, tree nuts, peanuts)
  - Increased prevalence b/c of hygiene hypothesis
  - RFs: other atopic diseases
- Mechanism
  - Most proteins are broken down into non-immunogenic peptides/aa but some immunogenic proteins pass thru the intestinal epithelium and these proteins can elicit different hypersensitivity reactions
- Types (NB can be allergic even if cooked, usually pts are allergic to just one food, most children outgrow allergies except peanuts, tree nuts, fish, shellfish)
  - **Cow Milk (5% of infants)**
  - **Egg White (NB don't give flu vaccine)**
  - **Fish**
  - **Shellfish**
  - **Tree Nuts**
  - **Peanuts**
  - **Wheat**
  - **Soy**
  - **Seeds**
  - **Banana**
- S/S
  - Type I Immediate Hypersensitivity Reaction (IgE Mediated)
    - Oral Allergy Syndrome (pruritus/angioedema of lips/mouth/pharynx, usually seen in fruit/vegetable allergies)
    - GI Anaphylaxis (ab pain/cramping, N/V, D along w/ skin/pulm Sx)
  - Type IV Delayed Hypersensitivity Reaction (T-Cell Mediated)
    - Celiac Disease (refer)
    - Dietary Protein Induced Eosinophilic Proctocolitis, Enterocolitis Syndrome, Enteropathy (seen in infants)
  - Very Mixed Process
    - Allergic Eosinophilic Esophagitis/Gastritis/Enteritis/Colitis (refer)
- Dx
  - Double Blind Placebo Controlled Oral Food Challenge (DBPCOFC)
  - IgG to certain foods?
  - Skin Prick Test (SPT) / Atopic Patch Test (APT) / RadioAllergoSorbent Test (RAST) if you suspect IgE Mediated Reaction
  - Elimination & Challenge Diets if you suspect non-IgE Mediated Reaction
- Tx
  - Avoidance
  - NB allergy shots do NOT work but new Tx are being developed including SL immunotheraphy, Xolair (anti-IgE), genetically engineered plants
  - NB antihistamines and steroids are not that effective

Eosinophilic Disorders

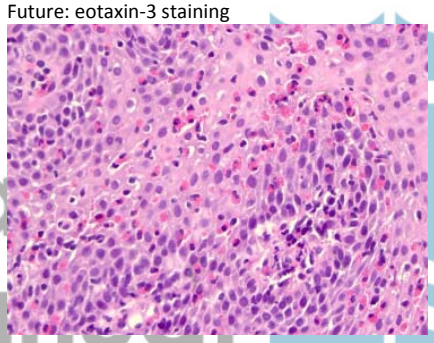
- Mechanism
  - During gestational development eosinophils are directed from the BM into the GI tract and other hematopoetic organs (LNs, Thymus, Spleen, NB only a small percentage reside in the blood) mediated by IL-5 and eotaxin-1
    - NB it is proposed that there role in the GI tract is to prevent parasitic infections and regulate tissue growth
    - NB in the GI tract they are normally concentrated in the lamina propria of the stomach, SI, colon
    - NB other parts of the GI tract (i.e. esophagus) and locations in the GI wall (i.e. muscularis) are normally devoid of eosinophils
  - Genetically predisposed pt (supported by the fact that familial clustering occurs in 10% of pts) exposed to an environmental antigen (in most cases the exposure is not in the GI tract aka food allergen but respiratory tract aka respiratory allergen, generally not one Ag but many suggesting a breakdown in Ag tolerance) → release of eotaxin-3, IL-5 and IL-13 which traffic additional eosinophils to different parts of the GI tract → release of preformed toxic granules (containing a cocktail of major basic protein (MBP), eosinophilic cationic protein (ECP), eosinophilic derived neurotoxin (EDN), eosinophilic peroxidase (EPO)) along with cytokines, neuromediators, etc which propagate the immune response → inflammation
    - NB recognition of these mediators is important clinically as they can be diagnostic markers and therapeutic targets
    - Early disease (children) is found to be associated w/ specific SNPs in the eotaxin-3 gene
    - Eosinophil recruitment can occur in ANY condition that damages the squamous epithelium
- Classification

- Secondary
  - Hypereosinophilic Syndrome
  - Myeloproliferative Disorder (CML, PV, ET)
  - Helminth Parasites (Strongyloides)
  - Meds (Gold, Azathioprine, Gemfibrozil, Enalapril, Carbamazepine, Clofazaminine)
  - CTDs (Scleroderma, DM/PM, Churg-Struass Vasculitis)
  - GI **(GERD, Leiomyomatosis, Recurrent Vomiting, IBD, Celiac Sprue, HP)**
- Primary aka Eosinophilic GI Disease (EGID) EGIDs ranging from IgE predominant diseases to non-IgE mediated diseases
  - Atopic
  - Non-Atopic
  - Familial (10% of cases)

- Eosinophilic Gastroenterocolitis
  - Usually lumped together even though dz location and wall involvement is variable resulting in variable Sx (dysmotility, malabsorption, exudative ascites, loss of protein) and endoscopic findings (inflammation, ulceration)
  - Remember, unlike in the esophagus, there are baseline eosinophils in the stomach, SI, colon making dx much more challenging (typically >20 HPF)
  - Rare in comparison to EoE, if present EoE is also present
  - Colon dz is uniquely seen in infants p/w bloody diarrhea and is 2/2 food proteins cow's milk and soy protein
  - Tx: prednisone 20-40mg/d induction w/ 5-10mg/d maintenance
- Eosinophilic Esophagitis (EoE)
  - Epidemiology
    - first adult case was reported in by Dobbins JW, et al. in 1977 in Gastroenterology, there were likely earlier cases that were falsely attributed to GERD
    - incidence is rising ("mini-epidemic") and not simply b/c of increasing recognition
    - very common in pediatric population but becoming a more common finding in the adult population
    - 3:1 M, mean age 38yo w/ range 14-89yo, no clear ethnic predilection but of note there are no cases in Africa reported in the literature but recent evidence reports increasing incidence in elderly African Americans who p/w atypical reflux
    - familial clustering has been reported in the literature and it has been observed that 10% of pts have an affected first degree family member
    - seasonal exacerbations (1° spring) correlating theory that respiratory allergens are the cause
  - New Concepts
    - EoE represents a disease spectrum from active inflammation (child) to scarring (adult) resulting in variable Sx
    - The interaction b/t GERD and EoE is complicated in that it is unclear whether GERD just looks like EoE or is the tipping point for the development of EoE (acid/pepsin from GERD damages the tight junctions b/t epithelial cells resulting in increased permeability to allergens which otherwise would not pass, therefore Tx of GERD might make EoE quiescent and might be the only Tx needed) or EoE only causes GERD (eosinophils products reduce LES pressure and dysmotility deceases reflux clearance)
  - S/S
    - Generally vary w/ age: infant (feeding difficulty/FTT), young child (vomiting), old child (ab pain), adult (below)
    - dysphagia w/ or w/o a morphologic abnormality in that a stricture is not always present, in fact in most cases it is likely 2/2 impaired smooth muscle function 2/2 inflammation affecting the muscular layers
      - should always be excluded in adults
      - 50% of pts report a h/o food impaction
    - GERD-like Sx that is poorly responsive to GERD meds and/or there is a lack of objective evidence of reflux on pH studies
    - even though an "esophagitis" odynophagia is not a common complaint
    - associated w/ other EGID resulting in a different Sx complex
    - h/o atopy dz w/ AR, asthma, food allergy, eczema
  - Complications
    - Anatomic Deformation: strictures, rings, narrowing, etc
    - Food impaction
    - Instrumental, emesis induced and sporadic esophageal mucosal laceration to transmural perforation has been reported in the literature
    - Metaplasia/dysplasia has not been observed but long-term studies are lacking
  - Dx
    - Clinical Picture
    - Esophagram (usually the first test as dysphagia is the predominant Sx)
      - Normal (50%)
      - abnormal in advanced cases where stricture develops
    - Endoscopy
      - Normal (30%)
      - Proximal/Middle/Distal Strictures
      - Multiple Circular Rings aka "Trachea/Feline-like"
      - Vertical Linear Furrowing and Corrugation

- Luminal Narrowing
- Edema/Friability
- “Crêpe Paper” Mucosa (loss of mucosal elasticity and shearing after passage of endoscope)
- Multiple whitish granular exudates (often confused for Candida, represents eosinophilic abscesses)
- NB one should get six biopsies along the length of the esophagus including both normal and abnormal appearing mucosa, in addition gastric/duodenal biopsies are recommended to r/o concurrent EoG/E

▪ Pathology
- Eosinophils
  - ≥15eos/hpf (400x) in the squamous epithelium in at least one specimen despite acid suppression w/ a PPI x2mo or normal pH study which is critical b/c eosinophils can be seen w/ GERD (the cutoff of eosinophil number b/t EoE/GERD is unclear as one can see dense eosinophils in unTx GERD but generally <7 is GERD and >20 is EoE)
    - NB unlike in GERD, histologic changes in EoE affect the entire length of the esophagus and is often patchy
    - NB density of eosinophils does not correlate w/ Sx
- Other Specific Findings
  - eosinophilic microabscesses
  - surface layering of eosinophils w/ sloughing of necrotic squamous cells
  - extracellular deposition of eosinophilic granules
- Other Non-Specific Findings (seen in all types of inflammation)
  - basal cell hyperplasia
  - lamina propria papillae lengthening
  - lamina propria fibrosis
- Future: eotaxin-3 staining



▪ Other
- Peripheral Eosinophilia (more common/pronounced in children than adults w/ levels usually normal in adults thus not a good surrogate marker for activity)
- Elevated IgE (similar to peripheral eosinophilia)
- SPT/APT/RAST (may be helpful)
- Future: eotaxin-3 levels

o Tx

▪ General
- very few controlled studies evaluating and defining optimal treatment
- most literature reported is clinical experience or case series
- f/u & frequency of clinical/endoscopic follow-up is unclear
- current approach is to divide EoE into inflammatory disease (children) = Tx: 1° steroids + PPI then allergen avoidance 2° immunomodulators vs fibrotic disease (adults) = Tx: 1° dilation + PPI 2° allergen avoidance or steroids
- if Sx return while pt is on steroids then consider infection (Candida/HSV)
- A big issue is what is the endpoint: Sx relief vs endoscopic resolution vs histologic improvement, need for r/u endoscopy, need more maintenance Tx vs repetitive/pulse Tx (dose/duration/frequency is unknown)
- Problem: most studies are short term, none address maintenance vs repetitive/pulse Tx, endpoints are unclear

▪ PPI
- as noted earlier a 2mo course should be done prior to Bx to make a proper dx
- it may be useful to prevent further damage from physiologic GER on top of inflamed esophagus from EE
- it is important to know that GERD can coexist w/ EoE suggested if pts have a good response to just PPI
- questionable whether considered a cotherapy vs primary Tx
- new studies suggest that omeprazole actually blocks IL-13 induced eotaxin-3 secretion

        - Dilation
            - reserved for pts w/ strictures/rings
            - do so carefully as there is increased r/o tears/perforation compared to other causes dysphagia requiring dilation, it is important to gently inspect the esophagus after dilation
            - several studies have demonstrated that symptom-freedom from dilation is quite durable similar to that of glucocorticoid Tx, however, the underlying inflammatory process and subsequent chronic remodeling is not altered
            - post procedural pain more common when compared to other causes for dilation
            - b/c dz in adults is more of a scarring process repetitive dilations might all that be needed
        - Allergen Avoidance
            - specific allergen restriction based on SPT/APT/RAST (70% success rate in children) → general 6-food elimination diet: cow-milk protein, soy, wheat, egg, peanut, seafood (75% success rate in children) → elemental diet (eg. free amino acids) which limits the intake of all potential food allergens but not tolerated at all b/c it requires a feeding tube (95% success rate in children)
            - Problems: risk of nutritional deprivation, hard to do, etc
        - Glucocorticoids
            - systemic forms
                - effective but SEs and long term need limit their role
            - topical forms x2-8wks (very unclear)
                - 1° fluticasone 220mcg/spray 2 sprays swallowed NOT inhaled BID-QID w/o spacer to ensure delivery to esophagus and not lung, inspire and hold and depress inhaler and swallow and then take a sip of water to carry fluticasone from pharynx to esophagus and then breath and then not eat/drink for 30min
                - 2° budesonide suspension 0.5mg/10mL 120mL PO BID NB take 0.5mg Pulmicort Respules used for nebs and 5g Splenda and mix with water to make 10mL of viscous liquid
                - pts typically respond w/in 1wk
                - 45% relapse rate at 24wks indicating that repeat therapy may be needed
                - SEs: candida esophagitis is seen in 15% of pts and there have been case reports of herpes esophagitis, systemic SEs are rarely associated with topical steroids
        - Antihistamines/Mast-Cell-Inhibitors/Leukotriene Inhibitors
            - very mild effect
            - not supported in the literature
        - Anti-IL-5 (mepolizumab-Bosatria) humanized monoclonal antibody against IL-5
            - NB Anti-IL-13 and Anti-IgE (Xolair) are being studied
    - Prognosis
        - No evidence of spontaneous remission but there is seasonal variation w/ abatement during the winter
        - Recurrence after Tx is common
        - There is evidence that the reason why Sx differ b/t children and adults is because the disease itself progresses to a fibrotic stage characterized clinically w/ dysphagia
        - associations w/ Celiac Dz has recently emerged in the literature despite different antigen cause and immune response

Cystic Fibrosis

- **Stomach**
    - **GERD** (2/2 unknown but for some reason these pts have a higher r/o GERD, the problem is that PPIs increased r/o pneumonias)
- **Intestine**
    - **Pediatric Meconium Ileus → Adult Meconium Ileus Equivalent aka Distal Intestinal Obstruction Syndrome DIOS** (2/2 inspissation, acute Sx (unlike gradual onset in constipation), thickened stool aka meconium at ICV (unlike colon in constipation), can cause partial or complete obstruction, palpable RLQ mass, bubbly stool in RLQ on KUB, Px: daily Miralax and pancreatic enzymes, Tx: IVF and GoLytely Prep over 8 hours → Hypaque enema and be sure and tell radiologist to reach TI (NB there is high r/o perforation) → surgery)
    - **Constipation w/ Fecal Impaction**
    - **Mucosal Malabsorption**
    - **Intussusception**
    - **Rectal Prolapse**
    - **Appendicitis**
    - **SIBO**
- **Pancreas** (Tx: pancreatic enzymes, fat soluble vitamin replacement)
    - **Acute Recurrent to Chronic Pancreatitis** (2/2 inspissation)
    - **Exocrine/Endocrine Insufficiency** (2/2 chronic pancreatitis)
- **Biliary** (Tx: URSO, prophylactic cholecystectomy)
    - **Cholestasis** (2/2 inspissation)
    - **Cholelithiasis** (2/2 decreased bile acid reabsorption resulting in more lithogenic bile)

- **Secondary Biliary Cirrhosis** (2/2 chronic cholestasis)
- **Steatosis** (2/2 malnutrition)
- **Congestive Hepatopathy** (2/2 R-CHF for pulmonary dz)

Gastrointestinal Heterotopia

- Definition
  - Abnormal localization of well differentiated normal tissue w/o anatomic or vascular continuity with the native organ
  - Can arise anywhere from the mouth to rectum
- Epidemiology
  - Age/gender of presentation is highly variable depending on type of tissue and location but in general these are found in younger symptomatic pts or incidentally on imaging/endoscopy in older pts
  - Though likely embryologic in origin pediatric cases are rare
- Mechanism (two proposed mechanisms)
  - (1) Embryonal (during development of the native organ there is considerable migration, contortion, invagination, etc of tissue that eventually leads to normal human anatomy, during embryogenesis remnant tissue can remain along the tract of migration resulting in heterotopic tissue)
    - Specifically in the esophagus: columnar epithelium of embryonic esophagus is not completely replaced by psuedostratified squamous epithelium during fetal development, this conversion begins at both ends of the esophagus and extends toward the upper middle hence the location of inlet patches, this persistent columnar epithelium differentiates in gastric mucosa, NB there is clear evidence that this lesion is not acquired based IHC comparisons b/t inlet patches and Barrett's which demonstrate that Barrett's is derived from immature GI stem cells while inlet patch is derived during embryogenic gastric tissue
  - (2) Metaplasia (conversion of one differentiated tissue to another after tissue injury)
- S/S
  - Many are asymptomatic however significant disease can occur
  - Depending on type of tissue and location
  - Tissue is generally functional
  - All pathologies that can occur in normal localized tissue can occur in heterotopic tissue including bleeding, cancer, -itis, infection
- Dx
  - Histologically looks like the native tissue
- Types
  - Pancreatic Heterotopia aka "Pancreatic Rest", mainly occurs in the submucosal layer, 1° stomach 30% (mainly antral greater curvature), 2° duodenum 30%, 3° jejunum 20%, 4° esophagus/GB/CBD/spleen/mesentery/mediastinum
    - Surprisingly common (0.3-13.7% of population)
    - usually seen as an umbilicated submucosal (25% of time it is in a different layer) 1-4cm lesion
    - S/S: usually clinically silent unless complicated by enzyme secretion leading to surrounding inflammation w/ S/S of pain and bleeding and obstruction if large
    - Other complications can occur as in the normal pancreas including: Pancreatitis, Cysts, Psuedocysts, Abscesses, Adenocarcinoma
    - EUS (hypoechoic submucosal lesion)
    - Tx: if symptomatic then resect otherwise observe
  - Gastric Heterotopia
    - 1° Esophageal Inlet Patch (refer)
    - 2° Meckel's Diverticulum (refer)
    - 3° tongue, jejunum, gallbladder, rectum, scrotum

Radiation Injury

- Depends on total dose, fraction size, treatment volume, treatment techniques, addition of chemo/surgery
- Mech: radiation causes ionization aka release of an electron which then damages DNA and/or interacts w/ water forming free radicals which collectively kills rapidly dividing cells i.e. cancer cell or mucosa
  - NB rule out recurrence of cancer as cause of Sx as endoscopic findings are sometimes not clear
- Dx: acute (basal epithelial layer injury w/ thinning and vacuolization and inflammation) vs chronic (epithelial regeneration, fibrosis w/ strictures)
  - NB try to avoid endoscopy to make Dx b/c of r/o perforation secondary to insufflation
- S/S: early (during or shortly after radiation) vs late (months to years)
  - Oral: mucositis/stomatitis, infection, salivary gland damage w/ xerostomia, dental carries, osteoradionecrosis of the jaw, taste dysfunction, trismus
  - Esophagus
    - Acute: esophagitis (begins 2wks after initiation, lasts up to several weeks following cessation of therapy, 50% risk)
    - Chronic: stricturing (begins 3mo after initiation, obviously Sx can last a life time if not treated, 60% risk), dysmotility (begins 4-12wks after initiation)
  - Stomach
    - Acute: gastritis (begins 1wk after initiation, lasts 3wks following cessation)

        - Chronic: atrophic gastritis w/ impaired secretion
    - Intestine (small intestine more susceptible than large intestine)
        - Acute: enteritis (begins 3wks after initiation but can occur even a few hours after starting therapy, lasts 2-6wks following cessation)
        - Chronic: malabsorption, dysmotility, stricturing, infection w/ abscess, fistulization,
    - Rectal
        - Acute: proctitis w/ tenesmus, diarrhea, bleeding
        - Chronic: chronic radiation proctitis (CRP, 2/2 radiation for prostate or female GU cancer, bleeding and proctalgia for several months to years, telengectasias and mucosal friability on endoscopy, Bx: obliterative endarteritis, Tx: APC or now w/ the new Halo 90 degree radiofrequency ablation, NB topical steroids/5-ASA have been tried in the past)
- Px: amifostine-Ethyol (binds radicals preventing their damage), decorin-? (neutralizing antibodies to TGF-beta suppressing fibrosis)
- Tx: very difficult to Tx, just Tx the Sx, try HBO, surgery if stricturing dz

Peritoneum, Mesentery, Omentum, Diaphragm

- Peritoneum: single sheet of mesothelial cells, sealed bag in males while females there is an opening at the ostia of the fallopian tubes, overall there is only a few mL of peritoneal fluid acting as a lubricant, parietal surface (somatic innervations, covers ant/lat/post ab wall, diaphragm, pelvis and anterior surface of the retroperitoneal organs: duodenum, L/R colon, pancreas, kidney, adrenals) & visceral surface (visceral innervation, covers intraperitoneal organs which are suspended by thick bands of peritoneal ligaments and subdivide the abdomen into compartments), mesentery (peritoneum that connects parietal and visceral peritoneum and thus holds organs in place), omentum (peritoneum that connects stomach w/ other organs, greater omentum connects the greater curvature to the transverse colon vs lesser omentum connects the lesser curvature to the liver, NB the R lateral edge of the lesser omentum is the hepatodeuodenal ligament and the opening posterior to this is the foramen of Winslow and is the only connection b/t the greater/ lesser peritoneal sacs)
- Primary Peritonitis: SBP aka infection of ascites, PD, TB/Fungal/Parasites 2/2 HIV (refer to pleural fluid for findings), Chlamydia w/ Fitz-Hugh-Curtis Syndrome, Powder on gloves used in laparotomies, CTD resulting in a serositis, FMF
- Secondary Peritonitis: any adjacent inflammatory process (eg. perforated PUD, appendicitis, diverticulitis, etc), leakage of blood or bile, etc, peritoneum sequesters inflammation thru fibrin trapping via adhesions and omental loculation, 75% are anaerobe/aerobe polymicrobial, Tx: abx ± surgery (ex-lap to make Dx, washout, consider laparostomy w/ secondary intention closure)
- Peritoneal Tumors
    - tumors that metastasize to peritoneum include ovary/stomach/colon/breast/pancreas/lung/lymphoma/sarcoma aka peritoneal carcinomatosis, cytology is 90% sensitive, S/S are ascites, Tx: paracentesis and if SAAG >1.1 then diuretics will work, consider intraperitoneal chemo w/ Mytomycin C and peritonectomy, very poor prognosis w/ 25% survival at 3mo
    - psuedomyxoma peritonei: broad condition referring to the presence of gelatinous substance in the peritoneal cavity, rare, F>M, from perforation and leakage of a mucus producing tumors esp 1° appendix 2° ovarian/gastric/colon, Dx: imaging ("jelly belly" w/ bowel compressed centrally and thick fluid around bowel unlike other causes of ascites where bowel floats throughout fluid), paracentesis, Tx: paracentesis and Tx the underlying cancer
    - mesothelioma: ¼ of mesothelioma affects the peritoneum
    - pelvic lipomatosis: normal fat deposits found in the perirectal/perivesical spaces may develop non malignant overgrowth associated w/ a fibrous reaction, seen in adult black men, can cause HTN, proliferative cystitis, urinary tract obstruction, GI Sx, etc, must differentiate from liposarcoma
    - benign peritoneal cysts
- Diseases of Omentum/Mesentery
    - Hemorrhage/Infarction
    - Tumors (mesenteric cysts, various sarcomas, etc)
    - Inflammatory to Fibrotic Syndrome (very confusing syndrome w/ various presentations and various terms including retractile mesenteritis, mesenteric panniculitis, retroperitoneal fibrosis, etc)
    - Epiploic Appendagitis (primary inflammation of the colonic epiploic appendices, often confused w/ appendicitis)
- Diseases of the Diaphragm
    - Hernias (refer) vs Eventration (not a true hernia but an area of weakness that can lead to bulging of viscera into thorax)
    - Hiccups (refer)

Protein Losing Gastroenteropathy

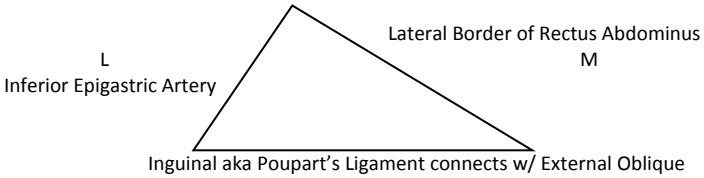
- Definition
    - Group of disorders characterized by excessive loss of serum proteins into GI tract
    - Normally 1%/10% of total-protein/albumin is lost in GI tract, this can increase to 6%/60% in protein losing gastroenteropathies, most protein in GI lumen is derived from sloughed enterocytes and pancreatic/biliary secretions
    - Lost proteins are degraded like food proteins and thus recirculated but when loss exceeds the body's capacity to synthesize then hypoproteinemia
    - Adaptive changes in endogenous protein catabolism occur resulting in unequal loss of specific proteins: normal high turnover proteins are not affected (insulin, clotting factors, IgE) vs low turnover proteins are affected (albumin, all Ig except IgE)
- Classification
    - Mucosal Injury resulting in increased permeability to plasma protein
        - 1°: Menetrier's, HP Gastritis, Allergic Gastroenteropathy, SLE

        - Other: HIV, Viral GE, Sprue, Collegenous Colitis, EGE, Parasites, Vascular Ectasia, SI Bacterial Overgrowth, Lymphocytic Gastritis/Colitis, Hypertrophic Hypersecetory Gastropathy
    - Mucosal Erosions/Ulcerations resulting in loss of protein rich inflammatory exudate
        - 1°:
        - Other: Alpha Chain Dz, Amyloidosis, Behcets, Carcinoid, IBD, Erosive Gastritis, GI Carcinomas, GVHD, HP Gastritis, Bacteria GE, Ischemic Colitis, KS, Lymphoma, NF, NSAID Enteropathy, Sarcoid
    - Lymphatic Obstruction resulting in leakage of lymph
        - 1°:
        - Other: CHF, IBD, GI Endometriosis, Lymphagiectasia, Lymphatic Enteric Fistula, Mesenteric Venous Thrombosis, Mesenteric TB/Sarcoid, Lymphoma, Portal Hypertensive Gastroenteropathy, Retroperitoneal Fibrosis, Sclerosing Mesenteritis, SVC Thrombosis, TB Peritonitis, Whipple's
- S/S
    - Edema b/c of protein loss
    - Various GI S/S based on the underlying cause
    - Impaired Immunity, Dyslipidemia, Emphysema, Coagulaopathy, Endocrine Imbalance are actually very rare
- Dx
    - General: hypoproteinemia esp hypoalbuminemia, decreased Ig, decreased lipoproteins, decreased alpha-1-antitrypsin levels, decreased fibrinogen, decreased hormone binding protein
        - NO cirrhosis, nephrotic syndrome, malnutrition
        - NB all serum proteins are lost (there is no filtering of smaller proteins, etc) unlike say in Nephrotic Syndrome
    - Screen: Alpha-1-Antitrypsin plasma clearance x72hrs (>24mL/d in a pt w/ no diarrhea or >56mL/d in a pt w/ diarrhea = protein loss)
        - NB GIB causes false elevations, cannot be used for gastric causes as low pH degrades it and thus cannot be measured in stool
    - Confirm: radiolabeled ^{99m}Tc-human serum albumin scintography to locate area
        - NB measurement of fecal loss of ^{131}I-polyvinylpyrrolidone, ^{51}Cr-albumin, ^{67}Cu-ceruloplasmin, etc markers given intravenously (not clinically done b/c cumbersome)
    - Endoscopy w/ Lesion/Random Bx, CT Ab/P, Lymphangiogram
- Tx
    - Treat underlying disease
    - High protein diet
    - Octreotide (decrease protein secretions)
    - If stomach is where disease is occurring consider gastrectomy

Hernias

- General
    - protrusion of peritoneum thru weak wall w/ sac made of peritoneum w/ abdominal contents (NB don't confuse hernia w/ diastasis recti (separation of rectus abdominis muscle w/o defect in fascia, defect is wide/long and no ring can be palpated, no repair))
    - Reducible vs Incarcerated (cannot be reduced and when you cannot then apply ice, steady pressure and call surgery) → Obstructed (obstructed GI tact) → Strangulation (ischemic GI tract, small hernias more dangerous than large hernias)
    - PEx: place finger along spermatic cord into canal and have pt cough (direct = side of finger vs indirect = tip of finger)
- **(1) Diaphragmatic (refer)**
- **(2) Internal**
    - **Internal:** not thru ab wall but thru spaces/defects created during/after surgery from adhesions or division of mesentery (esp RYGB), developmental anomalies (abnormally large foramen of Winslow, abnormal opening of mesentery, etc), obturator, sciatic notch, perineum
- **(3) Abdominal Wall**
    - **Inguinal**
        - **Direct**
            - Pt: old male
            - Etiology: age related breakdown of wall
            - Mech: extend from peritoneal cavity thru Hesselbach's triangle along inguinal canal towards but rarely into scrotum
            - Test: place finger at exit of inguinal canal and ask pt to cough and hernia will press along SIDE of finger
            - S/S: strangulation uncommon
            - Tx: herniorrhaphy by returning contents into peritoneal cavity then repairing inguinal canal floor defect aka Bassini, McVay or Shoudlice repair w/ addition of polypropylene mesh to make tension free aka Lichtenstein repair
        - **Indirect**
            - Pt: young males aka infants esp if premature
            - Etiology: congenital birth defect where processus vaginalis does not close
            - Mechanism: extend from peritoneal cavity lateral Hasselbach's triangle thru inguinal canal into scrotum

        - Test: same test but hernia will press on TIP of finger
        - S/S: strangulation common
        - Tx: herniorrhaphy (same)
    - **NB Pantaloon** (combo of Direct + Indirect)



- **Incisional** thru a poorly healed incision, 5% of laparatomies, 0.5% of trocar sites, higher risk if vertical, post-op wound infection, impaired wound healing (from chronic steroid use, old, sick), midline, hematoma, along stoma sites aka parastomal
- **Spigelian** thru ab wall precisely at the jxn of semilunar line aka lateral edge of rectus abdominus and semicircular line of Douglas aka where the transverse abdominus and internal oblique aponeuroses change to pass anteriorly to the rectus muscle, usually below level of umbilicus, very rare
- **Epigastric aka Epiploceles** thru midline defect of linea alba above umbilicus, often multiple and small, rarely bowel is involved b/c in upper abdomen rather usually peritoneal fat or omentum, very common but often asymptomatic and undiagnosed
- **Umbilical** thru umbilicus, congenital African children or acquired in adults with pregnancy, ascites, etc, breakdown can occur leading to rupture
- **Femoral** (rare) thru empty space of (Lateral - "NAVEL" – Medial), below inguinal ligament unlike inguinal hernias medial to femoral vessels, more common in females
- **Little's** Hernia (hernia containing Meckel's diverticulum)
- **Amyand's** Hernia (hernia containing appendix)
- **Richter's** Hernia (only one side of bowel herniates therefore no obstruction)

FIstula

- Definition
    - Abnormal anatomic connection b/t two epithelialized surfaces
- Description
    - **Anatomic**: internal (eg. ileocolic) vs external (eg. enterocutaneous) w/ first part origin and last part drainage
    - **Physiologic**: high output (>500cc/d) vs moderate output (200-500cc/d) vs low output (<200cc/d)
- Dx
    - Oral/rectal contrasted CT vs fistulogram in which contrast is injected retrograde thru fistula
    - If it is unclear if the cutaneous lesion is a post-op fistula vs wound drainage you can give oral charcoal and see if it appears in the fistula
- Etiology/Tx
    - Spontaneous (20%) 2/2 inflammation, infection, cancer, radiation, foreign body, etc
        - Usually internal
        - Tx: unlikely to close therefore need surgery
    - Post-Op (80%)
        - Usually external
        - Tx: likely to close w/o surgery therefore medical manage fluid/electrolytes (**generally fistula output is iso-osmotic and high in potassium therefore replace mL for mL with NS and added potassium and if there are still electrolyte imbalances then send fluid off for analysis**), wound care w/ wound VAC, ensure adequate drainage by incision and placing a catheter in the fistula??? b/c if not then pooling of fistula contents in abdomen can cause abscess formation, ostomy bag?, nutrition (enteral nutrition promotes fistula closure but many pts need TPN esp if fistula is from proximal small bowl and is high output, some have tried reinfusion of succus entericus back into small bowel if electrolyte imbalance is complicated), treat underlying problem eg. anti-TNFs for Crohn's, octreotide to decrease output if high output (1: decreases GI hormone thus decreasing GI secretion, 2: relaxes smooth muscle increasing compliance of bowel, 3: increase GI absorption), once stabilized assess if fistula will likely close on own (signs of self closure: output <500cc/d, <40yo, proximal small bowel site, well nourished, cause is anastomotic breakdown), new studies are looking into fibrin glue, collagen plugs, gelatin sponges, etc to close chronic fistulas, if no closure in 4-6wks then surgery

Phlegmon → Intra Abdominal Abscess (IAA)

- Etiology
    - Perforation/Surgery/Trauma
    - Inflammation esp Acute Pancreatitis
    - Cancer esp ?
- Pathogens
    - Mixed aerobic/anaerobic
- Dx

    - CT (extraluminal loculated fluid density (sometimes higher) that has enhancing wall w/ contrast, sometimes there is gas, sometimes difficult to distinguish unopacified bowel from abscess)
    - US good for diagnosing abscess in liver/spleen/pelvis
    - Indium/Gallium Scan
- Tx
    - CT/US Guided Percutaneous Aspiration
        - **equivalent in success and less risk compared to surgery and thus should be the procedure of choice except for interloop/intramesenteric abscesses, diffuse peritonitis and deep abscesses in which surgery is the best option**
        - **± Thombolytics** if loculations or when thick debris
        - **± Drainage Catheter** (Jackson Pratt or Penrose Drain) if **>3cm** and remove catheter if **<20mL/d (NB if high output for awhile then consider fistula and assess by instilling Gastrograffin thru catheter and then fluoro)**
        - Complications: transient sepsis, organ injury, hemorrhage, pain, pneumoperitoneum
    - Multiple Surgical Washout w/ Wound Vac followed by secondary closure
    - IV Abx: Invanz or Flagyl+3rdCeph/FQ
- NB **if poor response consider Candida superinfection**