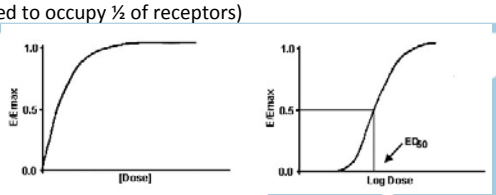
Household Terms

- ¼ gallon = 1 quart = 2 pints = 4 cups = 32 ounces = 66 tablespoons = 200 teaspoons = 1000 drops (gtt) or cc or mL
- 1 pound = 16 ounces = 0.45kg
- French Catheter System = 3 x diameter (in millimeters) = outside circumference of cylindrical objects
- Gauge Catheter System = 1 / diameter (in inches)

Pharmacology

- General
  - c = with, s = without, x = except, p (post) = after, a (ante) = before, pc (come) = after meals, ac = before meals, O/A-D/S/U = eye/ear-right/left/both, UD = as directed
  - any extended release and enteric coated meds cannot be crushed and sent down tubes
- Drug Development
  - In Vitro Studies (~2yrs)
  - Animal Testing for Mechanism (~2yrs)
  - Investigational New Drug (IND) Period: Phase 1 for Safety and Pharmacokinetics w/ Normal Volunteers, Phase 2 for Efficacy in Sick Pts, Phase 3 for Two Double Blinded Placebo/Old-Drug Controlled Trials (~4yrs)
  - DRUG IS RELEASED
  - New Drug Application (NDA) Period: Phase 4 for postmarketing surveillance
  - Drug expires: (patent lasts20yrs)
  - NB in general a pharmaceutical company must project a 1 billion revenue to go ahead with developing a drug!!!
- **PharmacoDynamics (PD)** (effect of drug on body)
  - Affinity = Ka ([ ] needed to occupy ½ of receptors)



  - Efficacy = two drugs can similar affinity for a receptor but their effect is different (agonists, partial agonists, antagonists, etc)
  - Therapeutic Index (TI) = LD50/ED50
- **PharmacoKinetics (PK)** (effect of body on drug)
  - General: collectively PK determines loading/maintenance dose, route, site, etc and over all Half Life (t1/2 = 0.7Vd/Cl) of the drug
  - **Absorption**
    - Drugs are usually absorbed passively (rarely actively) in the GI tract (stomach and intestine) b/c drugs are usually lipophilic/small/non-ionic
    - The non-ionic state of drugs depends on the pH of the environment they are in hence the passage of drugs across enterocytes is a fxn of mucosal pH (some drugs absorb thru acidic (stomach/jejunum) vs alkaline (ileum/colon) surfaces)
    - Bioavailibilty (F) fraction of dose that gets into blood from GI tract
    - First pass metabolism by enterocytes and liver
  - **Distribution**
    - Volume of Distribution (Vd = amount of drug in body / plasma drug [ ]) % of drug that moves from blood compartment into interstitium into cells based on hydrophobicity/size/capillary structure/plasma proteins esp albumin/organ-blood-flow
    - NB areas (placenta, CSF, milk) are difficult to penetrate by meds
  - **Metabolism**
    - Some drugs are prodrugs and must be converted to the active form
    - Phase I (CYtochrome-P450 Enzymes (Redox/Hydrolysis) = creating a slightly polar molecule w/ variable activity = drug enters urine but can be selectively absorbed/reabsorbed)
      - NB [CYP] highest in ER and [ER] highest in liver/enterocytes hence highest [CYP] is in liver/enterocytes, there are several families but the most important one are 3A, there is extensive polymorphism b/t people, CYP enzymes can also have inducers/inhibitors therefore when you are giving a drug that has a narrow therapeutic index (TI) determine what its CYP is and then determine what the CYP's inducers/inhibitors so as to avoid them
        - -3A: grapefruit juice, cimetidine, ACE abx, -azoles esp ketoconazole
        - +3A: St. John's Wart, carbamazepine, rifampin, rifabutin, ritonavin
    - Phase II (Conjugating Enzymes (Acetylation/Glucuronidation) = creating a very big molecule = drug enters bile and into gut and cannot be reabsorbed)
  - **Excretion**
    - liver and kidney
    - clearance (volume of plasma from which a drug is completely eliminated)

- zero order (linear decrease in [drug] ~ rate is regardless of [drug]) vs first order (exponential decrease in [drug] ~ rate is proportional to [drug])

Complementary Alternative Medicine (CAM)

- Medicines (refer to specific sections for specific drugs): probiotics, prebiotics, herbals, vitamins, supplements, functional foods
- Actions: acupuncture (based on the Chinese energy (*qi*) which circulates among organs along channels (meridians) and w/ the placement of needles at specific points the flow of qi is restored), hypnosis, yoga, massage, meditation, cognitive behavioral therapy, colonic irrigation, Ayurveda (Indian holistic system that provides dietary and lifestyle recommendations)
- Allopathic (Western Medicine) vs Homeopathy (believe that you Tx a dz by giving a very small dose of that which caused the disease), Osteopathy (believe that dz is due to bone imbalance and thus manipulation is the Tx), Chiropractor (believe dz is due to impinged nerves)
- Insurance is now covering CAM except meds
- In US CAM costs = MD costs!!!
- Pt: rich, educated, white female
- No government FDA regulation or standardization
- Belief: CAM is safer than conventional medicine but the reality is that many herbals have been link w/ liver/renal failure and are contaminated w/ toxins and heavy metals
- Studies are Bad: NOT RDBPCT, underpowered, non-English, no quality control or consistency b/t products
- CAM can make false claims like "good for digestive health" but cannot make false truths "this will cure your IBD"
- CAM must have a disclosure statement
- www.nccam.nih.gov

Pre/Pro/Anti-biotics

- Pre: poorly absorbed but fermentable carbs that are meant to stimulate growth of "good" bacteria eg. *Lactobacilli* and *Bifidobacteria*
  - Germinated Barley Foodstuff (GBF)
  - Oligosaccharides in Breast Milk
  - Fiber
  - Pomegranate Juice
  - Oligofructose
  - Inulin-type Fructans
  - Galactosaccharides (GOS)
  - Pyrodextrins
  - Isomalto-Oligosaccharides
  - NB also found in banana, garlic, wheat, rye, asparagus, onion, chicory, leeks
- Pro: give "good" bacteria to repopulate gut
  - General: *Enterococcus fecalis, E.coli Nissle* 1917
  - Specific Ones for IBD, IBS, AAC, etc (refer to individual conditions)
  - Stool Transplant
- Anti: kill off the "bad" bacteria
  - rifaximin (Xifaxin)
  - neomycin (Neo-Fradin)

Mouth

- **vicodin elixir** 7.5mg/15mL 5mL PO Q8hrs prn
- **viscous lidocaine** 2% 5-10mL Q4hrs prn dispense 100mL
- **stomatitis cocktail:** formulated by pharmacy equal parts liquid Benadryl, viscous lidocaine, Maalox, 1tbsp S&Spit or S&Swallow Q4hrs prn
- **artificial saliva substitute (Caphosol)** 15mL, S&Spit, QID

Other

- **cromolyn (Gastrocrom)** for systemic mastocytosis and food allergies
- **belladonna alkaloids + AlMgOH + Simethicone + Phenobarbital (Pink Lady)** for GERD
- **phenobarbital / hyoscyamine + atropine + scopolamine (Donnatal)** for IBS
- **simethicone (Mylicon, Gas-X, Phazyme)** 50mg/tabs or 40mg/0.6mL liquid, 80-120mg PO Q6hrs w/ max of 480mg/d, chew tabs before swallowing, give after meals
- **sucralfate (Carafate)**
  - Dosing: 1gm/tab or 1g/10mL solution, 1gm PO Q6hrs, give 1hr before meals
  - Uses: FDA approved for DU but studies also show that is helpful for GU, in addition has effect against mucosal irritation from bile or pancreatic juices
  - Mech: aluminum salt of sulfate sucrose, exact mechanism is unknown, likely anionic sulfates forms a complex w/ cationic proteins exposed in damaged mucosa forming a viscous adhesive paste
  - SEs: interferes w/ med absorption therefore take separate from medicines, constipation, aluminum toxicity in RF, bezoar formation, some say has NO role in GI dz
- **octreotide (Sandostatin)**
  - 14aa native protein (somatostatin) has a short t1/2 ~4min vs 8aa modified protein (octreotide) has a longer t1/2 ~90min

- Mech: universal "stop" hormone found in CNS/GI and has both NT/autocrine/paracrine effects
- Action: inhibits gut secretion, inhibits gastric emptying, inhibits GB motility, decreases mesenteric blood flow BUT has a paradoxic effect on gut motility actually increasing it hence its use in pseudo-obstruction
- Dose: 50-100mcg/hr IV or 50-100mcg IV TID or 50-200mcg SC TID (nasal spray is being developed) or 10-40mg IM Qmo
- Use: NET (decreases hormone secretion and has a brief antineoplastic effect), dumping syndrome, GIB (NB there is some use in pancreatitis Px b/f ERCP, chronic diarrhea, fistula output)
- SEs:
  - abdominal upset (nausea, pain, bloating, diarrhea) for the first few weeks
  - pancreatic insufficiency (give enzymes)
  - hyperglycemia (give insulin)
  - GB sludge/stone
  - burn at injection site (put ice cube on site before injection)

Pancreatic Tx = Lipase/Protease/Amylase

- Types
  - **Enteric Coated: Creon, PancreaZe, Ultrase, Zenpep** (gastric acid breaks down the enzymes hence they are enteric coated, cannot crush/chew capsules but you can open the cap and sprinkle on food)
  - **Non-Enteric Coated: Viocase** (there is no enteric coat therefore you have to inhibit gastric acid w/ H2B)
- Approach
  - pancreas makes 720,000 U of lipase per 500 kcal meal, if >10% of normal pancreatic is needed to prevent steatorrhea than at least 72,000 U of lipase is needed per 500 kcal meal (average meal), most people use Creon 24 and give three w/ each meal (one before, one during, one after) and one w/ each snack (one before) then adjust based on Sx, weight, etc
  - another way of doing dosing is based on weight where you give 500 Lipase U per Kg
  - NB recently the FDA has mandated clinical trials demonstrating the effectiveness and as such some are off the market, some names and doses have changed, the cost has gone up

Bile Acid Tx

- CAM
  - Tumeric (increased biliary secretion and promotes GB contraction)
- Bile Acid Dissolution: (1) symptomatic gallstones in non-surgical candidates and (2) cholestatic conditions esp PBC, pregnancy, etc
  - **UrsoDeoxyCholicAcid-UDCA aka URSOdiol-URSO (Actigall)** 250,500mg tab 10-30mg/kg/d divided w/ each meal
    - NB by giving this bile acid [cholesterol]<<<[bile acid] allowing for dissolution of stones however this bile acid is NOT effective in replacing physiologically effective bile acid used to absorb fat (only cholic acid can do this)
    - NB from Chinese black bear
    - NB chenodeoxycholic acid was the first one but had lots of SEs
- Bile Acid Replacement: (1) deficiency states that result in steatorrhea
  - **cholic acid (Ox Bile)** 1g w/ each meal, can only get on internet (Jarro Company)
    - NB overflow into colon can cause diarrhea similar to that seen in post-cholecystectomy therefore titrate up dose to where you don't have steatorrhea along with no diarrhea
- Bile Acid Resins/Binders: (1) bile acid excess states as in post-cholecystectomy diarrhea, (2) cholestatic pruritus
  - **cholestyramine (Questran) – nasty powder but cheap $30/mo, colestipol (Colestid) – large pill or powder but cheap $30/mo, colesevelam (Welchol) – best b/c small pill or powder but expensive $60/mo**
    - NB positively charged resins that bind negatively charged BAs in the SI preventing their absorption at the TI and preventing them from acting on LI to cause diarrhea
    - NB directions usually say to take with meals b/c they are designed to lower cholesterol but don't take it this way rather take at night b/c that is when the GB usually stores BA and if not present they stay in the SI and at night the migratory complex acts to clean out the SI carrying these BA into the LI acting as a laxative
    - NB start at low dose and build up slowly
- Bile Acid Transport Inhibitors (under development)

Anti-Diarrheals

- General
  - Consider stopping all acid reducing agents
  - Probiotics (refer above)
  - Herbals
    - Clove (Syzgium aromaticum)
    - Berberine
    - Arrowroot
  - Texture Modifiers, Absorbants, Bulking Agents
    - Banana Flakes
    - Attapulgite, Kaolin, Charcoal, Bismuth
    - Fibers (psyllium, methylcellulose, pylocabopil)
- Diet Modification

- Rehydration (in general you want a solution that has equal elemental nutrients (glucose, etc) and electrolytes principally sodium b/c you want to use the glucose-Na channel which does not require ATP and pulls water with it (goal concentration: glucose 55mM and Na higher)
    - Hospital
        - IV NS w/ KCl if severe
    - Purchased
        - WHO, Pedialyte, Rehydralyte, Resol, Ricalyte
        - New formulas: hypo-osmolar amylase resistant starch to enhance colonic SCFA and water absorption
    - Home Made
        - 1/2tsp salt, 1/2tsp baking soda, 4tbsp sugar, 1L water = solution of glucose and electrolytes
        - bowl rice and drink water = solution of glucose and amino acids
    - NO Gatorade (designed to replace sweat losses not diarrhea), Soda, Fruit Juices, Jello, Tea, et al b/c contain so much more sugar than electrolytes that you just overwhelm absorption resulting in an osmotic diarrhea
- bland foods eg. BRAT Diet (Banana, Rice, Apple Sauce, Toast), malt o'meal, cream of wheat, mashed potatoes
- back to regular foods but avoid…
    - dairy products (b/c of secondary lactase deficiency which can last up to 1yr!!!)
    - caffeine (inhibits phosphodiesterase resulting in increased intracellular cAMP and increased secretion)
    - alcohol (irritates the intestine)

- Anti-Motility Agents to slow motility and allow for more absorption
    - Opiates
        - General
            - decrease motility, decreases fluid secretion, increases absorption, increasing anal sphincter tone
            - theory that they should not be used in infectious diarrhea has not been proven in studies nevertheless they should be used cautiously in pts w/ dysentery
            - if chronic give as prophylaxis four times a day (before bedtime and with meals to prevent food as a motility stimulus)
            - titrate up every few days so as to allow CNS tolerance (remember that there is NO GI tolerance) and taper when stopping to avoid withdrawal symptoms
        - Mild (OTC)
            - Loperamide (Imodium) 4mg PO x1 and then 2mg PO Q6hrs prn
        - Mod (Rx)
            - Diphenoxylate/Atropine (Lomotil) 2.5/0.025mg/tab or 2.5/0.025mg/5mL or Difenoxin/Atropine (Motofen) 1/0.025mg, 2tabs or 10mL PO x1 then 1tab or 5mL PO Q6hrs prn (NB the anti-cholinergic atropine actually has very little effect on diarrhea, rather it is used to prevent abuse b/c of its anti-cholinergic effects)
        - Severe (Triplicate)
            - Deodorized Tincture of Opium (DTO-?) 10mg/mL (NB 20gtts=1mL) start at 1gtt PO QID and increase 1gtt at each dose to when Sx are managed (max is usually 20gtts), bad taste therefore mix w/ juice in shot glass
            - Camphorated Tincture of Opium (CTO-Paregoric) 0.4mg/mL, better taste
            - Morphine Liquid (Roxanol) 20mg/mL
            - Codeine (?) 15-60mg PO QID, don't use the Tylenol combo, take w/ food b/c can give nausea
    - Enkaphalinase Inhibitors (eg. Acetorphon only in Europe) (increase endogenous opiates)
    - CCB (eg. Verapamil)
    - 5-HT3 Antagonists: alosetron (Lotronex) not only decrease visceral hypersensitivity but also slows transit time, very severe SEs including extreme constipation, ileus, obstruction which can progress to ischemic colitis and perforation, only FDA approved for women with very bad IBS-D refractory to all other meds >6mo
    - Anticholinergics (refer below)
- Increase Electrolyte/Water Absorption
    - Clonidine 0.1-0.3mg PO TID (alpha-2 receptor on enterocytes and when activated there is increased Na/Water absorption, in addition there are effects on opiates receptors (hence its use in opiate withdrawal), use in pts with hypertension and diabetics)
- Decrease Electrolyte/Water Secretion
    - Bismuth Salicylate (bismuth is antimicrobial while salicylate is antisecretory)
    - Octreotide (if hormone mediated, dumping syndrome, chemo induced or any type that is refractory and very high volume)
    - Empiric Bile-Acid Resins
    - Empiric Pancreatic Enzyme Replacement
    - Other: Berberine, Calmodulin, PG Inhibitors (eg. Indomethacin), Chloride Channel Blockers, Nicotinic Acid, Corticosteroids

Anti-Spasmotics

- CAM

    - Methol in Peppermint Oil (Alkaloids, Colpermin, Elanco LOK) from *Mentha piperita* flowers (has CCB activity relaxing smooth muscle acting as a antispasmodic but there is NO anticholinergic effect, many RDBPCT)
    - STW5 (Iberogast): spasmolytic effect, 9 herbs the main one being Clown's Mustard plant aka Iberis amara, used in Europe, many RDBPCT, endorsed by Dr. Oz, find on internet, mix 20 drops w/ warm drink three times a day, SEs: liver injury, bleeding, alters metabolism of drugs)
    - Caraway from *Carum carvi*
    - Ceandine from Chelidonium majus
    - Valerian from *Valeriana officinalis*
    - Artichoke Leaf Extract from *Cynara scolymus*
    - Tong-Xie-Yao-Fang
    - Tong-Xie-Ning
- Anticholinergics (-M3)
    - Mech: (refer to general CNS notes) but in pre NT bind nicotinic and post NT bind muscarinic with M-3 being the predominant one in the GI by increasing glandular secretions, increasing contraction amplitude (not stimulating), etc
    - GI drugs either agonize/antagonize the M3 receptors
    - Uses: spasming in IBS, diarrhea, used in the 1950s for PUD by decreasing acid
    - SEs: "spacy", sedating
    - Binary Amines (very effective but more CNS SEs)
        - **atropine**
        - **scopolamine (Scopace)** 0.4mg tabs, 0.4-0.8mg PO Q4hrs, patch
    - Tertiary Amines
        - **hyoscyamine (Anaspaz, Levsin, NuLev)** 0.125mg tabs/SL/SC/IM/IV, 0.125-0.25mg PO/SL/SC/IM/IV Q4hrs prn w/ max 1.5mg/d, anticholinergic, Duration: 4hrs, **Levbid** is an ER form that comes in 0.375mg tabs that can be taken Q12hrs
        - **dicyclomine (Bentyl)** 10,20mg tabs or 10mg/5mL liquid or 20mg IM, 20mg PO Q4hrs prn w/ max of 160mg/d, anticholinergic and inhibits bradykinin, Duration: 6hrs, no long acting form
    - Quaternary Amines (not as effective but less CNS SEs)
        - **clidinium/chlordiazepoxide (Librax)** 5/2.5mg tabs, 1-2tabs PO Qd, anticholinergic/anxiolytic, Duration: 24hrs
        - **methscopolamine (Pamine)** 2.5mg tabs, 2.5mg PO QID 30min before meals, anticholinergic used in PUD
    - Other
        - **Phenobarbital/Hyoscyamine/Atropine/Scopolamine (Donnatal)** 1tab PO BID
    - Old Drugs Not Used Anymore: Donnatal, many others
        - **propantheline (?)** 7.5,15mg tabs, 15-30mg PO BID, anticholinergic used in PUD
        - **glycopyrrolate (Robinul)** 1mg solution, 1-2mg PO/IV/IM TID w/ max 8mg/d, anticholinergic used in PUD

Anti-Emetics (-H1,-D2,-M1,-5HT3, etc)

- **NB the anti-emetic cocktail used for chemo induced N/V at MD-Anderson is Haldol/Ativan/Benadryl**
- CAM
    - Ginger 0.5-1g/d (-5HT3 activity, in morning and motion sickness, SEs: anti-platelet and mutagenic effect)
    - Pyridoxine <250mg/d (mechanism unknown, used in morning sickness, SEs: changes drugs levels, allergic rxn, neuropathy)
    - Acupuncture (specifically at the neiguan P6 point which is 3 fingerbreaths above the proximal palmar crease on the volar aspect of the midline wrist)
- Anti-Histamines (first generation) (-H1) = labyrinthine N/V
    - **Meclizine (Antivert)**
    - **Diphenhydramine (Benadryl)**
    - **Dimenhydrinate (Dramamine)**
    - **Hydroxyzine (Atarax/Vistaril)**
    - **Cyclizine**
    - **Cinnarizine**
    - SEs: sedation, weight gain, metabolic syndrome
- Anti-Cholinergic (-M1) = labyrinthine N/V
    - **Scopolamnine (Scopase)** PO/Patch
    - SEs: dry mouth, constipation, blurry vision and dilated pupils, urinary retention, tachycardia, dry skin (if severe can cause "Central Anticholinergic Syndrome" characterized by the addition of delirium)
- Anti-Serotonin (-5HT3)
    - **Ondansetron (Zofran)** 4,8,16,24 tabs or 4,8 ODT or 4/5mL solution = 8mg PO/ODT/IV/IM Q8 prn, SEs: headache, dizziness, constipation
    - SEs: abnl LFTs, headache
    - Mechanism: increases serotonin release from the first neuron in the complex neuro system that regulates motility thereby activating the whole system
    - **Granisetron (Granisol)**
    - **Dolasetron (Anzemet)**
    - **Tropisetron**
- Anti-Benzo (-GABA) = NV from anxiety
    - **lorezapam (Ativan)**

- Pro-Cannibinoid (+CB) = N/V from anxiety
  - **dronabinol (Marinol)** 2.5-10m BID (better than MJ b/c of predictability)
- Pro-Steroids (+Steroids) = N/V from chemo
  - **dexamethasone (Decadron)** 20mg IV
- Anti-NK1 (-NK1) = N/V from chemo
  - **aprepitant (Emend)**
- Benzamides (-D2/-M1/-5HT4) = N/V from GI stasis
  - **metoclopramide (Reglan)** 5,10mg tab or 5/5mL solution, 10-20mg PO/IM/IV/SC 30min before each meal and at bedtime, max duration 12wks!!! Mandated by FDA in 02/2009, use the liquid version not the pill, have pts sign a waiver w/ informed consent detailing SEs (mild SEs in 30% of pts and severe SEs in 10% of pts), use lowest effective dose, try drug holidays
  - **domperidone (Motilium)** less BBB crossing, acquire from outside the US or get FDA approval for research use, 10-30mg PO QID, check EKG for QT prolongation and electrolytes periodically!!!
- Phenothiazine & Butyrophenones (-D2/-H1/-M1)
  - **Promethazine (Phenergan)** 12.5,25,50 tabs/supp or 6.25/mL solution = 6.25-25mg PO/PR/IV/IM Q6 prn
  - **Prochlorperazine (Compazine)**
  - **Chlorpromazine (Thorazine)**
  - **Perphenazine (Trilafon)**
  - **Haloperidol (Haldol)**
  - **Droperidol (Inapsine)**
- SEs of Dopamine Blockade = increase LES and proximal stomach tone w/ only mild increase in motility
  - "Extra Pyramidal Symptoms" (EPS)
    - Acute Dystonia (occurs after ~4hrs) (common in young males) (Tx based on reciprocal relationship between acetylcholine and dopamine hence anticholinergics: Benztropine (Cogentin), Biperiden (Akineton), Trihexyphenidyl (Artane), Diphenhydramine (Benadryl) and never use Reglan again)
      - spasming of neck/back (opisthotonos) resulting in pt arching forward
      - spasming of SCM in neck (torticollis) resulting in neck moving to side
      - spasming of torso (pleurothotonos) resulting in a leaning posture
      - spasming of extraocular (oculogyric crisis) eyelid (blepharospams)
      - spasming of laryngeal muscles (laryngospams) resulting in resp compromise
      - spasming of mouth/tongue/jaw
      - spasming of vocal cords
    - Akinesia (occurs after ~4d) (treat with anticholinergic agents or dopamine agonists)
      - Parkinsonian-like symptoms
    - Akathesia (occurs after ~4wks) (treat with beta blockers, benzodiazepines, or vitamin E, decrease dose and switch to other agent)
      - inner restlessness/anxiousness manifesting as difficulty remaining still
    - Tardive Dyskinesia (TD) (occurs after ~4mo usually >1yr) (irreversible if agent is continued, do NOT use anticholinergic, interestingly reducing dopamine blocker actually temporarily worsens TD, best approach is prevention w/ judicious use of neuroleptic and drug holidays)
      - tongue fasciculations (tongue darting) → lingual/fascial hyperkinesias (lip smacking and chewing)
  - Hypothalamic Effects
    - increased prolactin (resulting in decreased libido, amenorrhea, gynecomastia, galactorrhea), change in appetite, change in temperature regulation
  - Neuroleptic Malignant Syndrome (refer to general ID)

Upper Prokinetic

- **Dopamine Antagonists** (refer)
- **Serotonin Agents**
  - **Tegaserod**
  - **Prucalopride**
- **Motilin Agonists**
  - **Erythromycin** 250mg PO TID or 3mg/kg IV Q8hrs, IV better than PO, give 30min before EGD for GIB, no antiemetic effect, NB tachyphylaxis occurs, SEs: cramps, N

Lower Prokinetic (Anti-Constipation)

- Definition
  - Laxatives (anything that promotes defecation)
    - Purgatives (laxative that produces large volume)
    - Lavages (laxative that results in no net absorption/secretion)
    - Emollients/Aperients/Softeners (laxative that increases water content)
- General Approach (sometimes it is good to purge the pt w/ PEG for a few days to clear everything out and then titrate PEG back until pt has 1 BM/d, if impaction is a problem use a suppository or enema every day,
  - 1st: fluids (>2L/d), exercise, avoid constipating meds, dietary bulk laxatives, education (promptly respond when you feel the urge to defecate, capture the gastrocolic reflex, schedule a time to defecate every day, place a support under feet to keep hips flexed as much as possible like squatting in a forest, use chest/ab muscles when bearing down, etc)

- 2nd: supplementary bulk laxatives (Benefiber, Citrucel, Fibercon, PEG)
- 3rd: mild osmotic laxatives (magnesium salts)
- 4th: mild stimulant laxatives (bisacodyl)
- 5th: enemas (soap suds, tap water, saline, PEG) & suppositories (glycerine, bisacodyl)
- 6th: strong osmotic laxatives (lactulose)
- 7th: strong stimulants laxatives (senna)
- 8th: strong enemas (Hypaque)
- 9th: last resort drugs and consider primary constipation workup (above)

- *Bulk Laxatives* (very large molecules that do not add any osmotic force rather they just trap water so that it can't be absorbed creating a large bulky mass that stimulates peristalsis, no alteration of water/electrolytes, the more bacterial breakdown the less effective and more SEs of bloating and flatulence, take with plenty of water b/c if not obstruction can occur, should not be taken before/with meals b/c can delay gastric emptying, only effective in pts with normal transit times and normal defecation dynamics, add more fiber (20-30g/d) to your diet by eating more food w/ whole grains, raw bran, vegetables but there are SEs of bloating/flatulence and if pts are unable to naturally increase fiber diet then consider OTC supplements 4-6g/d, there is also an increased r/o impaction)
  - **1st Line (synthetic fibers that undergo no bacterial degradation): Methylcellulose (Citrucel), Pylocarbophil (Fibercon, Equalactin)**, **Polyethelene glycol-PEG (MiraLax, GlycoLax, Dulcolax)** 17g (~1 scoop) in 8oz of water PO QD until BM but highly variable in dosing
  - **2nd Line: Guar Gum from seed of the *Cyamopsis tetragonoloba* plant (Benefiber)** (natural fiber that undergoes LITTLE bacterial degradation)
  - NB Psyllium from husk of the *Ispaghula* plant (Metamucil) (natural fiber that undergoes bacterial degradation, there are reports of asthma/anaphylaxis therefore avoid if possible)
  - **Dietary Soluble Fibers**
    - Dissolve in water and are ferments by colon bacteria
    - Action:
    - Examples: Oat Bran, Pectins, Gums, Mucilages, etc
  - **Dietary Insoluble Fibers**
    - Do not dissolve in water and are not fermented by colon bacteria
    - Action: add bulk to stool promoting bowel movements
    - Examples: Wheat Bran, Cellulose, Ligan, etc
- *Osmotic Laxatives* (draw water into lumen which softens stools, can be given chronically unlike stimulant laxatives)
  - Poorly Absorbed Ions (create a hyperosmolar lumen pulling water in, try to avoid b/c they teach your colon bad habits such that some pts cannot have a BM w/o a laxative also pts can easily get magnesium toxicity if they have CKD or young/old)
    - Mg Salt: **magnesium citrate (Evac-Q-Mag)** 150-300mL PO QD-BID until BM, **magnesium hydroxide (Phillips MOM)** 15-30mL PO QD-BID until BM, **magnesium sulfate (Epsom Salt)** 15g PO QD until BM
    - SO4 Salt (rarely used)
    - PO4 Salt (rarely used)
  - Poorly Absorbed Sugars
    - **lactulose (Kristalose)** 10g/15mL 15-30mL PO QD-BID until BM (does undergo bacterial degradation leading to bloating and flatus, lactulose is like lactose except that the bond connecting to the two sugars is flipped)
    - sorbitol (Cystosol)
  - Other
    - **glycerin**
- *Stimulant Laxatives* (directly act on mucosa (epithelia/nerves/muscle) increasing motility and secretion of water via electrolyte secretion, exact mechanism is unclear, avoid long term use b/c pts can theoretically develop tolerance and cathartic colonic atony b/c of smooth muscle atrophy and damage to myenteric plexus, not actually true nevertheless only use on PRN basis <3x/wk)
  - Diphenylmethanes
    - **bisacodyl (Dulcolax, Correctol)** 5-15mg PO Qhs prn
    - picosulfate (Lubrilax, Sur-Lax)
    - Other: phenolphthalein (can cause cancer!!!)
  - Anthraquinones (produced by plants, converted by colonic bacteria to active forms, metabolites can be detected in urine, causes psuedomelanosis coli (refer))
    - **senna (Senakot, Ex-Lax)** 187mg PO QD prn
    - **Other: cascara, castor oil, aloe, senna, rhubarb, frangula** (not used much anymore b/c of severe cramping)
- *Enemas* (softens stool, stimulates colonic muscle to contract, and physically helps with evacuation of hard stool, always direct nozzle posteriorly)
  - **Soap Suds 1500mL, Tap Water 500mL, Saline 500mL Enema** (greater return but more discomfort and mucosal irritation)
  - **Polyethylene Glycol w/ Electrolyte Enema** (less return but less discomfort and mucosal irritation)
  - **Sodium Biphosphonate (Fleet Enema)** (NB no longer used b/c can cause hyperPO4!!!)
  - **Hypaque/Veripaque Enema** (water soluble contrast material like gastrografin but used for colon, good b/c clears out colon but also is like a barium enema therefore use for also used for diagnosis when you are suspecting constipation due to an anatomic problem like volvulus, done by radiology)
- *Suppositories* (good for immediate effect)
  - **Glycerin** suppository PR prn
  - **Bisacodyl** suppository PR prn

- *Stool Softeners* (main effect is the detergent effect which allows water to interact more effectively with solid stool thereby softening it, does not actually work even though it sounds like it would be effective)
    - docusate sodium (Colace, Regulax SS, Surfak) 100mg PO QD-BID prn
- *Lubricating Emollients* (lubricates the outside of stool, aspiration can result in lipoid pneumonia, long term use can cause fat-soluble vitamin deficiency and anal seepage, hence not used much anymore)
    - mineral oil (Fleet Mineral Oil) 12-45mL PO Q6-8hrs prn
- *Last Resort Drugs*
    - New Drugs
        - Promoting bile acid presence into colon via cholic acid (Ox Bile) or a new drug called A3309 which inhibits TI bile acid transporter
    - CAM
        - Herbals
            - Aloe (*Aloe barbadensis*) stimulant
            - Apple pectin (?) fiber
            - Cascara (*Rhamnus purshianus*) stimulant
            - Hibiscus (*Hibiscus sabdariffa*) stimulant
            - Raspberry (*Rubus idaeus*) ?
            - Rhubarb (*Rheum palmatum*) stimulant
            - Yellow Dock (*Rumex crispis*) ?
        - Colonic Irrigation ("Colonics")
            - colonics are administered by a "trained" person unlike enemas which are self-administered
            - device that controls water flow, temperature, pressure
            - the idea was born out by Sir Arbuthnot Lane in the early 1900s who theorized that toxins originating in the intestine enter circulation and poison the body
            - SEs: amebiasis, rectal perforation
    - Chloride Channel Type 2 (ClC-2) Agonists (allowing for increased chloride secretion into lumen pulling sodium and thus water with it)
        - **lubiprostone (Amitiza)** 8-24mcg PO BID prn (SEs: SOB/N/D/HA for a few hours after taking medicine)
    - 5-HT4 Agonists
        - **tegaserod (Zelnorm) and cisapride (Propulsid)**
        - **prucalopride (Resolor)** is a new agonist that does not interact w/ hERG channel (human Ether-a-go-go Related Gene) which is thought to be the channel that the above agents interact with causing lethal dysrhythmias
        - **? velusetrag**
        - **? naronapride**
        - **? renzapride**
    - Cholinergic Agonists(+M3) (appear to be effective in constipation due to anticholinergic effects of other drugs)
        - Uses: constipation by increasing coordinated muscle activity, ACPO, can also be used to alleviate the anticholinergics SEs of meds like Elavil, consider in GERD b/c increased LES tone but always give with a PPI b/c cholinergics increase acid production
        - SEs: N/V, defecation, cramping, sweating, salivation, urination
        - **Agonist: bethanechol (Urecholine)** 10mg PO QD for constipation
        - **ACE Inhibitor: neostigmine (Prostigmine)** 15mg PO TID-QID for ACPO
    - Prostaglandin Agonists
        - **misoprostol (Cytotec)** 100-200mcg PO BID-QID (significant SEs and data limited therefore rarely used)
        - **colchicines (Colsalide)** 0.6mg PO TID (significant SEs and data limited therefore rarely used)
    - Opiate Antagonists methylnatrexone/alvimopan (opioid antagonist like naltrexone but with methyl group so it doesn't cross into CNS therefore not blocking analgesic effects) (refer to motility notes)
    - Neurotrophic Factors NeuroTrophin-3 (NT-3) (growth factor involved in the development of the enteric nervous system, its action or role in adults is unclear (may promote neuron growth or modulate synaptic transmission) nevertheless a multicenter RDBPC study assessed the effect of 4wks of 3mg 3x/Qwk SC injection NT-3 in 107 pts w/ Rome III defined functional constipation and found that NT-3 led to significant increases in BM frequency, complete BMs, colon transit)
        - Parkman HP, et al. Neurotrophin-3 Improves Functional Constipation. AJG. 2003;98:1338.
    - Guanylate Cyclase-C Agonist **linaclotide (Linzess)**
    - Inhibit Bile Acid Uptake: **elobixibat**

Antacids

- History: crushed coral, milk products eg. Sippy diet, etc
- Mech: weak base that reacts with gastric acid to form water and salt and since pepsin is inactive at pH>4.0 enzyme activity is diminished, all act nearly immediately but must take frequently to have a lasting effect b/c one dose is short lived (~1-2hrs)
- Types: Tums ($CaCO_3$), Rolaids ($CaCO_3$), Maalox ($CaCO_3$), AlternaGel (AlOH), Mylanta (AlOH/MgOH), Alka-Selzer ($NaHCO_3$)
    - NB Citric Acid/ Na Citrate (Bicitra) (Cytra-2) is no longer used
    - NB OTC magnesium alginic acid (Gaviscon) mixes with saliva to form a highly viscous solution that floats on the gastric pool acting as a mechanical barrier
    - NB some have simethicone with it
- Dosing: 1-2 or 5-10mL Q4hrs (liquids are better)

- SEs: metals can chelate medicines therefore take 2hrs after taking other meds, since Ca stimulates gastrin release its effect is counterproductive and one can have rebound acid afterwards, constipation (Al) vs diarrhea (Mg), hyper-metal in pts w/ RF, white speckled stool, belching/flatulence/stomach-rupture from increased CO2, hypernatremia precipitating HTN/CHF

Histamine 2 Blockers (H2Bs)

- Mech: reversibly inhibit histamine activation of parietal cells from producing cAMP which in turn stimulates proton pump secretion of gastric acid
- Tachyphylaxis is controversial but does occur when you are concurrently taking PPI therefore when taking a PPI take H2B prn Qhs (effective at night b/c of the nocturnal secretion of gastrin/ACh) or before certain refluxogenic meals (eg. Mexican food)
- Faster acting than PPI therefore good for symptomatic relief while PPI are for good long term effect
- Compared to PPI H2B are not as good at inhibiting acid but they are still pretty good

H2B	Equivalent Dose (NB OTC doses are ½ the Rx dose) (NB PO=IV)	PK	PD	SEs HA, AMS, D, rash, hepatitis, nephritis, increases EtOH levels, myelosuppression (very uncommon)
famotidine (Pepcid) OTC Generic Formulary 40mg	20,40mg tabs or 40mg/5mL solution 20-40mg PO BID (can be crushed and go down NGT) 20mg IV Q12	Onset: 2hr Duration: 8hrs	All are Hepatically Metabolized (except Axid) and Renally Cleared	• Both are generally equivalent Zantac works a little faster
ranitidine (Zantac) OTC Generic 150mg	150,300mg tabs or 15mg/mL solution 150-300mg PO BID 50mg IV Q6h	Onset: 1hr Duration: 8hrs		
nizatidine (Axid) OTC Generic 150mg	150mg tabs or 15mg/mL solution 150-300mg PO BID NO IV	Onset: 1hr Duration: 8hrs		• Not used much anymore
cimetidine (Tagamet) OTC Generic 300mg	200,300,400,800mg tabs 400-800mg PO TID 300mg IV Q6	Onset: 1hr Duration 6hrs		RARELY USED BC OF SEs • P450 enzyme inhibition resulting in decreased metabolism of several drugs • Antiandrogen and prolactin stimulation • metabolic encephalopathy in older pts esp with liver/kidney dz

Proton Pump Inhibitors (PPIs)

- History: in the 1970s antiviral for HCV were being developed and one of them was accidentally found to decrease acid in the stomach
- Mech: when exposed to acid they activate but b/c the stomach is so acidic they are actually destroyed hence PPIs are enteric coated (NB Zegerid uses NaHCO3 to protect it), they reach the SI intact, absorbed, circulate in blood taking 1-2hrs to reach parietal cells, cross membranes and activate in acidic environments forming an irreversible covalent bond w/ PPs inhibiting them (hence concurrent H2B use actually makes PPIs less effective, hence take 30min-1hr b/f breakfast so that when PPIs reach the parietal cell there is a stimulus aka food for acid to allow for their activation, when fasting only 5% of PPs are active vs during meals 70% of PPs are active!!!)
- NB PPIs do not make the pt fully achlorydric
- NB in ZES you need very high doses like 240mg/d
- Isomers (Dexilant and Nexium) last longer b/c they are stereoisomers
- Vimovo (naproxen and esomeprazole) is coming out soon
- Lifelong PPI: erosive esophagitis, HP negative ulcer dz who require chronic NSAIDs, ZES if all of tumor cannot be resected, esophageal stricture, Barrett's
- BID PPI if persistent esophagitis or documented low pH on QD
- Always try to titrate down dose b/c of rebound hyper acid secretion
- All are comparable except Dexilant which is the strongest and less food dependent
- Drug Interaction
    - Least (Dexilant) vs Most (Prilosec) others less studied
    - Interactions

        - (1) increase gastric pH which could affect the non-ionized state and thus absorption of certain meds that are absorbed in the stomach (even though this occurs it likely accounts for only a small percentage of drug interactions rather it is the effect on CYP that is of main concern)
        - (2) alter P-glycoprotein system
        - (3) alter CYP-2C19/3A4 (3% of whites and 15% of Asians are deficient)
    - Even though there might be in-vitro drug-drug interactions in most cases there is minimal in-vivo effect (eg. Plavix) nevertheless if you suspect a problem just change to Protonix and separate 12hrs from other meds
    - Types
        - Decrease: Clopidogrel, PIs, PCNs/Cephs, Iron, Azoles (requires acidic environment for absorption), Mesalamine (premature dissolution of enteric coated granules in acidic pH), Coumadin, PCNs
        - Increase: Benzos, SSRIs, ACE, MTX, Cyclosporine, Digoxin (requires alkaline environment for absorption), Phenytoin
    - Plavix (NEW STUDY INDICATES THAT DEXILANT DOES NOT INTERFERE)
        - P450 2C19 isoenzyme converts pro drug clopidogrel (no AP activity) to active metabolite ? (AP activity) & PPIs competitively inhibit 2C19 isoenzyme
        - this prompted many studies which demonstrated that the concurrent use of omeprazole w/ clopidogrel resulted in impaired platelet fxn via ex vivo platelet function assay and this resulted in the FDA placing a black box warning on 11/17/09
        - this sparked much debate including post hoc analyses from prior RCTs: Clopidogrel for the Reduction of Events During Observation (CREDO) & Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition (TRITON-TIMI) = there was no change in endpoints of death/MI/CVA with concurrent Plavix/PPI use, but these post hoc analysis need to be validated w/ RCTs, the first was Clopidogrel and Optimization of Gastrointestinal Events (COGENT) but was prematurely stopped b/c of financial problems however the initial data indicated that there was no change in CV outcome (CV death, MI, CVA) (RRR 0.99, CI 0.68-1.44) in pts who received Aspirin+Plavix w/ omeprazole vs Aspirin+Plavix alone but there was decreased GI events (RRR 0.34, CI 0.18-0.63) over a 6mo period
        - so despite the attenuation of the pharmacodynamic effects clinical outcomes are not affected, regardless most say just to separate meds 12hrs apart though this is not supported by any trial, the effect of other PPIs is unclear therefore switching to another is not recommended
        - NB cimetidine and AA may have similar effects but other H2B should be fine

Name	Route (IV = PO)	PK	PD	SEs
Pantoprazole (Protonix) Generic	20,40mg tab/granule 40-120mg BID	Duration: 24hrs (tells you how frequent to take medicine, but after each meal new PPs are made hence some advocate taking before each meal, this is in contrast to H2B which when they inhibit they inhibit parietal cells)	M: Hepatic E: Renal/Hepatic But no adjustments need to be made for liver/renal impairment Acid labile and thus are enteric coated or given with antacids: omeprazole + NaHCO3 (Zegerid)	Approach: check Qyr labs (Ca, Mg, VitB12, Iron Studies, VitD), have pt get a DEXA by their PCP, advise about med interactions, remind that polyps are common, at higher risk of infections, headache is the most common SE, review meds • Drug Interaction (refer above) • Growths o concern that hypergastrin state would stimulate ECL tumors like Carcinoid and CRC (this is seen in rats but not in humans) o fundic gland polyps • Infection o Pneumonia o C.diff and other enteric infections o SBP o SIBO • Other o Headache (most common!!!) o Interstitial Nephritis (rare but important to know b/c serious) o Microscopic Colitis • Deficiencies o Osteoporosis, still very controversial, mechanism: (1) inhibited gastric acid diminishes Ca absorption, (2) hypergastrinemia induces hyperparathyroidism, (3) directly modify acid-related enzymes in bones that regulate remodeling o VitB12 malabsorption b/c PPI decrease acid which is necessary to
ESomeprazole (Nexium) S isomer of omeprazole	20,40mg cap/powder/IV 20-40mg QD	Duration: 72hrs		
Omeprazole (Prilosec) Generic OTC	10,20,40mg tab/cap/liquid 20-40mg QD	Duration: 72hrs		
Dexlansoprazole (Kapidex, Dexilant) S isomer of lansoprazole	30,60mg tabs 30-60mg PO Qd	Duration: 24hrs		
Lansoprazole (Prevacid) Generic OTC	15,30mg Cap/Tab/Granule, 15-30mg PO Qd	Duration: 24hrs		
Rabeprazole (Aciphex) • Different P450 metabolism	PO (Tablet) 20	Duration: 24hrs		

therefore good in pts who are refractory others or who are elderly and on a bunch of meds				cleave VitB12 from protein and also decreases acid in SI which leads to SIBO and VitB12 consumption o Hypomagnesemia, mechanism is unknown, on 03/11 the FDA announced a warning of symptomatic hypomagnesemia, rare but when it occurs it is significant w/ EKG changes and refractory to IV therapy o Iron Deficiency (in theory but not clinically seen)

Pain

- **General**
  - **Acute** (painful stimulus is appropriately appreciated) **vs chronic** (aberrant sensation)
  - **Pathway:** Nociceptor (free nerve ending in tissue) can be activated in various ways (chemical, mechanical, thermal) and their cell bodies are in the dorsal root ganglion (other inputs include interneurons and descending inhibitory neurons) and then a second neurons mediate the signal to the thalamus (spinothalamic tract which mediates intensity/localization of pain and the spinohypothalamic tract which mediates autonomic response to pain) neurons are then sends signal to sensory cortex (where pain is), limbic system and frontal lobe (affective response to pain), hippocampus (memory of pain)
    - +: glutamate, substance P, calcitonin gene related peptide, brain derived neurotrophic factor, bradykinin, histamine
    - -: encaphalins, beta-endorphin, GABA, glycine, 5-HT
- **Nociceptive Somatic** (aching, stabbing, throbbing, etc) damage to soft tissue
  - Tx: Tylenol then NSAIDs then Opioids/Tramadol
- **Neuropathic & Nociceptive Visceral** (unfamiliar, burning, electric, tingling, numbness, etc) damage to nerves, NB Paresthesia (non-painful tingling) vs Dysethesia (painful tingling) vs Allodynia (pain 2/2 to a stimulus that does not normally cause pain) vs Hyperalgesia (mild noxious stimulus results in out-of-proportion pain)
  - Tell pts that these meds are used to Tx various other painful conditions like migraines, postherpetic neuralgia, diabetic neuropathy and that they are not at the dose used to Tx psychiatric conditions even though some pts might need that strength
  - Tx (start w/ low doses, must try for >1mo to say a drug is working or not, taper very slowly if stopping)
    - Calcium Channel Ligands: Gabapentin (Neurontin) first then Pregabalin (Lyrica) b/c of cost
    - AEDs: carbamazepine (Tegretol) 800-1200mg QD, take w/ food, many SEs, follow CBC/LFTs
    - TCAs (increase by 5mg Qwk)
      - amitryptiline (Elavil) 10-50mg PO Qhs (does not change mood at these doses, takes a few weeks to work, use cautiously in elderly, can constipate b/c of anticholinergic effects)
      - nortriptyline (Pamelor) 10-50mg PO Qhs (less sedating)
      - desipramine (Norpramin) 10-50mg PO Qhs (less anticholinergic activity thus less constipating)
    - SSRIs: (less effective but use if SEs despite low dose TCAs)
    - SNRIs: esp duloxetine (Cymbalta) and venlafaxine (Effexor) (recently studied and found to be helpful)
- Other modalities of achieving analgesia
  - Injections, Nerve Blocks, Spinal Cord Stimulators, Rhizotomy (surgically cut neurons at dorsal root ganglion), Neuraxial Infusion, Biofeedback, Transcutaneous Electrical Nerve Stimulation (TENS), Acupuncture (life force aka "qi" runs thru meridians through-out the body, disruption of this flow causes Sx and this can be reversed via puncture of acupoints), Hypnosis, Massage Therapy, Bisposphonates (bone pain), muscle relaxants, steroids can actually improve pain, topical local anesthetics (Lidoderm, Emla, Capsaicin, OTC LMX4), methylacrylate for vertebreal compression fractures
  - Lidocaine Patch
  - Capsaicin (selectively impair nociceptive C-type pain fibers, derived from a pepper)
  - "OT Consult for Complementary Tx of pain"
  - PM&R Consult
  - Screen for Depression and Tx

Opioid Ladder

- Approach
  - Begin IR Opiates (Q2-4hrs NEVER Q6hrs) (eg. 15mg of Morphine-PO = 1mg of Sublimaze-IV)
    - morphine suflate (Morphine-PO/PR ~15, Roxanal-Transmucosal Dropper ~15, Morphine-IV ~5)
    - hydrocodone (?-PO ~10)
    - oxycodone (OxylR/Oxydose/OxyFast-PO ~10)
    - hydromorphone (Dilaudid-PO/PR ~3, Dilaudid-IV ~0.75)
    - fentanyl (Actiq-Lollipops ~1, Sublimaze-IV ~1)

    - After stable for a few days look at total need for opiates past 24hrs and calculate for SR Opiates along w/ breakthrough opiates but decrease dose and frequency (NB convert all IR opiates to Morphine-PO equivalents and then convert to SR opiates)
        - morphine sprinkles (Avinza, Kadian) Q12-24hrs
        - morphine pill (MS Contin, Oramorph SR) Q8-12hrs
        - fentanyl transdermal patch (Duragesic) Q48-72hrs
        - oxycodone pill (Oxycontin) Q8-12hrs
- NB opiates not used anymore
    - Hydrocodone (?) never used alone, always in combination
    - Codeine (?) never used except as antitussive
    - Propoxyphene (Darvon) never used ???
    - Meperidone (Demerol) is no longer used b/c pts really like it b/c it gives them a high thus high r/o addiction and there is increased r/o seizures when used chronically
    - Methadone (Methadose) rarely used b/c long QT except in pts w/ renal failure, when all other opiates have failed, in pts w/ concurrent neuropathic pain
- General
    - Opioids: exogenous (opiates) vs endogenous (endorphins-mu, enkaphalins-delta, dynorphins-kappa) NB narcotics are any drug that causes you to sleep
    - Mechanism: bind mu (all exogenous drugs, affects all organs) / kappa (no exogenous drugs, only brain analgesia) / sigma (no exogenous drugs, only spinal cord analgesia) receptors
    - Effects (tolerance develops to CNS effects but NONE of the other organ systems!!!)
        - CNS: euphoria, analgesia, sedation, miosis, decreased respiratory drive
        - GI: N/V, C, sphincter of oddi contraction
        - Skin: pruritus
        - GU: urinary retention
        - Pulm: antitussive
    - Intoxication: naloxone (Narcan) IV works w/in 1-2min but short t1/2 therefore you might have to give several doses NB naltrexone (Revia) PO is only used to decrease analgesic effect of alcohol
    - Withdrawal: clonidine
    - Heroine is very lipophilic hence more can get into brain and much more quickly
    - for liver pts use tramadol (Ultram, SEs: SEIZURES), opioids at lower doses, weaker opiates
    - for renal pts similar to liver pts but try to use methadone
    - there is no ceiling dose (some pts require a lot of opioid) but combination products do have ceilings b/c of Tylenol/NSAIDs
    - remember that opiates peak @30-60min for oral and @10-30min for IV
    - if pt is chronic opiates try to rotate them to determine the best opioid in terms of efficacy/SEs
    - always coadminister laxatives (consider Relistor/Alvimopan if severe)
    - If pt is having sedating effects 2/2 opiates add stimulants (Ritalin, Provigil, etc)
- PCA Pump
    - 1st choose opioid based on allergy, asthma, kidney dz, liver dz
    - 2nd choose dosing based on if pt is normal, has greater analgesic needs (SCD crisis, palliative care, opioid tolerance) or risk for overdose (old, OSA, obese, COPD, opioid naïve)
    - NB there exists an order set and call pharmacy to help with dosing

	Morphine	**Dilaudid**	**Fentanyl**
Loading Dose	2.5-4mg	0.2-1mg	12.5-50mcg
Pt Controlled Bolus Dose	0.7-1.2mg Q6min prn	0.1-0.4mg Q8min prn	10-40mcg Q10min prn
Nurse Controlled Bolus Dose ?			
Continuous Dose	0-2mg/hr	0-0.3mg/hr	0-25mcg/hr
Precautions	allergy, asthma, kidney dz, liver dz	allergy, liver dz	allergy, kidney dz

Analgesic Combos

- Mild: hydrocodone+tylenol (Lortab, Lorcet, Norco, Vicodin), propoxyphene+tylenol (Darvocet), propoxyphene+aspirin+caffeine (Darvon), codeine+tylenol (Tylenol #2(15/300), #3(30/300), #4(60/400)), codeine+aspirin (Empirin w/ Codeine), tramadol+tylenol (Ultracet) NB only use combos w/ 325mg Tylenol
- Mod: oxycodone+tylenol (Percocet), oxycodone+aspirin (Percodan) NB these are rarely used
- For Liver Pts: same just specify <2g/day APAP

Muscle Relaxants

- Other: stretching, hold off on intense exercise, address stess, hydrate, check and correct electrolytes sme just give tums and potassium, quinine

- Skeletal: carisoprodol (Soma), metaxaline (Skelaxin), baclofen (Lioresal), cyclobenzaprine (Flexeril TID vs Amrix QD take at night to sleep well and then it wears off during the day so you are not sedated), methocarbamol (Robaxin), tizanidine (Zanaflex), orphenadrine (Norflex)
- Smooth: CCB, Nitrates

Acetaminophen (Tylenol)

- (refer to acute liver disease)
- Effects
    - **Analgesic**
    - **Antipyretic**
    - NOT an Anti-Inflammatory (b/c acts only at the CNS not in the periphery where inflammation occurs)
- NB phenacetin (no longer made b/c of renal toxicity)

NSAIDs (refer to stomach notes)