Bone, Joint and Rheumatology

Gout

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Signs/Symptoms

- Uric Acid Elevation
- Pain
- Redness
- Swelling
- Usually singular joint

Classic Risk Factors

- Obese
- Alcohol (excessive)
- Meats/Seafood
- Drugs

Classic Drugs That Increase Uric Acid

- Diuretics (thiazides)
- Niacin
- Cyclosporine

Acute Treatment Options

- NSAIDs
  - GI, CHF, Kidney
- Steroids
  - Hyperglycemia, GI, Insomnia
- Colchicine
  - Diarrhea
  - 3A4 inhibitors may increase concentrations

Chronic Management

- Xanthine Oxidase Inhibitors
  - Allopurinol
  - Febuxostat
- Colchicine
  - Diarrhea, GI adverse effects
  - Dose adjusted with poor kidney function
- Probenecid
  - Rarely used
  - May raise penicillin anbx concentrations
  - Promotes excretion of uric acid through kidney (avoid in CrCl <30)

Osteoarthritis

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Osteoarthritis Symptoms

- Pain after longer periods of use
- Stiffness after resting
- Potential change in the shape of ends of fingers (DIP)
- Not much inflammation (differentiator from RA)

Pain Impact

- Quality of life
- Sleep
- Function/ability
- Work/Volunteerism
- Appetite
- Exercise
- Mood

Treatment for OA

- Trial of hot/cold
- Massage
- Acetaminophen
- NSAIDs
- Opioids
- Steroid injections
- Topicals

Acetaminophen

- 4 gram max
- Lots of variation in dose
- Short half life
- Safest agent especially in elderly
- Combo products

NSAIDs – Risk

- GI
- CKD
- CHF
- HTN
- Cardiovascular risk boxed warning

NSAID Pearls

- Ibuprofen
  - OTC
  - Short ½ life
- Naproxen
  - OTC
  - Longer ½ life
  - Maybe cardiovascular risk is less/neutral
- Ketorolac
  - 5 days or less (boxed warning)
- Indomethacin
  - Higher GI risk

COX-2 Inhibitor

- Celecoxib
  - Same issues as NSAIDs
  - Exception: GI bleed is less
    - Remember that elderly patients are usually on antiplatelet/anticoagulant therapy
    - Risk similar if on baby aspirin

Common Opioids

- Tramadol
- Tylenol #3
- Morphine
- Oxycodone
- Fentanyl
- Hydrocodone
- Methadone

Important Approximate Conversions

- Morphine (oral) 30 mg
- Oxycodone 20 mg
- Tramadol 300 mg
- Fentanyl (patch) 12 mcg
- Hydrocodone 30 mg

Opioid Adverse Effects

- GI
- Constipation
- Sedation
- Cough suppression
- CNS
- Itching
- Tolerance/Dependence/Addiction risk

Opioid Pearls

- Oxycodone
  - In combo with APAP or alone
  - Very commonly used
- Hydrocodone
  - Combo with APAP

Opioid Pearls

- Tramadol
  - Seizure
  - Serotonin
- Morphine
  - Kidney disease
  - Gold standard
  - Hospice
- Codeine
  - Prodrug (2D6)
  - Acetaminophen

Opioid Pearls

- Fentanyl patch
  - Very potent
  - Disposal concerns
  - Slow onset/offset
  - Potential absorption issues
  - Convenient
- Methadone
  - QTC
  - Conversion sucks
  - Sometime seen in hospice

Topical Medications

- Good option for elderly if only a few locations of pain
- Capsaicin
  - Avoid prn use
  - Substance P
- IcyHot, BenGay etc.
- Lidoderm patch
  - $$$

Steroids

- Acute inflammation
- Injection to site of pain
  - Still has systemic effects

Glucosamine/Chondroitin

- Potential option for OA
- Takes time to work
- Be sure dose is adequate – target 1,500 mg
- If beneficial continue…if not, DC

Osteoporosis

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WHO Classification

- Normal; T-score greater than or equal to -1.0
- Osteopenia; -1.0 to -2.5
- Osteoporosis; -2.5 or below

Risk Factors

- Female
- Age
- Low BMI
- T-score
- Steroid use
- Smoking
- ETOH
- Hyperthyroidism (chronic)
- Prior Fracture
- RA

Treatment

- Bisphosphonates
- Denosumab
- Calcitonin
- SERM (Raloxifene)
- Teriparatide
- Estrogen

Bisphosphonates

- Bone resorption inhibitors
- Administration Procedure
  - Before other meds/food
  - Glass of water
  - Remain upright
  - Try to avoid esophageal ulceration
- Osteonecrosis
  - Extremely rare, most occurrences surrounding oral surgery
- IV (zoledronic acid, ibandronate)
- Reassess use after 5 years

Denosumab

- SubQ injection every 6 months
- Hypocalcemia risk; monitor phosphorus and magnesium as well
- Rare osteonecrosis risk
- $$$

Calcitonin

- Nasal spray used most often
  - Rhinitis and nose bleed
- Potential compression fracture benefit
- Storage/Admin pearls
  - Store upright
  - Prime 5 times before use
  - Discard after 30 doses or 35 days

Raloxifene

- Breast cancer indication
- DVT/Cardiovascular disease warning
- Side effects
  - Hot flashes
  - Edema

Teriparatide

- Builds Bone (osteoblasts)
- SubQ – once daily
- $$$
- Warning – osteosarcoma in rats
  - Use longer than 2 years is not recommended

Other Considerations

- Vitamin D
- Calcium
- Exercise, strength building, weight bearing
- Fall risk

Classic Medication Contribution

- Steroids
- Anticonvulsants
- Thyroid supplements
- PPI’s
- TZD’s

Rheumatoid Arthritis

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Rheumatoid Arthritis

- Inflammation
- Painful
- Joint Swelling (big difference with OA)
- Typically symmetrical
- CRP, RF, ESR, ANA

RA Versus OA

- RA
  - Onset middle age/anytime in life
  - Quick onset – Weeks to months
  - Inflammation/Swelling
  - Both sides of the body affected
  - Stiffness can last much longer throughout the day
  - Whole body symptoms possible (fatigue, feeling sick)

DMARDs

- Methotrexate
  - Once weekly up to 20-30 mg
  - LFT’s, CBC, immune system suppression, Folic acid
- Sulfasalazine
  - GI upset, rash, CBC, LFT’s
- Hydroxychloroquine
  - CBC, LFT’s, eye exams
- Leflunomide
  - LFT’s, CBC, diarrhea, skin reactions, hair loss

DMARDs - Biologics

- Etanercept (once weekly), adalimumab (every 2 weeks), infliximab (infusion), etc.
- Injection site reaction
- Infection risk

Flare Medications

- Steroids
  - Minimize dose
  - Minimize duration
    - Osteoporosis, GI, Diabetes, Insomnia, Weight gain, HTN
- NSAIDs
  - GI, Kidney, HTN, CHF

Cardiovascular

Advanced Cardiac Life Support

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Symptoms – Cardiac Arrest

- Unresponsive
- No respirations
  - Or irregular gasping with no definable breaths
- Pulse unidentifiable
- 911
- CPR performed
  - 30/2 – compressions/breaths
- AED

VFib - VTach

- Shockable rhythm
- CPR if still applicable, patient still unresponsive
- Shock twice
  - If no effective administer epinephrine every 3-5 minutes
- Amiodarone third line consideration if Epinephrine and AED shock failure

Asystole, Pulseless Electrical Activity (PEA)

- Non-shockable rhythm
- Epinephrine every 3-5 minutes
- Continue CPR compressions/breaths

Other Agents

- Adenosine for supraventricular tachycardia
  - Slows conduction through AV node
- Atropine for bradycardia (HR <50)
  - Anticholinergic
  - Blocks effects of vagus nerve, increases heart rate
- Dopamine
  - Second line agent if atropine not beneficial for bradycardia
  - Increase in HR and contractility

Take a Look – ACLS Algorithm

- https://www.uwhealth.org/files/uwhealth/docs/pdf4/EEC/acls_algorithms.pdf

Acute Coronary Syndromes

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ACS

- STEMI
  - S-T Elevation
  - Biomarkers
- Non-STEMI
  - No S-T Elevation
  - Biomarkers
- Unstable Angina
  - Chest pain at rest
  - New onset, limits activity
  - Increase or worsening in symptoms
  - No Biomarkers

Symptoms of MI

- Chest pain
- Pressure
- SOB
- N/V
- Fainting
- Women can present with atypical symptoms

Causes of MI

- CAD
- Plaque Buildup
- Spasm
- Coronary artery embolism

Immediate Care

- MONA
- Aspirin
- Nitroglycerine for chest pain
- Oxygen
- Morphine

Percutaneous Coronary Intervention (PCI)

- STEMI – PCI is treatment of choice
  - Within 12-24 hours
- If cannot do PCI, fibrinolytic therapy is alternative option
  - More likely in non-US locations/extremely remote locations
- Heparin based products given in conjunction
  - Bivalirudin is an alternative option in those who can’t use heparin/enoxaparin

Fibrinolytics

- Tenecteplase, alteplase, streptokinase
  - Tenecteplase – best safety profile, similar efficacy to alteplase
  - Streptokinase – cheap, less effective, less intracranial bleeding
- Considered if PCI not an option, or don’t have access in 120 minutes or less
- Contraindications
  - Any significant internal bleeding
    - Intracranial hemorrhage
    - Active GI bleeding
    - Uncontrolled, unresponsive hypertension (>180/110)

NSTEMI/Unstable Angina

- Higher score, more likely to do early invasive strategies (i.e. PCI)
- Thrombosis in Myocardial Infarction (TIMI) risk score
  - Age >65
  - CAD or CAD risk factors like smoking, hypertension, hypercholesterolemia, diabetes, tobacco
  - Recent aspirin use (last 7 days)
  - Severe angina
  - Elevated cardiac marker
  - ST change >0.5

Classic Medications on Hospital Discharge

- Aspirin
- P2Y12 inhibitors (i.e. clopidogrel)
- ACE or ARB
- Beta-blocker
- Statin

Atrial Fibrillation

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Symptoms of Atrial Fibrillation

- General fatigue
- Rapid and irregular heartbeat
- Fluttering or “thumping” in the chest
- Dizziness
- Shortness of breath and anxiety
- Weakness
- Faintness or confusion
- Fatigue when exercising

Classification of AFib

- Paroxysmal (<7 days)
- Persistent (>7 days and won’t go back to normal on its own)
- Permanent (continuous Afib)

Controlling Rate

- Beta-blockers
- Calcium Channel Blockers
- Digoxin

Clinical Medication Pearls

- Beta-blockers
  - Usually first line
  - Generally avoid non-selective unless compelling indication
- Calcium Channel Blockers
  - Non-dihydropyridines
  - Heart failure risk
- Digoxin toxicity
  - GI symptoms, CNS, weight loss, bradycardia
  - Renal elimination
  - Target concentration <1ng/mL vs. CHF (0.5-0.8)

Rhythm Control

- Potassium Channel Blockers
  - Amiodarone
- Sodium Channel Blockers
  - Flecainide (Tambocor®)
  - Propafenone (Rythmol®)

Amiodarone Pearls

- Extremely long half life
- Liver toxicity
- Pulmonary toxicity
- Thyroid impact
- Drug interactions
- QTc prolongation

Anticoagulation

- Clot formation is one of the major risks with atrial fibrillation
- To be discussed further – see NOACs/Warfarin section
- CHADS2Vasc
  - CHF
  - Hypertension
  - Age (65-74 +1; 75 or greater +2)
  - Diabetes
  - Stroke (+2)
  - Vascular Disease history
- Score of 2 or greater; anticoagulation indicated

Valvular Heart Disease

- Anticoagulation – Mechanical Heart Valve(s) Replacement
  - Warfarin = Drug of Choice
  - Target higher INR – 2.5-3.5
- Direct oral anticoagulants
  - Not indicated for use in valvular replacement

CHF

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CHF Characteristics

- Inability to effectively pump blood
- Elevated BNP (or pro-BNP)
- SOB, cough
- Fatigue, weakness
- Edema

Acute Management of CHF

- Loop diuretics are mainstay of therapy (dose will depend upon patient, preexisting medication regimen)
- Oxygen if difficulty breathing/PO2 <90
- Severe hypertension
  - Nitroprusside (watch out for cyanide toxicity)
- May add nitroglycerin in normotensive/mild hypertensive, non-responders to diuretic therapy alone
- Inotropes for patients with inadequate cardiac function, systolic failure with low ejection fraction (i.e. dobutamine or milrinone)
  - Avoid beta-blocker which can suppress function

Medications Frequently Used in CHF

- Diuretics
  - Loops
  - K+ sparing
  - Thiazide Like
- ACE/ARBs
- Beta-blockers
- Digoxin

Loops

- Furosemide
- Mainstay of therapy
- Fluid loss
- Risks
  - Electrolyte depletion
  - Dehydration/Kidney Failure
  - Frequent urination

Aldosterone Antagonists

- Spironolactone, Eplerenone
- Hyperkalemia
- Gynecomastia
- 100mg spironolactone/40 mg furosemide

Thiazide Like

- Metolazone
  - One hour before furosemide
  - Used to augment furosemide
  - Significant hyperkalemia risk when used with furosemide
  - Sometimes only need to use once or twice/week
- True thiazides (i.e. HCTZ)
  - Generally not used for CHF/fluid loss
  - Likely not as beneficial with CrCl <30

Beta-blockers/ACE Inhibitors

- See Hypertension for more clinical breakdown
- Generally try to push the dose
  - Not that easy in the elderly
  - Falls
  - Weakness
  - Kidney function

Digoxin in CHF

- Increased mortality at higher levels
- Target 0.5-0.8
- Monitor closely
  - Changing renal function
  - Symptoms of toxicity

Classic Drugs that Exacerbate CHF

- NSAIDs
  - Sodium retention
  - Also risk of Kidney damage with ACE/Diuretics on board
- CCB’s
  - Increase edema
- TZD’s
  - Pioglitazone
- Pregabalin

Coronary Heart Disease and Cardiovascular Risk

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Coronary Heart Disease

- Atherosclerosis, Coronary Artery Disease (CAD), Ischemic Heart Disease (IHD)
  - Plaque formation
  - Hardening of the arteries
- Can lead to;
  - Angina
  - Myocardial Infarction

Cardiovascular Risk Stratification Considerations

- Age
- Sex
- Family history
- Smoking
- Obesity
- Alcohol
- Hypertension
- Diabetes
- Metabolic Syndrome
- Physical activity
- Lipid levels
- Diet

ACC/AHA Risk Calculator – Primary Prevention

- Age
- Gender
- Race
- Cholesterol/HDL (doesn't use LDL in calculator, but if >190 recommend likely starting statin)
- Blood Pressure (level plus if on medication)
- Diabetes
- Smoking
- ***Provides 10 year risk as well as if aspirin is recommended

Links to Calculators

- http://www.cvriskcalculator.com
- http://www.mayoclinic.org/diseases-conditions/heart-disease/in-depth/heart-disease-risk/itt-20084942

Heart Risk Calculator

Home | About | Contact

17.9%

10-year risk of heart disease or stroke

On the basis of your age and calculated risk for heart disease or stroke over 10%, the USPSTF guidelines suggest you **start taking aspirin 81mg every day** if you are not at increased risk for bleeding and are willing to take it every day for at least 10 years.

On the basis of your age, your calculated risk for heart disease or stroke over 7.5%, and diabetes, the ACC/AHA guidelines suggest you should be on a **high intensity statin.**

Based on your age and race, your blood pressure is **poorly-controlled**, and you should initiate lifestyle interventions and consider starting a **thiazide diuretic, ACEI/ARB, or calcium channel blocker.**

Demography	Cholesterol	Blood pressure	Risk factors
Age: 55	Total: 132	Systolic: 155	Diabetes: yes
Gender: male	HDL: 55	Diastolic: 134	Smoking: yes
Race: not African-American		On medication: yes	

http://www.cvriskcalculator.com

Goal – Reduce Risk of MI/Stroke

- Platelet inhibitors
- Statins
- Smoking Cessation
- Weight loss
- Anti-angina medications
- Antihypertensives

Antiplatelet medications

- Aspirin
- ADP inhibitors commonly used with aspirin in stenting, ACS
  - Clopidogrel

Statin Consideration

- Adherence is critical
- Past history
- Some recommended to be dosed at night and some aren’t
- Cost
- Life expectancy

Anti-Angina Medications

- Nitrates
  - Long acting
  - Short acting
- Beta-blockers
- CCB’s

Antihypertensive Therapy

- ACE/ARB
- Beta-blocker
- CCB

Hyperlipidemia

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Hyperlipidemia Basics

- LDL is primary focus for statin medications
  - More of a shift towards risk factors, irrespective of levels
- Triglycerides – primary target >500
  - Fibrates
  - Niacin

Cardiovascular Risk Stratification Considerations

- Age
- Sex
- Family history
- Smoking
- Obesity
- Alcohol
- Hypertension
- Diabetes
- Metabolic Syndrome
- Physical activity
- Lipid levels
- Diet

ACC/AHA Risk Calculator – Primary Prevention

- Age
- Gender
- Race
- Cholesterol/HDL (doesn't use LDL in calculator, but if >190 recommend likely starting statin)
- Blood Pressure (level plus if on medication)
- Diabetes
- Smoking
- ***Provides 10 year risk as well as if aspirin is recommended

Links to Calculators

- http://www.cvriskcalculator.com
- http://www.mayoclinic.org/diseases-conditions/heart-disease/in-depth/heart-disease-risk/itt-20084942

High Intensity Examples

- Atherosclerotic CVD
- LDL >190
- Diabetes and CVD 10 year >7.5%
  - Age 40-75
- Age 75 – magic number to assess risk/benefits and aggressiveness of therapy

Table 1. Statin Therapy

Intensity	Definition	Dosage
Low	Daily dose lowers LDL-C by <30%, on average	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg Pitavastatin 1 mg
Moderate	Daily dose lowers LDL-C by approximately 30% to <50%, on average	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg
High	Daily dose lowers LDL-C by approximately ≥50%, on average	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg

C: cholesterol; XL: extended-release.
Source: Reference 1.

Clinical Pearls

- Rosuvastatin/Atorvastatin for high intensity
- Generally avoid simvastatin if not on/hasn’t tried others
  - CYP3A4 interactions (amlodipine, amiodarone, diltiazem, etc.)
- Rosuvastatin
  - Most potent LDL lowering, less strict on interaction with gemfibrozil
- Atorvastatin
  - Covers moderate/high intensity nicely
  - Does have some 3A4 interaction potential
- Lovastatin
  - 3A4 potential

Clinical Pearls

- If myopathy on CYP3A4 agent, try an alternative that doesn't use that pathway
  - If tried atorvastatin, avoid lovastatin, simvastatin if alternatives have not been tried
  - Look for drug interactions that might be contributing
  - Co-Q10?
- Hydrophilic may help reduce myopathy
  - Pravastatin
  - Rosuvastatin
  - Fluvastatin
- Lipid checks – recommended to assess adherence

Alternative Options – High Risk Patients

- Rechallenge with statin is recommended
- Ezetimibe
- PCSK9 inhibitors

Triglycerides

- Gemfibrozil
  - Interaction with statins (rhabodomyolysis, CPK etc.)
- Fenofibrate
  - Maybe less risk with statin interaction/myopathy
- Niacin
  - Better at increasing HDL
  - Flushing/Uric acid

Hypertension Pearls

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Complications/Risks

- MI
- Stroke
- Kidney
- Vision
- Heart Failure
- Aneurysm

Goals

- JNC-8
  - <150/90
  - Exception: 140/90
    - CKD
    - Diabetes

Drug Induced Hypertension

- NSAIDs
- Stimulants
- Corticosteroids
- Estrogen
- SNRI’s
- ESA’s

Medical Induced Hypertension

- Sleep apnea
- Thyroid
- Adrenal gland problems
- Illicit drug use/addiction
  - Opioid withdrawal

Hypertension Medications

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ACE Inhibitors

- Common Side Effects
  - Cough
  - Kidney impairment
    - Worry about 30% changes or more
    - Diuretics/NSAIDs
  - Hypotension
  - Hyperkalemia

Clinical Pearls

- ACE inhibitors can exacerbate CKD, but can also help be renal protective
- Lisinopril most commonly used
- Classic medication cause of angioedema (extremely rare)
- In some cases, African Americans may not respond to ACE Inhibitors as well as other ethnicities
- Avoid ACE/ARB combo

Compelling Indications

- Diabetes
- Stroke
- CAD
- CKD
- CHF

Angiotensin Receptor Blockers

- Losartan
- Valsartan
- Irbesartan

ARB Clinical Pearls

- Think ACE minus the cough
  - Hyperkalemia
  - Kidney function
  - Angioedema
  - Similar compelling indications

Thiazide Diuretics

- Memorable Side Effects
  - Increase urine output
  - Frequent urination
  - Electrolyte depletion
  - Low blood pressure
  - Hyperuricemia
  - Hypercalcemia
  - Increased risk of kidney failure

Use Caution

- Gout
- Poor kidney function (CrCl <30)
- Timing near night
- Hyperglycemia

Calcium Channel Blockers

- Dihydropyridines – amlodipine, nifedipine, felodipine
- Non-dihydropyridines – verapamil, diltiazem
- Dose dependent edema
- Constipation
- Simvastatin interaction

Calcium Channel Blockers

- Compelling Indications
  - Angina
  - Atrial Fibrillation (diltiazem, verapamil)
  - CVD risk
- Caution
  - Heart failure

Beta-Blockers

- Cardioselective
  - Metoprolol
- Non-selective
  - Propranolol
- Alpha and Beta blockade
  - Carvedilol

Beta-blockers

- Compelling Indications
  - CHF
  - MI
  - Angina
  - Afib

Beta-blocker Pearls

- Asthma/Airway disease
- Pulse
- Hypoglycemia masking
- Risk of rebound hypertension
- Non-selective uses
  - Tremor
  - Esophageal varices
  - Thyroid storm
  - Migraine

Alpha-Blockers (for hypertension)

- Doxazosin
- Prazosin
- Terazosin

Alpha-Blocker Pearls

- Orthostasis
- BPH compelling indication
- Typically dosed at night
- Prazosin off label for nightmares

Hydralazine

- Multiple doses
- Contraindicated in coronary artery disease
- Lupus type syndrome
- Vasodilator – hypotension risk may be a little greater than other antihypertensives

Clonidine

- Centrally acting side effects (depression, sedation, dizziness)
- Bradycardia
- Dry mouth
- Avoid in elderly
- Lots of unique uses
  - Opioid/nicotine withdrawal
  - ADHD
  - Clozapine excessive salivation

NOACs

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Factor 10A Inhibitors

- Gaining popularity
- Drug interactions
- Less monitoring
  - Is that good or bad?
- When might you not choose them
  - Prosthetic valves
  - Adherence issues (t ½ longer for warfarin)
  - CKD
  - Cost/insurance coverage
  - Provider comfort/preference

Rivaroxaban

- Rivaroxaban
  - Once daily
  - 3A4/P-glycoprotein interactions possible
  - <30mls/min avoid use
  - DVT – 15 mg BID for 21 days followed by 20 mg daily
  - DVT prophylaxis – 10 mg daily; up to 35 days
  - Afib – 20 mg daily
  - May have to reduce dose in elderly with CrCl btween 30-50 mls/min

Apixaban

- Apixaban
  - Twice daily
  - Possible dose adjustments based upon age, creatinine, weight
  - DVT Treatment 10 mg BID for 7 days then 5 mg BID
  - Afib – 5 mg BID
  - 2 or 3; age>80, body weight <60, or creatinine >1.5; reduce dose to 2.5 BID
  - Post op prophylaxis – 2.5 BID
  - Specific dose adjustements for 3A4 and P-glycoprotein inhibiotrs like clarithromycin, ketoconazole, itraconazole, ritonavir

Edoxaban

- Edoxaban
  - >95 mls/min boxed warning (stroke)
  - Once daily
  - Creatinine clearance 15-50 mls/min – dose reduction)30 mg daily
  - Usual dosing = 60 mg daily
  - Reduced dose with 3A4/P-glycoprotein inhibitors (rivaroxaban)
  - Avoid in very obese/low weight extremes

Dabigatran

- Direct Thrombin Inhibitor
- GI bleed risk >75 y/o
- Reversal agent available
- Dose adjustment in CKD
- Twice daily

Peripheral Vascular Disease

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Factors That Can Contribute to PVD

- Atherosclerosis
- Hypertension
- Clot formation
- Viscosity of the blood

Peripheral Vascular Disease

- Intermittent claudication
- Ischemia
- Sharp, stabbing pain
- Pedal pulses absent
- Risk amputation

Medications

- Smoking Cessation
- Aspirin/Clopidogrel
- Statins
- Antihypertensives

Cilostazol

- Trial for 3 months
  - If no improvement discontinue
- Administer on empty stomach
- Boxed warning – don’t use in heart failure
- Possibility to alter bleed risk
- 3A4 interactions

Pentoxifylline

- Possible antiplatelet activity
  - Reduces blood viscosity
  - Increase bleed risk potential
- Generally not that effective
  - Rarely see it used

Warfarin

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Warfarin Common Indications

- Atrial Fibrillation (2-3)
- DVT/PE (2-3)
- Prosthetic Mechanical Mitral Valve
  - 2.5-3.5
- Lower goals
  - High bleed risk
  - High fall risk

Warfarin - Pharmacokinetics

- Metabolized by
  - S-warfarin: CYP 2C9 (potent)
  - R-warfarin: CYP 1A2, 2C19, 3A4
- Bound to albumin
- Half-life = 36-42 hours

Warfarin – Adverse Effects

- Bleeding
- Purple Toe Syndrome
  - Don’t load warfarin

Warfarin – How long does it take to work?

- Half-life of clotting factors
  - II 60 hrs

  (prothrombin)
  - VII 6 hrs
  - IX 24 hrs
  - X 40 hrs

  (reduction of II and X = prolongation of PT)

- Half-life of anticoagulants
  - Protein C6 hrs
  - Protein S 72-96 hrs

Causes of INR Variation

- Adherence
- Diet
- Drug Interaction
- Changes in Disease States
  - Liver
  - CHF
  - Fever

Vitamin K

- Elevated INR and bleeding
- INR greater than 9
- Not going to work instantly
- Transfusion for acute, severe blood loss
- INR 5-9, no bleeding
  - May give vitamin K, don’t have to

Dermatologic

Burn Management

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Burns – Factors to Consider

- Depth
- Size of area
- Type of burn
  - Electrical
  - Chemical
  - Inhalation

- Severity
- 1st degree
  - Red, dry, painful, superficial
- 2nd degree
  - Wet, red, painful
- 3rd degree
  - Leathery/dry/waxy in appearance
- 4th degree
  - Deepest; may involve tendon and bone

Complications – Severe Burns

- Fluid/electrolyte status
- Infection risk
- Cosmetic/appearance

Supportive Care - Acute

- Fluids
  - Crystalloids
- Possible oxygen/intubation
- Antibiotics (IV)
  - Typically not recommended unless signs of infection/sepsis are present
- Assess for anticoagulation
  - ICU/immobility

Parkland Formula – Fluid Replacement

- Fluid (mls) = (4 mls crystalloid) X (% body surface affected) X (Body weight)
  - 24 hour replacement
- Higher % affected, more fluid requirement
- Bigger patient, more fluid required
- ***Use as general guide; consider other factors (i.e. CHF)
- Dopamine may be added to try to improve renal blood flow

Burn Management

- Topical antibiotics – not recommended for minor burns (i.e. sunburn)
  - Bacitracin
  - Mupirocin
    - MRSA coverage
  - Silver sulfadiazine
    - Antibacterial activity
    - Typically doesn’t cause pain when applied
- Simple burns
  - Aloe vera
  - Petrolatum

Dermatologic Disorders

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Dermatitis

- Contact, Atopic (Eczema)
  - Inflamed skin
  - Redness
  - Itchy
- Treatment
  - Topical Steroids
  - Calcineurin Inhibitors (i.e. tacrolimus)

Common Steroids

- Determinants of potency
  - Drug
  - Percentage
- Table
  - https://www.psoriasis.org/about-psoriasis/treatments/topicals/steroids/potency-chart

Medication Causes of Skin Disorders

- Rash
  - Antibiotics
    - Sulfa
    - Penicillins
    - Macrolides
- SJS risk
  - Antiepileptic (i.e. carbamazepine, lamotrigine)
  - Allopurinol
  - Penicillins
- **Timing, Timing, Timing

Yeast Infection

- Candida albicans
- Risks
  - Diabetes
  - Antibiotics
  - Immunosupression
- Treatment
  - Topical nystatin, clotrimazole
  - Systemic, fluconazole

Pressure Ulcer

- Staging:
  - 1 – red, no breaks in skin, potentially pain
  - 2 – skin broken open
  - 3 – deeper into the skin, fat potentially showing
  - 4 – deepest, possible visual presence of bone, tendon, or muscle
- Risk of osteomyelitis or sepsis with deeper stages (3 or 4 typically)

Dry Skin

- Xerosis
  - Common in the elderly
  - Cracks/Infection risk
  - Itching
- Common treatment
  - Moisturizers

Psoriasis

- Inflammation
- Excessive growth in the epidermis
  - Raised, rough skin
  - Scaly appearance
- Most common location
  - Elbows
  - Knees
  - Scalp
- Can result in pain in the joints (psoriatic arthritis)

Management

- Localized areas
  - Topical corticosteroids
    - Triamcinolone, betamethasone, etc.
  - Vitamin D analogs calcipotriene, calcitriol
  - Calcineurin inhibitors
    - Can increase risk of skin cancer
  - Coal tar
    - Messy

Management

- Moderate to Severe Disease
  - Systemic retinoids (acitretin)
    - Birth defect in females
  - Methotrexate
    - LFT, CBC
    - Similar dosing to RA – 10-25 mg per week
    - Folic acid
  - Cyclosporine
    - Immunosuppressive
    - HTN, nephrotoxicity, infection/malignancy risk
    - Tons of drug interactions
  - Biologics (etanercept, infliximab, etc.)
    - Risk of malignancy, infection
    - Injection/infusion
    - Expensive

Steven Johnson’s Syndrome

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SJS

- Severe skin reaction
  - Pain
  - Redness
  - Hives
  - Blisters/necrosis
- Complications
  - Sepsis
  - Cellulitis
  - Respiratory involvement
  - Skin damage

At Risk Patients

- Immunosuppressed
  - HIV
- Previous history of SJS
- HLA-B 1502 Gene
  - Chinese
  - Indian
  - Southeast asia

Medication Related Causes

- Allopurinol
- Lamotrigine
- Carbamazepine
  - HLA-B*1502 gene may place at higher risk
- Barbituates
- Phenytoin
- Sulfa
- PCN’s
- NSAIDs
- Acetaminophen

Management

- Stop offending agent
- Simple analgesics for pain
- Monitor/treat as appropriate
  - Sepsis
  - Cellulits
- Corticosteroids to reduce inflammation, pain as necessary
- Wound care as needed

Endocrine

Addison’s Disease and Cushing’s

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Addison’s Disease

- Defined by a deficiency in cortisol (from adrenal gland)
  - Corresponding aldosterone deficiency
- Results in; - possible adrenal crisis
  - Low blood pressure
  - Hyperkalemia
  - Hyponatremia
  - Hypoglycemia
  - Skin darkening

Management

- Exogenous steroids
  - Prednisone/hydrocortisone
  - Lifelong therapy likely unless identifiable/treatable reason for deficiency
- Mineralocorticoid replacement
  - Fludrocortisone
    - Helps with hyponatremia
    - Side note – often used in the management of severe hypotension due to dialysis

Adrenal Crisis

- Acute, severe, symptomatic adrenal gland failure
  - Hypotension
  - Loss of consciousness
  - Hyperkalemia, hyponatremia
  - N/V
- IV glucocorticoid (hydrocortisone)
- Fluid replacement
- Sodium monitoring
- Dextrose – to treat hypoglycemia

Cushing’s

- Opposite of Addison’s
  - Excessive corticosteroid (cortisol)
  - Caused by oversupply of exogenous
- Weight gain
- Hyperglycemia
- Moon face/buffalo hump – fat distribution changes
- Acne
- HTN
- Osteoporosis

Treatment – Cushing's

- Remove exogenous steroids
  - SLOWLY!!!
- Abrupt discontinuation of long term steroids
  - Adrenal insufficiency
- Treat underlying cause if not due to excessive supplementation of steroid
  - I.e. cancer
  - Surgery, radiation
- Cabergoline – may help normalize production of cortisol
  - Low success rate
  - Dopamine agonist
    - May see used for elevated prolactin levels
    - Psych/GI adverse effects

Diabetes: Compelling Indications, Complications, and Goals

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Diabetes Monitoring

- A1C
- Blood sugars
- Kidney, eye, feet
- Goals
  - 6.5-8
  - Trend toward less strict control as we age/life expectancy declines and keen sense of hypoglycemia risks

Complications

- Cardiovascular Disease
- Neuropathy
- Nephropathy
- Retinopathy
- Gastroparesis
- Amputation risk
  - Infection risk

Statin Use

- Recommended for majority of patient with diabetes
- Many patients at high risk
- Drug Interactions
- Factors to discontinue?
  - Tolerability
  - End of life

Table 1. Statin Therapy

Intensity	Definition	Dosage
Low	Daily dose lowers LDL-C by <30%, on average	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg Pitavastatin 1 mg
Moderate	Daily dose lowers LDL-C by approximately 30% to <50%, on average	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2-4 mg
High	Daily dose lowers LDL-C by approximately ≥50%, on average	Atorvastatin 40-80 mg Rosuvastatin 20-40 mg

Courtesy:
uspharmacist.com

Hypertension

- ACE OR ARB
  - Renal protection
- CCB
- Thiazide

Aspirin

- Most likely, but
  - Consider risk with other medications (i.e. Warfarin, NSAIDs, etc.)
  - Past history
  - Bleeding
  - Risk calculators (See CHD lecture)

Diabetic Neuropathy

- Gabapentin/pregabalin
- SNRI’s
- Topical Lidoderm
- TCA’s

Gastroparesis

- Cause of GI nausea/upset in diabetes patients
- Metoclopramide
  - Parkinson’s disease risk
- Erythromycin
  - Drug interaction risk
- Be careful with anticholinergics
  - Exacerbate gastroparesis

Changes That Can Impact Diabetes

- Steroids
- Beta-blockers
- Infections
- Dementia
- Medications that suppress or stimulate appetite

Treatment of Hypoglycemia

- Glucagon
  - Alertness compromised
- Sugar replacement
  - Aspiration
  - Choking

Diabetes Insipidus

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Diabetes Insipidus

- Urination of large volumes
  - Dilute urine <300 mOsm/kg
- Polydipsia
- Nocturia
- Hypernatremia
- Causes
  - Lack of ADH secretion (Central)
  - Renal resistance to ADH action (nephrogenic)

Management

- Dehydration avoidance
  - Ensure adequate fluid replacement
- Hypo-osmolar solution if IV replacement is necessary
  - Reduce hypernatremia
    - Reduction target 0.5 mEq/L/hr
- Desmopressin – drug of choice
  - Synthetic ADH
    - Water reabsorption
  - Boxed warning for hyponatremia

Other Alternatives

- Chlorpropamide
  - Sulfonylurea that can cause SIADH
- Carbamazepine
  - SIADH
- Thiazides
  - ***Drugs that can all contribute to hyponatremia

Type 2 Diabetes; The Medications

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Metformin

- First line
- Kidney function
  - Target 45 mls/min
- GI side effects
- Weight neutral to weight loss
- Low risk hypoglycemia
- B12

Sulfonylurea’s

- Glipizide, glimepiride, glyburide
- Hypoglycemia
- Weight gain
- Chlorpropamide (rarely used) SIADH risk

DPP-4 Inhibitors

- Sitagliptan, linagliptan etc.
- Well tolerated
- Increases incretin
  - Post-prandial
  - Promotes fullness
- Weight neutral
- $$$
- Generally low hypoglycemia when used alone

TZD’s

- Reduces insulin resistance in peripheral
- Weight Gain
- Edema
- CHF risk

SGLT-2 Inhibitors

- Glucose loss through the urine
- Low hypoglycemia when used alone
- UTI/genital infections
- Lower BP (mildly)
- Hyperkalemia
- Kidney function
- $$$

GLP-1 Agonists

- Incretin
  - Post-prandial
- GI SE’s
- Injection
- $$$
- Thyroid tumor risk

Insulin

- Sliding Scale
  - Short term use
- Long Acting
  - Targets fasting
- Rapid Acting
  - Targets post-prandial
- Diet Changes

Hyperparathyroidism

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Hyperparathyroidism types

- Primary
  - Surgery
- Secondary
  - Most commonly due to CKD complications

CKD Induced Hyperparathyroidism

- Vitamin D is converted to active form by the kidney
  - In CKD this process is reduced
  - Possible resulting hypocalcemia
- Hypocalcemia signals PTH release
- Phosphorus elevations can signal PTH release as well

Management

- Depends upon calcium level
- If low calcium level
  - Utilize active vitamin D (calcitriol)
- If low calcium and high phosphorus
  - Utilize calcium based phosphate binder
- If hypercalcemia
  - Avoid medications that can increase calcium
  - Cinacalcet

Cinacalcet

- Mimics calcium, but doesn’t contribute to hypercalcemia
- Risk of hypocalcemia and elevations in phosphorus
- Monitor levels closely upon initiation of therapy

Osteoporosis Prevention

- Bisphosphonates
- Reduce calcium loss from bones
- Adverse effects/risk
  - Oral – GI ulceration
  - Burdensome administration procedure
  - Osteonecrosis

Polycystic Ovarian Syndrome

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Polycystic Ovarian Syndrome (PCOS)

- Disorder of hormones regulation
  - Hypothalamus, pituitary, ovary
  - Estrogen
  - Androgen

Presentation/Symptoms

- No ovulation
  - Patients may present with difficulty conceiving
- Excess androgen production
  - Hair growth
  - Obesity
  - Metabolic Syndrome
  - Diabetes/hyperglycemia

Management

- Non-drug interventions
  - Weight loss
  - Exercise
- For those who aren’t trying to conceive
  - Oral Contraceptives
    - Regulate menstrual cycle
    - Helps reduce androgen overproduction

Pregnancy Desired

- Weight Loss
- Exercise
- Clomiphene
  - Stimulates ovulation (SERM)
  - 5 days of therapy every 30 days
  - 50 -100 mg dosing (can increase to 100 mg if 50 is ineffective)
  - Hot flashes
  - GI

PCOS Management

- Metformin
  - Helps with insulin sensitivity and hyperglycemia
  - Weight negative effects
  - Clinical Considerations
    - GI side effects
      - Loose stools
      - Nausea
    - Careful in Kidney disease

Systemic Lupus Erythematosus

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Systemic Lupus Erythematosus - The Disease

- Autoimmune disease “Lupus”
- Generalized Symptoms
  - Fatigue
  - Joint Pain
  - Selling
  - “Butterfly rash” – cheeks/nose
  - Anemia
  - Clotting disorder
  - Can be associated with Raynaud’s
    - Fingers turning blue/white when cold

Risks/Complications

- MI/Stroke
- Renal failure
- Inflammation of lung/heart
- Blood clots/vasculitis
- Osteoporosis

Autoimmune Nature

- DMARDs
  - Hydroxychloroquine
  - MTX
- Rashes
  - Corticosteroid creams
- Inflammation and Pain
  - NSAIDs
  - Acetaminophen
- Immunosuppression/inflammation
  - Steroids
  - Azathioprine, cyclophosphamide
- Treatment guided by severity of disease

Drug Induced Lupus/Exacerbate Lupus

- Sulfamethoxazole or other sulfa containing drugs
- Hydralazine
- Procainamide

Thyroid Disorders

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Hypothyroidism - Diagnosis

- Usually elevated TSH and low T4
- Symptoms
  - Lethargy
  - Cold
  - Weight Gain
  - Constipation
  - Hair loss/Skin Dryness
  - Lack of energy

Levothyroxine

- Usual starting dose 25-50 mcg/day
- Binding interactions
  - Consistency with administration
- Follow up – 6 weeks to 3 months

Drugs That Can Impact Thyroid Function

- Amiodarone
  - Hyperthyroid or Hypothyroid
- Lithium

Levothyroxine Interactions

- Enzyme Inducers
  - Phenobarbital
  - Carbamazepine
- Binding interactions
  - Calcium
  - Cholestyramine
  - Sucralfate
  - Iron

Hyperthyroidism

- Methimazole
- PTU
  - Liver toxicity
- Risk
  - Weight Loss
  - Tachycardia
  - Insomnia
  - Nervousness
  - Osteoporosis

Thyroid Storm

- Symptoms
  - Tachycardia
  - Anxiety
  - Agitation
  - Psychosis
  - Elevated temp
- Treatment
  - Beta-blocker
    - Helps with tachycardia/anxiety
  - Antithyroid medication
    - I.e. PTU/Methimazole

Eyes, Ears, Nose and Throat

Allergic Rhinitis

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Allergic Rhinitis

- Make sure not from acute illness
- Reassess treatment throughout the year

Treatment

- Nasal Steroid
  - i.e. Fluticasone
  - May take some time for max effect
- Antihistamine nasal spray
  - I.e. Azelastine
- Many patients will know what works best for them

Antihistamines

- 1st Generation
  - i.e. diphenhydramine
  - Avoid, highly anticholinergic
- 2nd Generation
  - Loratadine
  - Cetirizine

Other Therapies

- Oxymetazoline
  - Nasal
  - Use only short term (3-5 days)
    - Rebound congestion risk
- Pseudoephedrine/phenylephrine
  - Avoid if possible
  - Raise blood pressure
    - Assess recent BP and ensure controlled and not high risk patient
  - BPH
  - Insomnia risk

Other Therapies

- Montelukast
  - If allergies and asthma coexist – decent option
- Cromolyn
  - Generally safe
  - Likely less effective than steroids, antihistamines

Eye Disorders

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Common Eye Disorders in the Elderly

- Macular Degeneration
- Glaucoma
- Diabetic Retinopathy

Macular Degeneration

- Clinical Pearls
  - Central vision loss
    - Reading
    - Driving
  - Use of VEGF inhibitors (Bevacizumab)
  - Smoking can increase risk
  - Dry can progress to Wet (wet is worse)

Glaucoma Pearls

- Leading cause of blindness worldwide
- Peripheral loss
- Borderline Pressure 18-25
  - Assessment for damage
  - If damage, treatment
  - Some may argue >22
- Greater than 25 - treatment

Drugs

- Prostaglandins
- Beta-blockers
- Adrenergic agonists
- Carbonic Anhydrase Inhibits
  - Rarely oral used (acetazolamide)

Preventing Diabetic Retinopathy

- Blood sugar control
- Hypertension
- Regular Exams

Medications – Eye Problems

- Hydroxychloroquine
- Ethambutol
- Tamsulosin
  - Floppy iris syndrome
  - Concern in cataract surgery
- Dry eyes
  - Cornea scratch/damage
  - Anticholinergics
  - Diuretics
- Cataract
  - Steroid use

Ophthalmic Infections

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Symptoms

- Redness
- Itching
- Discharge
- Foreign Body Sensation

Bugs

- Staphylococcus
- Streptococcus
  - Classic gunky, yellow, mucous like discharge
- Viral infections
  - Watery discharge

Common Antibiotics

- Erythromycin
- Ofloxacin
- Ciprofloxacin
- Trimethoprim/polymixin

Shingles

- Reactivation of “Chicken Pox”
- Risk of vision loss
- Acute retinal necrosis
- Treatment
  - Acyclovir
  - Steroids

Eye Drop Administration Pearls

- Don’t touch tip to eye
- Avoid contact lenses
- Recommendation 5 minutes between drops
- Drops before ointment
- For more info
  - http://www.cc.nih.gov/ccc/patient_education/pepubs/eyedrops.pdf

Fluid, Electrolyte and Nutrition

Acid Base Disorders

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Acid Base Disorders

- Normal pH – 7.35-7.45
- Acidosis <7.35
- Alkalosis >7.45
- Asymptomatic with mild acid/base disorder
- Symptomatic
  - Neurologic changes; coma, seizures, acute delirium
  - CV changes; reduced cardiac output/contractility
  - Electrolyte changes

Type of Acidosis/Alkalosis

- Metabolic acidosis
  - pH <7.35; bicarb <24 mEq/L
- Respiratory acidosis
  - pH <7.35, PCO_2>40 mmHg
- Metabolic alkalosis
  - pH >7.45, bicarb >24 mEq/L
- Respiratory alkalosis
  - pH >7.45, PCO_2 <40mmHg

Anion Gap

- Anion Gap
  - Normal level 10-12 mEq/L
- Calculation of anion gap
  - Anion gap = Sodium - (chloride + bicarb)
- Elevation most likely indicative of metabolic acidosis

MUDPILES – Metabolic Acidosis, AG >16

- Methanol
- Uremia
- Diabetic ketoacidosis (also starvation)
- Paraldehyde, paracetamol (acetaminophen)
- Iron
- Lactic acidosis
- Ethanol (alcohol)
- Salicylates, aspirin

Metabolic Acidosis

- Normal AG
  - Diarrhea
  - Fistulas
  - Hyperkalemia
  - Renal problem
    - Increase bicarb excretion

Respiratory acidosis

- pH <7.35, PCO_2>40 mmHg
- Respirations
  - Reduce CO_2 (blow off CO_2)
- Slow or decreased ventilation can cause respiratory acidosis
  - Opioid toxicity
  - Sleep apnea
  - Lung disease
    - COPD
    - Asthma

Metabolic Alkalosis

- pH >7.45, bicarb >24 mEq/L
- Causes
  - Excessive bicarb administration
  - Diuretics (loops/thiazides)
  - Mineralcorticoid excess (Cushing's)
  - Hypokalemia

Respiratory Alkalosis

- pH >7.45, PCO_2 <40 mmHg
  - Caused by hyperventilation
    - Anxiety
    - Pain
    - Fever

Treatment

- Body will compensate with respirations as well as Bicarb shift
- Fix identifiable cause
  - Toxin removal
  - Diabetes
  - Pain/anxiety management
- Bicarb administration
  - Option in acidosis
  - Controversial; use with caution to avoid overcorrection and inducement of alkalosis

Electrolyte Abnormalities

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Symptoms/Signs of Hyponatremia

- Fatigue
- Cramps
- Confusion
- Dizziness
- Seizures (rare, usually with acute changes)
- Normal Sodium 135-145 mEq/L

Causes of Hyponatremia

- Diuretics
- SIADH
  - Oversecretion of ADH
  - Water retention
  - Dilutes Na+
  - Resulting Hyponatremia
- Heart Failure
- Cirrhosis
- Polydipsia

Causes of SIADH

- CNS changes
  - Trauma
  - Stroke
- Cancer
- Drugs
  - Carbamazepine/oxcarbazepine
  - SSRI’s
  - Chlorpropamide

Correcting Hyponatremia - Chronic

- If chronic, asymptomatic – correct slowly and/or monitor
  - Typically done outpatient
- Correct identifiable problem
- Remove offending medication(s)
- Medication management
  - Sodium chloride tablets
  - Demeclocycline
    - Tetracycline derivative
    - GI side effects, binding interactions, sun sensitivity

Correcting Hyponatremia - Acute

- Symptomatic
- If hyponatremia happened within the last 24-48 hours, can correct more quickly
- Hypertonic saline
  - Target initial 4-6 mmol/L
  - No more than 12 mmol/L/day correction recommended
  - Risk of osmotic demyelination syndrome (ODS)
- ”Vaptan” drugs – Vasopressin Antagonists (conivaptan, tolvaptan)
  - Stimulates release of free water in the urine

Hypernatremia

- Correct imbalances by 8-10 mEq/d
  - May be slightly more aggressive if acute hypernatremia
- Use isotonic saline if patient has fluid losses
- Free water if fluid status is stable
- Diuretics
  - Can help eliminate sodium
- Desmopressin (DDAVP)
  - Hyponatremia boxed warning

Hypokalemia

- Signs/symptoms
  - Muscle cramps
  - Weakness, fatigue
  - Arrhythmias
  - Normal 3.5-5.1 mEq/L
- Acute management
  - Replace potassium
  - EKG monitoring
  - Reduce diuretics
- Chronic
  - Reduce diuretics
  - Replacement
  - Increase/add medications that can increase K+ (ACE, ARB, Aldosterone Antagonist)

Hyperkalemia

- Acute – EKG changes or >6.5
- IV calcium and insulin
  - Dextrose to avoid hypoglycemia
- If acidosis and hyperkalemia, consider bicarb
- Diuretic therapy
- Sodium polystyrene sulfonate (SPS)
- Discontinue offending agent(s)
  - ACE, ARB, Aldosterone antagonist
- Dialysis
- Beta-agonist
  - Albuterol – can cause intracellular shift of potassium

Hypomagnesia

- Normal 1.5-2.2
- Symptoms
  - Muscle weakness, cramping, EKG changes, seizures
- Causes
  - Alcoholics
  - Diarrhea/vomiting
  - Drugs
    - Diuretics
    - PPI’s

Hypocalcemia

- Normal total calcium (9-10.2 mg/dL)
- Abnormal albumin can erroneously report total calcium
  - 1 gram change albumin is approximately 0.8 change in calcium level
- Symptoms
  - Neuromuscular, tingling, cramps, Arrhythmias
- Drug causes
  - Loops
  - Bisphosphonates
  - Cinacalcet
  - Estrogen

Obesity

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Obesity

- BMI >30
- Complications
  - Diabetes
  - Cardiovascular risk
  - Pain/physical complications
  - Sleep Apnea
  - GERD

Options for Treatment

- Diet changes/calorie reduction
- Exercise
- Medications
  - OTC/Herbals
- Surgery

Orlistat

- Blocks fat absorption in GI tract
- Relatively safe
- Problematic oily diarrhea if patient has significant fat intake in diet
- May decrease fat soluble vitamin absorption
  - ADEK
  - Supplement with multivitamin may be necessary

Lorcaserin

- Serotonin activity
- Reduces appetite
- $$$
- GI side effects
- Avoid if poor kidney function CrCl <30

Phentermine

- Stimulant
  - Acts via norepinephrine effects
  - Warnings/precautions regarding patient with cardiac complications/risk
    - Hypertension
    - Atrial fibrillation
  - Insomnia
- Controlled substance
  - Caution/avoid if history of addiction/drug abuse

Topiramate

- Seizure medication/migraines
- Cognitive slowing
- Combination product with phentermine

Bupropion

- Stimulating type antidepressant
- Avoid in seizures
- Smoking cessation benefit

Diabetes Medications

- GLP-1’s
  - Liraglutide – higher 3 mg dosing
  - Exenatide
- Metformin

Avoiding Weight+ Medications

- Antidepressants
  - Mirtazapine
  - TCA’s
  - Paroxetine
- Sulfonylureas
- Pioglitazone
- Depakote
- Antipsychotics

Gastrointestinal

Cirrhosis

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Cirrhosis – Major Complications

- Edema
- Ascites
- Esophageal Varices
- Hepatic encephalopathy

Common Medications

- Spironolactone
- Loop diuretics
- Propranolol
- Lactulose

Edema/Ascites

- Diuretic Combo
  - Furosemide 40mg
  - Spironolactone 100mg
- Close electrolyte monitoring
- Gynecomastia

Hepatic Encephalopathy

- Accumulation of toxins due to poor liver function
  - Toxins impact the brain
    - Cognitive symptoms (i.e. confusion, lethargy)
- Ammonia (NH_3)
- Lactulose
- Neomycin, rifaximin

Portal Hypertension

- Increased pressure in portal venous system
- Veins can swell and increase due to this increased pressure
  - Leading to rupture and possible bleed
    - Esophageal varices
- Non-selective beta-blocker used to treat
  - Propranolol

Crohn’s and Ulcerative Colitis

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Symptoms

- Diarrhea
- Cramping
- Pain
- Possible blood

Crohn's Versus Ulcerative Colitis

- Major Difference
  - Crohn's located "patches" throughout intestinal system
    - Can impact all the way through the intestine
  - Ulcerative colitis – continuous area in the colon and typically just the inner lining

Crohn's Major Options

- 5-Asa Compounds
  - Sulfasalazine
    - GI/rash
    - Rare – Elevated LFT's, neutropenia, thrombocytopenia
  - Mesalamine
    - Diarrhea, nausea
  - Maybe not so great if large small intestine component
- Corticosteroids
  - Budesonide (Entocort EC)
  - Used for short term active disease/maintenance over 3-6 month period
    - Long term not recommended
  - Much less systemic absorption than alternative steroids

Crohn’s Major Options

- Antibiotics
  - Metronidazole
  - Ciprofloxacin
- Immunosuppressive
  - I.e. Azathioprine
- Biologics
  - I.e. Infliximab, adalimumab

Ulcerative Colitis Major Options

- 5-Asa based compounds
  - Sulfasalazine
  - Mesalamine
- Steroids

Symptom Management

- Antidiarrheal
  - Loperamide
  - Cholestyramine
  - Colestipol

Diarrhea and Constipation

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Changes in Regularity

- Diet
- Exercise
- Fluid intake
- Drugs
- Disease

Medical Causes of Diarrhea

- C. Diff
- Viral
- Rare bacteria (giardia etc.)
- IBS

Medical Causes of Constipation

- Hypothyroid
- IBS
- Parkinson’s
- MS
- Colon Cancer

Medications that Cause Diarrhea

- Metformin
- Acetylcholinesterase Inhibitors
- Antibiotics
- PPI’s
- GLP-1
- Colchicine
- Laxatives

Medications that Cause Constipation

- Opioids
- Anticholinergics
- CCB’s
- Bile Acid Sequestran
- Calcium/Iron

Diarrhea Treatment

- Identify Cause
  - Medical?
  - Drug?
- Loperamide
- Diphenoxylate/atropine
- Bile acid sequestrans

Constipation Treatment

- Non-drug (fluid, fiber, exercise)
  - Ideal management
- Docusate (prevention)
  - Usually very well tolerated
- Stimulants
  - Cramping, pain can be bothersome for some patients
- PEG
  - Requires volume intake, rare chance for electrolyte changes

Constipation Treatment

- Lubiprostone
  - Expensive
- Lactulose
  - Excessively sweet taste, used in elevated ammonia levels
- Enemas
  - Caution with fleets type products and patients with poor kidney function
  - Used for quick results
- Mineral Oil
  - **Avoid
  - Pneumonitis, reduce absorption of fat soluble vitamins

GERD, PUD, and Dyspepsia

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GI Risk Considerations

- GI Diagnosis
  - PUD (Don’t forget about H. Pylori)
  - GERD
  - Heartburn
  - Barrett’s
- Length of medication use
- Reason for initiation

Proton Pump Inhibitors

- Incredibly common medication
- Often used for prophylaxis
- Often never reassessed
- Sometimes necessary long term

PPI Risks

- Fracture
- C. Diff
- Low Magnesium
- Pneumonia
- B12

PPI Drug Interactions

- Cefuroxime (concentrations reduced) – all PPI's
- Reduced iron absorption
- Rifampin/St. John's Wort – can reduce concentrations
- Omeprazole (2C19)
  - Clopidogrel (reduced concentrations)
  - Cilostazol (increased concentrations)
  - Citalopram/escitalopram

H2 blockers

- Kidney disease
  - Dose adjustments
- Confusion/CNS effects with accumulation
- Cimetidine – bad idea
  - Numerous 3A4 drug interactions

Antacids

- Calcium containing products
  - Constipation
  - Binding interactions
  - Work quickly
  - Don’t last long
  - Rare accumulation of calcium if frequent use
    - Combination with HCTZ

Step Down Versus Step Up

- Step Down
  - Reducing PPI to less potent acid blocker
  - H2 Blocker
- Step Up
  - Start with antacid and/or H2 blocker
  - Step up to PPI if inadequate control

Classic Medication Causes of GI Issues

- Steroids
- Bisphosphonates
- Digoxin toxicity
- NSAIDs
- Metformin
- Acetylcholinesterase inhibitors
- GLP-1
- Antibiotics

Irritable Bowel Syndrome (IBS)

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IBS versus IBD

- Irritable Bowel Syndrome
  - Similar symptoms
    - Diarrhea
    - Cramping
    - Pain
    - Constipation
- Irritable Bowel Disease
  - Marked by inflammation/damage
  - I.e. Crohn’s or UC

Treatment of IBS

- Antidiarrheal (if diarrhea)
- Constipation
  - Fiber/fluids
  - Osmotics (i.e. PEG)
- Spasms/pain
  - Anticholinergics
  - Dicyclomine, hyoscyamine

Awareness of Medication Adverse Effects

- Diarrhea
  - Metformin
  - Acetylcholinesterase inhibitors
  - Colchicine
  - SSRI’s (sertraline)
- Constipation
  - TCA’s
  - Opioids

Malabsorption, Malnutrition and Nutritional Deficiencies

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Malabsorption Disorders

- Lack of absorption of essential nutrients
- Cause
  - GI damage, alteration to GI tract
  - Surgery, Celiac disease, Crohn’s
- Symptoms
  - Diarrhea
  - Weight loss
  - Poor growth (kids)
  - Anemia
  - Fatigue

Contributors to Malnutrition

- Cancer
- Dental Issues
- Restricted diets
- Finances
- Depression
- Taste/smell alterations
- Socially eating
- Alcoholism

Weight Loss – Medication Causes

- Digoxin
- Stimulants
- Acetylcholinesterase Inhibitors
- Diuretics
- *Be aware of timing of medication changes

Malnutrition Concerns

- Weight Loss
- Vitamin Deficiency
  - I.e. B12, thiamine, folic acid, etc.
- Low Albumin
  - Phenytoin
- Frailty

Replacement of Essential Nutrients

- B12
- Vitamins A, D, E, K
- Iron
- Thiamine
- Folic acid
- Electrolyte replenishment
  - Magnesium
  - Potassium
  - Calcium

Vitamin B12

- Deficiency
  - Can cause cognitive impairment/dementia if severe enough
  - Metformin, PPI's – possible contributors
  - Pernicious Anemia
    - Lack of intrinsic factor
    - GI absorption compromised
    - B12 injections
- Folic acid, iron, B12
  - See anemia

Thiamine

- Supplementation common for alcoholics
- Deficiency
  - Wernicke’s encephalopathy
  - Acute delirium
  - Amnesia

Vitamin D

- Treatment of deficiency
  - Vitamin D 50,000 units weekly X 8 weeks
- Maintenance
  - Vitamin D 50,000 units/month
  - Vitamin D 1,000-2,000 units/day
- Target levels >30 (some may argue a little higher)
- Medication contributors
  - Anticonvulsants (phenytoin, phenobarbital, carbamazepine)
  - Leuprolide

Parenteral Nutrition

- IV nutritional supplementation
- Use oral when possible due to risks
  - Infection risk
  - Electrolyte/fluid abnormalities
  - Hyperglycemia
  - Refeeding syndrome*
  - Liver damage

Refeeding Syndrome

- Body adaptation to replacement of nutrients after starvation period
- Lipids/protein are energy sources in fasting state
  - Shift to carbs with TPN
  - Cells shift to storing/synthesizing fat/protein
    - Requires use of electrolytes
  - Electrolyte deficiencies possible
    - Potassium
    - Phosphorus
    - Magnesium
- Close monitoring of electrolyte/fluid status when initiating TPN

Caloric Requirements

- Harris Benedict equation
  - Weight, height, age, gender
  - Don’t memorize
- Stress level on patient
  - Mild – 20-25 kcal/kg/day
  - Moderate 25-30 kcal/kg/day
  - Severe 30-40 kcal/kg/day
    - Severe burn patient example

Kcal Per Nutrient

- Carbs
  - 3.4 kcal/gm
  - D10% 340 kcal/L
- Protein
  - 4 kcal/gm
- Lipids
  - 9 kcal/gm
  - 10% lipid solution – 1.1 kcal/ml

Targeted Replacement (TPN)

- Carbs
  - 5 grams/kg/day
- Protein
  - 1-2 gram/kg/day (higher stress, target higher replacement)
- Fat (20-40% of caloric intakes)
- Fluid replacement (30-40 mls/kg/day)
  - 70 kg = 2,100 - 2,800 mls

Sample Calculation

- https://health.csusb.edu/dchen/368%20stuff/TPN%20calculation.htm

Nausea and Vomiting

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Causes of Nausea and Vomiting

- Chemo
- Gastroparesis
- Motion Sickness
- Drugs
- Infection
- Severe Pain
- Migraine
- Pregnancy

Challenges

- Huge diagnostic differential
- Polypharmacy
- Easy to treat symptoms and hard to identify cause

Medications for Nausea/Vomiting

- Ondansetron
  - Serotonin activity (5-HT3)
    - Rare issues, but look out for other serotonergic meds
  - Be cautious with other QTC Prolonging agents

Dopamine Antagonists

- Meclizine
- Prochlorperazine
- Metoclopramide
  - May have serotonin activity as well
- *Movement disorders

Corticosteroids

- Dexamethasone
  - Chemo
  - Risks
    - GI Upset
    - OP, Cushing’s, insomnia, etc.

Nausea and Vomiting in Pregnancy

- Non-drug interventions
  - Small meals
  - Mild/simple foods
- Pyridoxine – first line medication, excellent safety profile
- Doxylamine
- May see these used, but we try not to
  - Chlorpromazine/prochlorperazine
  - Diphenhydramine
  - Metoclopramide
  - Ondansetron

Classic Medication Causes of Nausea/Vomiting

- Antibiotics
- Acetylcholinesterase inhibitors
- GLP-1
- Digoxin toxicity
- Opioids
- Metformin
- NSAIDs
- Iron
- Antidepressants
- Alcohol

Pancreatitis

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Pancreatitis

- Symptoms
  - GI pain (possibly radiating)
    - Upper abdomen
  - N/V
  - Fever
- Major roles - pancreas
  - Digestive enzymes
  - Insulin
- Elevation
  - Amylase
  - Lipase

Causes of Pancreatitis

- Gall stones
- Alcohol
- Infection
- High Triglycerides
- Medications

Medication Causes (Acute)

- Azathioprine
- Thiazides
- VPA
- Sulfasalazine
- Bactrim
- Tetracycline
- GLP-1 agonists
- DPP-4 inhibitors

Treatment

- Treat the cause
  - Gallstone removal
  - Hypertriglycerides (500 or greater)
    - Fibrates
    - Niacin
    - Fish Oil
  - Digestive enzymes
  - ETOH treatment

Stress Ulcer Prophylaxis

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Stress Ulcer Prophylaxis Indications

- Mechanical ventilation for >48 hours
- GI bleed history (<1yr)
- Low platelets (50K)
- INR >1.5
- TBI/spinal cord injury
- Burn
- Two or more
  - Sepsis, ICU >7 days, occult GI bleed, glucocorticoid use

Medications

- H2 blockers
  - Ranitidine, famotidine
  - May require renal dose adjustments
    - CNS side effects possible in elderly, high dose, poor kidney function
  - IV/PO options
  - Less expensive
- PPI’s
  - Pantoprazole, omeprazole, etc.
  - IV/PO options
  - More efficacious?

Infrequently Used Options

- Antacids
  - PO only
  - Keep an eye on magnesium/calcium levels if these are being used; generally not as effective as PPI's/H2 blockers
- Sucralfate
  - PO only
  - Aluminum toxicity risk (rare)
- Misoprostol
  - diarrhea

Possible Risks

- Pneumonia
  - Rise in GI pH
- C. Diff

Hematologic

Anemia

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Signs/Symptoms of Anemia

- Fatigue
- Low Hemoglobin/Hematocrit
  - Elderly often can feel normal despite levels below normal
  - WHO (men<14, women <12.3)
- Dizziness/Falls
- Skin pallor
- Weak
- Confusion

Classic Causes of Anemia

- Blood loss
- Iron
- B12
- Folic Acid
- Chronic Disease (esp. CKD)
- Chemotherapy

B12 Deficiency Causes

- PPI
- Metformin
- ETOH
- Intrinsic Factor - pernicious

Drug Causes – Folic Acid Deficiency

- Methotrexate
- Trimethoprim
- Phenytoin

Treatment of Anemia

- Transfusion
- ESA (i.e. darbepoetin)
- B12
- Iron
- Folic Acid
- No treatment (if asymptomatic)

Megaloblastic Versus Microcytic

- B12/FA
  - Megaloblastic
  - MCV>100
    - Homocysteine
    - MMA
- Iron
  - Microcytic
  - MCV <80
  - Ferritin

- *Elderly often present with mixed type of anemias and normal MCV

Pernicious Anemia

- Lack of intrinsic factor
- Poor oral B12 absorption
- B12 toxicity rare
- B12 shots

ESA Pearls

- Kidney produces erythropoietin
- Hold orders based on hemoglobin
- Iron shortage causes failure
- Risk of CV Event/Hypertension/Blood Clot
- Consideration for starting if hemoglobin <10
  - Reduce dose if >1 point increase in hemoglobin in less than 2 weeks

Blood Disorders and HIT

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Factor V Leiden

- Mutation in gene
- Thrombophilia (clot formation likely)
- Anticoagulation (warfarin chronic, heparin type product for acute treatment)

Von Willebrand Disease

- Von Willebrand Factor
  - Required for platelet aggregation
  - Bleed risk increased
- Treatment
  - DDAVP (desmopressin)
  - Stimulates release of VW factor

Thrombocytopenia

- Low platelets
- Increased bleed risk
- Symptoms
  - Bruising
  - Bleeding
  - Anemia

When to Worry - Thrombocytopenia

- 150-450k = normal
- <150k = “thrombocytopenia”
- Trends are important
- <50k severe

Medication Causes of Thrombocytopenia

- Aspirin
  - (NSAIDs)
- Clopidogrel
- Heparin
- Seizure medications
- Sulfonamides
- PCN antibiotics
- Chemo

Heparin Induced Thrombocytopenia

- HIT – Heparin induced thrombocytopenia
  - Type 1 – occurs within hours to a couple of days
    - Direct effects on platelet aggregation (non-immune response)
  - Type 2 – What most people think when they hear “HIT”
    - 4-10 days after initiating, immune response
    - May see skin reaction at injection site, fever, chills, SOB after administration
  - Drop in platelets >50%
- Alternative anticoagulation
  - Argatroban, bivalirudin (PCI), fondaparinux, warfarin

DVT/PE

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Risk Factors for DVT/PE

- Patient history
- Hypercoagulable Disorders
- Immobility
- Atrial Fibrillation
- Medications
- Smoking
- Cancer

Medications – Increased Risk of DVT/PE

- Estrogen
- Megesterol
- SERM

Important Considerations DVT/PE Treatment

- Drug Selection
  - LMWH
  - Heparin
  - NOACs
  - Warfarin

Considerations in Selection

- Low-molecular weight heparin
  - Immediate action (unlike warfarin)
    - Often used for bridging
  - Drug of choice in pregnancy
  - Needle phobia
  - 1mg/kg BID or 1.5 mg/kg daily
  - Obesity – higher doses
- Contraindications
  - Heparin induced thrombocytopenia
  - Derived from pork products
  - Avoid in dialysis
- Warfarin/NOACs – See separate presentations

Length of Therapy

- First Episode (usually 3-6 months)
- Known Cause
- Risk Factors

Sickle Cell Disease

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Sickle Cell Disease

- Genetic disease
- Abnormally shaped RBC's
  - Look like a sickle - not round (half/quarter moon shape)
  - Do not transport oxygen very well
- Symptoms
  - Chest pain
  - Pulmonary HTN
  - Infection risk
  - Stroke

Management

- Hydroxyurea
  - Helps with pain associated with sickle cell disease
  - Warning on myelosuppression
    - Low WBC, Platelets
- Antibiotic therapy (penicillin anbx), Vaccination
  - Infection prevention
- Pain can be a manifestation
  - Simple analgesics
  - SNRI
  - Gabapentin
  - TCA
  - Opioids
- Transfusion

Immunologic

Angioedema and Anaphylaxis

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Angioedema

- Signs
  - Swelling, tingling of mouth, lips, throat
  - Quick onset
  - Difficulty breathing is very concerning, medical emergency
  - Mild cases, limited to minor lip swelling can be managed outpatient

Anaphylaxis

- Respiratory distress
- Swelling/hives
- Hypotension
- Tachycardia

Goals of Therapy

- Medication treatment urgent
- 911
- Supportive care
- Identify cause
  - Avoidance to prevent future occurrence

Medications

- Epinephrine
  - Drug of choice in anaphylactic reaction
  - 0.15 mg dose in peds/0.3 mg dose in adults
  - Beta and alpha agonist activity constricts vessels
  - Beta/alpha blockers can blunt response
- Antihistamines
  - I.e. diphenhydramine
  - Used for allergic reaction in non-life threatening situation
  - Reduces reaction, can help with itch, hives

Medications

- Corticosteroids
  - Inflammation reduction
  - Alternative/add on to antihistamine in allergic reaction
  - Epinephrine used first line in anaphylaxis
- Glucagon
  - Possible option for those non-responsive to epinephrine
  - Helps avoid beta-blocker blunting effects
- Beta agonists
  - Inhaled – supportive care for continued breathing issues

Drug Induced Angioedema

- Generally not associated with urticaria
- ACE Inhibitors
  - African descent
  - Female
  - Age>65
  - Smoking
  - Seasonal allergies history
- NSAIDs
- Discontinue offending agent

Febrile Neutropenia

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Febrile Neutropenia

- Fever and low WBC (particularly ANC)
- ANC <500
- ANC <1,000 with anticipated drop further
  - Chemo just done
- Temp >38 Celsius

Highest Risk Patients

- ANC closer to 0 (<100)
- Underlying disease/conditions
  - Respiratory disease
  - CNS changes
  - Hypotensive
  - Chronically low ANC
- In these high risk patients with febrile neutropenia, antibiotic therapy is nearly always recommended

Antibiotics

- Broad spectrum
  - Pip/tazo
  - Penems
- Targeted therapy if source/bug identified
  - Vancomycin – MRSA
  - Aminoglycosides – Gram (-)
  - ESBL – Penems
  - Pseudomonas – pip/tazo
  - VRE – linezolid/daptomycin

Factors in Risk Stratification - Neutropenia

- Age
- Burden of disease
- Previous history
- Hypotension
- COPD
- Onset of fever (in hospital or outpatient)
- Dehydration requiring fluid replacement

Colony Stimulating Factor Use

- >20% risk of febrile neutropenia
  - Use CSF
- 10-20%
  - Possibly use
  - Patient history assessment
- Palliative chemo
  - More likely to reassess dose of chemo versus utilize CSF

Filgrastim

- Clinical pearls
  - Bone pain
    - Simple analgesics
  - Labs
    - Can elevate alk phos, uric acid
    - Usually transient
  - Injection site reaction

Medications for Organ Transplantation

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Calcineurin Inhibitors

- Cyclosporine, tacrolimus
  - Adherence is very critical
  - Change in dosage forms can result in changes in levels/bioavailability
- Monitoring
  - Immunosuppression/infection/cancer
  - Hypertension
  - Hyperglycemia
  - Hyperkalemia
  - GI side effects

Calcineurin Inhibitors

- Trough concentrations drawn
  - Goals can vary based upon:
  - Infection risk
  - Adverse effects
  - Risk of rejection
  - Time from transplant
  - 100-400 target levels
- Consistent timing of administration recommended
- CYP3A4 drug interactions
  - Monitor levels closely with changes

Corticosteroids

- Infection
- Cushing’s
- Hyperglycemia
- Osteoporosis
- GI Risk

Mycophenolate

- Adverse effects
  - GI
  - Hypertension
  - Edema
  - Immunosuppressive effects
- Administer on empty stomach

Signs of Rejection

- Loss of function of organ – examples:
  - Jaundice (liver)
  - Worsening renal function
- Patient feeling poorly
  - Flu like symptoms
- Pain/swelling
  - Location of organ
- Acute rejection
  - Week to 3 months; chronic >3 months
- Review for adherence/interaction/adverse effect potential

Infectious Diseases

Surgical Antibiotic Prophylaxis

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Considerations

- Location, location, location
  - Not just for real estate
  - Location of surgery
    - Allows us to speculate type of bugs to protect against
- Typically concerned (skin entry)
  - Staph
  - Strep

Skin Targets - Antibiotics

- Staph and Strep
  - 1st or 2nd generation cephalosporin (i.e. cefazolin)
  - Ampicillin
  - MRSA possibility
    - Vancomycin
  - For those allergic to PCN/Ceph
    - Clindamycin

GI surgery

- Gram negatives
  - Quinolones
- Anaerobes
  - Metronidazole
  - Clindamycin

Urologic

- Remember bugs that commonly cause UTI's
  - E. coli and the rest…
- Antibiotics
  - Sulfa/TMP
  - Quinolones (i.e. ciprofloxacin)

Bacterial Prostatitis

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Symptoms

- Pain
- Inflammation
- Change in urine consistency
  - Blood
  - Frequent urination
- Often not bacterial infection

Bacterial

- Simply remember standard UTI medications
- Length of therapy is different (next slide)
- Targeted bugs
  - Gram (-)
  - Enterobacteriaceae
    - I.e. E. coli

Chronic Bacterial Prostatitis

- 4-6 weeks treatment
  - Possibly up to twelve
- Bug Coverage
  - Quinolones (i.e. ciprofloxacin, levofloxacin)
  - TMP/Sulfa
  - Doxycycline

Adjunct Symptom Management

- Pain relief
  - NSAIDs
  - Acetaminophen
- Urinary flow
  - Alpha blockers

Common Drug Resistant Bacteria

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MRSA

- Methicillin Resistant Staphylococcus Aureus
  - Community acquired
    - Resistant to Penicillins, cephalosporins
    - Oral options: Doxycycline, Clindamycin, Sulfa/tmp
  - Inpatient medications
    - Vancomycin
    - Linezolid
    - Daptomycin (non-pneumonia)

Other Gram Positives

- Strep Pneumo.
  - Gram Positive
    - Resistance to penicillins, cephalosporins
    - Alternatives: Levofloxacin or moxifloxacin (avoid ciprofloxacin), clindamycin, vancomycin (IV only)
- Vancomycin Resistant Enterococcus (VRE)
  - Linezolid, daptomycin alternatives

Pseudomonas Aeruginosa

- Gram negative
  - Resistant to 1st, 2nd, 3rd generation cephalosporin's (exception ceftazidime), non antipseudomonal penicillins
  - Common Treatment
    - Quinolones (oral)
    - Pip/tazo
    - Meropenem
    - Colistin
    - Polymixin B

Extended Spectrum Beta Lactamases

- Klebsiella
  - Resistance to 2nd/3rd generation cephalosporins
  - Alternatives:
    - Imipenem
    - Colistin
- E Coli.
  - Resistance to sulfa/tmp, cephalosporins, quinolones
  - Nitrofurantoin, penems

Endocarditis

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Heart Infection

- Bugs are typically deposited from blood stream, usually from other areas of the body
  - Wound
  - Surgery
  - Mouth (dental prophylaxis
  - IV drug abusers

Likely Bugs

- Gram +
  - Staphlococcus sp.
  - Strepotococcus sp.
  - Enerococcus sp.
  - Less commonly Gram (-)

Management

- Empiric
  - Vancomycin
  - Linezolid
  - Daptomycin
- ID organism(s) and adapt treatment

Specific Targets

- MRSA
  - Vancomycin
- MSSA
  - Ampicillin
- Gram (-)
  - 3rd generation cephalosporins
  - Aminoglycosides

Prophylaxis Consideration

- Specific prophylaxis for procedures
  - (i.e. dental prophylaxis)
- Who might be candidates?
  - Endocarditis hx
  - Valve replacement
  - Pre-existing cardiac injury
  - Transplant patients
- Amoxicillin or clindamycin

Fungal Infections

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Tinea pedis

- Athlete's foot
  - Itching, burning, redness between toes, on feet
  - Warm moist environment
- Treatment
  - Topicals
    - Fungal infections can take a while to heal (up to 6 weeks)
    - Clotrimazole, miconazole, ketoconazole (imidazoles)
    - Terbinafine (allylamines)
  - Orals
    - Don't use for mild cases
    - Itra/fluconazole
      - Drug interactions! (3A4)
    - Terbinafine

Tinea cruris

- Jock itch
  - Warm/moist environments
    - Keep areas cool and dry as much as possible
    - May see higher incident in summertime/warm climate temps
- Topical agents, similar to Tinea pedis
  - Clotrimazole
  - Terbinafine
  - Miconazole

Ringworm

- Tinea family
  - Topical agents
    - Terbinafine
    - Ciclopirox
  - Orals
    - Systemic azoles
    - Terbinafine

Azole Clinical Pearls

- Adverse effects
  - Common – GI
  - Rare but serious – Liver function
    - More concerning with longer term/higher dose or those at risk for liver concerns
  - CYP3A4 inhibition
    - Warfarin, seizure medications, etc.
  - Possible QTc prolongation risk – highest risk in those on other agents
    - I.e. Amiodarone (+ 3A4 interaction)

Thrush

- Candida albicans
  - White gunk, pain, inflammation, difficulty swallowing
  - Immunosuppression from meds increases risk
    - Chemo, steroids (including inhaled)
  - Treatment
    - Clotrimazole troche
    - Nystatin topical (swish/swallow or swish/spit)
    - Systemic fluconazole for non-responders, adherence concerns, more severe disease
    - Ampho B – life threatening

Yeast Infection

- Candida albicans
  - Itching, burning, cottage cheese type discharge
  - May be exacerbated/caused by changes in normal flora
    - Recent antibiotics
  - Topical azoles
    - Clotrimazole, miconazole, etc.
  - Systemic
    - Fluconazole

Aspergillosis

- Tends to more problematic in immunosuppressed
  - Can cause pneumonia and CNS type symptoms
- Voriconazole typically first line
  - Isavuconazole
- Amphotericin B
  - Option for severe infection

Amphotericin B – Clinical Pearls

- Conventional and lipid based formulas
  - Not interchangable
  - Infusion reaction
    - Diphenhydramine with APAP or NSAID - pretreatment
      - Corticosteroids as option as well
  - Flu-like adverse effects (more common with first doses)
    - Chills, headache, pain, just not feeling well
  - Can drop K+, Mg+
  - Renal insufficiency – nephrotoxic
  - Boxed warning – use for severe, life-threatening infections

Blastomycosis

- Typically – lung infection
  - Mild symptoms, sometimes asymptomatic
    - Slow growing
  - Treatment
    - Itraconazole
    - Ampho B for severe

Histoplasmosis

- Lung infection
- Immunocompromised at highest risk (HIV/AIDS)
- Itraconazole
- Ampho B last line/severe

Cryptococcus

- Lung and CNS effects possible
- HIV/AIDS
- Fluconazole for mild to moderate
- Ampho B + flucytosine for severe with CNS involvement

PCP – Pneumocystis Pneumonia

- Pneumonia
- Sulfamethoxazole/TMP
  - Longer length of treatment usually necessary compared to UTI or antibacterial use (i.e. a few weeks)

GI Infections

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Infections

- 2 Classic Infections you need to know
  - Clostridium Difficile (C. Diff)
  - Helicobacter Pylori (H. Pylori)

C. Diff

- Watery diarrhea
- Cramping
- Pain
- Blood (severe)
- Spores can last for weeks to months
  - Horrible for healthcare facilities

Medication Risks

- Antibiotics
  - Minimize duration
  - Minimize spectrum
- PPI’s
  - Assess diagnosis for use
  - Risk/Benefit

Treatment

- Metronidazole
- Vancomycin
  - Oral ok
- Fidaxomicin

H. Pylori

- Major cause of GI ulcers
- Able to tolerate acid environment of stomach
- Symptoms
  - N/V
  - Abdominal pain
  - Weight loss
  - Burping

Treatment

- Typically 10-14 days
- Different regimens (see next slide for combo's)
  - Amoxicillin
  - Clarithromycin
  - Metronidazole
  - Bismuth
  - Tetracycline

Treatment

- Bismuth, metronidazole, tetracycline, PPI
- Amoxicillin, clarithromycin, PPI
- Clarithromycin, metronidazole, PPI
- Regimen considerations
  - Resistance
  - Previous treatments
  - Penicillin allergy

Clinical Pearls - Antibiotics

- Clarithromycin
  - Drug interactions via 3A4
  - QTc prolongation
- Metronidazole
  - Avoid alcohol
  - Neuropathy (more likely with long term use)
- Tetracycline
  - Binding interactions
  - Sun sensitivity

Hepatitis

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Hepatitis/Hepatotoxicity

- Hepatitis
  - Inflammation of the liver
  - Elevation in ALT/AST
  - 3x ULN
- Common causes
  - Hepatitis A, B, C
  - Drugs
  - Alcoholics
    - See cirrhosis

Drug Induced Causes

- Amiodarone
- Isoniazid
- RA drugs
  - MTX, leflunomide, sulfasalazine, hydroxychloroquine
- Valproic acid
- Rifampin
- Statins

Hepatitis A

- Vaccine available
- Fecal/oral transmission
  - Unsafe water in more 3rd world countries
- Symptoms
  - Mild fever, N/V, muscle pain, anorexia
- Usually self limiting, but rare cases of hepatic failure
  - Supportive care is mainstay
  - Immunoglobulin therapy – may be administered with vaccine

Hepatitis B

- Blood, semen, vaginal transmission
- Symptoms
  - N/V, anorexia, mild fever, muscle aches
  - Many patients will be asymptomatic
  - Immune response causes issues and can cause liver injury
    - Can lead to HE, coagulopathy, confusion, ascites
- Risk of liver cancer
- Vaccination available

Drugs

- PEG interferon alfa 2a
  - Boxed warning on psych, autoimmune, infectious issues
  - Hair loss, GI, CNS changes are common adverse effects
- Entecavir (nucleoside), tenofovir (nucleotide)
  - Lactic acidosis and hepatomegaly boxed warning

Hepatitis C

- Blood transmission (IV drug abusers)
- Patients born from 1945-1965 are at highest risk due to previously poor infection control practices
- Some cases will clear on their own, some will become chronic
- Direct acting antivirals are drugs of choice
  - Ledipasvir/sofosbuvir (Harvoni)
- No vaccine

Needle Stick Injuries

- Hepatitis B vaccination!
- Post Exposure Management
  - Information gathering
  - Patient exposure/past medical history
    - Hep B/Hep C testing – source
  - If cannot find out patient's history, must assume they are positive for disease
- Antibody titer – use this to assess vaccination status and to identify if post exposure prophylaxis is necessary

Hepatitis B - Immune Globulin

- Give within 24 hours of exposure if possible
  - 7 days at latest
- Hepatitis C
  - Monitor
    - Early treatment if infected
  - IG not available at this time
  - Vaccination not available

HIV/AIDS

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HIV/AIDS Pearls

- Drug resistance
  - Frequent mutations
  - Adherence CRITICAL
- Immune Deficiency
- Rare, opportunistic infections
- Monitoring
  - CD4 counts

Opportunistic Infections

- PCP (Pneumocystis pneumonia)
  - Sulfa/TMP
  - Glucocorticoids
- Kaposi Sarcoma
  - Chemo or radiation
- Mycobacterium Avian Complex (MAC)
  - Macrolide
  - Ethambutol
  - Rifampin

CD4 Count

- CD4 Count
  - 500-1500 is normal
  - Following trend
  - Lower = higher risk for infection
- If less than 200
  - PCP prophylaxis
- If less than 50
  - MAC prophylaxis

Medications for HIV/AIDS

- NRTI (Nucleoside)
  - Abacavir, Emtricitabine, Lamivudine
  - Adverse Effects: Fat redistribution (lipodystrophy –i.e. buffalo hump), lactic acidosis, fatty liver
- NRTI (Nucleotide)
  - Tenofovir
  - Adverse Effects: lactic acidosis, fatty liver, may increase cholesterol and decrease bone mineral density

Protease Inhibitors

- Atazanavir, Darunavir, Fosamprenavir, Lopinavir/Ritonavir
  - Lipodystrophy (buffalo hump)
  - CYP3A4 interactions
  - Rash
  - Hyperglycemia
  - (Ritonavir is a booster – increases concentrations of lopinavir)

NNRTI’s

- Efavirenz
  - Rash
  - CNS changes
    - Mood/Depression
  - Liver

Integrase Inhibitors

- Raltegravir, dolutegravir, elvitegravir
  - GI
  - Myopathy/elevations in LFT, CPK
  - Immune reaction
  - Skin reactions

Influenza

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Influenza Pearls

- Very contagious
- Institutionalized patient at high risk of transmission
- Vaccination
- Prophylaxis in an outbreak
- Mutations
- Elderly/young at higher risk for complications
  - Secondary pneumonia

Medications

- Antiviral – Neuraminidase Inhibitor
  - Prevents replication
- Oseltamivir
  - Drug of choice for treatment and prevention
  - Sooner the better with treatment (less than 48 hours)
  - Expensive
  - Watch kidney function/dose adjustments
  - Lower dose for prophylaxis (75 BID vs. QD)
  - GI, psych changes as most common AE’s

Intra-Abdominal Infections

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Intra-Abdominal Infection

- Signs
  - Fever
  - Pain
  - Possibly due to
    - GI tract infection
    - Gynecologic
    - Kidney
    - Liver
- Polymicrobial Coverage

Common Bugs

- Gram (-)
  - E. Coli
  - Klebsiella
  - Proteus
- Anaerobes
  - Bacteroides fragilis
- Gram (+)
  - Streptococci
  - Enterococci

Regimens – Low Risk Infection (Community Acquired)

- Can be used alone
  - Pip/tazo
  - Ertapenem
  - Ticarcillin/clavulanate
- Combination
  - Metronidazole
    - Plus one; cefazolin, ceftriaxone, quinolone

Severe Infections

- Imipenem-cilastin
- Pip/tazo
- Meropenem or doripenem
- Combo
  - Metronidazole
  - Plus 3rd generation cephalosporin or quinolone
- For Healthcare Associated Infection
  - May have to add linezolid, daptomycin for VRE risk
  - Vancomycin if MRSA suspsected

Meningitis

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Meningitis

- Sudden spike in temperature
- Neck stiffness
- Severe headache
- CNS effects
  - Confusion
  - Seizures
  - Sleepiness
  - Ataxia

Meningitis – Likely Causes

- Newborns
  - Group B Streptococcus, Strep pneumo, Listeria monocytogenes, E. coli
- Babies - young children
  - Strep pneumo, Neisseria meningitidis, Haemophilus Influenza B, Group B Streptococcus
- Teens/young adults
  - Neisseria meningitidis, Streptococcus pneumonia
- Older adults
  - Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus Influenza type B, Listeria monocytogenes

Medication Selection - Neonates

- 3rd generation cephalosporin
  - Majority of scenarios
  - Cefotaxime for neonates very young babies
    - Likely concerns with safety profile of ceftriaxone
- Ampicillin
  - Add on for neonates
- Gentamicin
  - Coverage for Listeria

Young Kids

- 3rd Generation cephalosporin
  - Ceftriaxone
- Resistant Streptococcus risk
  - Vancomycin
- Vaccination!
  - Haemophilus influenzae and Streptococcus pneumonia

Young Adult/Teens

- Neisseria meningitidis
  - Ceftriaxone
  - Ampicillin, fluoroquinolone alternatives
- Prophylaxis for patients in close contact – see ahead for agents
  - Dorms
  - Military

Elderly

- 3rd generation cephalosporin
- Maybe a little more likely for resistant Strep. Pneumoniae species
  - Vancomycin possibly a stronger consideration

Miscellaneous

- Don’t sleep on Lyme’s disease
  - Tick bite
  - Doxycycline
- Meningitis prophylaxis
  - Vaccinations
  - Rifampin
  - Cipro alternative
  - Ceftriaxone IM – pregnancy option

Osteomyelitis

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Osteomyelitis

- Infection of the bone
- Redness/swelling/pain at site
- Fever
- Long length of treatment (weeks)

Risk Factors

- Diabetes
- Immunosuppressed
  - Chemo
  - Corticosteroids
  - Biologics
- Illicit drug use
  - I.e. dirty needles
- Recent trauma or surgery

Procedures

- Debridement
- Improving blood flow
- Amputation

Bacteria

- Cultures Important!
- Most common: Staphylococcus
  - Need to be aware of MRSA (vancomycin, linezolid)
  - MSSA (Penicillins)
- Gram negatives possible
  - Quinolones
- Tough infections to treat
  - Likely at least 4-6 weeks on initial infection
  - Recurrent infections might require life long prophylaxis

Effective antibiotics

- Penicillin(s) - MSSA
- Clindamycin
- Sulfamethoxazole/trimethoprim
- Rifampin (used to prevent reinfection, prosthetic)
- Vancomycin (empiric gram positive)
- Linezolid
  - MRSA/VRE
- Quinolones (gram negative)

Otitis Media

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Otitis Media

- Infection of middle ear
- Viral infection is common in pediatrics
  - Should not be treated with antibiotics
- Signs/symptoms
  - Tugging on the ear
  - Pain
  - Fever >38 Celsius (100.4 Fahrenheit)
  - Insomnia
  - Appetite/stool change

Risk Factors

- Daycare
- Infants/toddlers
  - Anatomy of ear canal
- Fall/winter season
  - Enclosed enviroments
- Secondhand smoke
- Non-breastfed infants

Most Common Bacteria

- Streptococcus pneumoniae
- Haemophilus influenza
- Group A streptococcus
- Moraxella catarrhalis
- Staphylococcus aureus

Management

- Prevention – PCV vaccinations
- Watch/wait
  - Especially if mild symptoms
  - No diagnostic tool to identify viral versus bacterial
- Drugs of choice (antibiotics)
  - Amoxicillin 80-90 mg/kg/day
  - Amox/clavulanate
  - Cephalosporins (cefdinir, cefuroxime)
  - Azithromycin
- If MRSA suspected
  - Clindamycin
  - Sulfamethoxazole/trimethoprim
- Quinolones/tetracycline derivatives generally avoided

Pneumonia

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Common Bugs

- Strep. Pneumoniae
- H. Flu
- Staph Aureus
- M. Cat
- Atypical
  - Legionella
  - Mycoplasma

Risk Calculator for Hospitalization

- CURB-65
  - Confusion
  - Urea>20
  - Respirations >20/min
  - BP <90 or diastolic <60
  - Age >65

Vaccination

- Polysaccaride-23 Vaccine
- Conjugate-13 Vaccine
- Influenza

Healthcare Associated

- Hospitalization
- Long term care
- Bugs to be fearful of
  - MRSA
  - Pseudomonas
  - Resistant gram negatives

Community Acquired Treatment

- Macrolide
- Macrolide +/- beta lactam
- Doxycycline
- Respiratory fluoroquinolone

Risk Factors – Resistant Pathogens

- Previous antibiotic use
- Hospitalization
- Immunosuppressive deficiency
- Spreading in the community

Coverage for MDR Organisms

- Pseudomonas
  - Ceftazidime
  - Pip/Tazo
  - Cefepime
  - Penem (excluding ertapenem)
- MRSA
  - Vancomycin
  - Linezolid
- If concern for MDR Gram negatives
  - May add respiratory quinolone
  - Or aminoglycoside

Outpatient MDR Organisms

- MRSA
  - Bactrim
  - Clindamycin
  - Linezolid
- Pseudomonas
  - Quinolones

Sepsis and Septic Shock

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Sepsis

- Fever 38.3 Celsius or higher
- Tachycardia
- Tachypnea

Severe Sepsis

- Potential organ damage
  - CNS status change
  - Change in urine output
  - Change in cardiac output
  - Respiratory difficulty

Septic Shock

- Signs of Sepsis as earlier described
- Hypotension that doesn’t respond to fluid replacement
- Risk/increasing incidence
  - Elderly
  - MDR bacteria
  - Immunosuppressed

The Basics

- Don’t delay antibiotics
- Target likely source of infection for antibiotic selection
  - I.e. UTI, pneumonia, etc.
- Get cultures
- Fluid replacement first in sepsis
- Vasopressors for hypotension unresponsive to fluid

Vasopressors

- Norepinephrine
  - Generally first line in septic shock
  - Alpha agonist activity
    - Primary activity on vessels
  - Lower risk of increasing cardiac output/heart rate

Vasopressors

- Dopamine
  - Has potential to stimulate heartrate
  - Possible use with existing bradycardia
- Epinephrine
  - Drug of choice if anaphylaxis

Antibiotic Selection

- Assess for MDR bacteria
- MRSA, Pseudomonas, ESBL
- Local patterns for resistance
- Source of infection identification
  - Pneumonia
  - Skin and soft tissue infection
  - UTI

Shingles

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Shingles

- Caused by Varicella Zoster virus
  - Chicken pox
  - Reactivation
- Painful skin rash/reaction
  - Inflammation of nerve
  - Blisters

Treatment

- Vaccination (prevention)
  - Best efficacy in the 60's
  - Indicated for age 50 or greater
  - ACIP now recommends Shingrix (over Zostavax)
    - Shingrix (two doses + cost a little more)
    - More effective
- Antiviral treatment
  - Get started ASAP
  - Acyclovir
  - Valacyclovir

Antivirals

- Acyclovir dosed 5 times/day
- GI SE's
- CNS toxicity rare, but possible
  - More likely with poor kidney function
- Potential for renal issues if other kidney toxic medications or dehydration

Pain Management

- Gabapentin
- Pregabalin
- TCA’s
- Topical
  - Capsaicin
  - Lidocaine

Sinusitis

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Sinusitis

- Nasal discharge plus obstruction
- Facial pain, headache, pressure sensation
- Most common cause is viral
- Signs that may point bacterial
  - Persistent symptoms >10 days and no improvement
  - Fever >102
  - Purulent discharge, facial pain for extended period of time – 3 or more days
  - Continued symptoms after initial improvement

Treatment

- Bacterial
  - Amox/clav
    - N/V/D
  - Doxycycline (PCN allergic patients)
    - Binding interaction
    - Sun sensitivity
    - Avoid in pregnancy
  - Respiratory quinolones (levofloxacin, moxifloxacin)
    - Generally avoid if possible
    - QTc prolongation, tendon rupture, CNS effects, renal dosing
  - Macrolides
    - Commonly prescribed, generally now discouraged due to resistance

Supportive Care

- Simple analgesics
  - NSAIDs, acetaminophen
- Nasal steroids
  - Fluticasone, mometasone, etc.
- Nasal saline
- Decongestants
  - Pseudoephedrine (be a little careful depending upon patient population)
- Antihistamines
  - Second generation

Skin and Soft Tissue Infections

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Important Bugs

- Staphylococcus
- Streptococcus
- Pseudomonas

Cellulitis

- Beta-hemolytic Streptococcus
- MSSA
  - Drugs
    - Cephalexin
    - Penicillin
    - Clindamycin

Pseudomonas and MRSA Empiric

- Pseudomonas
  - Quinolones
- MRSA
  - Clindamycin
  - Sulfa/TMP
  - Tetracycline
- Inpatient, higher risk patients
  - Vancomycin
  - Daptomycin
  - Linezolid

Animal/Insect Bites

- Pasteurella multocida (dog/cat bites)
  - Amox/clav
  - Doxycycline
- Lymes (Borrelia burgdorferi)
  - Doxycycline
  - Amoxicillin

Sexually Transmitted Diseases

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Chlamydia

- Usually asymptomatic (especially early after infection)
  - Easily transmissible at this time
- Burning, itching, discharge
- Can cause pelvic inflammatory disease (infertility)
- Treatment
  - Azithromycin 1 gm single dose
    - Best for adherence
  - Doxycycline 100 mg BID

Gonorrhea

- Neisseria gonorrhoeae
- Can be asymptomatic
  - Carrier
- Can cause PID
- Treatment
  - Ceftriaxone IM + single dose 1gm azithromycin
- Assessment of partners and treat accordingly

Syphilis

- Treponema pallidum
- 4 stages
  - Primary – sore at sight of infection
  - Secondary – skin rash, fever, swollen lymph nodes
  - Latent – asymptomatic
  - Tertiary – severe medical problems; neurological problems, impact on cardiac function
- Treatment
  - Penicillin G IM

Genital Herpes

- HSV 1 and 2 subtypes
  - Most genital cases caused by subtype 2
- Antivirals – therapy for outbreaks
  - Not curative
  - Acyclovir, valacyclovir, famciclovir
    - 7-10 days course for initial episode
  - Can consider long term suppressive therapy for those with frequent outbreaks
- Avoid sex when lesions or prodrome symptoms

Human Papillomavirus

- Genital warts
- Topical agents (applied by patient)
  - Imiquimod
  - Podofilox
  - Sinecatechins
- Clinic/office treatment
  - Cryotherapy
  - Trichloroacetic acid
  - Surgical removal
- HPV vaccination
  - Gardasil 9 given to most patients (protective effects on cervical cancer as well as warts)
  - Target 9-26 y/o patients

Bacterial Vaginosis

- Gardnerella vaginalis
  - Flora changes
  - Recent antibiotic use
  - Change in estrogen production
- Vaginal discharge and odor
- Metronidazole oral
  - Vaginal gel
- Clindamycin vaginal gel

Trichomoniasis

- Trichomonas vaginalis
  - Protozoal infection
  - Itching, burning, discharge
- Metronidazole 2 gm single dose
- Tinidazole 2 gm single dose

Tuberculosis

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Tuberculosis

- Latent
  - No symptoms
  - Not contagious
- Active
  - Cough
  - Fever
  - Fatigue
  - Weight loss
  - Contagious
- Difficult to treat - https://www.cdc.gov/tb/topic/treatment/guidelinehighlights.htm

Immunosuppression and TB

- Most immune systems will suppress the infection
  - TB goes from latent to active in immunosuppressed
- HIV/AIDS
- Chemo
- Transplant
- Biologics

Drugs

- Isoniazid
  - Boxed warning for liver toxicity
    - Look out for high risk patients (i.e. other hx liver disease, alcoholics, etc.)
  - Possibility for neuropathy
    - Pyridoxine supplementation may be helpful
- Rifampin
  - Enzyme inducer
    - Look out for high risk meds (anticoagulants, amiodarone, seizure medications, etc.)
- Ethambutol
  - Hepatotoxic
  - Eye exams – optic neuritis, potential blindness
- Pyrazinamide
  - Exacerbate gout
  - LFT monitoring

Urinary Tract Infections

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Definition

- UTIs in women are defined as at least 100,000 colony-forming units (CFU)/ml in a pure culture of voided clean catch urine
- In men, the presence of just 1,000 CFU/ml indicates a UTI

UTIs

- Asymptomatic bacteriuria: $>10^5$ bacteria in the urine without symptoms
- Recurrent UTIs: culture confirmed UTIs with a frequency of >3 in 1 year or >2 in 6 months.
  - Relapse occurs within 2 weeks of treatment and is caused by the same pathogen
  - Reinfection occurs >4 weeks after an earlier UTI and usually involves a different pathogen
- Catheter-Associated UTIs

Common Pathogens

- E. coli (70-80%)
- Proteus mirabilis
- Staphylococcus saprophyticus
- Klebsiella pneumoniae

Antibiotics

- Common treatment regimens include:
  - Trimethoprim/Sulfamethoxazole
  - Nitrofurantoin monohydrate/macrocrystals
  - Ciprofloxacin and other fluoroquinolones
  - Third-generation cephalosporins

Treatment Regimens for Uncomplicated UTIs

- TMP-SMX 160/800mg BID for 3-7 days
- Trimethoprim 100 mg BID for 3-7 days
- Ciprofloxacin 250 mg BID for 3 days
- Levofloxacin 250 mg QD for 3 days
- Nitrofurantoin 100 mg BID for 7 days
- Fosfomycin 3 grams x 1 dose
- Cefpodoxime 100 mg BID for 3 days

Complicated

- Structural abnormality
  - Surgery
  - Urinary retention
  - Males
- Renal insufficiency
- Transplant
- Immunosuppression
- Diabetes

Treatment of Complicated UTIs

- Usually a 7-14 day treatment for mild cases
- Avoid Nitrofurantoin and Fosfomycin if suspected pyelonephritis
- Symptomatic cases require hospitalization and IV antibiotics
- Fluoroquinolones
  - Ciprofloxacin 500mg BID for 7 to 14 days
  - Levofloxacin 250 mg for 10 days or 750mg QD for 5 days
  - Can be used outpatient

Inpatient

- Extended-spectrum beta lactams:
  - Ceftriaxone 1-2 grams IV/IM q24h or in divided doses twice a day
  - Ceftazidime 500mg IV/IM q8-12h
- Aminoglycosides
  - Ototoxicity
  - Nephrotoxicity
- If ESBL
  - Carbapenems

Trimethoprim-Sulfamethoxazole (TMP-SMX)

- Considered 1st-line for uncomplicated UTIs
- Good activity against many pathogens (except *Enterococcus* species)
- Growing resisitance to *E.coli* (20%)
- Common side effects: GI upset and rash
- Crystalluria may occur- take with a full glass of water
- Contraindicated in patients with sulfonamide allergies
- Syrup available

Fluoroquinolones (ciprofloxacin and levofloxacin)

- Effective against gram (-) organisms, but only fair coverage against gram (+)
- Administer (oral) at least 2 to 4 hours before or 6 hours after antacids or other products containing calcium, iron, or zinc.
- Common side effects: N/V/D
- Rare side effect: tendonitis
- Avoid excessive exposure to sunlight
- Reduce the dose by half if CrCl< 30 ml/min
- Caution: may increase effects of warfarin/QTc prolongation

Nitrofurantoin (Macrobid)

- Provides good antibacterial coverage
- Common side effects: N/V/D
- Take with food- increases serum concentrations
- Avoid alcohol
- Avoid in suspected pyelonephritis
- May discolor urine brown
- Contraindicated in patients with CrCl < 60ml/min
  - Some evidence now that it may be ok in CrCl 30-60 mls/min

Fosfomycin

- Studies showed equally effective to nitrofurantoin and TMP-SMX
- Can be given as a single dose
- Expensive- not generally used
- Avoid in suspected pyelonephritis

Pharmacologic Prophylaxis

- Regimens
  - Bactrim/Septra double strength 3x/week or single strength QD
  - Trimethoprim 100 mg QD
  - Macrobid (nitrofurantoin) 100mg QD

Non-Pharmacologic Prophylaxis

- Cranberry juice
  - 300 ml/day of standard juice or 60 ml/day of concentrated juice
  - 400 mg QD of cranberry extract
  - Common side effect: calcium oxalate kidney stones

Neurological

CNS Hemorrhage

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CNS Hemorrhage

- Bleeding within the brain, CNS
- Can lead to inadequate perfusion/damage
  - Hemorrhagic stroke
  - Less common stroke than thromboembolic/atherosclerotic blockage
- Primary concern as pharmacists
  - Worry about blood thinning medications

Management

- Supportive
  - Lower blood pressure
    - Target mean arterial BP <130 (but don’t go too low)
    - Labetalol, nicardipine
  - Intubation as necessary
  - Monitor intracranial pressure – options for elevated pressure
    - Hyperventilation
    - Mannitol

Management

- Blood volume monitoring
  - Maintain adequate perfusion
  - Use normotonic solutions
- Correct bleeding factors
  - Reversal agents as appropriate/available
  - Vitamin K, 4-Factor Prothrombin Complex Concentrate (Kcentra)
  - Heparin – protamine
  - Dabigatran – idarucizumab

Other Management Tools

- Seizure prophylaxis
  - May or may not be necessary
  - Levetiracetam
  - Fosphenytoin/lorazepam if active seizure
- Pain management
  - Generally avoid NSAIDs
    - Platelet effects
  - Use acetaminophen

Delirium

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Definition

- Delirium – “an ***acutely*** disturbed state of mind that occurs in fever, intoxication, and other disorders and is characterized by restlessness, illusions, and incoherence of thought and speech”

Causes

- Medical
  - Infection
  - Pain
  - Electrolyte imbalances
- Prescription Drugs
- Drugs of abuse
  - Opioids
  - Alcohol
  - Methamphetamines
  - LSD

Drug Causes

- Anything that acts on the CNS
- Classic Examples
  - Benzo’s
  - Opioids
  - Anticholinergics
  - Antispasmotics
  - Z-drugs
  - Sinemet
  - Drug levels (Digoxin, phenytoin, lithium)
  - Drug interactions

1st Line Therapy

- Identify and solve existing problem
- Redirect Patient
- Enlist patient in an activity
- Offer snacks and beverages to patient.
- Go to the bathroom

When Drugs Are Necessary

- Haldol
  - Most experience
  - Higher incidence of AE’s
- Newer AP’s
  - Risperidone
  - Quetiapine
    - Less EPS
    - Less experience

Treatment of Delirium - Avoid

- Benzo’s
  - Can aggravate
- Opioid
  - Pain can be cause of delirium
  - Use non-opioid if possible to treat delirium suspected to be caused by pain

Dementia

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Major Types of Dementia

- Alzheimer’s
- Vascular
- Lewy Body

MMSE

- *Higher = Better
  - 24-30 Normal
  - 20-23 Mild
  - 10-19 Moderate
  - <10 Severe

Medications

- Acetylcholinesterase Inhibitors
  - Donepezil, Rivastigmine, Galantamine, Tacrine
- NMDA Receptor Antagonists
  - Memantine

- *Do NOT Reverse Dementia

NMDA Antagonists - Memantine

- Moderate to Severe
- XR and Immediate release
- 28 mg to 20 mg conversion
- CrCl
- Usually well tolerated
  - CNS Changes

Acetylcholinesterase Inhibitors

- All oral except rivastigmine patch option
  - Less GI ($$)
- Tacrine – liver toxicity
- GI (NVD)
- Weight Loss
- Low risk of bradycardia (think about Atropine)
- Mild-moderate

The One Million Dollar Question

- When to DC?
- Questions to think about
  - Adverse Effects?
  - Function Left?
  - Family opinions?
  - What would the patient think?
  - Another problem identified?
- Risk of DC?
  - Deterioration
  - Increase in behaviors

Behaviors

- Wandering
- Restless
- Agitation
- Physical Aggression
  - Hit, bite, kick
- Hallucinations
- Delusions

Behavior Identification

- Contributing factors
  - Individual person
  - Time of day
- Rule Out Causes
  - Pain
  - Infection
  - Medication changes

Solutions

- Non-drug approaches
- Solve underlying problem
- Creativity
- Make sure problem is distressing to patient before treating
- Medications last resort
  - Drugs don’t often “treat” behaviors effectively

Common Psych Medications Tried

- Antipsychotics
- Benzodiazepines
- Mood Stabilizers
- Antidepressants

Falls

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Why do we Care About Falls?

- Mortality
- Injury
  - Fracture
  - Head injury
- Bleeding risk
- Fear of falling

Risk Factors

- Cognition
- Balance
- Dizziness
- Orthostatic BP
- Anemia
- Medications
- Stroke

Body Systems

- Muscle weakness/pain
- Accumulation of medications and risk of toxicity due to reduced metabolism and clearance
- Visual changes
- Disease
  - Parkinson’s
  - MS
- Stiffening vessels, less responsive to body’s adaptations (i.e. orthostasis)
- Loss of feeling (PVD or neuropathy)

Common Medications Implicated with Falls

- Psych medications
  - Benzodiazepines
  - Antipsychotics
  - TCA’s
  - Antidepressants
- Blood pressure medications
- Parkinson’s medications
  - Dopamine agonists
  - Carbidopa/levodopa

Environmental Considerations

- Steps
- Walking areas
  - Clutter
- Footwear

Vertigo

- Difficult diagnosis to make for physicians
- Medications
  - Meclizine
  - Antiemetic
  - Anxiety

Dizziness Follow Up

- Timing of Falls
  - Medication changes
- Vitals
- Diagnosis

Fibromyalgia

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Fibromyalgia

- Pain
  - Often non-specific, non-localized
- Fatigue
- Non-inflammatory
- Insomnia
- Mental cloudiness
  - Fibro Fog
- Laboratory negative

Medication Induced Symptoms - Differential

- Hypothyroid
  - Amiodarone
  - Lithium
- Lupus
  - Hydralazine
- Skeletal Muscle Pain/Myopathy
  - Statins

Fibromyalgia Treatment

- Initial – Non-drug interventions
  - Exercise program
  - Sleep hygiene
  - Patient education about disease
  - Cognitive Behavioral Therapy

- Second Line
  - Medication Management

Fibromyalgia Treatment

- TCA’s
- SNRI’s
- Anticonvulsants

Fibromyalgia Treatment

- Selection considerations
  - Cost
  - Adverse effect profile
    - Sedation
  - Agents tried in past
  - Adherence
- FDA approval
  - Duloxetine
  - Milnacipran
  - Pregabalin

TCA’s

- Amitriptyline, nortriptyline
  - Anticholinergic
    - Dry eyes
    - Dry mouth
    - Constipation
    - Urinary retention
    - Sedation
    - QTc prolongation
    - Sexual dysfunction
    - Weight gain
  - Can be useful in insomnia management
  - Younger populations will tolerate better
  - Inexpensive

SNRI's

- Duloxetine, milnacipran, venlafaxine
  - Duloxetine better studied than venlafaxine
  - If venlafaxine used, consider trying to get to higher doses
  - SE's
    - GI
    - Norepinephrine effects at higher doses especially
      - HTN, Tachycardia
    - Sexual dysfunction
    - Tends to be less sedating than TCA's
  - Milnacipran $$$

Anticonvulsants

- Gabapentin, pregabalin
  - Sedating
  - Dizziness
  - Edema/fluid/weight gain
  - Accumulation in kidney disease
  - Dosed multiple times per day, could use at night for sedative effects if daytime symptoms are manageable

Other Options

- Simple analgesics
  - NSAIDs
  - Acetaminophen
- Opioids
  - Avoid

Headache

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Types of Headache

- Tension
- Migraine
- Cluster
- Medication Overuse/Rebound

Management of Tension Headache

- Non-pharmacologic
  - Reduce stress
  - Avoid triggers
  - Rest
- Pharmacologic
  - Acetaminophen
  - NSAIDs
  - Combination with Caffeine
  - Triptans
  - Opioids

Medication Overuse/Rebound

- Often precipitated by initial onset of headache
- Repeated use of medication over time to relieve headache
- Drug Causes
  - NSAIDs
  - Acetaminophen
  - Triptans
  - Opioids

Migraine Treatment

- Triptans
- NSAIDs/APAP in Combo
- Dihydroergotamine
- Antiemetics
  - Prochlorperazine
  - Metoclopramide
- Dexamethasone

Migraine Prophylaxis

- Propranolol
  - Sedating, pulse monitoring
- Valproic Acid
  - Lab monitoring (CBC, LFTs), hepatic issues, weight gain
- Topiramate
  - Cognitive slowing
- Tricyclic antidepressants
  - Highly anticholinergic
- SNRI’s
- CCB’s

Cluster Headaches

- Acute
  - Oxygen
  - Triptans
- Prophylaxis
  - Verapamil

ICU Sedation

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ICU Problems

- Agitation, anxiety, delirium
- Identifying cause can be incredibly difficult
- Common causes
  - Pain
  - Hypoxemia
  - Hypoglycemia
  - Hypotension
  - Withdrawal
  - Adverse effects
  - Infection

Non-Pharmacological Interventions

- First line for problems
  - Comfort
  - Appropriately assessing analgesia
  - Reorientation
  - Maintaining normal sleep patterns

Sedation

- Minimal sedation possible
  - Light sedation
    - Able to arouse patient
  - Deep sedation
    - Patient is unresponsive
- Choice of sedating agent will vary depending upon situation/tolerability

Sedation Scale Examples

- RASS (Richmond Agitation-Sedation Scale)
  - Subjective
    - Combination of sedation and agitation/combativeness level
    - Ideal score is “0” – alert and calm (+4 combative; -5 unarousable)
- Sedation Agitation Scale (SAS)
  - 1-7 (level of agitation (7 is highest, striking out at staff, pulling out IV tubing etc.)
  - 1 is unarousable
  - Subjective
- Brainstem auditory evoked potentials
  - Objective
  - Electrodes placed on scalp (measures response to auditory stimulus)

ICU Sedation - Medications

- Propofol
  - Binds to multiple receptors (GABA, nicotinic, muscarinic, glycine)
  - Rapid on/offset
  - Dissolved in lipid emulsion
    - Rare but serious Propofol Infusion syndrome (PRIS)
    - Hypertriglyceridemia, rhabdomyolysis, acidosis, hypotension, hyperkalemia, arrhythmia, AKI, Liver dysfunction
  - Dose-dependent
    - Hypotension
    - Respiratory depression

Benzodiazepines

- GABA activity
- Elderly may be more sensitive to effects
- Midazolam, lorazepam, diazepam
  - Midazolam has quickest onset
  - Lorazepam – contains propylene glycol and may cause toxicity depending upon amount used (monitor serum osmol gap)
- Tolerance can develop
- Great choice in status epilepticus

Dexmedetomidine

- Selective alpha2 receptor agonist
  - Less respiratory depression than other agents
- Hypotension
- Bradycardia
- Typically patient is more easily arousable

Opioids

- I.e. Fentanyl
  - Avoid overusing if possible
  - Respiratory depression
  - Can extend mechanical ventilation time
- Be cautious about tapering down if has been on chronic opioids
  - Withdrawal can cause agitation
- If on other agents for sedation, be careful about patient waking up in pain

Insomnia

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Insomnia Concerns

- Troubles
  - Getting to sleep
  - Staying asleep
- Quality of Life
  - Motivation
  - Ability to perform at work/school

Non-Drug Interventions

- 1st Line Therapy
- Sleep Hygiene
  - Regular schedule
  - Snacks/warm milk
  - Avoiding Caffeine near bedtime
  - Minimize stimulation before bed
  - Exercise earlier in the day
  - Pain
  - Avoiding other stimulants

Pharmacotherapy

- Z-drugs
- Anticholinergics
- Melatonin
- Trazodone
- Benzo’s
- Ramelteon
- Mirtazapine
- Suvorexant

Z-Drugs

- Fall risk
- Confusion
- Risk of dependence
- Abnormal sleep behaviors
- Zolpidem, eszopiclone
  - Dose restriction on zolpidem – limit to 5 mg, risk of next day impairment at 10 mg

Anticholinergics

- Diphenhydramine, doxylamine, TCA’s
- Retention
- Dry eyes
- Dry mouth
- Constipation
- Fall risk
- Confusion (interacts with dementia meds)

Trazodone and Mirtazapine

- Trazodone
  - Usually higher doses required for antidepressant effect
  - Orthostasis
  - Dry mouth
- Mirtazapine
  - Low dose
  - Weight gain

Melatonin

- OTC
- Tends to regulate the sleep cycle
- Some patients use as needed

Antipsychotics for Sleep

- Can be sedating
- Always avoid unless compelling indication
  - Hallucinations unresolved by other methods
  - Schizophrenia

Multiple Sclerosis

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Multiple Sclerosis

- Immune dysregulation – attacks nervous system
- Unique sensations
  - Fatigue
  - Weakness
  - Tingling
  - Balance problems
- Vision problems

Interferon

- Beta-interferons
- Disease modifying
- Adverse drug reactions
  - Injection site reaction (High percentages – 50%+)
    - Flu-like symptoms
    - Fever
    - Pain
  - Pretreatment with acetaminophen/ibuprofen
  - Neutropenia
  - Lots of other unique reported side effects; thyroid, hepatotoxic, SLE, etc.

MS Complications

- MS Flares
  - Corticosteroids
- Spasms/pain
  - Baclofen
  - Tizanidine
  - NSAIDs
  - Acetaminophen

Bladder/Bowel Issues

- Spasms/Incontinence
  - Anticholinergics
- Constipation
  - Stool softeners
  - Stimulants

Other Associated Risks

- Mood disorders
  - Depression
- Epilepsy

Neuropathy

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Neuropathy

- Painful
- Burning
- Tingling
- Needles/pinprick type pain
- Diabetes
  - Control blood sugars
  - Lower A1C
- Falls risk with loss of sensation

Treatment

- Gabapentin/Pregabalin
  - Sedation
  - Renally cleared
  - Cost concern with pregabalin
  - Edema/weight gain
    - Dose dependent
  - Gabapentin requires transporter in gut
    - Dose dependent absorption
  - 300 gabapentin – approx. 50 mg pregabalin
  - Multiple daily doses

Treatment

- SNRI’s
  - Duloxetine with most evidence
  - Likely need higher doses of venlafaxine
  - Antidepressant effect can be nice
  - HTN possible at higher doses

Treatment

- TCA’s
  - Generally avoid in elderly
  - Really nice inexpensive option
  - Highly anticholinergic
    - Retention, constipation, dry eyes, dry mouth, CNS effects
  - Nortriptyline possibly better tolerated in elderly

Topical Agents

- Capsaicin
  - Regular, frequent use
  - PRN generally not effective
- Lidoderm patch
  - Needs to be small areas
  - Expensive (limits use)
  - On/off 12 hours

Orthostasis

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Orthostasis

- Drop in blood pressure with position changes
  - 20mm Hg drop in blood pressure
- Dizziness, syncope, fainting
- Fall risk

Causes of Orthostasis

- Medications
- Dialysis
- Medical
  - Parkinson’s
  - Dehydration

Medication Causes of Orthostasis

- Antihypertensives
  - Central acting alpha-2 agonists
  - Alpha blockers
- Carbidopa/levodopa
- PDE-4 inhibitors

Treatment of orthostasis

- Remove offending medication
- Fludrocortisone
  - GI upset
  - Edema
  - Adrenal suppresion
  - Immunosupression
- Midodrine
  - Raise BP
  - Exacerbate BPH

Parkinson’s Disorder

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Parkinson’s Symptoms

- Tremor
- Rigidity
- Akinesia
- Postural instability
- Can be challenging to diagnose
  - Trial Sinemet

Drugs for Parkinson’s

- Sinemet
- Dopamine Agonists
- MAOI’s
- COMT’s
- Anticholinergics

Sinemet

- Gold Standard
- Frequent dosing
  - CR product available
- GI
- Psych AE's
  - Psychosis
- Orthostasis
- Drug/Food interaction – protein
- Unusual obsessive behaviors
  - I.e. gambling, eating

Dopamine Agonists

- Ropinirole, pramipexole
- RLS treatment
- Orthostasis
- Edema
- Unusual obsessive behaviors
  - I.e. gambling, eating

COMT’s

- COMT’s
  - Preserve levodopa
  - Need to be dosed with Sinemet
  - May need to reduce dose of Sinemet
  - Entacapone, tolcapone
    - Tolcapone – liver toxicity

MAOI's

- Selegiline
  - Reduce Sinemet dosing – 10-30%
  - Serotonin interaction concern
  - Tyramine interaction potential
    - Hypertensive crisis
  - Increases Sinemet effects so may see side effect profile similar to Sinemet

Anticholinergics

- Rarely used due to adverse effect profile
  - Constipation
  - Dry eyes
  - Confusion/CNS changes
  - Dry mouth
  - Urinary retention
- Trihexyphenidyl
- Benztropine

Drug Induced

- Antipsychotics
  - Typicals – the worst
  - Quetiapine – the best
- Metoclopramide
  - Used for GI problems, but DA blocking activity

Seizures

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Causes of Seizures

- CVD
- Dementia
- Trauma
- Cancer
- Withdrawal
  - Benzo’s
  - Barbiturates
  - ETOH

Medications that Increase Seizure Risk

- Bupropion
- Tramadol
- Cancer medications
- Hypoglycemia
- Antipsychotics
- Stimulants

Common Seizure Medications

- Phenytoin
- Levetiracetam
- Carbamazepine
- Lamotrigine
- Valproic Acid
- Topiramate

Phenytoin

- Complex Kinetics
  - Dose depending increase in concentration
  - Small doses can lead to disproportionately large increases in drug levels
- Free versus total levels
  - 1-2, 10-20
- Vitamin D deficiency
- General toxicity symptoms similar to alcohol
  - Vertical nystagmus
- Enzyme inducer
- Gingival Hyperplasia

Carbamazepine

- Enzyme inducer
- Hyponatremia
- Bipolar and trigeminal neuralgia
- Bone loss
- Levels
  - 4-12
- Cousin *oxcarbazepine

Levetiracetam

- Watch kidney function
- Drug levels not routinely done
- Adjust dose based upon SE’s/seizures
- Less drug interactions
- SE’s; sedation, confusion, GI, behavioral changes, increase in BP

Lamotrigine

- Very slow dose titration
- Interaction with Valproic acid and enzyme induces
  - Quicker titration with enzyme inducers like phenytoin
  - Slower titration with VPA
- Drug induced rash (SJS)
  - Life threatening

Topiramate

- Cognitive slowing
- Weight loss
- Migraine indication
- Metabolic acidosis
- Kidney stone formation

Valproic Acid

- Weight gain
- GI
- Hair loss
- Rare (ammonia elevations, LFTs, thrombocytopenia)
- Migraine, Bipolar indications, might also see off label for aggressive type behaviors versus use of antipsychotics

Sexual Dysfunction

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Psych

- SSRI’s
- TCA’s
- MAOI’s
- Better options
  - Bupropion
  - Mirtazapine
- Antipsychotics (typicals maybe a little worse as well as risperidone)
- Lithium

Cardiac Medications

- Beta-blockers
- Thiazide Diuretics
  - Alternatives for HTN – ACE/ARB/CCB
- Clonidine, methyldopa

Other Medications

- Finasteride
- Dutasteride
- Antihistamines (drugs with anticholinergic effects)

Use of PDE-5 Inhibitors

- SE’s
  - Dizzy, drop in blood pressure
  - Headache
  - Visual changes
  - Flushing
- Nitrate Interaction

Spinal-Cord Injuries

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Spinal Cord Injury

- Trauma
  - MVA
  - Sports injury
- Initial pain management
- Spinal fractures
- Initial assessment
  - May involve X-ray, CT, neurological assessment
- Initial Complications
  - Paralysis of limbs
  - Cardiac, respiratory complications

Spinal Cord Injury

- Numerous possible long term complications
  - Spasticity, immobility
  - Pain (likely nerve pain, spasms)
  - Bladder dysfunction
  - Changes to GI tract (low motility)
  - Sexual dysfunction
  - DVT
  - Pressure ulcer risk
    - Due to immobility

Muscle Spasticity

- Baclofen
  - Intrathecal pump
    - Boxed warning on abrupt withdrawal (risk of hyperthermia, CNS changes, rebound spasticity, muscle rigidity, rare cases of rhabdomyolysis)
  - Oral – sedation, CNS effects, GI side effects
- Tizanidine
  - Alpha2 agonist
  - Dizziness, low BP, dry mouth, sedation
- Diazepam – benzo effects
- Dantrolene
  - Boxed warning hepatotoxicity
  - Sedation, dizziness, CNS effects

Collateral Damage Management

- Bladder
  - Spasms
    - Anticholinergics (oxybutynin, tolterodine)
  - Retention/emptying problems
    - Alpha blockers
    - Cholinergic agonists (bethanechol)
      - Diarrhea side effect
- Sexual dysfunction
  - PDE inhibitors (i.e sildenafil)

Collateral Damage Management

- Constipation
  - Stool softeners
  - Stimulants
  - Fiber
  - Enemas
- DVT – anticoagulation as appropriate
- Pressure ulcer risk
  - Repositioning

Status Epilepticus

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Potential Causes

- Epilepsy
- Hypoglycemia
- Acid/base disorder
- Toxicity

Medication Management

- Benzodiazepines
  - Lorazepam
    - Typically first line
    - May stay in CNS a little longer than diazepam
  - Diazepam
    - Most lipophilic
    - May get to CNS a little quicker, but may redistribute out of CNS quicker as well
- Likely going to load patient with tradition antiepileptic agent in addition to doing benzodiazepine

Anticonvulsants

- Fosphenytoin/phenytoin
  - Slower onset than benzodiazepines
  - Generally not used alone in status epilepticus
- Fosphenytoin
  - Can be administered more quickly
  - Reduced risk of purple glove syndrome and phlebitis compared to phenytoin

Refractory Agents

- Phenobarbital/pentobarbital
  - Likely will require intubation if using these agents
  - 3rd or last line agent
  - Slow onset to peak efficacy compared to benzodiazepines
- Propofol
  - Anesthetic agent
  - Ventilation/intubation
- Midazolam
  - Benzodiazepine
  - More water soluble, may take a little more time to get to CNS for activity

Stroke and TIA’s

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Types of Stroke

- Hemorrhagic
- TIA
- Ischemic
  - Local (Atherosclerotic)
  - Heart (Atrial Fibrillation)

Classic Signs

- Face drooping
- One sided arm weakness
- Slurred Speech
- Confusion
- Vision changes
- Fall

Acute Ischemic Stroke Management

- Reperfusion
  - tPA
- Quicker the better for tPA administration
  - Best outcomes 90 minutes or less
    - Good evidence of benefit in 3 hours or less
  - 3-6 hours range, less evidence

Exclusion Criteria - tPA

- History of intracranial bleeding
- Active bleed/hemorrhage (last 21 days)
- BP > 185/110
- Recent head trauma/surgery (3 months)
- INR >1.7, heparin, or other anticoagulant (including DOACs)
- Platelets < 100,000
- Glucose < 50
- Endocarditis

Classic Risk Factors

- Hypertension
- Smoking
- Atrial Fibrillation
- Diabetes
- Hyperlipidemia
- Age
- Genetics

Prevention of Stroke

- Manage modifiable risk factors
  - Hypertension
  - Smoking
  - Weight loss
  - Diabetes
  - Statins

Options for Long Term Management of Stroke

- Atherosclerotic
  - Aggrenox (Aspirin/Dipyridamole)
  - Clopidogrel
    - Ticlopidine - neutropenia
  - Aspirin
- Cardioembolic (Atrial Fibrillation)
  - Warfarin
  - DOACs
  - Aspirin

Substance Abuse

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Most Common Substance Abuse

- Alcohol
- Tobacco
- Methamphetamine
- Prescription Drugs
  - Opioids
  - Benzo’s

Signs of Alcohol Abuse

- Higher tolerance
- Blackouts
- Concerns from friends/family
- Legal or financial issues
- Liver disease

Alcohol Addiction

- Loss of control
- Lack of other interests
- Withdrawal symptoms
  - Sweating, shaking, anxiety, DT’s
- Guilt
- Worry
- Change in relationships

Alcohol Treatment

- Withdrawal seizures/DT’s
  - Benzodiazepine
- Craving/Pleasure reduction
  - Naltrexone
  - Acamprosate
- Negative feedback
  - Disulfiram

Smoking Cessation

- Nicotine replacement
- Varenicline
  - Vivid dreams, CNS adverse effects
  - $$$
- Bupropion
- TCA’s
- Counseling

Methamphetamine

- Stimulant
  - Psychosis
  - Agitation
  - HTN
  - Tachycardia
- Medications for management of addiction
  - None have good evidence
  - Counseling

Prescription Drug Misuse

- Using for legitimate reason, but not under supervision of a healthcare provider
- Medication hoarding
- Opioids, Benzo’s

Signs of Opioid Overdose

- Respiratory depression
  - Snoring like noise
- Unconsciousness
- Pinpoint pupils
- No bowel sounds
- Response to naloxone

Signs of Opioid Withdrawal

- Withdrawal when stopping use
  - Nausea
  - Sweating
  - Anxiety
  - Insomnia
  - Chills
  - Irritability

Drugs to Treat Opioid Addiction

- Withdrawal
  - Clonidine
  - Diphenhydramine
  - Trazodone
  - Simple analgesics
- Buprenorphine/naloxone
- Methadone
- Naltrexone

Benzodiazepine

- Withdrawal
  - Anxiety
  - Irritability
  - Tremor
  - Confusion
  - Nausea
  - *Seizures
  - Psychosis

- Reversal agent
  - Flumazenil

Traumatic Brain Injury

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TBI

- Blunt trauma to the brain
  - MVA, fall, etc.
- Alters functioning of the brain
- Can lead to all sorts of complications
- Alterations in blood flow/perfusion can lead to oxygen deficiency in various areas
  - Leading to death of brain tissue

Elevated Intracranial Pressure

- Medication options – goal is to pull fluid across blood-brain barrier to ultimately reduce pressure
  - Mannitol
    - Monitor fluids, lytes, kidney function
    - Volume depletion
    - Renal failure
    - Metabolic acidosis
  - Hypertonic saline
    - Sodium monitoring

- **Target BP >90, PaO2 >60

Sedation

- Agent selection based upon various factors
  - Onset/offset desired
  - Amnesia properties
  - Seizures or risk of seizure
  - Analgesia required

Sedation Agents in TBI

- Propofol
  - Quick onset
  - Low drug interaction risk
  - May help lower ICP
- Benzodiazepines
  - Midazolam
  - Amnesia
  - Quick onset
  - Seizure management/prevention
  - Disinhibition – exacerbate delirium
  - Accumulation if poor renal function

Sedation Agents in TBI

- Barbiturates
  - Lower ICP
  - Seizure management
  - Hypotension risk
- Fentanyl
  - Analgesia benefit
  - Likely no change or increase in ICP
  - Respiratory suppression

Complications

- DVT
  - Prophylaxis (pneumatic compression)
  - Risk of bleed in TBI (R vs. B)
- Seizure prophylaxis
  - Levetiracetam
  - Phenytoin (more drug interactions/complex medication)
- Delirium, aggression, anger
  - Antipsychotics for acute management in the event of non-drug intervention failure

Tremor

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Essential Tremor

- Rhythmic, consistent movement of body part
  - Often hands
- Consistent frequency
- Severity can vary
- Interfere with life activities

Treatment

- Propranolol
  - Pulse
  - BP
  - Selectivity for beta receptors
- Primidone
  - Phenobarbital is metabolite
  - Sedation
  - Confusion
  - Fall risk

Drug Induced Tremor

- Lithium
- Beta-agonists
- Theophylline
- Hyperthyroidism (or over supplementation)
- VPA
- Stimulants

Vertigo and Dizziness

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Potential Causes

- Benign Paroxysmal Positional Vertigo
- Inner ear disorders
  - Infection
  - Inflammation
  - Motion Sickness
- Meniere’s Disease
- Migraines
- Drugs

Rare, but Serious Causes

- Stroke
- TIA’s
- MS
- CNS Tumor/cancer

Treatment – Underlying Cause

- Bacterial Ear Infection
  - Antibiotics
- Meniere's
  - Salt restriction/Diuretics
  - Corticosteroids
- Migraines
  - Typical treatment

Treatment - Symptomatic

- Meclizine, dimenhydrinate
  - H1 antagonist as primary mechanism
  - Sedation, dry mouth
- Glycopyrrolate, scopolamine
  - Anticholinergics
- Benzodiazepines
  - Short term
- Dopamine blockers
  - Promethazine
  - Prochlorperazine

Drug Induced Dizziness

- Antihypertensives
- Antiepileptics
  - Gabapentin, pregabalin, carbamazepine, phenytoin, etc.
- Opioids
- Psych Medications
  - Antipsychotics
  - Antidepressants
  - Benzodiazepines
- ***Timing, interactions, metabolic changes (renal/liver function)

Obstetrics and Gynecology

Men’s Health and Urology

BPH

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BPH Characteristics

- Enlargement of the prostate
- Impairs urination
  - Frequency
  - Incomplete bladder emptying
  - Low flow
  - Incontinence

BPH Treatment

- Alpha Blockers
- 5-Alpha Reductase Inhibitors
- Surgery (TURP)

Alpha-Blockers

- Tamsulosin
  - Not used for hypertension
  - Works quickly
- Non-selective agents
  - Terazosin
  - Doxazosin
- Risks
  - Orthostasis

5-Alpha Reductase Inhibitors

- Finasteride, Dutasteride
- Takes weeks/months to begin to work
- Actually shrink prostate
- Decreased libido
- Pregnancy risk

Drugs That Exacerbate Frequency

- Diuretics
- Caffeine
- ETOH

Drugs That Exacerbate Retention

- Anticholinergics
- Alpha agonists (Midodrine)
- Pseudoephedrine

Contraception

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Contraception

- Primary goal:
  - Reduce risk of pregnancy
- Options
  - Oral contraceptives (estrogen, progestin combination)
  - Progestin only
  - Vaginal option (ring)
  - Patch
  - IM injection
  - Implant/IUDs
  - Emergency contraceptives

Selection Factors

- Adherence
- Adverse Effects
- Cost
- Lifestyle
  - Patient preference
- Previous experience

Adverse Effects – Oral Contraceptives

- Weight gain
- GI (nausea)
- Mood changes
- Breast tenderness
- Variable spotting
- DVT
- CV events
  - Smoking, age (>35)

High Risk Patients – Oral Contraceptives (E/P)

- Age >35/smoking
- CVD risk factors (smoking, diabetes, hypertension, older age)
- Uncontrolled hypertension >160/100
- Clotting disorder
  - Hx of stroke/DVT
- Valve replacement/anticoagulation
- Breast cancer

Estrogen Component

- Higher estrogen
  - GI
    - May get used to this
  - More breast tenderness
    - May get used to/tolerant
  - DVT risk
- Less estrogen
  - Breakthrough bleeding

Progestin Only Pill

- “Minipill”
- Consistent administration key!
  - Take at same time every day
  - Risk of breakthrough bleeding or pregnancy
- Option for breastfeeding

Other Options

- Patch (E/P)
  - Weekly change
  - Higher clot risk?
  - Not as effective in obesity
- Ring (E/P)
  - Refrigeration
    - Insert once every 3 weeks, then off 1 week
- Medroxyprogesterone injection
  - Q 3 months
  - Weight gain
  - Warning – low BMD

Other Options (cont.)

- Subdermal implant – progesterone
  - 3 year implant
  - Irregular bleeding
- IUD
  - Non-hormonal (copper)
  - Heavy menstrual bleeding
- IUD
  - Levonorgestrel
  - 3-5 years

Emergency Contraception

- Levonorgestrel (progestin)
- “Morning after pill”
- Take ASAP after unprotected sex
- Best within 72 hours, possibly effective up to 5 days

Endometriosis

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Endometriosis

- Overgrowth of the lining of the uterus
- Damage/scarring to pelvic tissue
- Patient complaints/concerns
  - Pain
  - Bleeding
  - Infertility
  - Intercourse discomfort/pain
  - Increased risk of ovarian cancer

Medications to Know

- Oral contraceptives (combination E/P)
  - Suppress ovarian action
  - Can lead to pain relief
  - Continuous (skipping placebo pill week) can maximize benefit
- Progestin only
  - medroxyprogesterone
  - Inhibits menstruation
  - Causes atrophy in uterine lining
    - Prevents overgrowth

Medications to Know

- Gonadotropin releasing hormone agonists (GnRH)
  - Leuprolide
  - Lowers estrogen levels
  - Adverse effects
    - Decrease BMD
    - Hot flashes
    - Vaginal atrophy
- NSAIDs
  - Pain management

Estrogen Replacement

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Estrogen Risks

- Clots
- CHD
- Breast Cancer
- Endometrial Cancer

Benefits of Estrogen

- Osteoporosis
- Colorectal Cancer
- Improve menopausal symptoms

Goals of Estrogen Therapy

- Treat symptoms
- Limit length of use
- Minimum Effective Dose
- Avoid use
- Discontinue

Alternatives for Menopausal Symptoms

- SSRI
- SNRI
- Gabapentin
- Clonidine
- Topical Estrogen (vaginal atrophy/dryness)

Infertility

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Infertility

- Inability to become pregnant
  - Usually consider 1 year
- Patients may have irregular or no period
- Hormone testing can be done
- Semen analysis

Risk Factors of Infertility

- Advance maternal age
- Tobacco
- Alcohol
- Obese/frail
- Inactivity/excessive activity
- PCOS
- Chemo/radiation induced

Medications

- Metformin
  - Typically used in PCOS
  - Weight negative effects can be good in obese
- Clomiphene
  - Induces ovulation
  - Can help sperm production in males
  - More likely for multiple babies (i.e. twins, triplets)
- Letrozole
  - Induces ovulation

Medications

- hCG
  - Used to trigger ovulation
  - Used if other options fail
- In vitro
  - Fertilization in a lab and implanting embryos

Lactation

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Use of Medications – Breastfeeding Mom

- Challenges
  - Chronic disease
    - HTN, Depression, Anxiety
  - Acute problems
    - Infections
  - Pain management
- Common sense principle
  - If baby can take it, breastfeeding mom should be able to take it

Meds that Impact Breast Milk Production

- Pseudoephedrine
  - Suspected suppression of prolactin
- Dopamine agonists
  - Remember that antipsychotics can cause elevated prolactin levels (and cause lactation)
- Estrogen
  - Birth control
  - May need to use progestin only BC

Mastitis

- Infection/inflammation of breast tissue
- If infected
  - Beta-lactam
    - Dicloxacillin
    - Cephalexin
    - **if baby can take it, mom should be able to as well

Baby Deficiencies

- Iron
  - Premature babies
- Vitamin D
- B12

Common Drugs Considered ”Generally Safe”

- Breastfeeding
  - Analgesics – APAP, ibuprofen
  - Antibiotics – PCN, Cephs, Macrolide
  - Big molecule drugs – heparin type products/insulin

What to do?

- If minimal data
  - Play it safe
  - Minimize dose
  - Minimize duration
  - Choose alternative agent
  - Factor in mother’s health
    - Anxiety/depression
  - Provide information to patient
  - Avoid breastfeeding

Menstrual Disorders

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Menstrual Disorders

- Dysmenorrhea
  - Painful menses
- Menorrhagia
  - Excessive bleeding during menses
  - Can lead to anemia

Dysmenorrhea

- Management
  - Simple analgesics
    - NSAIDs
    - Acetaminophen
  - Oral contraceptive
    - Regulates cycle, may reduce pain

Menorrhagia

- Oral contraceptive are first line
  - Reduces blood loss
- Tranexamic acid
  - Non-hormonal option
  - Displaces fibrinogen from fibrin and inhibits fibrinolysis
  - Increased risk of clot
- NSAIDs may be helpful
- Iron/B12/Folic acid assessment if anemic

Pregnancy and Medication Use

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Preeclampsia

- Increase in blood pressure late in pregnancy
- Hypertension drugs of choice
  - Nifedipine (CCB)
  - Methyldopa
    - Rare, notable precautions – edema, thrombocytopenia, liver issues
  - Labetalol
    - IV and oral option
  - Hydralazine
    - IV and oral option
- 100% Avoid
  - ACE, ARB, Aldosterone antagonists

Constipation

- Common complaint in pregnancy
- Non drug interventions first line
  - Fluids/fiber
  - Exercise
- Stool softeners generally considered safe
- Metamucil type products

Nausea/Vomiting (Morning Sickness)

- If serious enough, can lead to dehydration, nutritional concerns
- Non-drug interventions for mild to moderate
  - Small, frequent meals
  - Bland foods
  - Avoiding trigger foods/smells
- Pyridoxine (vitamin B6)
- Doxylamine
  - First generation antihistamine
- Other options – reserved for refractory cases
  - Chlorpromazine
  - Prochlorperazine
  - Diphenhydramine
  - Metoclopramide
  - Ondansetron

UTI's

- Rare case where asymptomatic bacteriuria treatment is indicated
- Drugs of choice
  - Cephalosporins
  - Penicillins
- Nitrofurantoin
  - Contraindicated at full term due to risk of hemolytic anemia in infant
    - 38-42 weeks
- Fosfomycin
- Sulfa – decent safety record early (1st and 2nd trimesters)
- Quinolones, Trimethoprim, Tetracyclines generally avoid

Heartburn

- Non-drug interventions
  - Small, frequent meals
  - Elevated head of bed if nighttime problems
- Antacids (calcium, magnesium based)
- Sucralfate
  - Minimal systemic absorption
- H2 blockers (i.e. ranitidine)
  - Generally considered safe, use for shortest duration possible
- PPI's – less data available compared to H2's; reserved for severe/refractory cases
- Metoclopramide – option if nausea and vomiting as well

Pain Management

- Non-drug
  - Heat, ice
- Acetaminophen
  - Drug of choice for pain/headache
- Educate to avoid NSAIDs
  - Risks>benefit
  - Ibuprofen, aspirin, naproxen, etc.

Depression/Anxiety

- SSRI's drug of choice if have to start one during pregnancy
  - Sertraline, fluoxetine generally have the most data
  - Avoid paroxetine
- Depression and/or anxiety can be detrimental to health of the mother and health of the baby too
- Weigh risk of treatment compared to benefit of treatment

Gestational Diabetes

- Risk of hypertension, high birth weight baby, early delivery
- First line
  - Diet management
- Insulin is typically first line if medication management is necessary
  - Most experience
    - NPH
    - Regular
- If patient refuses injections
  - May consider sulfonylurea/metformin

Urinary Incontinence

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Definitions

- Incontinence
  - Go when you don’t want to (can’t control)
  - Weakness or loss of voluntary control of urinary sphincter
- Frequency
  - Feeling of having to go all the time
- Retention
  - “retaining” – incomplete emptying of the bladder
    - Most common cause (males) - BPH

Types of urinary incontinence

- Stress
  - Physical exertion (i.e. sneeze, cough)
- Urge
  - Over Active Bladder (OAB)
  - Feel the need to go, but maybe don’t make it in time
  - Immobility
  - MS, Parkinson’s, Diabetes
- Overflow
  - Blockage (BPH)
  - May dribble urine
- Functional
  - Patient who has dementia

Drugs – Clinical Pearls

- Anticholinergics
  - Confusion
  - Dry eyes, mouth
  - Constipation, slows GI motility
  - Retention
- Beta agonist (mirabegron)
  - Tachycardia
  - HTN
- 5-alpha reductase inhibitors
  - Sexual dysfunction
  - Fatigue
- Alpha agonists
  - Hypertension
- Diuretic timing/sleep
  - Urinary frequency
- Alpha blockers
  - Hypotension

Stress Incontinence Treatment

- Kegel Exercises
- Alpha agonists
  - Midodrine
  - Pseudoephedrine
- Anticholinergics tried, but may not be that effective
  - Could be mixed incontinence if beneficial

Urge Incontinence

- Treatment
  - Anticholinergics
  - Beta agonist (mirabegron) – selective for Beta-3
  - Estrogen (topical)

Overflow

- Medication Treatment
  - Alpha-blockers
  - 5 alpha reductase inhibitors (BPH)

Oncology

Breast Cancer

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Risk Factors

- Genetics
  - BRCA1 and BRCA2 genes
    - Increase risk of breast and ovarian cancer
- Estrogen excess
  - HRT
- Female
- Age
- Obesity
- No children

Targeted Medications

- Targeted therapy
  - Estrogen receptor positive (ER+)
    - SERMs
    - Aromatase inhibitors
    - Fluvestrant
  - Human Epidermal Growth Factor Receptor 2
    - Trastuzumab, pertuzumab, lapaptinib

SERMs

- Tamoxifen
  - Prodrug via CYP2D6 (inhibitors can decrease effectiveness)
  - Side effects
    - Hot flashes, increase clot risk, vaginal atrophy, night sweats
- Raloxifene
  - Useful in osteoporosis
  - Hot flashes, vaginal atrophy, blood clots

Estrogen Targeting Drugs

- Anastrazole, letrozole, exemestane (Aromatase inhibitors)
  - Prevent production of estrogen
  - Use only in postmenopausal women
  - Hot flashes, osteoporosis risk, vaginal atrophy
- Fulvestrant
  - Disables estrogen receptors
  - Menopausal type side effects
  - Post menopausal indication only

HER2

- Human Epidermal Growth Factor Receptor 2 targeted drugs
  - Trastuzumab, pertuzumab, lapatinib
  - Only used in HER2 overexpression
  - GI/flu like side effects
  - Increase stroke, heart failure risk

Cervical Cancer

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Human Papilloma Virus

- Most common cause of cervical cancer
- HPV subtypes
  - 16 and 18 – most common for cervical cancer
    - 6, 11 associated with genital warts
- Sexual transmission

Vaccination

- Gardasil-9 (9 subtypes)
  - Includes 6,11, 16, 18
- 2 dose schedule approved
  - Patients <15
  - Target patients before sexually active
- Vaccination recommended in immunocompromised
  - AIDS patients may be at higher risk (i.e. AIDS is often sexually transmitted)
- Males benefit as well
  - Cancer, warts protection

Chemotherapy

- Platinum drugs
- 5-FU
- Taxanes
- Bevacizumab
- Topotecan
- ***Agents selected may vary based upon many factors; common chemo agents discussed in separate section

Colon Cancer

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Symptoms

- Bowel pattern changes
  - Weeks/months
- Blood
- Pain
- Weight loss
- Fatigue

Screening

- 50 is the magical age
- Colonoscopy every 10 years
- Flexible sigmoidoscopy every 5 years
- Fecal occult blood test
- Risk factors may increase recommended screening frequency
  - Genetics
  - History of polyps
  - Smoking

Management

- Prevention
  - Aspirin may have some evidence as reducing the risk
- Early stages
  - Polyp removal
- Radiation, surgery (colectomy)
- Targeted agents
  - Bevacizumab, ramucirumab, aflibercept
    - Vascular endothelial growth factor (VEGF)
    - Boxed warning on GI perforations, wound healing and bleeding
    - HTN, DVT/PE

Management

- Cetuximab
  - Epidermal growth factor
  - Boxed warning for cardiac arrest, infusion reaction
  - Rash, hypomagnesia
- Metastatic disease
  - Irinotecan
  - Oxaliplatin
  - 5-FU
  - Capecitabine
  - Leucovorin

Leukemia

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Leukemia

- Cancer impacting bone marrow
- Abnormal/dysfunctioning WBC’s
- Infection risk
- Bone pain
- Fatigue
- Bruising/bleeding

Leukemia

- Subtyping of leukemia
  - ALL (Acute Lymphoblastic Leukemia)
  - AML (Acute Myeloid Leukemia)
  - CLL
  - CML

Treatment

- Radiation
- Stem cell transplantation
- Chemo regimens
  - Know side effects versus selection – see chemo agents section
- Imatinib (Gleevec)
  - CML
  - Tyrosine kinase inhibitor
  - Precautions
    - Bone marrow suppression
    - Heart failure
    - Moderate emetic potential
    - Hepatotoxicity
    - Tumor lysis syndrome

Lung Cancer

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Lung Cancer Stats

- US – 200,000+ new cases
- US – 150,000+ deaths
- Leading cause of cancer death
- Non-small cell lung cancer (NSCLC)
  - 80-85% of lung cancer
- Small cell lung cancer
  - 10-15% of lung cancer
- Staging; 1-4
  - 4 being the worst

Lung Cancer Risk Factors

- Smoking
  - Don’t forget about second hand smoke
- Radon
- Asbestos or other carcinogenic toxin
- Family history

Agents

- EGFR inhibitors
  - Erlotinib, afatinib, gefitinib
  - Fatigue, rash, GI
  - 3A4, 1A2 metabolism
- ALK protein
  - Crizotinib, certinib, alectinib
  - Edema, neuropathy, GI
  - Immunosuppression risk
  - Elevated LFT’s
  - QTc prolongation
  - Eye/pulmonary toxicities
- See Chemo agents

Chemotherapy Agents

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Anthracyclines

- Doxorubicin, daunorubicin
- Cardiotoxicity
  - Dexrazoxane may be used to help prevent this
  - Beta-blockers may also be utilized
- High risk of N/V when used in combination with cyclophosphamide
- Neutropenia
- Anemia
- Hair loss

Taxanes

- Paclitaxel, docetaxel
  - Neutropenia risk is high compared to other agents
  - Neuropathy risk is high compared to other agents
  - N/V (low risk agents)
  - Bone marrow suppression
  - Anaphylaxis type infusion reaction

Cyclophosphamide

- N/V/D
  - Highest risk if dose greater than 1,500 mg/m2
- Appetite suppression
- Bladder cystitis
  - Fluids and mesna for prevention
- Hair loss
- Myelosuppression

Platinum Drugs

- Cisplatin, Carboplatin
- Cisplatin
  - highest risk category for CINV
  - Amifostine to prevent ototoxicity and renal toxicity
- Carboplatin – moderate risk
- Class effects
  - Neutropenia
  - Neuropathy
  - Hair loss
  - CNS changes

Vinka Alkaloids

- Vincristine
  - Very significant neuropahty
  - Vesicant warning – avoid extravasation
  - Elevations in uric acid
    - Can cause nephropathy
  - Minimal CINV

5-fluorouracil

- Stomatitis
- Neutropenia
- Photosensitivity
- Diarrhea

Methotrexate

- Myelosuppression
- Hepatotoxic
- Renal elimination
  - Increased risk of toxicity in CKD
- Pneumonitis
- Tumor lysis syndrome
  - See next slide
- Leucovorin rescue (folinic acid)
  - Administer within 24-36 hours of methotrexate

Tumor Lysis Syndrome

- Cells destroyed, release contents into blood stream
- Laboratory assessment (Cairo-Bishop)
  - Elevated uric (>8mg/dL)
  - Potassium >6 mEq/L
  - Phosphorus >4.5 mg/dL
  - Calcium <7 mg/dL
- Prevention
  - IV hydration
  - Allopurinol
  - Rasburicase
    - Avoid in glucose-6 phosphate dehydrogenase

Prostate Cancer

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Prostate Cancer

- Slow growth
- Symptoms
  - Flow issues
  - Pelvic pain
  - ED
  - Blood in urine
  - Incontinence

Prostate Cancer

- Prostate specific antigen
  - Can be elevated in any type of damage
    - Infection
    - Cancer
    - Inflammation/damage
  - Not necessarily specific to cancer

Management

- Considerations for monitoring
  - Slow growth nature
  - Age
  - Symptoms
- Radiation

Medications

- Luteinizing hormone-releasing hormone (LH-RH) agonists
  - Leuprolide, goserelin, triptorelin, histrelin
  - Reduce testosterone production which feeds the cancer
  - ED, hot flashes, decreased BMD, weight gain
  - Vitamin D deficiency, calcium monitoring; OP treatment may be necessary
- Anti-androgen
  - Bicalutamide, flutamide, nilutamide
  - Similar SE profile to LH-RH
- Metastatic disease
  - Docetaxel, cabazitaxel, mitoxantrone, estramustine

Skin Cancer

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Skin Cancer Stats

- Most common 5+ million cases
- 1/5 develop skin cancer
- Actinic keratosis
  - Precancer (58+ million affected)
- 90% caused by UV radiation
- Most treatable/least serious
- Melanoma (<1% of skin cancer)
  - Majority of deaths

Types

- Basal cell
  - Bump on skin, brown/flesh color
  - Usually only occurs on sun exposed areas
- Squamous Cell
  - Red nodule or scaly type surace
- Melanoma
  - Not necessarily on sun exposed areas
- Kaposi’s Sarcoma
  - Red/purple patches
  - AIDS defining illness

Increased Risk of Sunburn

- Drugs
  - Tetracyclines
  - Diuretics
  - Quinolones
  - Sulfa drugs
  - Retinoids
- Fair skin
- Lack of sunscreen and excessive exposure
- Immunosuppressed

Prevention

- Long sleeves
- Avoiding tanning
- Sunscreen
  - SPF 30 or greater
  - 30 minutes before exposure and every 2 hours thereafter

Management

- Cryotherapy
- Surgery
- Radiation
- Phototherapy
- Electrosurgery
- Drugs

Topical Agents

- 5-FU
  - Apply to localized area
  - Clean/wash area, wash hands before and after application
  - Hazardous medication
  - Increased sunburn risk on application area
  - SE – dry, scaling, pain, redness, burning
- Imiquimod
  - Local SE's similar to 5 FU
  - Photosensitivity
  - $$$

Psychiatric

Attention Deficit Hyperactive Disorder

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Symptoms

- Fidgits
- Constantly moving
- Can sit still
- Forgetful
- Disruptive behavior
  - Relationships
  - School function/learning

Drugs

- Stimulants (methylphenidate, amphetamines)
- Atomoxetine
- Bupropion
- Central alpha-2 agonists
  - Clonidine, guanfacine

Selection Considerations

- Adverse effect profile
  - Weight
  - Vitals
  - Sleep pattern
- Dosage forms/frequency of dosing
- Cost
- Family considerations
  - Ensure non-drug interventions have been exhausted
  - Controlled substance

Stimulants

- Amphetamine salts (Adderall)
  - Extended release and immediate release
- Methylphenidate
  - Capsule, patch, solution, extended release
- Adverse effect/monitoring
  - Weight
  - Cardiovascular
  - Insomnia

Atomoxetine

- Norepinephrine reuptake inhibitor
- Insomnia
- GI upset
- Suicidal thinking
- Will typically not work quickly like stimulants

Other Agents

- Bupropion
  - Avoid in seizure disorder
  - Non-controlled
  - Takes a while to work
- Clonidine, guanfacine
  - Antihypertensive effect
    - Rebound hypertension (drug holiday not advised)
  - Non-controlled
  - Immediate benefit not likely
  - Fatigue

Anxiety

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Association of Anxiety

- PTSD
- Substance Abuse
- OCD

Assessment

- GAD-7
  - 7 questions
  - Example: Feeling afraid something awful might happen
  - Scored from 0-3 for each question
    - Not at all
    - Several days
    - More than half the days
    - Nearly every day
  - Higher the score the worse
  - Obviously might not work in our dementia type patients

Acute Treatment

- Identify underlying cause
  - Pain
  - Infection
  - Hyperthyroid
  - Medications
    - Stimulants
    - Alpha/beta agonists

Medications

- SSRI’s
- Benzo’s
- Buspirone
- Other antidepressants
- Antipsychotics (usually with comorbidities)

SSRI’s

- Won’t work quickly
- Preferred for long term maintenance over benzo’s
- Selection based upon adverse effects

Benzodiazepines

- Work quickly
- Controlled substance
- Avoid long acting if using as needed
- LOT in elderly
  - Less likely to accumulate
  - Inactive metabolites

Buspirone

- Usually well tolerated
- Takes time to work
  - Similar to SSRI’s
- Not a controlled substance

Bipolar Disorder/Schizophrenia

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Acute Mania Treatment

- Antipsychotics
- Valproic Acid
- Lithium

Lithium

- Target Concentration
  - Acute 0.8-1.2
  - Maintenance 0.6-1.0
- AE’s
  - GI
  - Tremor
  - Slurred Speech
  - TSH
  - Kidney function
- Drug Interactions
  - NSAIDs
  - Thiazides
  - ACE Inhibitors

Bipolar Depression

- Lamotrigine
- SSRI’s
  - Can induce mania
  - Often used with mood stabilizer (i.e. Lithium, VPA, Carbamazepine)

Schizophrenia

- Elderly Adults
  - Likely tried numerous agents
  - May be able to or have to decrease doses
- Metabolic Syndrome
- TD risk

Antipsychotics

- Typical
  - Haloperidol
- Atypicals
  - Ripseridone
  - Quetiapine
  - Aripiprazole
  - Clozapine
  - Olanzapine
  - Ziprasidone

Side Effect Profile, Clinical Considerations

- Sedation
- Weight Gain
- EPS
- Prolactin
- Anticholinergic
- Agranulocytosis
- QTC prolongation

Antipsychotic Pearls

- Weight gain/metabolic syndrome
  - Olanzapine, clozapine
  - Aripiprazole, ziprasidone better
- QTc
  - Ziprasidone, typicals (i.e. haloperidol) tend to be worst
- EPS
  - Typicals, risperidone
  - Quetiapine tends to be best
- Prolactin elevation
  - Risperidone

Depression

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Depression – Kind of a Big Deal

- Suicide
- Circumstances
  - Finances
  - Job Loss
  - Living alone
  - Aging
  - Loss of Family/Friends

Common Diseases That Increase Risk of Depression or Depressive Symptoms

- MS
- Parkinson’s
- Dementia
- Cancer
- Hypothyroid
- Nutritional factors
  - B12

Antidepressant Pearls

- Take time to work
- Selection
  - Adverse effects
  - Compelling indications
- Monitoring
  - PHQ-9
  - Higher number/worse depression
  - Not perfect

Common SSRI’s

- Sertraline
- Escitalopram
- Citalopram
- Fluoxetine
- Paroxetine
- Fluvoxamine

SSRI Clinical Pearls

- Citalopram
  - QTc prolongation, limit dose in elderly to 20 mg daily; omeprazole interaction
- Fluvoxamine
  - Generally avoid, multiple 3A4 drug interactions
- Fluoxetine
  - A little more activating
- Sertraline
  - Loose stools/serotonergic
- Paroxetine
  - Generally avoid in elderly, mildly anticholinergic
  - 2D6 interactions
  - Tends to be more sedating/weight gain
- Controversial effect on platelets and bleeding

Common SNRI's

- Duloxetine
- Venlafaxine
  - Pain at higher doses
  - Challenging to taper down/off

Trazodone/Nefazodone

- Nefazodone – rare use, hepatotoxic
- Trazodone
  - Low doses insomnia
  - Orthostasis
  - Dry mouth
  - Sedation

Mirtazapine

- Weight gain
- Sedation
  - Lower doses

Bupropion

- Smoking cessation
- Activating
- Caution - Seizure disorder

TCA's – lots of them!

- Nortriptyline, Desipramine, Amitriptyline, Imipramine
- Anticholinergic
- Risk in overdose
- Nortriptyline – possibly better tolerated in elderly
- QTc prolongation
- Good for corresponding pain syndrome
  - Fibromyalgia
  - Neuropathy

Less Common Antidepressants

- Serotonin modulators and stimulators
  - i.e. vilazodone
- MAOI’s
- Antipsychotic augmentation
- OTC’s
  - St. John’s Wort

Opioid and Alcohol Overdose/Withdrawal

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Opioid Effects

- Overdose
  - Respiratory depression
  - Confusion
  - Sedation
  - Miosis
  - Bowel sounds absent
  - Blue extremities (inadequate oxygen supply)
- Withdrawal
  - Insomnia
  - Anxiety
  - Irritability
  - Sweating
  - GI upset
    - N/V/D
  - Cramping/muscle pain

Opioid Withdrawal Agents

- Clonidine as needed
  - Sweating, hypertension, tachycardia
- Trazodone
  - Insomnia
- Diphenhydramine
  - Anxiety/insomnia
- Simple analgesics
  - Muscle cramps/pain

Alcohol

- Overdose
  - Confusion
  - Sedation
  - Ataxia
  - Slurred speech
  - Unconscious
- Withdrawal
  - N/V
  - Anxiety/insomnia
  - Seizures
  - DT’s
    - Confusion, hallucinations
    - Sweating
    - Tachycardia
    - Life threatening

Alcoholism Deficiencies

- Thiamine (risk of Wernicke's encephalopathy)
  - Acute delirium symptoms
- Folic acid
- Potassium
- Magnesium
- B-vitamins
- Malnutrition

Miscellaneous Agents

- Benzodiazepines
  - Used in alcohol withdrawal
  - Reduces seizure and DT risk
- Naloxone
  - Opioid antagonist
  - Drug of choice for opioid reversal
  - Can induce withdrawal
- Flumazenil
  - Reverses benzodiazepines
  - Boxed warning for seizure risk

Renal

Acute and Chronic Kidney Disease

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Signs of Kidney Failure

- Rise in serum creatinine
  - Generally 30%
- Rise in Blood urea nitrogen
  - Both are removed by the kidney
  - In renal disease, both accumulate
- Hyperkalemia/cardiac changes

Cockcroft-Gault Formula for Estimating Creatinine Clearance

$$\text{CrCl (mL/min)} = \frac{(140\text{-age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \quad (\times 0.85 \text{ if female})$$

Acute Renal Failure

- Prerenal
  - Inadequate perfusion
- Post renal
  - Blockage (stones, BPH)
- Intrinsic
  - Infection
  - Toxic agents
  - May be marked by elevated protein in the urine

Acute Kidney (Injury) Disease - Prerenal

- Common causes
  - Reduced blood flow to kidney
  - Caused by
    - Dehydration
    - Significant acute blood loss
    - Severe N/V/D
- Medications
  - ACE/ARB
  - NSAIDs
  - Diuretics

Classic Medication Causes - Intrinsic

- Aminoglycosides
- Cisplatin
- Amphotericin B

Treatment of ARF

- Supportive care
- Prerenal
  - Volume replacement with dehydration
- Intrinsic
  - Remove offending agent
  - Inflammation
    - Steroids
- Post renal
  - Remove blockage

Stages of Chronic Kidney Disease of all Types

Stage	Qualitative Description	Renal Function (mL/min/1.73 m^2)
1	Kidney damage-normal GFR	≥90
2	Kidney damage-mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	End-stage renal disease	<15 (or dialysis)

Source: http://guidelines.diabetes.ca/

Problem: Dosing Medications

- Many drugs are dosed by CrCl
- Lab reports GFR
- Keep an eye on changes in kidney function
  - Drugs can accumulate
  - Cause toxicity

Incredible # of Medications Dose Adjusted

- Chronic medications
  - Use common sense
  - Check levels (i.e. digoxin)
  - Start low go slow
  - Should you change dose if no side effects
    - Gabapentin
    - Ranitidine
    - Allopurinol

Collateral Damage - CKD

- Fracture risk
  - Vitamin D deficiency
- Anemia
  - Kidney = source of EPO
- Fluid retention
- CVD
- Hyperkalemia

Preventing Kidney Problems

- Diabetes
  - Blood sugar control
  - ACE inhibitors
- Hypertension management
- Smoking cessation
- Obesity management

Dialysis Complications

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Electrolyte Complications

- Hyperkalemia
- Hyponatremia
- Hypocalcemia
- Hypermagnesia

Complications

- Infection risk
  - Access site
  - Think about potential causes/source
    - Skin (gram +)
- Bleeding
  - May already be anemic
    - EPO production lacking
  - Many on antiplatelet/anticoagulant therapy
- Hypotension

Management/Monitoring

- Electrolytes
  - Replace as appropriate
  - EKG if significant deviations from normal
- Hypotension
  - Fluid bolus for acute management
    - Saline
    - Lactated ringers can elevate potassium
  - Hold/alter antihypertensives

Medication

- Hypotension Associated with Dialysis
  - Medication NOT first line
  - Reassess goal weight
  - Holding BP meds
- Midodrine
  - Alpha agonist
  - Exacerbate BPH
  - Raise BP
- Dose given 15-30 minutes before dialysis

Nephrolithiasis

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Nephrolithiasis

- Kidney stones
  - Severe side/back pain
  - Change in urination
    - Blood, urine consistency, flow
  - Severe pain causing N/V

Causes/Risks

- Excessive Calcium intake
  - Key component of stones
- Dehydration
- Hyperparathyroidism
- Obesity
- Genetic

Potential Medication Contributors

- Theophylline
- Acetazolamide
- Glucocorticoids
- Antacids (calcium)
  - Excess vitamin D
- Vitamin C

Acute Management

- Surgery, shock waves
- Pushing fluids
- Pain management
  - Simple analgesics
  - Opioids
- Alpha blockers (ok to use in females)
- Uric acid based stones
  - Allopurinol
  - Febuxostat

Pulmonary

Asthma

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Asthma Versus COPD

- Reactive
- Younger onset
- Reversible
- Triggers
- Wheeze
- Inflammation

Drug Selection

- SABA
- Steroids (inhaled)
- Dose escalation
- Addition of LABA
- Montelukast

Factors in Classification

- Frequency of exacerbations requiring oral steroids
- SABA use
- Interference with activity
- Nighttime awakenings
- FEV
  - Target 80% of predicted or better

Steps in Asthma Treatment

- Intermittent – SABA
- Mild Persistent – SABA + Low dose inhaled corticosteroid
- Moderate Persistent – SABA + Medium dose inhaled corticosteroid
- Severe Persistent – SABA + ICS + LABA and/or montelukast
- Last options for severe asthma
  - Oral corticosteroids (chronic)
  - Anticholinergics
  - Theophylline
  - Cromolyn

Rule of 2 in Asthma

- < or equal to 2 times/week – use of albuterol
- < or equal to 2 nighttime awakenings/mo
- > 2 refills per year on rescue
- ER visits/hospitalizations
- https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

Nebulizers

- Pediatrics/elderly
- Albuterol
- Ipratropium
  - Combination with albuterol
- LABA
- Budesonide

COPD

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GOLD Classification

- 1 – mild (FEV >80% of predicted)
- 2 – moderate (FEV 50-80)
- 3 – Severe (FEV 30-50)
- 4 – Very Severe (FEV <30)
- http://goldcopd.org/wp-content/uploads/2016/12/wms-GOLD-2017-Pocket-Guide.pdf

General Medication Flow

- SABA/Short Acting Anticholinergic
  - Or Combo
- Long Acting Anticholinergic
- Long Acting Beta Agonist (LABA)
- Inhaled corticosteroids
- Roflumilast
- Theophylline

Adverse Effects Beta Agonists, Anticholinergics

- Beta Agonists (i.e. albuterol, salmeterol)
  - Tachycardia
  - Tremor
- Anticholinergic (i.e. ipratropium, tiotropium)
  - Dry mouth

Inhaled Corticosteroids

- Reduces Exacerbations
- Not used as monotherapy in COPD
- Systemic Corticosteroids
  - Avoid long term if possible
  - OP, GERD, HPA suppression, Diabetes

Roflumilast

- Reduces exacerbations
- $$
- SE risks
  - Weight loss, GI
  - Psychiatric concerns

Other Alternatives

- Theophylline
  - Drug levels
  - Drug interactions
    - Quinolones, macrolides
    - Sympathomimetics
  - Systemic effects
- Azithromycin

Classic Medication Causes of Respiratory Issues

- Amiodarone
- Nitrofurantoin
- Beta-blockers
  - Can blunt response to medications (beta-agonists)

Other Considerations

- Oxygen
- Vaccination
- Smoking
- Alpha-1 antitrypsin deficiency (AATD) screening

Lung Abscess

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Lung Abscess

- Necrotic area of pulmonary tissue
  - Maybe a complication following pneumonia
- Anaerobes common
  - Don’t need oxygen/blood flow
  - Bacteriodes, Peptostreptococcus, Fusobacterium, Microaerophilic
- Aerobes
  - Common bugs that cause pneumonia (i.e. Strep.)
- Fungal contributors
  - Aspergillus
  - Cryptococcus

Coverage

- Clindamycin
  - Anaerobes – good coverage
- Metronidazole (likely won’t use alone)
  - Anaerobic coverage
- Imipenem/cilastin

Other Considerations

- Known resistant bugs involved
  - MRSA
    - Vancomycin
  - Pseudomonas
    - Piperacillin/tazo
    - Antipseudomonal cephalosporin

Fungal Coverage

- Aspergillus
  - Voriconazole
- Cryptococcus
  - Fluconazole
  - Ampho B for severe/resistant infections
- Will discuss Fungal Infections more in separate video

Pulmonary Hypertension

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Pulmonary hypertension

- Elevated pressure in lung arteries
  - Narrowing, damage, blockage
- Can result in right side heart failure
  - SOB
  - Fatigue
  - Edema
  - Poor perfusion
  - Tachycardia

Management

- Prostanoids (i.e. epoprostenol, iloprost)
  - IV administration for acute issues (epoprostenol)
  - Potential for tolerance and rebound if abruptly discontinue
  - Bleed risks – platelet inhibition
- Endothelin Receptor Antagonists
  - Ambrisentan, bosentan
  - REMS program – pregnancy, fetal risks

PDE-5 Inhibitors

- Sildenafil, tadalafil
  - Nitrate interaction
  - Flushing
  - Headache
- CCB’s
  - Last line
  - Usually well tolerated

Respiratory Failure

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Respiratory Failure

- Failure of gas exchange in the lungs
  - Goals of the lungs
    - Bring in O2
    - Eliminate CO2
- Low oxygen is most common form of respiratory failure
  - PaO2 <60 mm Hg
  - Normal or low PCO2
  - Pneumonia, pulmonary edema
- Hypercapnic
  - Elevated PCO2 >50 mm Hg
    - Asthma, COPD, drug overdose

Management

- Get O2 levels up if low oxygen saturations
  - Respiratory failure
    - Most common reason for intubation
    - Target >60 mm Hg PaO2
      - Oxygen saturations >90%
- Elevated CO2 usually not primary concern
  - Exception might be substantial acidosis
    - pH<7.2

Medication Management

- Treat identifiable cause
  - Pneumonia – antibiotics
  - Pulmonary Edema - Diuretics
  - COPD – Anticholinergics/beta agonists/steroids
  - Asthma – beta agonists, steroids, etc.

Intubation - Medications

- Induction
  - Etomidate
    - Inhibits GABA receptors
    - No drop in BP
  - Propofol (quick on/quick off)
    - More likely to impact BP (drop)
  - Ketamine
    - Possibly increase ICP/BP
  - Midazolam
    - Slower onset, generally not used

Intubation - Medications

- Lidocaine
  - Helps suppress gag reflex (pre-medication)
  - Possibly helps prevent increases in HR, Intracranial pressure, MAP
- Fentanyl
  - Blunt sympathetic response to physical act of intubation
- Neuromuscular Blocking agents
  - Discussed Elsewhere

Supportive Care

- DVT Prophylaxis
- Stress ulcer prophylaxis
- Management of issues causing respiratory failure
- If used, monitor for VAP
- Minimizing sedation as much as possible

Sleep Apnea

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Sleep Apnea

- Patient stops breathing during sleep
  - Reduced respiration
- Gasping/choking/snoring sounds
- Drop in oxygen sats
- Waking up
  - Patients don’t feel rested
  - Daytime sleepiness
- ***Important cause of resistant hypertension

Typical Management

- No drugs
- CPAP
- Change in sleeping position
- Smoking Cessation
- Weight Loss
- Alcohol Cessation

Medications – Daytime Sleepiness

- Despite adequate CPAP/management of sleep apnea
- Modafinil/armodafinil
  - Stimulant
  - Aids in wakefulness in partial responders to CPAP/other therapies
  - Monitor BP/HR
  - Be a little careful in patient with psychiatric history (psychosis, mania)

Sleep Apnea - Risky Medications

- Opioids
- Benzodiazepine
- Barbituates
- Alcohol

Health Maintenance and Public Health

Biostatistics

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Hypothesis Testing

- Ho – null hypothesis
  - No difference between groups
  - Example: comparing new drug to placebo
    - People studying new drug will want p-value less than 0.05
  - If the p-value is low (<0.05), null hypothesis must go
- Ha – alternative hypothesis
  - Ha is accepted when the null hypothesis is rejected

P-Value

- Also referred to as alpha (α)
- Represents the probability that your study is wrong
- The lower the p-value, the less likely your study is incorrect
  - <0.05 (5%) is set by convention as a statistically significant study
- Type 1 error
  - Detecting a difference when one doesn’t actually exist

Beta

- Beta (β) represents the probability of type 2 error
  - Type 2 error is the inability to detect a difference and one actually exists
  - Underpowered studies
    - Inadequate sample size
- Power = 1-Beta
  - Target power is 80% or greater (0.8)
  - Target Beta is 0.2

Variables

- Independent
  - What the researches set as variables
  - Drugs, doses, etc.
- Dependent
  - They depend upon the independent variables
  - Drop in blood sugar, blood pressure, etc.
- Control variable
  - No intervention is made
  - Comparison group

Types of Variables

- Nominal “name”
  - Placing patients in groups/categories
  - Those with MS, those without
- Ordinal
  - Order
  - No specific distance between variables
  - Subjective scales/surveys are included in this group
    - Staging of pressure ulcer
    - Pain scale
    - Rating a speaker
  - Ordinal and Nominal are also called discrete variables (only take on a limited # of values within a range

Types of Variables

- Continuous (can have fraction of numbers)
  - Ratio
    - Has an absolute zero
    - Example: height
  - Interval
    - Similar to ratio
    - No absolute zero
    - Fahrenheit/Celsius temperature scale

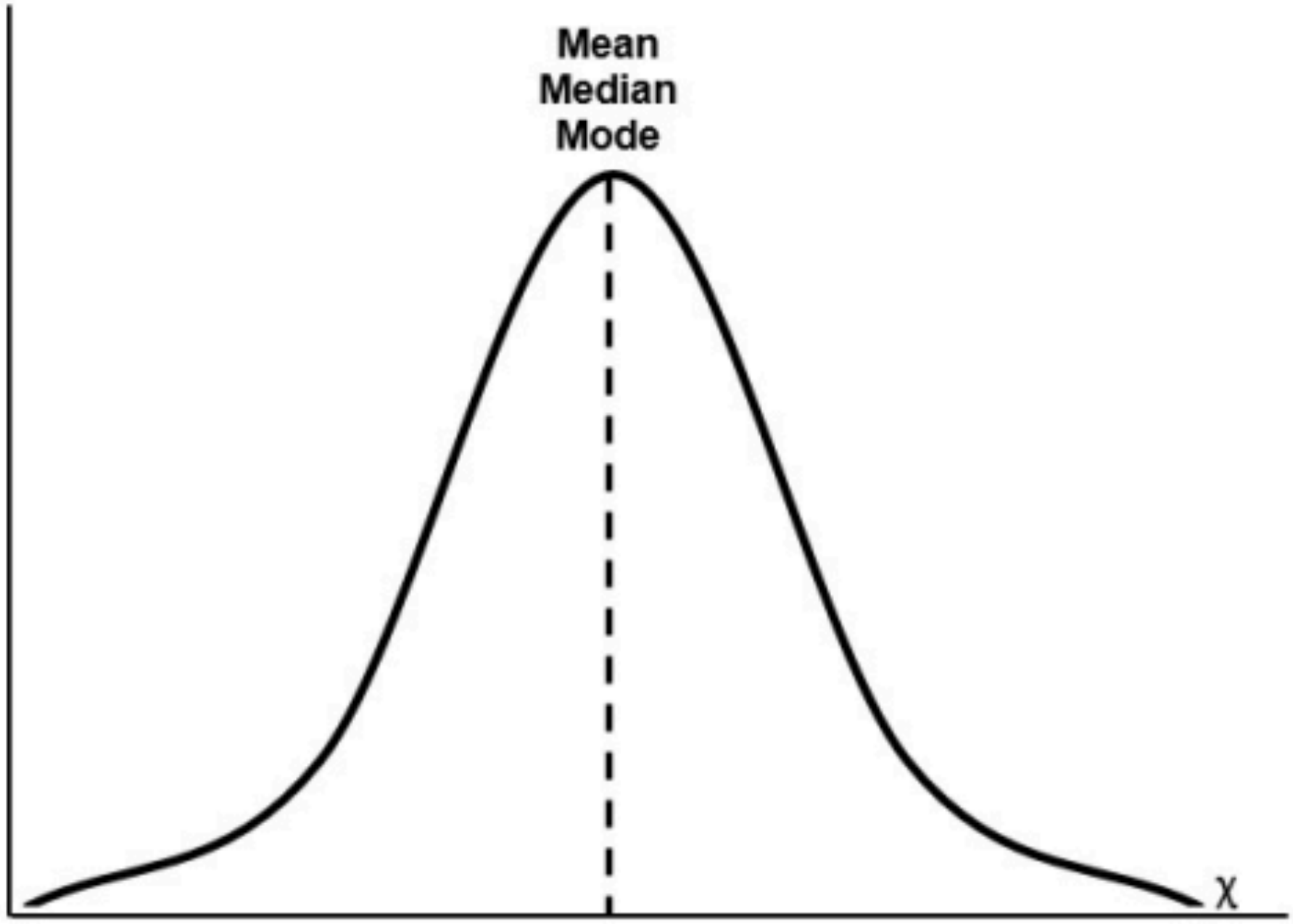
Confidence Intervals

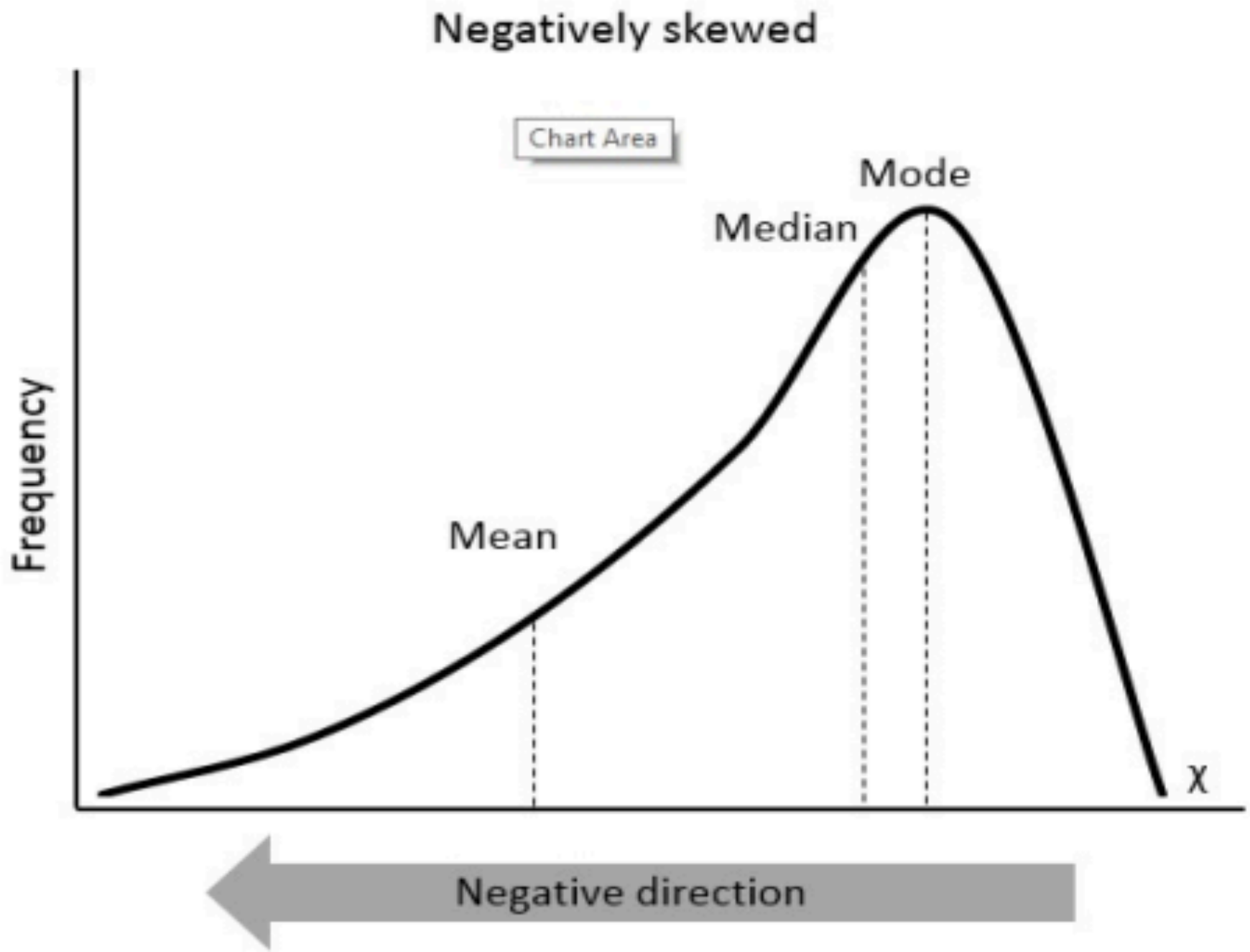
- Range of values that you believe the true value lies between
  - Traditionally set at 95%
  - I.e. you are 95% confident that the values lie between two values
- If you are looking for a change, does your confidence interval contain "0"
  - Change in blood sugar on prednisone; 95% CI = 4-25
- If you are looking for a deviation from normal comparing two confidence intervals (groups), do they overlap?
  - Comparing two different dosages
  - Drop in systolic blood pressure (2.3-6.8) vs. (4.5-8.1)

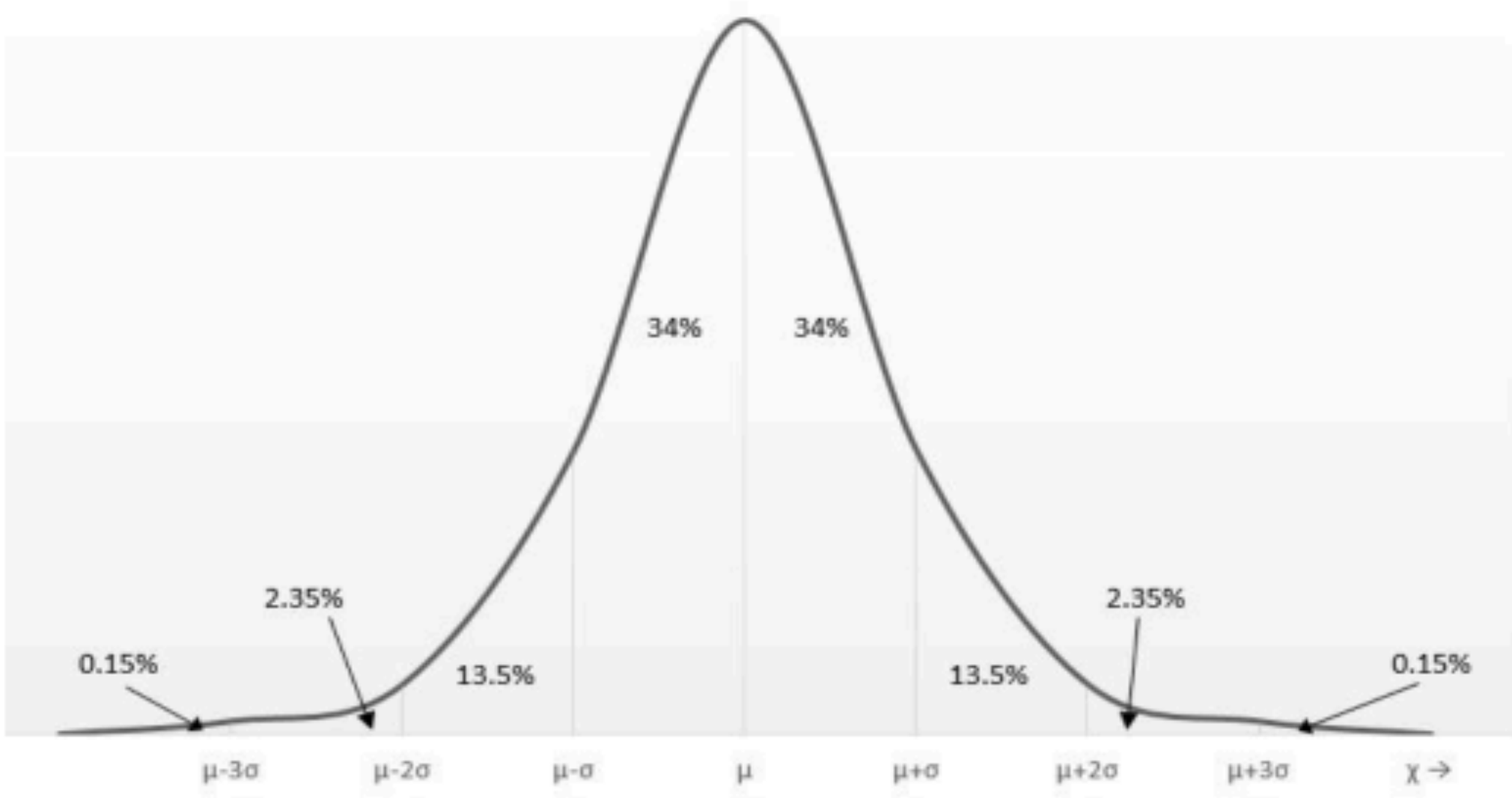
Normal Distribution – Continuous Variables

- Also termed parametric data
- Mean = Median = Mode
- Mean – average
- Median – middle number
- Mode - # (or value) that occurs most often
  - Bell Curve
- ***Do NOT use for ordinal data
  - Ordinal, nominal are considered nonparametric data

Normal (no skew)




Negatively skewed
Chart Area
Mode
Median
Mean
Frequency
X
Negative direction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-2
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0
1
2
3

Statistical Testing – Paired/Unpaired Groups

- Paired
  - Data measured from same subject
  - Before and after treatment
    - Washout period when using drugs
- Unpaired
  - Two different groups being compared
  - Assume a normal distribution in the population
    - No before and after comparison for an individual research participant

Statistical Testing

- Ordinal
  - Sign test
  - Wilcoxon test
    - Used for two paired samples
  - Unpaired Samples (two)
    - Mann-Whitney
  - Three or more unpaired samples
    - Kruskal-Wallis test
  - Spearman correlation
    - Correlation for two paired samples

Statistical Testing - Continuous

- Continuous (t-test or sometimes called Student's t-test)
  - Paired t-test
    - Two paired continuous groups
  - Unpaired t-test
    - Two unpaired continuous groups
- ANOVA (analysis of variance)
  - Three or more samples
- Pearson correltation

Nominal Data

- Chi-squared χ^2
  - Unpaired samples
- Paired samples
  - Sign test
- Correlation comparison
  - Contingency coeffecients

	Dataset		
	Nominal	**Continuous**	**Ordinal**
Example of Variable	Separation of patients into Afib and non-Afib groups	Readings of blood pressure from several patients	Pain Scale
Is mean (average), standard deviation applicable?	No	Yes	No
Example of appropriate Statistical Test (dependent upon samples)	χ^2 (chi-squared)	One-sample t test	Sign test or Wilcoxon test
Compare two paired samples	Sign test	Paired t test	Sign test or Wilcoxon test
Compare two unpaired samples	χ^2 square Fisher's exact test	Unpaired t test	Mann-Whitney test
Compare three or more unmatched samples	χ^2 test	One-way ANOVA	Kruskal-Wallis test
Quantify association between two paired samples (correlation)	Contingency coefficients	Pearson correlation	Spearman correlation

Absolute Risk

- Simply take the difference between the raw %
  - 60% of smokers develop lung cancer
  - 20% of non-smokers develop cancer
- Absolute risk reduction
  - Not smoking is 40% (0.4) absolute risk reduction

Number Needed to Treat

- NNT
  - Good comparison of agents/pharmacoeconomics
  - Also good to compare risks (adverse effects) versus benefits of medication therapy
- Lower NNT = more effective treatment
  - How many people will get benefit
- NNT = 1/ARR
  - Difference between groups is 5% MI rate versus 10% MI rate
  - ARR = 0.05
  - NNT = 1/0.05 = 20

Number Needed to Harm

- Similar to NNT
- Demonstrates tolerability/risk of ADR's in medication studies
- Higher NNH is better
  - Less likely that an adverse effect will happen
- Risk of renal failure is 1% in placebo group and 2% in treatment group
  - NNH = 1/Absolute risk
  - NNH – 1/0.01 = 100 patients treated, 1 patient will have renal failure from the medication

Odds Ratio

- Most often presented as 95% CI
- CI containing 1 will not be considered statistically significant
  - 0.7-1.31
- Range less than 1
  - Demonstrates that outcome is less likely to happen
- Range greater than 1
  - I.e. 1.23 – 1.61
  - Demonstrates that outcome is more likely to happen

Hazard Ratio

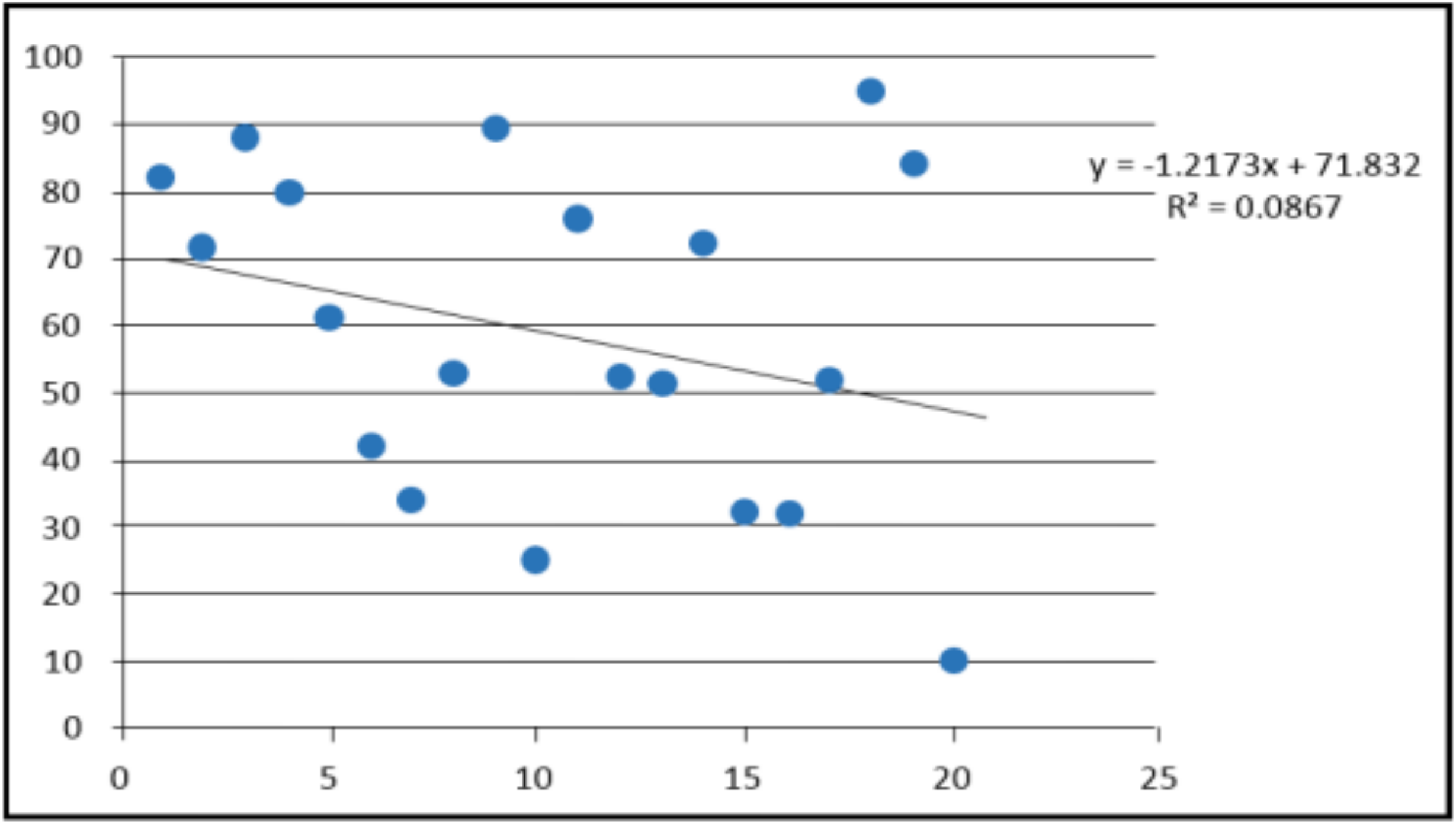
- Often related to adverse events
  - CI less than 1 and doesn’t contain 1
  - Protective effect
- Adverse effects more likely
  - CI that doesn’t contain 1 and is greater than 1

Correlation

- Association
- Negative
  - Variables go in opposite direction
- Positive
  - Variables go in the same direction
- Correlation does not mean causation***
  - Patients with COPD develop lung cancer

Correlation Coefficient

- Correlation coefficient = r
  - Value ranging from -1 to 1
- R-squared
  - Lies between 0-1
  - Tells us how accurately we can predict where values fall
  - 0 = no correlation
  - 1 = perfect predictability of the model


100
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70
60
50
40
30
20
10
0
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5
10
15
20
25
y = -1.2173x + 71.832
R² = 0.0867

Bias in Studies

- Selection
  - Study participant groups differ
- Observation
  - Investigator ”seeing” something or exaggerating the response
- Recall
  - Memory recall
- Misclassification
  - Incorrect incorrect classification of a study participant
  - Misdiagnosis

Confounding Variables

- A variable that is impacting your study results
  - Known or unknown
- Confounding Variable
  - Lead to incorrect assumptions/association
  - Kind of similar to correlation does not mean causation

Clinical Literature

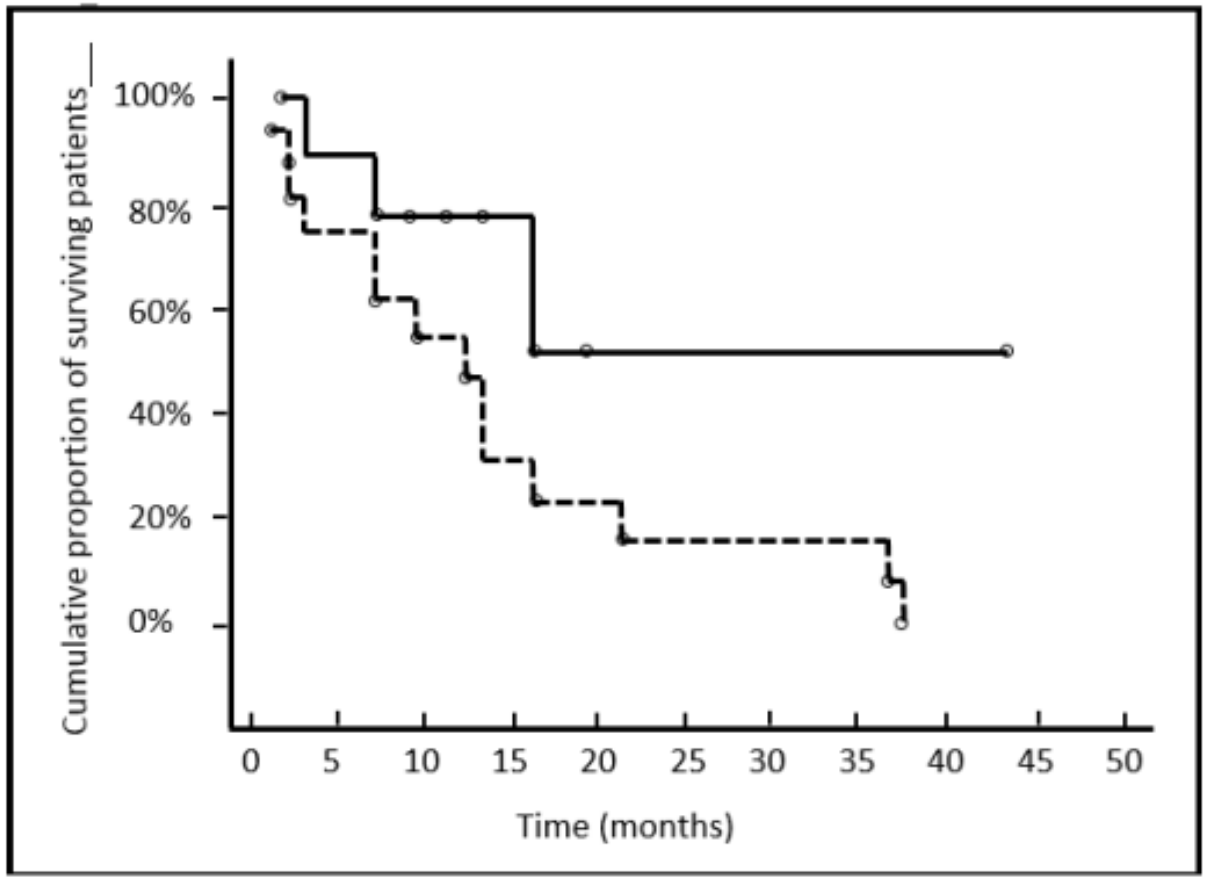
- Primary
  - Clinical trial/study
- Secondary
  - Review article breaking down a particular topic
- Tertiary
  - Large compilation of information
  - Textbook

Study Design Strength

- Randomized Controlled Trials
  - Direct comparison under controlled environment to identify
  - Gold Standard
- Meta-Analysis
  - Comparison of similar studies to draw conclusions
- Cohort
  - Following a group of patients over time on a drug/with a disease etc. and monitor some effect (done prospectively)
- Case Control series
  - Look back at information to identify trends/associations
- Cross Section Surveys
  - Snap-shot in time
- Case Studies
- Expert opinion

Kaplan Meier

- Estimation of survival over time



Regulatory

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The Joint Commission (TJC)

- Evaluate/Accredit Healthcare Organizations
- Non-profit
- Accreditation process based on quality of care
  - Performance standards
  - Best practices
- TJC aims to ensure HCO’s provide
  - Quality
  - Safety
  - Effective
  - Value

Survey

- Unannounced visit
- 18-36 month window from last visit
- On-site
- Deficiencies
  - Called Requirements for Improvement (RFI's)
  - Entities must respond to the deficiencies
    - Evidence of standards compliance (Plan of correction)

Survey Process

- Initial planning session
- Orientation/conference
- Leadership session
- Tracer method of review*** (next slide)
- Competence assessment
- Review of credentialing
- Environmental review (look over building)
- Exit conference

Tracer Method

- Review process for TJC
- Review/track patient care experience
- Walks through the entire healthcare process
- Looks at how well services are integrated
  - Coordination
  - Communication
- Medication Management is an important aspect of providing care

TJC and ORYX Initiative

- ORYX – publicly reported quality data
- Incorporates Quality Measures into the accreditation process
  - eCQM (electronic quality measures)
- TJC is working closely with CMS
- Helps TJC identify/review weaknesses
  - Look at process and what organization is doing to make improvements
- Accountability Measures
  - Alter over time
  - Examples – next slide

Historic Examples of Quality Measures

- Acute MI
- Tobacco treatment
- VTE
- Substance abuse
- Asthma
- Perinatal care
- Immunizations

TJC Benefits

- “Voluntary”
- Competitive edge
- Public appearance
- Recognition by payers
- Ensure best practices are being utilized/followed
- May reduce liability costs for hospital

Medication Management

- Handling of hazardous/high risk medications
- Look alike/sound alike list
- Formulary approval process
- Non-formulary process
- Storage
  - Preparation
  - Labeling
  - Beyond use dating
  - Security

Criteria for Drug Selection - Hospital

- Effectiveness
- Drug interactions
- Indications for use
- Potential for errors and abuse
- Adverse drug events
- Sentinel event advisories
- Population(s) served (for example, pediatrics, geriatrics)
- Other risks
- Costs

Process for Drug Events

- Medication errors
- Adverse drug reactions
- Drug Diversion
- Tracks/collects data
  - Errors, controlled substances, patient scanning/med scanning
  - Continuous improvement based on data
  - Hospital needs to take action on data

CMS – Centers for Medicaid and Medicare

- Falls under HHS umbrella
- Medicare part A – Hospital/skilled nursing/hospice
- Medicare part B – Medical/clinic/labs/imaging healthcare benefits
- Medicare Advantage (Part C) – puts everything together; part A, part B, and often vision, hearing, and possibly prescription coverage
  - Often require “networks”
- Medicare part D – outpatient dispensing pharmacy benefit

HCACHPS

- Hospital Consumer Assessments of Healthcare Providers and Systems
- CMS mandate
- Patient satisfaction surveys
- Allows patient comparisons of hospitals
- Surveys can/are used as payment incentives/disincentives
- Goal – increase transparency in care, consumer help in determining quality of care provided

LEAPFROG

- Independent, non-profit organization
- Collect data and support public initiatives to improve safety
- Goal – reduce unnecessary healthcare injuries
  - Medication errors
  - Injuries
  - Preventable infections
- LEAPFROG hospital survey
  - Allows comparison between institutions

HIPAA

- Standards for handling patient information
- Protects patients personal information
- Also provides access to healthcare professionals who need the information to make informed decisions with the patient
- No restrictions of de-identified data/info

Common Sense Violations - HIPAA

- Anything that could possibly reveal a patient's identity/condition/etc.
- Discussion PHI in a public area
- Obtaining more information than is necessary to treat the patient
- Releasing information about minors without parental consent
- Leaving computer screen up/not logging off

Food and Drug Administration

- Regulatory Agency
- Role in Drug Approval
- OTC
- Prescription
- Role in Drug monitoring after approval
- Supplements
- Food

Center for Drug Evaluation and Research

- CDER
- Part of FDA
- Monitors drugs for safety/effectiveness
- Reviews New Drug Applications (NDA's)
- OTC approvals
- Rx approvals
- Removal from the market
- Ensures Good Manufacturing Practices (GMP's)

Division of Medication Error Prevention and Analysis

- DMEPA
- Under CDER umbrella (which is under FDA umbrella)
- Review medication error reports
- Work closely with
  - Institute of Safe Medicine Practices (see later slide)
  - United States Pharmacopeia (USP)

Institute of Safe Medication Practices

- ISMP – Non-profit organization
- Medication Errors Reporting Program (MERP)
  - Voluntary
  - Reports forwarded to FDA
  - Identify trends (look alike, sound alike, dosing concerns)
- Send out reports to HCP's
- ***my favorite – do not crush list

ISMP - Vaccines

- Separate from MERP
- Voluntary
- Vaccine errors
- Good catches can be reported as well
  - I.e. similar labels etc.

Vaccine Adverse Event Reporting System

- VAERS
- Part of Department of Health and Human Services
- Post marketing vaccine reporting only
  - May be hard to identify rare reactions in clinical trials due to # of patients
- Non-preventable adverse reactions
- Analyze reports
  - Identify trends
- NOT mandatory

Process for New Drug Approval

- Discovery
- Development
- Study in non-humans (pre-clinical research)
- Apply/receive IND approval
- Three phases of clinical trials***see next slide
- Phase 4 – post-marketing monitoring

Human Clinical Research

- After receiving Investigational New Drug application approval
- Phase 1 Clinical Trials
  - 20-100 healthy volunteers
  - Safety/dosing
  - Usually at least a few months
- Phase 2
  - Up to several hundred people (have disease being studied)
  - Months to years
  - Efficacy and adverse effects

Human Clinical Research

- Phase 3
  - Hundreds to 1,000's of study participants
  - Often up to a few years
  - Efficacy, adverse drug reactions
- Drug approval after Phase 3
- Phase 4
  - Post Marketing Surveillance
  - Safety and efficacy
  - Rare adverse events
  - Drugs removed from market or have restrictions
    - Rosiglitazone
    - Darvocet

Generic Drug Approval

- Do NOT require clinical trials
- Simply have to prove bioequivalence
  - This is why they are a lot cheaper!
- ANDA
  - Abbreviated New Drug Application is what generic medication manufacturers submit

MedWatch

- FDA program
- 3500B form for consumers
  - Report serious reactions from medications
  - Quality concerns/product malfunction problems (i.e. devices0 etc.
- MedWatch goals
  - Ensure availability of safe/effective drugs
  - Ensure integrity of drugs on the market
  - Promote safe use of available drugs

Center for Biologics Evaluation and Research

- CBER
- Under FDA umbrella
- Biologic medication approval
- Biosimilar approval
- Monitoring of these products

Risk Evaluation and Mitigation Strategy (REMS)

- Ensure the benefit>risk of medication
- Used for certain medications that pose a significant risk of problems (or a small risk of VERY serious problems)
- Above usual Rx designation
- Examples
  - Clozapine registry (WBC monitoring)
  - Isotretinoin (iPLEDGE – fetal risks in pregnancy)

REMS Program

- Drug sponsor designs program
  - FDA reviews/approves REMS program
- Program is generally developed based upon the risk of the medication (clozapine, isotretinoin is pretty intensive)
- Can be class effect or just a specific drug
- May be required with initial approval
  - OR may be due to post-marketing surveillance
- REMS Medication Guides
  - Given to patient in patient friendly language

ETASU

- Elements to assure safe use (may be part of REMS program)
  - Tasks that need to be completed before Rx/dispensing
  - Time consuming
  - May require
    - Special training
    - Special administration (maybe in a controlled setting by HCP)
    - Lab testing
    - Patient may have to enroll in registry

National Institute of Health

- Government agency
  - Biomedical research
- Under HHS umbrella
- Clinical trials funded via taxpayer expense
- Goal is to improve understanding/knowledge in the medical community

Institute of Medicine

- Agency that released “To Err is Human” report
  - Opened discussion about medical/medication errors
  - Fostered environment for care improvement
  - Development of safeguards
- Shifted focus to system problems
  - Versus blaming humans (staff) for errors

Agency for Healthcare Quality and Research

- AHQR
- Under HHS umbrella
- Fosters evidence based medicine in making healthcare more accessible, affordable, safe, and equitable
- Improve delivery of healthcare
- TJC will often incorporate research from AHRQ information

ACO's

- Accountable Care Organization = ACO
- Group of physicians, hospitals, healthcare professionals who voluntarily commit to provide high quality, highly coordinated care to Medicare patients
- Attempt to reduce costs
  - Avoiding duplicate services
  - Minimize excessive care (delivering care in least expensive way) – I.e. avoiding expensive ED/hospital care
- Payment models shifting to quality of care reimbursements, not fee for service

National Quality Forum

- Agency that provides guidance on standards/quality measures
  - Endorses
  - Makes recommendations on quality measures that should be incorporated into payment models
- Source for provider/healthcare tools
  - Reports
  - Guidance on how to improve quality
  - Guidance on how to meet standards

Meaningful Use

- Electronic health record use
  - Improvement of quality, safety, sharing information, care coordination
- Benefit to population health
  - Vaccine tracking
  - Sharing between organizations
  - Allows patients to access their own records in efficient manner
  - Allows streamlined communication with healthcare professionals
  - Allows for better tracking, reporting, and analytics

Presenting Materials

- Who’s the audience
  - Ensure presentation matches education level
- What is the objective
  - Is there a need?
  - Weakness to be improved?
- Assessment of education delivered
  - Testing
  - Improvement in practice
  - Teach back

Barriers to Providing Education

- Language
- Cultural
- Educational
  - Non-healthcare professionals
- Hearing problems
  - Written materials
- Visual problems
  - Audio materials
- Cognition concerns

OSHA

- Occupational Safety and Health Administration
- Protects workers safety
- Reviews standards for risky medication handling by HCP’s
  - Handling
  - Administration
  - Storage
  - Disposal
  - Transportation

Pharmacy Legislation

- Biologics Control Act of 1902
  - Ensured safety and purity of products that were used to treat and prevent diseases
- Food and Drugs Act of 1906
  - Prohibited interstate commerce of adulterated and misbranded drugs
- 1938 Food, Drug, and Cosmetic Act
  - New drugs approved must be proven safe
  - Factory inspections began

Pharmacy Legislation

- Durham-Humphrey Amendment of 1951
  - Delineates categories for two types of drugs
    - OTC versus prescription
- Kefauver-Harris of 1962
  - Ensure efficacy and enhance safety
  - **thalidomide use in pregnancy
- Tamper Resistant Packaging 1982
  - Tylenol/cyanide poisoning

Pharmacy Legislation

- Orphan Drug Act of 1983
  - FDA promoted research for drugs for rare diseases
  - Conditions affecting 200,000k or less
  - Financial incentives
- Prescription Drug Marketing Act
  - Required wholesalers be licensed
  - Restricted reimportation of drugs
  - Bans sale/trade/purchase of drug samples
  - Bans diversion of Rx drugs from commercial channels

Pharmacy Legislation

- Medwatch initiated – 1993
- DSHEA - 1994
  - Dietary Supplement Health and Education Act
  - Classifies dietary supplements as food (not medication)
  - Allows FDA to encourage GMP for supplements
- FDA Modernization Act of 1997
  - Regulated off label advertising

Pharmacy Legislation

- Medicare Prescription Drug Improvement and Modernization Act of 2003
  - Medicare part D
  - Implemented in 2006
- Affordable Care Act 2010 (Obamacare)
  - Allowed children to remain on plan until age 26
  - Set up fee for not having insurance
  - CMS Innovation Center
    - Developed to test healthcare models to reduce cost, maximize service
    - MTM model received expanded testing

Institutional Review Board

- Responsible for monitoring, reviewing, approving research within an entity
- Protects the rights and looks out for human research participants
- Reviews planned research process
  - Informed consent
  - Proposed study
  - Patient education

Institutional Review Board

- IRB – needs to register with HHS if doing FDA research
- Doesn’t have to be set up by institution
  - Can use an outside IRB
- IRB members can be paid
- Conflicts of interest should be considered when selecting members
- IRB Members
  - At least #5
  - Varying backgrounds (need more than one profession)
  - Mix of men and women – recommended but not required
  - One member – scientific background
  - One member – non-scientific background

Pharmacy and Therapeutics Committee

- P&T
- Interdisciplinary Team
  - Nurses, pharmacists, physicians, administration, quality personnel
- Responsibility
  - Creating drug formulary
  - Updating formulary
  - Review of evidenced based medicine, safety, as well as cost effectiveness of drug therapy
  - Review ADR’s, errors, processes, risks, guidelines, etc.

Medication Use Evaluation

- MUE sometimes called Drug Utilization Reviews (DUR)
- Analysis of medication use process
  - Prescribing, ordering, preparing, dispensing, administration, monitoring
- Prevent errors, injuries
- Supports ideal use of medication therapy
- Best practices
- Continuous improvement
- Identify areas of weakness
- Minimize costs
- Regulatory requirements

Bioterrorism

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Notable Infectious Agents – High Risk

- Smallpox
  - Fever, aches, rash (pustules)
- Ebola
  - Fever, N/V/D, muscle pain, weakness
- Anthrax
  - Inhalation – pneumonia type symptoms
  - Skin infection
- Botulism
  - Flaccid muscles
- Tularemia
  - **symptoms depend upon entry into the body
  - Fever, chills, headache, skin ulcer at site if from an animal bite

Useful Therapies

- Ciprofloxacin
  - Anthrax (Bacillus anthracis)
  - Tularemia (Francisella tularensis)
  - Plague (Yersinia pestis)
- Doxycycline
  - Alternative for Cipro
- Antitoxins
  - Anthrax, botulism, ricin

Physiological Changes in the Elderly

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GI Tract

- Decreased GI Motility
- Decreased Gastric Acid Secretion
- Higher PH

Distribution

- Increase in body fat
  - Increased volume of distribution for lipophilic drugs
    - Example Diazepam
- Reduction in Muscle
  - Fall risk
  - Lower creatinine (doesn’t necessarily mean improved renal function)
    - Creatinine clearance equation includes age

Kidney

- Reduced elimination of medications
- Remember muscle mass decreases
  - If creatinine stays the same, it doesn’t mean kidney function does change
- Increased half-life of kidney cleared meds
  - Digoxin
  - Allopurinol

Liver Changes

- Decrease in metabolic activity
  - CYP enzyme system
- Reduced hepatic blood flow
- Changes are complex
- Need to reduce doses, but no standard

Albumin

- Protein in the blood
- Drugs frequently bind to it
- Less found in the elderly/malnourished
- Higher free fraction of certain medications
  - Phenytoin
  - Warfarin

Infection Risk

- Reduced immune response
  - Example: fever
- Skin thinning
- Urinary changes
- Natural flora
- Immunosuppressant medications
- Nutrition
- Antibiotic use

Vaccines

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Pediatric Vaccines

- Hepatitis B
  - First dose at birth, series completed at about 6 months
  - Inactivated
- Rotavirus
  - 2 or 3 doses depending upon product
  - Live Vaccine
  - Severe diarrhea
- DTaP (Diphtheria, tetanus, and acellular pertussis
  - 5 doses (2, 4, 6, 15 months and 4-6 y/o)
  - Inactivated
- Haemophilus influenzae (Hib)
  - Potential risk of pneumonia, meningitis
  - 4 dose series (2, 4, 6, 12-15 months0
  - Inactivated

Pediatric Vaccines

- Pneumococcal (PCV13)
  - 4 dose series
  - Additional dose for high risk patients
    - Lung disease, diabetes, sickle cell, HIV infection, renal failure, heart disease, CSF leak, cochlear implant, asplenia, nephrotic syndrome, immunosuppressed (transplant, leukemia, etc.)
- Inactivated Polio (IPV)
  - 4 dose series (2, 4, 6, 4-6 years)
- Influenza
  - Annual

Pediatric Vaccines

- MMR (Measles, mumps, rubella)
  - Live vaccine
  - 2 doses
- Hepatitis A
  - Inactivated
  - 2 doses
- Varicella
  - Chickenpox
  - Is sometimes combined with MMR (MMRV)
  - Live Vaccine
    - Avoid catch up in pregnant females
  - 2 doses

Adolescent Vaccines

- Tdap
  - One booster shot 11-18 y/o
- Human papillomavirus (HPV)
  - 2 shots 6-12 months apart
  - Age 11-12
  - If started after 14, needs 3
  - Inactivated
- Meningococcal B (MenB)
  - 2 or 3 doses depending upon product
  - Teenagers/early 20’s at highest risk
- Influenza
  - Annual

Adult Vaccines

- Pneumococcal
  - PCV13
  - PPSV23
- Influenza
- Zoster Live Vaccine
- Tetanus, diphtheria, pertussis

Zoster Pearls

- Same virus as chicken pox
- Live vaccine
  - Immunosuppressed
- Storage in freezer (fridge for 72 hours)
- Age 60-69 best benefit
  - Indicated at age 50

Pneumococcal (Strep Pneumoniae)

- PCV13
  - Give age >65 once
  - Aim for one year between PCV13 and PPSV23
  - Do not co-administer
- PPSV23
  - Give twice if given before age 65
  - Give 5 years apart if given twice

Influenza

- Annually
- Inactivated injection
- High dose available
  - Somewhat more expensive
  - CDC not recommending high dose yet
    - Many target 65 and older
  - Some clinicians will target high risk patients
    - I.e. COPD/Asthma
  - Probably more effective
    - http://www.cdc.gov/flu/protect/vaccine/qa_fluzone.htm

Tdap/Td

- Tetanus, Diphtheria, Pertussis (whooping cough)
- Revaccination
  - Every 10 years (one time dose of Tdap)
  - Td for all other doses
- Inactivated
  - Immunosuppressed patients ok