PHARMACOLOGY – A Class Act

• “The arrival of a good clown exercises a more beneficial influence on the health of a town than 20 asses laden with drugs.”

• Dr. Thomas Sydenham (1624-1689)
The Numbers...

• 30 years ago there were 900 drugs to choose from in the PDR
• Today there are over 11,000...
Don’t PANIC....

• Know the 30 or 40 drugs you use daily in your clinical practice as well as the most common drugs most likely used by your patients...(age and gender specific)

• Helpful hints...
Generics vs. Brand names

As a general rule, classes of drugs have the same generic “last” name:
- “Prils” — ACE inhibitors
- “Sartans” — ARBs (angiotensin receptor blockers)
- “Triptans” — treatment of acute migraine headache
- “Statins” — Lower LDL-cholesterol
- “Dipines” — calcium channel blockers
- “Tidines” — H2 blockers reduce nighttime acid
- “Prazoles” — Proton Pump Inhibitors, GERD
- “Azoles” — antifungal
“Prils”—The ACE inhibitors

- Captopril (Capoten)
- Enalapril (Vasotec)
- Lisinopril (Prinivil, Zestril)
- Perindopril (Aceon)
- Moxepril (Univasc)
- Benazepril (Lotensin)
- Quinapril (Accupril)
- Trandolapril (Mavik)
- Ramipril (Altace)
A little refresher on the kidney...

- At any given moment, the kidney is “sensing” the pressure and volume of blood flow throughout the body.
- Low volume or low BP, the kidney will release renin from a small area (the JGA) just inside the afferent arteriole.
- Renin (the messenger) → (liver) angiotensin 1 → angiotensin 2 → via Angiotensin Converting Enzyme (ACE).
- Angiotensin 2 triggers the release of “AL” from the adrenal cortex.
So, let’s get back to the original story... Who is ACE and why do we want to inhibit him?
What does “angie’ do?

• “Tenses” your “angios”—vasoconstricts the arterioles and increases blood pressure

• Triggers release of “AL”—aldosterone (from the adrenal cortex to save Na+ & H2O († BP) and excrete K+...but that’s not all...

ANGIOTENSIN 2 ALSO...

• Increases inflammation in the arteries

• Prothrombotic

• Increases tissue resistance to insulin

• Potent growth factor— “remodels tissues”
So, if you were an ACE inhibitor, what would you do?

1. Anti-hypertensive agent via vasodilation and inhibition of aldosterone (Na+ and H2O diuresis)
2. Treatment of heart failure by inhibiting renin-angiotensin-aldosterone—CHF is a HYPER-RENNEMIC state
3. Anti-inflammatory
4. Anti-thrombotic
5. Hypoglycemic (be careful when starting ACE inhibitors in diabetics)
6. Decrease growth of tissues or “remodeling”

Is “remodeling” a good word? Hmmmmm....yes, in your...
But NOT...

- In your heart after a myocardial infarction, OR
- In your heart with chronic heart failure, OR
- In your blood vessels with hypertension,
- OR
- In your kidneys with diabetes
- “Angie is a bad girl...”
To summarize...ACE inhibitors are used for:

- Hypertension (*night time dosing of anti-hypertensive drugs—dippers (10% decline @ night) vs. non-dippers”) (American Journal of Kidney Diseases December 2007)

- Decrease the remodeling of the heart in heart failure patients and post-MI patients (clearly beneficial in MI patients 65-74 years of age, but not so clear in patients older than 75)

- Beneficial in patients with anterior ST-elevation MIs and in patients with MIs complicated by HF or significant LV systolic dysfunction with LV ejection fractions less than 40%
To summarize...ACE inhibitors are used for:

• Decrease the risk of 1\textsuperscript{st} and 2\textsuperscript{nd} myocardial infarctions in high-risk patients due to anti-inflammatory effects

• Stroke prevention

• Prevention of diabetic nephropathy

• Decrease insulin resistance and reduce the risk of progression to type 2 diabetes
“Sartans”--ARBs

• Angiotensin receptor blockers (bypass ACE) and work by blocking the angiotensin-2 receptors on tissues
• Who are they? The “Sartan Sisters”...
  • losartan—Cozaar
  • valsartan—Diovan
  • candesartan—Atacand
  • irbesartan—Avapro
  • telmisartan—Micardis
  • olmesartan—Benicar
  • eprosartan--Tevetan
A new class of drugs...

- Direct renin inhibitors (DRI)
- Aliskirin (Tekturna)
- Blocks the entire RAA system
“Olols, alols, ilols”—Beta blockers

- acebutolol (Sectral)
- atenolol (Tenormin)
- betaxolol (Kerlone)
- bisoprolol (Zebeta)
- carvedilol (Coreg) (non selective, alpha-1 blocker)*
- Esmolol (Brevibloc)
- labetalol (Trandate) (Normodyne)—safe during pregnancy
- metoprolol succinate* and tartrate (Toprol XL, Lopressor) {Betaloc}* (not tartrate for CHF)
- *EBM (evidence-based medicine) for heart failure to prevent remodeling of the heart
Beta-blockers, continued...

- nadolol (Corgard)
- nebivolol (Bystolic)
- oxprenolol (Trasicor, Slow-Trasicor)
- penbutolol (Levatol)
- pindolol {Visken}
- propranolol (Inderal)(1968)(nonselective)
- timolol (Blocadren)
SNS receptors and actions

• B1—found on heart muscle; epinephrine binds to B1 and increases heart rate and strength of contraction (chronotropic and inotropic)

• B2—skeletal muscle (tremor), bronchioles of the lungs (bronchodilation), large arteries of the legs (vasodilation), piloerection (hairs stand up on back of neck and arms)
Same slide as last—throw in beta and alpha blockers

• B1—found on heart muscle; epinephrine binds to B1 and increases heart rate and strength of contraction (chronotropic and inotropic)—CARDIOSELECTIVE BETA BLOCKERS

• B2—skeletal muscle (tremor), bronchioles of the lungs (bronchodilation), large arteries of the legs (vasodilation), piloerection (hairs stand up on back of neck and arms)—NONSELECTIVE BETA BLOCKERS
Why don’t we pick just any old beta blocker? Because the non-cardioselective beta blockers block both the B1 AND B2 receptors and can wreak havoc in certain patient populations

• B2 blockade can cause bronchoconstriction and exacerbate COPD & asthma as well as vasoconstrict the femoral artery {exacerbate [peripheral artery disease]}

  propranolol (Inderal), nadolol (Corgard), timolol (Blocadren), carvedilol (Coreg)
“Olols, alols, ilols”...

- Cardioselective? (B1 receptors)—if you block the B1 receptors on the heart, the heart rate and contractile state decrease – cardiac output falls, heart rate falls (10-15%), blood pressure falls, workload of the heart decreases—angina, SVT
  
  atenolol (Tenormin), metoprolol (Lopressor), betaxolol (Kerlone); bisoprolol (Zebeta), nebivolol (Bystolic)@ doses <10 mg

- *Beta Blockers are NO longer considered FIRST line therapy for essential hypertension (diuretics, ACE inhibitors**, ARBs, and CCBs are better choices)
Beta blockers...other properties

• Water-soluble? (low lipophilicity)
  atenolol (Tenormin), nadolol (Corgard), labetalol (Trandate), nebivolol (Bystolic)

• Lipid-soluble? (high lipophilicity--cross the blood brain barrier)—CNS side effects—anhedonia (the “Blahs”)—BUT...the lipid-soluble can also “calm down” the brain

• propranolol (Inderal), timolol (Blocadren), metoprolol (Lopressor, Toprol XL), pindolol

• All of the others are moderately lipophilic
Functions of beta-blockers

- Decrease palpitations during panic attacks
- Decrease essential tremors
- Decrease situational anxiety
- Decrease symptoms of PTSD Episodic dyscontrol syndrome
- Decrease HR in patients with Grave’s disease
- Decrease portal pressure in patients with cirrhosis and esophageal varices
- Decrease migraine headaches by 50% in 50% of the patients (mechanism unknown)
- Preoperatively in cardiac patients undergoing noncardiac surgery
3 Classes of Calcium Channel Blockers...

1) Verapamil (Isoptin SR, Verelan and Verelan PM, Calan and Calan SR, Apo-Verap, Novo-Veramil, Nu-Verap,)—block calcium channels primarily on the coronary vessels and the AV node—increasing blood flow to the heart and decreasing impulses through the AV node—used to decrease workload of heart and slow the heart rate; HTN, angina, atrial fib

2) Calcium channels in bowels (elderly)
2) Diltiazem—Cardizem, Dilacor XL—dilates calcium channels on the coronary (1/5 affinity for coronary channels) and peripheral vessel calcium channels;

Clinical uses—

- Atrial fibrillation, Hypertension, Angina, Vasospasm

Less constipation
3) “DIPINES”—Peripheral vessel calcium channel blockers

- Amlodipine (Norvasc)
- Felodipine (Plendil)**
- Nifedipine (Procardia XL, Adalat)
- Nicardipine (Cardene)
- Isradipine (Dynacirc)
- Nisoldipine (Sular)
- Clevidipine (Cleviprex) for IV use
- MOA: Block the peripheral vascular calcium channels
Clinical uses of the “dipines”...

- Hypertension
- Vasospasm—Prinzmetal’s angina, Raynaud’s phenomenon, cocaine-induced vasospasms
- FYI: Ureteral spasm in patients with small kidney stones (try slow release nifedipine 30 mg qd x 5-7 days)
- “male contraceptive”
The “Statin Sisters”...

Who are they?
• lovastatin (Mevacor)
• simvastatin (Zocor)*--no more than 40 mg/d due to increased risk of rhabdomyolysis
• atorvastatin (Lipitor)
• fluvastatin (Lescol)
• pravastatin (Pravachol)
• rosuvastatin (Crestor)
• pitavastatin (Livalo)
The “Statin Sisters”...what do they do?

- Inhibits the enzyme HMG-CoA reductase in the liver
- HMG-CoA reductase is responsible for the production of the bad guy—LDL-cholesterol; works primarily at night to produce LDL, so the “statins” work the best when taken before bedtime (exception to the rule--atorvastatin)
- LDL is the most atherogenic of the cholesterol bunch and puts fat right smack dab into all of the arterial walls; therefore, statins decrease LDL-cholesterol
- Statins **decrease** CAD, PVD, CVD risk and **increase** survival rates
- Begin with a dose that drops the LDL-C by 30-40%
The “Statin Sisters”

- Reduce total cholesterol levels
- Decrease plaque formation
- Stabilize plaques and prevent plaque rupture
- Shrink plaques in all arteries (prevent stroke)
- **Anti-inflammatory effects (other clinical uses?)**
The “afils”—1998 and the Pfizer Riser (Viagra)...Erectile dysfunction

- Prior to November 1998...
- What are the causes of ED?
  Athero, neuro, drugs, ↓testo, psychological (the stamp test)
- Sildenafil (Viagra)(Revatio for pulmonary arterial hypertension)
- Vardenafil (Levitra)
- Tadalafil (Cialis)(Adcirca for PAH)—the “weekend warrior”
- Boost nitric oxide—potent vasodilator
- Can use in patients with stable CHD
Can’t use with nitroglycerin…

• “When was your last dose of Viagra?
• Can’t use Viagra or Levitra within 24 hours of receiving NTG; Cialis within 36 hours
• Side effects
  Hypotension
  Headaches
  GERD
  Blue vision
  Priapism
• A surprise side effect of the “afils”…
Sexually transmitted diseases have increased by over 300% in the over 60 crowd since the release of Viagra...

- More sex
- No pregnancy worries
- Swingin’ singles
- Who cares what the neighbors think?
- Swimming pools and golf courses
- Can you have a heart attack during sex?
- Only if...
The “dronates” for osteoporosis

- The “dronates” for osteoporosis
- Alendronate [Fosavance] (Fosamax + D), clodronate [Ostac, Bonefos], Risendronate (Actonel), ibandronate (Boniva)
- Zoledronic acid [Aclasta] (Zometa) (Reclast) and pamidronate (Aredia) -- cancer
- Trigger apoptosis of osteoclasts
- Osteoblasts continue to build bone matrix but without remodeling
- Any downside?
- Fractures? Negligible risk
- Osteonecrosis of jaw? Risk is highest with IV zolendronic acid and pamidronate for cancer Rx
The “prazoles”—Proton Pump Inhibitors*

- Omeprazole (Prilosec) (first released as Losec in U.S.)
- Lansoprazole (Prevacid)
- Dexlansoprazole (Dexilant/Kapidex - old name)
- Rabeprazole (Aciphex)
- Pantoprazole (Protonix)
- Esomeprazole (Nexium) -- “the purple pill”
- *BIG Exception: Aripiprazole/Abilify—an new antipsychotic—a dopamine system stabilizer
The “prazoles”—Proton Pump Inhibitors

- MOA—Inhibition of the proton pump at the lumenal surface of the stomach...especially after a meal
The “prazoles”

• Work within 4-7 days to reduce all acid in the stomach; take 30’-60’ before the *first* meal of the day or before the dinner meal (especially if nocturnal GERD is a problem)
• Blocking acid production also decreases the release of intrinsic factor which is necessary for binding B12
• Do you need B12? **YES.**
• Do you need acid to digest food? **NO**
• Do you need acid to zap food-borne pathogens? **YES**
• Do you need acid to absorb calcium? **YES** (use calcium citrate for low acid conditions—elderly and PPI use)
• **NO** acid, no IRON
The antifungals--the “azoles”

- Miconazole (Monistat)
- Clotrimazole (Mycelex)
- Fluconazole (Diflucan)
- Itraconazole (Sporanox)
- Ketoconazole (Nizoral)
- Voriconazole (Vfend)
- Posaconazole (Noxafil)—newest of the bunch (HIV)
- DRUG INTERACTIONS
- “You have a yeast infection...”
The antiherpeticsthe “cy{i}clovirsk

- Acyclovir (Zovirax)
- Famciclovir (Famvir)
- Valacyclovir (Valtrex)
- Ganciclovir (Cytovene) – CMV retinitis in HIV patients; CMV pneumonitis in transplant patients
The antiherpetic--VZV

- Acyclovir (Zovirax)(4000/d)
- Famciclovir (Famvir)(750/d)
- Valacyclovir (Valtrex)(3000/d)
- Ganciclovir (CMV retinitis)

Tx must be started within 48-72 hours after the first signs of a rash appear.

- +Prednisone

- Zostavax for prevention
The antibiotics—the fluoroquinolones, the “floxacins”...

- Ciprofloxacin (Cipro)* (2) (↑ INR)
- Lomefloxacin (Maxaquin)(2)
- Norfloxacin (Noroxin)* (2)
- Ofloxacin (Floxin)(2)*
  *uncomplicated UTI if resistance to TMP/SMX is ≥20%
- Levofloxacin (Levaquin) (3)—too broad spectrum for UTI
- Gemifloxacin (Factive)(4)
- Moxifloxacin (Avelox)(4)—effective against TB
- WARNINGS: *C. difficile* after the quinolones...
- acute tendonitis in elderly and patients on corticosteroids
It’s a “MAB, MAB, MAB” (monoclonal antibodies) world

- Infliximab (Remicade)—targeted against TNF-α, the culprit in Crohn’s disease, RA, psoriasis; TB testing prior to use
- Adalimumab (Humira)—as above
- Trastuzumab (Herceptin)—HER2-neu+ Breast cancers; when given in early stages, prognosis improves significantly
- Cetuximab (Erbitux)—colon cancer (Martha Stewart)
- Bevacizumab (Avastin)—inhibits angiogenesis; used to inhibit tumor growth; used to decrease neovascular growth in the retina; glioblastoma
THANK YOU...and remember...

- “Never under any circumstances take a sleeping pill and a laxative on the same night.”
- Barb Bancroft, RN, MSN, PNP
- www.barbbancroft.com
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