Good Presentation Topics

- Herbal medicines, supplements, vitamins (section 10.11 is a good start)
- Pharmaceuticals in our drinking water
- Other drugs – legal or illegal

Drug History

- India, 4500 to 1600 BC, early reference to using plants as drugs
- China, 3000 BC, refers to using a plant that we now know has ephedrine
- 400 BC, Hippocrates (famous doctor) made tea with willow bark. This lowered fevers, helped with pain and inflammation. A derivative is still in use today. What is the wonder drug???

The Wonder Drug?

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frequency</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drowsiness</td>
<td>Rare</td>
<td>4</td>
</tr>
<tr>
<td>Rash, hives, itch</td>
<td>Rare</td>
<td>3</td>
</tr>
<tr>
<td>Diminished vision</td>
<td>Rare</td>
<td>3</td>
</tr>
<tr>
<td>Ringing in the ears</td>
<td>Common</td>
<td>5</td>
</tr>
<tr>
<td>Nausea, vomiting, abdominal pain</td>
<td>Common</td>
<td>2</td>
</tr>
<tr>
<td>Heartburn</td>
<td>Common</td>
<td>4</td>
</tr>
<tr>
<td>Black or bloody vomit</td>
<td>Rare</td>
<td>1</td>
</tr>
<tr>
<td>Blood in the urine</td>
<td>Rare</td>
<td>1</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Rare</td>
<td>3</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>Rare</td>
<td>3</td>
</tr>
</tbody>
</table>

*The severity scale ranges from 1, life-threatening, seek emergency treatment immediately to 5, continue the medication and tell the physician at the next visit.


The wonder drug

- **Salicylic acid** is the original drug extracted from willow bark. The problem is that is some individuals experience stomach irritation.
- The derivative is **Acetylsalicylic acid** or aspirin. It was synthesized by Felix Hoffman and patented by the Bayer Company in 1893.
- Aspirin did not receive FDA approval. Why?

There was no approval process at that time! If there had been, aspirin would most likely been approved for prescriptions only, not over the counter!
The “Wonder Drug”? “The presence and properties of functional groups are responsible for the action of all drugs.” Look at the next slide and identify aspirin’s functional groups.

Aspirin

Carbon line drawings

• Carbon is so important the study of it is called organic chemistry
• Organic chemists use line drawings to represent carbon and hydrogens in organic molecules
• 12 million of the 27 million known chemical compounds are organic

• How many bonds does each carbon atom have in hexane? 4
• So how many electrons are around each C atom in hexane? 8

Functional Groups

• How many bonds does each carbon atom have? 4
• How is a single bond represented? Double?
• How many electrons are in a single bond? Double? 2, 4
• So how many electrons are around each C atom? 8

Here is another organic molecule. What generalizations can you make about the number of bonds around carbon? About the number of electrons around carbon?

Yes, carbon always has 4 bonds and 8 electrons around it. Carbon follows the OCTET RULE. Note: 4 bonds can mean 4 single bonds, 2 single + one double bond, 1 single + 1 triple bond, or 2 double bonds. Draw a carbon atom with all these options.
Draw this structure with the carbon and hydrogen atoms
How many bonds and electrons are around each C?

Draw this structure with the carbon and hydrogen atoms
How many bonds and electrons are around each C?

Draw this structure with the carbon and hydrogen atoms
How many bonds and electrons are around each C?

The Body's Chemical Communication
- Electrical pulses that travel along nerves triggers movement, breathing, heartbeats, and reflexes.
- But most messages in the body are chemical.
- Endocrine glands produce hormones. Hormones are the body’s chemical messengers.
  - Thyroxine regulates metabolism
  - Insulin regulates glucose use for energy
  - Adrenaline (epinephrine) regulates “fight or flight”

How Aspirin Works
Hormones regulate by altering cell metabolism. These body processes are regulated by hormones:
- Body Metabolism
- Growth
- Puberty
- Tissue Function
- Body Temperature
- Attitude (mood)

How Aspirin Works
- Aspirin and other anti-inflammatory drugs (NSAIDs) block the action of other molecules
- Aspirin blocks cyclooxygenase (COX)
- COX produces prostaglandins from arachidonic acid
- Prostaglandins cause fever, pain and swelling
Comparisons

- Acetaminophen (Tylenol) reduces fever, but does not stop inflammation.
- Ibuprofen (Advil and Motrin) is a better pain reliever and fever reducer than aspirin. Its anti-inflammatory action is 5 to 50 times that of aspirin.
- However aspirin is the only one that inhibits blood clotting. Which is why low doses are sometime prescribed to prevent heart attacks and strokes. But aspirin should not be given to those with ulcers or undergoing surgery.

Penicillin

- Molds used for treating infections for 2500 years.
- In 1928 Sir Alexander Fleming accidentally saw that in a petri dish of bacteria, the area contaminated by the mold Penicillium was free of bacteria. He correctly concluded that this mold inhibits bacterial growth.

- Mold spore from the next lab drifted in and contaminated Fleming’s dish. Fleming was on vacation and noticed this dish among dirty glassware! It was his experience that helped him recognize the importance.
- The development of other antibiotics followed similar experiments.
- Today we have extreme overuse however. We now have resistant bacteria.
- What can we do about overuse? What do you think about antibacterial soap?

The Ideal Drug

1. **Efficacy**: The ability to produce some desirable effect

2. **Specificity**: Should bind to its target receptor, but not other receptors or biomolecules. This can lead to the toxic effects of drugs
Let's look at some common drugs

- Steroids
- Statins: Lovastatin, Lipitor, Zocor, etc.
- Opiates: Morphine, Demerol, Vicodin, Percoset, Codeine, Darvocet
- Pseudoephedrine
- Anti-depressants
- Meth

### Steroids

- All have 4 ring backbone
- Many uses: birth control, abortion, body building, fighting asthma, allergies, rashes, inflammation
- Some steroids you may recognize: cholesterol, cortisone, corticosterone, prednisone, estradiol, testosterone
- Anyone know what these do???
  - Look at the pictures next – slight differences in functional groups greatly change the steroid

- Estradiol - predominant sex hormone present in females; present in males at lower levels, produced in the ovaries and testes, the main estrogen, promote female characteristics, regulate menstrual cycle
- Testosterone – hormone secreted in testes / ovaries, main sex hormone in males, regulates male characteristics (hair, Adam’s apple), anabolic steroid = builds up bone and muscle mass, men have about 8-10 times as much as females

### Statins

- Used to lower cholesterol by inhibiting the enzyme HMG-CoA reductase, which controls the speed of producing cholesterol in the liver.
- Lovastatin – first one developed. Occurs naturally in oyster mushrooms. Pictures above.
- Mevastatin – next one. Occurs in red yeast rice.
- Lipitor - Sales top $10 billion a year.
- Other meds – Zocor, Crestor, Pravachol, Vytorin
- May help with Alzheimer’s, prostate cancer, hypertension, preventing heart attack and stroke, dementia, colon cancer
Opiates

- Natural and semi-synthetic derivatives from opium which is from poppy plants
- Natural: morphine, codeine (milder).
- Semi-synthetic: heroin, oxycodone (Purdue’s OxyContin, & Percocet which is just oxycodone + acetaminophen), hydrocodone (Vicodin = hydrocodone + acetaminophen)
- Fully Synthetic: Demerol, methadone, tramadol
- They are used as analgesics (painkillers), cough suppressants, to stop diarrhea, and to stop anxiety
- The World Health Organization says opiates are essential in the treatment of severe pain. However, only six countries use 77% of them. Poor countries are severely lacking.

Opiates

- Work directly on the central nervous system, relieves pain by binding to the opioid receptors which blocks the transmission of pain in the spinal cord, creates higher levels of dopamine (feels good) tolerance can develop
- Adverse reactions: vomiting, drowsiness, dry mouth, constipation,
- Extremely unpleasant withdrawal symptoms: confusion, sweating, depression, pain, vomiting, nausea
- Often treat withdrawal with clonidine and antidepressants

Morphine

- for severe pain, very addictive
- Oxycodone – for moderate pain, often combined with NSAIDs, “hillbilly heroin” or “oxy”
- Hydrocodone – intermediate pain reliever and strong cough suppressant, possible addiction
- Methadone – treats chronic pain and used to get people off heroin and morphine, “junkie juice”
- Codeine – treats mild to moderate pain, cough, diarrhea, often with NSAIDS like Tylenol-3, not abused near as much as other opiates
- Heroin – made from morphine, 90% comes from Afghanistan, very addictive especially psychologically, aka diamorphine which can be prescribed in the UK, Netherlands, Germany, Switzerland
- Tramadol – treats moderate pain and restless leg syndrome, atypical of opiates, has SSRI and SNRI qualities, withdrawal is longer than most, lower risk of addiction

Morphine

- Decongestant
- Was over the counter, now behind the counter because it is a precursor of methamphetamine
- Replaced by phenylephrine in over the counter meds
- In the amphetamine class of drugs – can be a stimulant. Reportedly abused by truck drivers
- Can be extracted from ephedra plant species
- Adverse effects: dizzy, nervous, anxiety, sleeplessness, can trigger a manic episode in bipolar patients
- Banned in Olympic sports
Anti-depressants
• All inhibit the reuptake of neurotransmitters
• SSRI – selective serotonin reuptake inhibitors (Zoloft, Prozac, Paxil)
• SNRI – selective serotonin norepinephrine reuptake inhibitors (Effexor)
• NDRI – norepinephrine dopamine reuptake inhibitor (Wellbutrin)
• SSRI used for treatment against social anxiety, panic disorders, OCD, depression, posttraumatic stress, premature ejaculation
• NRI and DRI used for stimulation, energy, focus, alertness, desire, decrease appetite, used to treat ADHD, narcolepsy, fatigue, obesity

Meth
• Methamphetamine – increases alertness, self-image, energy, sexual pleasure
• Highly abused, increases levels of dopamine, serotonin, and norepinephrine
• FDA approved in the US to treat morbid obesity as Dexoyx currently
• Was approved to treat narcolepsy, depression, and hay fever but not anymore
• Made from ephedrine
• Used widely in WWII by German soldiers, suspected that Hitler used it until he died in 1945
• Illegal use really picked up in the 1960’s and is still increasing
• Part of the Patriot Act involves how much pseudoephedrine and ephedrine one can buy legally in a given time period

Green Chemistry
• All chemical manufacturing is trying to go green = less waste, less side-products
• Current way to make ibupfen is green. Previous method required 6 steps, used lots of solvent, generated lots of waste. Now made in 3 steps with hardly any solvent or waste. All starting material recovered. BHC company awarded the 1997 Presidential Green Chemistry award.
• Codexis, winner of the 1996 award, created a way to make Lipitor with increased yield, less by-products, less waste and less solvent which increases worker safety.

Drug Development
(Testing and Approval)

Animal Testing
• Controversial topic these days – lots of legislation over the world lately
• LD50 – lethal dose 50 – the dose size that will kill 50% of animals
• Vioxx example – Merck made about 1 billion dollars a year but in 2000 was seen to increase chance of heart attack, withdrawn in 2004, thousands of law suits followed. Scientists would like to prevent drug failures like this despite the animal testing.
• In 2009 EU banned many animal tests and will use biochips instead like Datachip and Metachip
• Frontier medicine – A new biochip holds hundreds of tiny white dots loaded with human cell cultures and enzymes. Scientists hope the chips can do away with the need to use animals to test new blockbuster drugs or wrinkle creams.
**Dangers of Prescription Drugs**

4. **Billie Holiday** (44) – Billie was a famous female jazz singer. She was originally named Eleanor Fagan. This singer used hard drugs (primarily heroin) and was involved in unhealthy relationships where abuse took place. Eventually she developed heart disease and liver complications. She died at the age of 44 from cirrhosis of the liver, a problem which arose from long-term drug and alcohol abuse.

5. **River Phoenix** (23) – This actor was the oldest of five children, one of whom is actor Joaquin Phoenix. He acted in films such as *Stand By Me*, *Little Nikita*, *The Thing Called Love*, and *Running on Empty*. Throughout his life he was a proud supporter of animal rights and refused to use animal products in the films he acted in. Phoenix died as a result of speedballs (a combination of cocaine and heroin) outside of the night club The Viper Room. He was 23 years old.

6. **Anna Nicole Smith** (39) – Smith was an actress and model. In fact, she was named Playmate of the Year in 1993. She was married three times during her lifetime, the most famous of which was to J. Howard Marshall. This oil executive was a billionaire and 63 years older than Smith. Anna Nicole Smith died at the age of 39 from accidental overdose of chloral hydrate and other prescription drugs.

**Dangers of Prescription Drugs**

7. **Jim Morrison** (27) – He is most famous for being a singer, but he also wrote a number of poems, directed films, and wrote his own songs. Morrison was a lead singer for the famous band, The Doors. Throughout his life, the singer struggled with both drug and alcohol abuse. He died at the age of 27. Although several stories have circulated regarding his death, the general consensus is that he died of a heart attack triggered by accidental heroin overdose.

8. **Chris Farley** (33) – comedian, cocaine and heroin overdose (speedball).

9. **Sigmund Freud** (83) – neurologist, long-term cocaine use, physician assisted morphine overdose (euthanasia).

10. **Judy Garland** (47) – singer and actress, barbiturate (secobarbital) overdose. Her death certificate states the overdose was "accidental" however there is speculation it was intentional.

11. **Jimi Hendrix** (27) – rock and roll musician, respiratory arrest caused by alcohol and barbiturate overdose and vomit inhalation.

**Dangers of Prescription Drugs**

12. **Howard Hughes** (70) – aviator, engineer, industrialist, movie producer, liver failure - physician administered overdose of codeine at "the highest clinical level ever recorded".

13. **Michael Jackson** (50) – musician, died June 25, 2009, lethal dose of propofol along with two sedatives.


15. **Heath Ledger** (28) – actor, accidental death Combined Drug Intoxication of various prescription drugs, including oxycodone, hydrocodone, temazepam, and others.

16. **Bruce Lee** (32) – actor, martial artist, died of acute cerebral edema due to a reaction to compounds present in the prescription pain killing drug Equagesic.

17. **Sid Vicious** (21) – musician, the Sex Pistols, heroin overdose.