Worksheet #1 Bimm 118
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The following is intended to give you some practice answering pharmacology questions. It is not intended to be used solely as a study guide. Remember that questions on the exam come from the notes from class, so be sure to know all material covered in class!

1. What is the difference between pharmacokinetics and pharmacodynamics? Also, give one example of a condition associated with pharmacogenetics. What causes this condition?

   See Notes!

2. Pain killers belong to what type of drug?

   a. Therapeutic
   b. Prophylactic
   c. Palliative

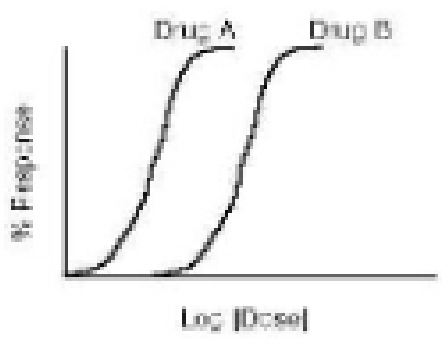
3. A competitive antagonist
   a) binds to the same site on the receptor as the natural ligand
   b) binds the receptor irreversibly
   c) elicits a response from the receptor
   d) shifts the dose-response curve to the right
   e) shifts the dose-response curve to the right AND down

4. What is the ED50?
   The dose that elicits a predefined response in 50% of the test subjects

5. What is the difference between the efficacy and potency of a drug?

   Efficacy refers to the capability of a drug, whereas potency compares the relative effectiveness of two or more drugs. Efficacy has nothing to do with how much you take. Two drugs can have similar efficacy, but different potency.

6. According to the diagram
   a) both drugs have the same efficacy
   b) Drug B has higher efficacy
   c) have different potency
   d) Drug B has the lower potency
   e) Drug A is a partial agonist



7. Describe the process involved in patenting a drug (be descriptive!)

   Phase I, Phase II, Phase III (see notes)

8. What are orphan drugs? What incentive was provided in the 1980's to encourage their development?

Drugs that affect less than 200,000 individuals in the US. Orphan Drug Act of 1983.

9. What is one concern with taking dietary supplements (concerning their development process)? Give one example of a dietary supplement discussed in class and what it has been proposed to be useful for.

No FDA approval process, no regulation. Ex: Leptoprin (weight loss)

10. What is involved in the preclinical trials portion of developing a drug? What is often a serious limitation here?

Study effects in-vitro (cells/organs). Study receptor-binding characteristics. Move into in-vivo animal model and then predict the potential therapeutic uses. Animal models are often limitations!

11. Define and describe three different types of toxicity testing that must be considered when developing a drug.

Mutagenicity, Carcinogenicity, Reproductive toxicity, acute toxicity, subacute toxicity, chronic toxicity. See notes for descriptions—be able to define these!

12. Give three routes of drug administration, describe an example of each.

Oral (pills, tablets, coated tablets, capsules…)
Topical/percutaneous (creams, lotions, eye drops, etc)
Rectal or Vaginal (birth control)
Pulmonal (inhalers)
Parenteral (needles, IVs)

13. Describe the difference between external and internal drug distribution barriers.

External: Skin (epithelium), creates tight junctions to create an unbroken phospholipids bilayer. Drugs must cross the lipophilic membrane to enter the body

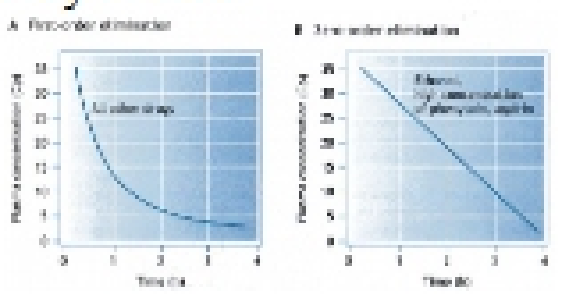
Internal (Blood-tissue): permeation occurring mostly in the capillary bed, developed differentially in various capillary beds (muscle, glands, gut, liver, CNS, placenta)

14. Rank in order of bioavailability (highest to lowest):

i. Oral
ii. Transdermal — Intraveneous>Transdermal>Rectal>Oral
iii. Rectal
iv. Intraveneous

15. Describe the difference between drug elimination through the kidney versus the liver. What is meant by first-order kinetics when describing drug elimination? Draw a graph that has both first-order kinetics as well as linear, zero-order elimination. Label all axes and lines that you draw!

Kidney=Filtration elimination, Liver=metabolism
First-order kinetics refer to the fact that the rate of elimination is proportional to drug concentration.



16. Make sure you can understand how to derive the clearance of a drug. What is the equation?

Clearance (CL) [ml/min]:
= Rate of Elimination [mg/min] / Drug concentration plasma (CP) [mg/ml]
where Rate of Elimination [mg/min] = k [1/min] x CP [mg/ml] x Vd [ml] and
Elimination rate constant (k) [1/min] = ln 2 / t1/2 (=half-life) (ln 2 = 0.693)
=> CL [ml/min] = Elimination rate constant (k) [1/min] x Vd [ml] = ln 2 x Vd / t1/2

- It is the sum of all separate organ clearances:
CL = CLrenal + CLliver + CLother

- Clearance is the volume of plasma cleared of all drug per unit of time (a constant for any given drug [ml/min])

- The actual quantity of drug [mg] removed per time unit [min] depends on both the clearance [ml/min] and the concentration [mg/ml].

17. Drug X is given as a rapid, single i.v. infusion to a 50 kg individual. The volume of distribution (Vd) for drug X is 2 L/kg. What is the predicted initial plasma concentration if a 500 mg dose is administered?

C=Dose/Vd. Therefore C=500mg/(50kg x 2L/kg)=> 500 mg/100 L or 5 mg/L.

18. Describe the difference between and maintenance dose. When is it most appropriate to use the loading dose as an estimate of how much drug to give a patient?

Loading dose is used for drugs with a long half-life. Loading dose must fill the Vd to achieve the target Cp. The maintenance dose refers to the the amoune that must replace the drug that is being eliminated over time.

19. Describe what is meant by the therapeutic index. What two very important factors go into this calculation? What are two problems with this measurement of the therapeutic range.

=Maximum non-toxic dose/Minimum effective dose. Does not take into account the variability between indivs. LD50 reflects only deaths, not other toxicities. ED50 depends on condition being treated and LD50 depends on the patients' overall condition.

20. Describe the steps involved in Phase I and Phase II Reactions during drug metabolism.

Phase I=Convert parent group into more polar metabolite. Often adds functional group to drug. Phase II=Conjugation with endogenous substrates to increase solubility in the body. Following these reactions, the body can better metabolize the drug.

21. Describe 3 examples of enzymes that are P450 enzymes. Give one example of a polymorphism that exists in the population that disrupts this interaction. How does the mutation affect this process?

PPAR ligands, CYP1, CYP2E, CYP2B
CYP2C19: Polymorphism that changes the ability of the enzyme to metabolize mephenytoin. Most prominent in Asian population.
CYP2D6: Defect in demethylation of codein (6-10% of Caucasians)

22. Give 2 examples of reactions that would represent oxidation of a drug. (On a test, understand what happens to the functional groups represented in the drug).