

FALL SEMESTER STUDY GUIDE (from 2003)

Drug Disposition/Pharmacokinetics

1. Name two routes of administration that may demonstrate a prominent first pass effect.
2. Which route of administration permits most careful control of the patients response?
3. Which route of administration is most suitable for irritating substances?
4. Which route of administration is most convenient and economical?
5. Which route of administration is associated with the greatest risk of anaphylactic reaction?
6. Drugs can cross membranes by which four mechanisms? What are the characteristics of each of these transport mechanisms?
7. Which mechanism of transport occurs most commonly for most drugs? Which chemical properties of a drug influence the extent and the rate of absorption?
8. A strong acid has a high pK_a . (T/F)
9. A strong base has a high pK_a . (T/F)
10. In general, which will be absorbed more completely at the gastric mucosa, a weak acid or a weak base?
11. Which would be absorbed more completely by the gastric mucosa: a weak acid with a high pK_a or with a low pK_a ?
12. If a weak base is administered intravenously it is possible to eventually find a higher concentration in the gastric juice than in the blood (T/F).
13. If a drug is mostly absorbed in the intestine, will its onset of action be fastest on a full stomach or an empty stomach? If a drug is mostly absorbed in the intestine, and it is coadministered with a second drug which slows gastric emptying, the second drug will (decrease or increase) the rate of absorption of the first drug.
14. If you wish to enhance the renal elimination of a weak base, you would (acidify or alkalinize) the urine with (bicarbonate or ammonium chloride).
15. If you wish to enhance the renal elimination of a weak acid, you would (acidify or alkalinize) the urine with (bicarbonate or ammonium chloride).
16. The bioavailabilities of two preparations of the same drug are the same only when the two

preparations achieve comparable plasma levels (T/F).

17. In a 70 Kg man what is the approximate volume of the total body water compartment? the extracellular fluid compartment? the intravascular fluid compartment?

18. What chemical and physiological factors affect the rate of drug distribution? What factors affect the extent of drug distribution?

19. Drugs can gain access to the interstitial fluid through the capillaries by passing through small pores in capillaries (T/F). By passive diffusion through the membranes (T/F). By pinocytosis (T/F). By active transport across the membranes (T/F). By facilitated diffusion (T/F).

20. Drug bound to plasma proteins is pharmacologically inert (T/F).

21. Extensive binding of drugs to plasma proteins retards the renal filtration of the drug (T/F). Retards the metabolism of the drug (T/F). Retards the renal secretion of drugs (T/F).

22. Which plasma protein is most important for drug binding, because it is quantitatively the most abundant plasma protein?

23. Plasma proteins have a limited number of binding sites for drugs (T/F). These binding sites are saturable (T/F). Different drugs usually compete for different sites and only rarely displace each other from plasma proteins (T/F).

24. "Phase I" drug metabolism reactions are also known as _____ reactions.
"Phase II" reactions are also known as _____ reactions.

25. What properties of the cytochrome P-450 family make it such a versatile drug metabolizing system?

26. Cytochrome P450 is most concentrated in which cell organelle? In which cell types? When liver is homogenized and subjected to differential centrifugation, the cytochrome P450 is associated with the (nuclear fraction/mitochondrial fraction/microsomal fraction/cytosolic fraction). [choose one]

27. When 2 drugs that compete for the same form of CYP, and inhibit each other's metabolism, are co-administered, what effects on the activities of each drug are often seen?

28. What is the effect of co-administration of two drugs, one of which induces a CYP form that metabolizes the other?

29. Name several Phase I reactions that are mediated by cytochrome P450.

30. Name several Phase I reactions that are not mediated by cytochrome P450.

31. Which conjugation reaction requires microsomes?

32. A hydroxyl group can be conjugated with _____ or _____.
33. A carboxylic acid can be conjugated with _____ or _____.
34. An amine can be conjugated with _____.
35. If a drug is eliminated by first order kinetics (a constant fraction or a constant amount) of drug is eliminated by the body per unit time.
32. If a drug is eliminated by zero order kinetics (a constant fraction or a constant amount) of drug is eliminated by the body per unit time.
33. If a drug is eliminated from the body at a rate of 10% per day, what is this drug's half-life?
34. If a drug is administered repeatedly, how many half-lives will it take to approach almost 95% of the steady-state concentration?
35. (T/F) Clearance is the amount of drug eliminated from a given volume of plasma per unit time.
36. How is clearance of a drug related to its half-life?

CHEMOTHERAPY

Antimicrobial Chemotherapy

1. What are four general mechanisms which commonly account for drug resistance?
2. What are four general mechanisms by which microbes acquire or inherit new traits? Which is the single-most important mechanism for acquiring resistance to antimicrobial drugs, especially, resistance to multiple drugs?
3. What is the mechanism of action of each of the following drugs, which interfere with cell wall synthesis
 - cycloserine
 - bacitracin
 - vancomycin
 - penicillins/cephalosporins
4. Name two "Natural penicillins". Which one is more resistant to gastric acids and may be taken orally? What is their characteristic spectrum of action? What is the unit of measurement of these drugs?
5. What is the single-most important mechanism that imparts penicillin resistance to some organisms? Draw a simplified cartoon of the penicillin molecule (just the rings) including the amide bond. Indicate which bond is hydrolyzed by bacterial enzymes and

- name the enzyme. Name a compound which is a "suicide inhibitor" of this enzyme.
6. Name the **six** penicillins which are resistant to hydrolysis by this enzyme. What is their **only** indication? If a bacterium is resistant to one, is it resistant to all? What is the treatment of choice for methicillin-resistant staphylococcus? Name one other drug which although not first choice, may also be effective.
 7. Name three important gram negative organisms which are covered by amoxicillin and ampicillin **but not** the natural penicillins. Are both of these drugs are effective orally?
 8. The carboxypenicillins and the uriedopenicillins have extended spectrums which include *P* _____ and *E* _____. However the carboxypenicillins are also effective against indole positive *P* _____; whereas the uriedopenicillins have activity against *K* _____. Which is the only drug in these two groups which may be administered orally?
 9. How are penicillins excreted? Which drug will significantly prolong the duration of action and what is the mechanism of action of this drug?
 10. What are the two repository forms of penicillin G. If equal units of each form are given to two different patients, which form will provide the longest duration of action? Which form will provide the shortest duration of action? Which form will produce the lowest peak plasma levels of penicillin? Which will produce the highest peak plasma concentration of penicillin? What is the basis for the different durations of action?
 12. What is the most common adverse effect of penicillins? Of the four types of this reaction, which is the rarest but most frequently fatal? Which drug should be used to treat this life-threatening reaction?
 13. Name three 1st generation cephalosporins; three 2nd generation cephalosporins; and three 3rd generation cephalosporins. What are the major difference that distinguish the first from the third?
 14. What is the chance of a cross-reaction to a cephalosporin in a patient that is sensitive to penicillin?
 15. What is the primary mechanism of action of each of the following drugs which inhibit protein synthesis? Indicate whether it binds to the 30s or the 50s ribosomal subunit. Indicate whether it is bacteriostatic or bactericidal.
 - aminoglycosides
 - tetracyclines
 - chloramphenicol
 - erythromycin
 - clindamycin
 16. Describe how aminoglycosides get inside bacteria. How does this affect their spectrum of activity? Which nosocomial infection are they used to treat? What are common two mechanisms of resistance.
 17. What are the three major side effects of aminoglycosides?
 18. List three major therapeutic indications for tetracyclines.
 19. What are the side effects of tetracycline on each of the following systems?
 - GI
 - bones and teeth
 - kidney
 - skin
 20. Why are tetracyclines contraindicated during pregnancy and in prepubescent children?

21. How are most tetracyclines eliminated? Which tetracycline is predominantly metabolized, and can be given without a dosage change in renal failure?
22. Chloramphenicol is usually bacteriostatic; however it is _____ against *H* _____. Why is chloramphenicol useful in the treatment of meningitis? Name one other **primary** indication for the use of chloramphenicol. What is the primary mechanism of resistance?
23. What is the most important side effect of chloramphenicol which limits its use because the effect is frequently fatal?
24. In neonates, it may cause grey baby syndrome. Describe the major clinical features. Why are neonates particularly vulnerable to grey baby syndrome?
25. The spectrum of activity of erythromycin most closely resemble that of _____. Though not a first line drug it is effective against both β -lactamase staphylococcus and _____-resistant staphylococcus. The estolate preparation (erythromycin estolate) is more resistant to stomach acid, but may cause _____.
26. The use of clindamycin is restricted because clindamycin the drug which **most frequently causes** _____ colitis. This colitis is caused by overgrowth of _____. It is **best** treated with _____.
27. What is the enzyme which is inhibited by sulfonamides? What is the substrate do sulfonamides **compete**. What local anesthetic is hydrolyzed to this substrate and may antagonize the antimicrobial effect of sulfonamides?
28. What enzyme is inhibited by trimethoprim? What is the name of the combined preparation of trimethoprim and sulfamethoxazole? What is the name of the combined preparations of trimethoprim and sulfadiazine? Are organism which are resistant to sulfonamides susceptible to these combination preparations? What is another rationale for combining these two types of drugs?
29. Sulfonamides may precipitate in _____ urine. This can be avoided by using triple sulfonamide treatment or by _____ing the urine.
30. What are the approximate half-lives of sulfadiazine and sulfamethoxazole? What is the approximate half-life of sulfadoxine. Explain the benefit of sulfasalazine in the treatment of inflammatory bowel disease.
31. Sulfonamides may cause hemolytic anemia in patients with a deficiency _____. What is the most serious manifestation of a hypersensitivity reaction to sulfamethoxazole or cotrimoxazole?
32. _____ are chemically distinct from sulfonamides, but have a similar mechanism of action. They are used to treat leprosy because they are effective against _____. The prototypical drug is called _____.
33. Name two fluoroquinolones. What is their mechanism of action? They are similar in their action to _____; however they are more potent.
34. What is the mainstay therapy for tuberculosis? What is another name for this drug? This drug competes in a variety of metabolic reactions with which co-factor? What are two primary side-effects caused by this competition? Both are prevented or reversed by co-

- administration of _____.
35. What is the primary route of metabolism of INH? Slow acetylators are more prone to develop _____. The elderly are more prone to develop _____. Patients with a deficiency of _____ may develop _____.
 36. What is the mechanism of action of rifampin? An ex-heroin addict is being treated with rifampin in conjunction with INH for tuberculosis. What effect will rifampin have on his plasma levels of methadone?
 37. What color is the urine and other secretions of a patient taking rifampin?
 38. What is the principal visual disturbance caused by ethambutol and how does this usually present in a patient? Does it progress to blindness?

Antifungal Agents, Antiprotozoal Agents, and Anthelmintic Agents

1. What is the mechanism of action of each of the following anti-fungal agents?
 - Griseofulvin
 - Amphotericin B
 - Ketoconazole
 - 5-Fluorouracil
 - Nystatin
2. What are the primary adverse effects of amphotericin B?
3. What drug-drug interaction occurs between ketoconazole and cimetidine?
4. Which antimalarial drug is most effective against the exoerythrocytic forms of *P. vivax* and *P. ovale*?
5. What is the mechanism of action of each of the following anti-protozoal drugs?
 - Primaquine
 - Chloroquine
 - Pyrimethamine
 - Quinine
 - Metronidazole
6. What is the mechanism of action of each of the following anti-helminthic drugs?
 - Mebendazole
 - Thiabendazole
 - Pyrantel pamoate
 - Piperazine
 - Praziquantel
 - Niclosamide
7. Which four drugs are used primarily to treat nematode infections? Which drug is used primarily to treat most trematode infections? Which drug is used primarily to treat cestode infections?

Anti-cancer chemotherapy

1. Make a diagram illustrating the stages of the cell cycle.
2. Briefly describe the rationale for using combination chemotherapy.
3. What are the **four** actions of alkylating agents on nucleic acids? Which of the four is **MOST** important for the cytotoxicity of alkylating agents? How does this last action

- affect DNA replication and transcription?
4. Name three prototypes for the nitrogen mustards. Which are effective when given orally? Which drug **must** be metabolized by cytochrome P450 to an active alkylating agent?
 5. Name the the prototype for the alkyl sulfonates. What is the only significant side-effect of this agent?
 6. Name two prototypes for the nitrosoureas. What are the abbreviations of their chemical names?
 7. Provide a concise, detailed explanation of the mechanism of action of each of the following drugs:
 - vinca alkaloids
 - etoposide
 - dactinomycin
 - doxorubicin
 - bleomycin
 - L-asparaginase
 - cisplatin
 8. What is the mechanism of action of methotrexate? What drug can be given immediately after methotrexate in order to reduce the toxicity of methotrexate?
 9. Name two pyrimidine analogs. Name two purine analogs.
 10. Briefly define "lethal synthesis".
 11. What drug-drug interaction occurs between allopurinol and 6-mercaptopurine? What enzyme is inhibited by allopurinol?
 12. What is the mechanism of action of each of the following as chemotherapeutic agents? Provide at least one primary indication for each drug:
 - prednisone
 - progesterone
 - estrogen
 - tamoxifen
 - aminoglutethimide
 13. Briefly define what is meant by the terms cell-cycle specific (CCS) and cell-cycle nonspecific (CCNS).
 14. For each chemotherapeutic agent, indicate whether the drug is CCS or CCNS. If the drug is CCS, then indicate which step of the cycle it is most active.
 - mechlorethamine
 - cyclophosphamide
 - carmustine
 - cisplatin
 - doxorubicin
 - mitomycin
 - dactinomycin
 - methotrexate
 - vinblastine
 - bleomycin
 - 5-fluorouracil
 - 6-mercaptopurine

15. Nearly all cancer chemotherapeutic agents (increase/decrease) the susceptibility of the patient to infection. Also they predominantly effect (rapidly/slowly) proliferating tissue such as _____, _____, and _____. Hence they almost all cause _____ and _____.
16. The following drugs produce toxicities for specific organs. Identify the organ specific toxicity associated with each drug.
- doxorubicin
 - bleomycin
 - cyclophosphamide
 - L-asparaginase
 - vincristine
 - cisplatin
 - vinblastine
17. What is the major difference in the toxicities of vincristine and vinblastine?

Immunosuppressants and Antiviral drugs

1. What is the mechanism(s) of action for the immunosuppressive action of corticosteroids?
2. What single drug has decreased the incidence of tissue rejection the most in transplantation surgery? What is the mechanism of action of this drug and what population of lymphocytes does it mostly affect?
3. What is the primary mechanism of action of each of the following antiviral drugs and which viral syndromes is each drug used to treat.
 - Amantadine
 - Acyclovir
 - Ganciclovir
 - Vidarabine
 - Retrovir