1. List the aminoglycoside antibiotics available in the US. Know which ones are obtained from *Streptomyces* ("mycins" and "kacins") and which from *Micromonospora* (micins”) and which are semi-synthetic.

2. What are the major common structural features for all AGs? What is the difference between a streptamine and deoxystreptamine ring and which AGs have which?

3. How are the aminosugars and aminocyclitol moieties linked? Which AGs are composed of three rings? Of four rings?

4. The biosynthetic schemes for streptomycin and gentamicin are included for your information and you will not be required to reproduce these.

5. Structural comparisons: How are neomycin and paromomycin related structurally? How does the structure of tobramycin differ from the kanamycins? How does amikacin differ from kanamycin A? How does the structure of Netilmicin differ from the gentamicins? How does spectinomycin differ from other aminoglycosides in structure?

6. What physicochemical properties are common to all of the AGs? How does this influence the products available (salt forms) and the form at physiological pH? How does this property contribute to antibacterial activity and resistance?

7. Are the aminoglycosides chemically stable in aqueous acid and base? If not, what decomposition products form?

8. What barriers must the AGs traverse to be effective against gram negative bacteria? By what mechanisms do the AGs get across these barriers (OM and IM)? What is “adaptive resistance”?

9. Why are the AGs ineffective against many anaerobes? Why are they not effective in bacterial infections that result in local acidosis?

10. What is the mechanism by which the AGs kill bacteria and what is the role of structure? Why are they cidal in action? Why are the AGs selectively toxic? Why do the AGs exert a “post-antibiotic effect”?

11. What are the four most important mechanisms of resistance to the AGs? Identify each as innate, plasmid-mediated or chromosomal. Which is most important for anaerobic bacteria? Which is most important for gram negative bacteria? Which mechanisms is commonly observed for streptomycin?
12. List the three enzymes of AG inactivation produced by many resistant microbes. How are the enzymes of resistance classified and sub-classified?

13. Know which reaction each enzyme class catalyzes and which AG functional group is modified? Be able to draw the products. By what mechanisms do the reactions of resistance eliminate AG activity?

14. Know which AG functional groups are attacked by specific enzyme sub-types, and be able to draw the products. Table 3 and Figure 10 will allow you to determine possible products.

15. List the factors that determine the efficacy of the AG inactivating process by bacteria that elaborate these enzymes.

16. How does the L-AHBA group of amikacin extend the spectrum of activity? Which functional groups are protected? How does the N-ethyl group of Netilmicin extend the spectrum of activity and which functional groups are protected? How is ring I of gentamicin C2 protected from enzymatic inactivation?

17. What other approach is used to modify AGs and make them resistant to enzymatic inactivation. What are examples of this?

18. What is “HLR”, why is it important for AG drug selection?

19. Characterize the antimicrobial spectrum for paromomycin, spectinomycin and streptomycin. When is kanamycin used?

20. Characterize the antimicrobial spectrum for gentamicin, tobramycin, netilmicin and amikacin including gram positive organisms, gram negative cocci and bacilli. What are the primary therapeutic uses of these AG products and combinations?

21. Describe and understand the advantages and disadvantages of AG which should be weighed when using these agents.

22. Why is the oral bioavailability of the AGs very low? Are they ever used orally? Which products are used orally, when and why?

23. How are the AGs administered for the treatment of systemic infections?

24. What is the extent of plasma protein binding for the AGs? Do they achieve adequate CSF levels when administered IM or SC? Which tissue(s) accumulate the AGs?

25. Describe the three phases of AG distribution and elimination. How are the AGs cleared? Is metabolism important? What is the mechanism of elimination? How does renal impairment impact on AG therapy? Why is this important?
26. What is conventional AG dosing and what are the therapeutic goals?

27. Define "loading" and "maintenance" doses. What pharmacokinetic factors determine loading doses? Which patients may require larger loading doses and why?

28. What pharmacokinetic factor determines maintenance doses and which parameter is used to modify maintenance doses?

29. What case-specific factors determine the target AG serum levels in multiple daily dosage regimens? Describe the procedures used to monitor AG therapy.

30. What is the rationale for "once daily" AG dosing? Which patient-specific factors are used to determine once daily dose regimens.

31. How do once-daily and multiple daily dosing compare generally in terms of efficacy and toxicity, according to currently available clinical data?

32. What are the three clinically significant adverse effects of the AGs?

33. What is the sequence of events believed to lead to nephrotoxicity? Which portion of the nephron and kidney is most effected by AGs? Are these effects reversible? What is the role of AG structure in nephrotoxicity?

34. What are the major risk factors for AG toxicity relative to patient status, AG administration and course of therapy? List several approaches to minimize AG-induced nephrotoxicity in various patients.

35. Describe the ototoxicities associated with AGs therapy? How are the target tissues for toxicity AG specific? Why do the AGs accumulate in ear tissues? Are these reversible or irreversible toxicities? Which AG is most ototoxic and which is least?

36. Explain the mechanism of AG-induced neuromuscular blockade. In which disease states is this adverse reaction most important?

37. What is the basis for the most significant AG-related drug interactions?