STUDY GUIDE

THE TETRACYCLINE ANTIBIOTICS

1. Identify the tetracyclines (TCs) as first or second generation agents and by duration of action (short, intermediate and long).

2. Be able to identify the TC rings (A, B, C and D) and number the entire ring system.

3. Which organisms biosynthesize TCs? What are the biochemical precursors?

4. Identify the TWO acidic functionalities of the TC ring system and explain why they are acidic. Identify the basic functionality of the TCs.

5. Why are the TSs compounds zwitterionic at physiological pH? Which salts (of the base) are used and why these salts?

6. Understand the epimerization reaction; where it occurs and what is its significance.

7. Explain the tetracycline elimination reaction involving substituents in Ring C. When and why does this occur? What electronic factor drives this reaction to completion?

8. Why is the elimination reaction less likely to occur with demeclocycline than tetracycline? Why is it less likely with minocycline than demeclocycline?

9. What are the elimination products generally called? Explain why methacycline and mecloxyline may also undergo an "elimination-type" reaction like those TCs with a 6-OH group?

10. Identify all of the TCs as acid unstable, intermediate acid stability and acid-stable and know why! Why is this reaction important?

11. What is an epianhydrotetracycline? How does it form and why is its formation important?

12. How do isotetracyclines form? What is the key functional group in this reaction? Why is this reaction important?

13. What is the chelation reaction, when does it occur and why is it significant?

14. Identify those TCs with the greatest phototoxic potential? Why?

15. Based on functional groups, identify all TCs as high, intermediate or relatively low lipophilicity. Why is lipophilicity important?

16. Which barriers must TCs traverse to express their antibacterial activity?
17. What is the mechanism of action of the TCs. What is the basis of antibacterial selectivity? Are they static or cidal agents?

18. What are the major mechanisms of TC resistance. What are their relative importance? Are they plasmid or chromosomal? What specific role do the “tet” proteins play in resistance?

19. Explain the rationale for the development of the “alkylthioTCs” and the “glycylglycineTCs”?

20. List three reasons that account for the limited therapeutic utility of the TCs?

21. How do the different TCs compare in terms of general activity and spectra of activity?

22. Characterize the activity of the TCs versus gram positive organisms of therapeutic significance.

23. Characterize the activity of the TCs versus gram negative organisms of therapeutic significance.

24. Characterize the activity of the TCs versus “atypical organisms of therapeutic significance.

25. What is the primary route of administration for TCs? Explain the role of acid stability, lipophilicity and chelation in oral bioavailability. Be sure you know the relationship between chemical structure and these properties.

26. List two limitations of IM administration of the TCs.

27. Explain the relationship between TC lipophilicity and protein binding and tissue distribution, including the CSF.

28. Explain the relationship between TC lipophilicity, protein binding and distribution to half-life.

29. Describe the elimination profile of the TCs and it's relationship to lipophilicity. What are the mechanisms of renal elimination? Why might TC doses need to be adjusted in hepatically impaired or renally impaired patients?

30. Explain the nature and significance of the various TCs in adverse reactions including GI tract disturbances, photosensitivity, bone/teeth deposition, hepatotoxicity, fanconi-like syndrome and neurotoxicity.

31. What is the chemical basis for TC-associated adverse reactions?

32. Explain the basis for the drug interactions between the TCs and antacids or iron products, diuretics and penicillins.