Pocket Examiner in Pharmacology

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A *Textbook of Pharmacology*, Bowman, W. C. and Rand, M. J., 2nd edn. (Blackwell Scientific Publications, Oxford, 1980)

B *Lewis's Pharmacology*, Crossland, J., 5th edn. (Churchill Livingstone, Edinburgh, 1980)

C *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, Gilman, A. G., Goodman, L. S. and Gilman, A., 6th edn. (Macmillan Publishing Co. Inc., New York, 1980)

D *Clinical Pharmacology*, Girdwood, R. H., 24th edn. (Baillière Tindall, London, 1979)

E *Principles of Drug Action*, Goldstein, A., Aronow, L. and Kalman, S. M., 2nd edn. (John Wiley and Sons, New York, 1974)

F *Medical Pharmacology*, Goth, A., 10th edn. (The C. V. Mosby Company, St. Louis, 1981)

G *Clinical Pharmacology*, Laurence, D. R. and Bennett, P. N., 5th edn. (Churchill Livingstone, Edinburgh, 1980)

H *Pharmacology: Drug Actions and Reactions*, Levine, R. R., 2nd edn. (Little, Brown and Company, Boston, 1978)

I *Review of Medical Pharmacology*, Meyers, F. H., Jawetz, E. and Goldfien, A., 7th edn. (Lange Medical Publications, Los Altos, California, 1980)

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Questions

PRINCIPLES OF DRUG ACTION

Drug identity and nomenclature

1 Are drugs always organic chemicals of an exogenous source or can a substance produced by the body, such as adrenaline, be regarded as such?

2 Do drugs confer new functions to tissues or organs?

3 How many names can each drug have?

4 Can the therapeutic effects of drugs always be assessed on normal subjects?

5 What properties should the ideal drug possess?

A Pharmacokinetics

Membrane transfer

6 What is the common barrier to drug absorption and what is its characteristic composition?

7 By which processes can drugs cross membranes?

8 Name the commonest process for drug transfer across cell membranes and explain why it is the commonest process.

9 Define partition coefficient and say how it is related to lipid solubility and why it is advantageous to know this property of a drug.

10 Is drug transfer across blood capillaries limited by lipid solubility?

11 What distinguishes enteral from parenteral routes of drug administration?

12 Which is the most common route of drug administration and why? When can it not be employed?

13 Are drugs which are ineffectively absorbed on oral administration of therapeutic value?

14 When are drugs administered sublingually? Give examples, outlining the limitations of this route.

15 Does the route of administration influence the therapeutic dose?

16 Do drugs penetrate intact skin?

17 Define the term bioavailability and explain its practical importance.

18 Give examples of drugs administered by inhalation and comment on their rate of absorption.

19 State the properties of a depot or sustained release preparation and say when such a drug would be employed.

20 State the major advantages and drawbacks of the intravenous route of drug administration.

21 Would you expect the rate of drug absorption to be altered by blood flow and can it be changed without the use of drugs?

22 List the reasons why and how food influences gastrointestinal drug absorption. When in relation to a meal should drugs be taken?

23 Name the major anatomical site of absorption of orally administered drugs and the reasons for this.

24 How are dissolution rate, particle size and absorption rate related?

25 Which physicochemical property of a drug is

most important for its absorption and how does it influence other processes?

26 Why does the pH at the surface of the cell membrane influence the rate of absorption and excretion of weak electrolytes?

27 If a weak acid has a pK_a of 4, what proportion of the total will be non-ionised at pH of 2 and at which part of the gastrointestinal tract may this occur?

28 If two weak acids have the same pK_a value, will they be absorbed across cell membranes at the same rate?

29 Explain why drugs possessing a quaternary ammonium group are notoriously badly absorbed and distributed.

Distribution

30 What factors govern the rate and extent of drug distribution?

31 Can one assume that a drug which is readily absorbed from the gastrointestinal tract will also be widely distributed?

32 What is the blood–brain barrier and how can it be bypassed?

33 Why does penicillin not readily enter the brain and cerebrospinal fluid?

34 Into which main body compartments do drugs distribute and what are their approximate volumes in a 70 kg man?

35 What is the 'apparent volume of distribution' of a drug and how is it evaluated?

36 Calculate the plasma concentration in an average man of 100 mg of drug which distributes uniformly throughout the body water.

37 Explain the influence of plasma protein binding on the volume of distribution of a drug. Does tissue protein binding have the same effect?

38 To which plasma protein do drugs most commonly bind and how is the rate of drug distribution influenced by such binding?

39 Which types of drugs are restricted in their distribution to plasma and which gain access to the extracellular and intracellular fluids?

40 Define drug redistribution, outline its important features and give examples.

41 List the possible consequences of plasma protein binding of drugs.

42 When a drug binds to plasma proteins which of its forms circulate in the blood and how do they differ in activity?

43 Assuming a drug is highly lipid soluble and not bound to plasma proteins will it distribute uniformly to all tissues after intravenous administration?

44 Can one predict the extent of binding and affinity of a drug for plasma proteins?

45 Give examples of drugs which are not distributed evenly in any of the recognized fluid compartments and explain why this occurs.

46 Which drugs are most liable to cross the placenta and by which process?

47 How readily will a fetus be affected by general anaesthetics, morphine, nicotine or *d*-tubocurarine administered to the mother?

48 How and why does adrenaline modify the duration of action of a local anaesthetic such as procaine and which drugs would have the same effect?

Biotransformation

49 What is meant by 'first-pass effect' and how can it be circumvented?

50 How is drug action terminated and by which processes are drugs eliminated?

51 What is the most important function of drug biotransformation?

52 Do all biotransformation reactions yield inactive compounds?

53 Are the terms biotransformation, drug metabolism and detoxification synonymous?

54 What are the major chemical reactions by which drugs are transformed?

55 Which is the major site of drug metabolism? Give examples of drugs metabolized at other sites.

56 Which type of compound can be conjugated and why is it a frequent type of biotransformation reaction?

57 Which is the major synthetic (conjugating) drug reaction? Give examples of drugs which undergo conjugation.

58 What are the hepatic microsomal enzymes?

59 What characteristics of relevance to drugs do microsomal enzymes exhibit and how do they compare with the non-microsomal enzymes?

60 At what reaction rate are most drugs biotransformed and which variable exerts the greatest influence?

61 Why do individuals differ in the rate at which they transform drugs? Give examples.

62 Can one infer from animal studies of drug metabolism that equivalent reactions will apply in man?

63 Does drug biotransformation to less lipid soluble derivatives also render them more water soluble?

64 Outline how the rate of drug biotransformation may be reduced.

65 Can drug biotransformation be enhanced?

66 With experimental evidence indicate the mechanism responsible for the increased microsomal enzyme activity induced by drugs.

67 How can termination of drug action by redistribution in practice be distinguished from termination by metabolism or excretion?

Excretion

68 Which is the principal route of drug excretion and of what relevance are other routes?

69 How do other routes of excretion differ from urinary excretion?

70 Describe the 'enterohepatic cycle', explaining how it modifies drug action.

71 With examples, explain how drugs excreted in the faeces get there.

72 Why do some drugs owe their duration of action primarily to excretion rate?

73 Why would an active drug be eliminated by the kidney?

74 Which mechanisms are responsible for urinary drug excretion?

75 Does plasma protein binding influence the rate of urinary excretion by glomerular filtration to the same extent as tubular secretion?

76 Illustrate mechanisms by which the rate of renal excretion can be altered.

77 Can renal clearances of all electrolytes be modified by changing urinary pH?

78 How is the excretion of salicylic acid, phenobarbitone and sulphamethoxazole influenced by the administration of sodium bicarbonate?

79 Explain the consequences of severe renal disease on renal drug elimination mechanisms. Which types of drugs would be most affected and what precautions must be taken?

80 What are the kinetics of accumulation and elimination of most drugs and why is this so? What other rates may apply?

81 What is the plasma half-life of a drug and is it a constant for an individual drug?

82 Does the plasma half-life change with the dose of drug administered?

83 Of what value are plasma half-life measurements?

84 If a drug which obeys first-order kinetics is given by a single intravenous injection how could one evaluate its plasma half-life and volume of distribution?

85 Which pharmacokinetic variables determine the fluctuations in plasma drug concentration and how can the magnitude of these fluctuations be reduced?

86 How do the graphical representations of plasma concentration versus time, for zero- and first-order elimination kinetics, compare?

87 How long would it take for the plasma concentration of most drugs to decline to approximately 7 per cent of their steady state level after administration ceases?

88 If a drug, which obeys first-order kinetics and is totally distributed in plasma, is intravenously infused in what time interval would its plasma concentration approach a steady state or plateau level?

89 To extend the duration of drug effect is it better to administer it more frequently or to increase the dose?

90 Does an increase in drug dosage cause a proportional increase in duration of action?

91 What is meant by maintenance dose rate and how is it derived?

92 When is the use of a loading or priming dose essential for effective drug therapy? How is it computed and what is its relation to the maintenance dose?

93 A drug which follows first-order elimination kinetics with a half-life of 10 min has a duration of action of 10 min after a single dose of 5 mg. How long would it act after single doses of 10 and 20 mg and by what factor would the initial dose have to be increased for its action to last for 1 hour?

94 When do drugs cumulate in the body and what is meant by cumulative toxicity?

B Pharmacodynamics

Dose-response relation, receptors, agonists, antagonists

95 What is the difference between the action and the effect of a drug?

96 What is the site of action of a drug and is it invariably located in the organ or tissue which ultimately responds to it?

97 What is the difference between drug dose and concentration and which term should be used?

98 With examples explain what is meant by a graded response. Are there other types?

99 What is a drug receptor and who formulated the concept of receptors?

100 Does an individual drug interact with only one functional receptor type? Give examples from drugs which influence the autonomic nervous system.

101 Is the receptor concept fundamental to drug action or can drugs produce their characteristic effect by other types of interactions?

102 How do drugs bind to receptors and which types of bonds occur most commonly?

103 Comment on which drug–receptor bond is ir-

reversible and, with relevant examples, indicate its incidence.

104 Do drugs bind only to their functional receptors?

105 With examples illustrate that enzymes can be regarded as receptors.

106 Explain how structure–activity relationships are obtained and the information they provide.

107 How can receptors be studied and what problems are associated with receptor isolation? Give examples of receptors isolated with a brief comment on their properties.

108 What is a true agonist and, with examples, illustrate how it can be distinguished from an indirect acting agonist?

109 What does the dose-response curve represent and what is its characteristic shape?

110 Why is the dose-response relationship plotted semilogarithmically and what is its shape? Which variable is on the logarithmic scale and on which axis is it plotted?

111 If the log dose-response curves of two agonists are parallel, what information could one obtain about their mechanism of action and potency?

112 What is meant by drug antagonism? List the various types of antagonists together with appropriate examples of pairs of antagonist : agonist combinations.

113 In terms of intrinsic activity how do full agonists compare with partial agonists and true receptor antagonists?

114 Does a drug which has a high affinity for a receptor also have a high efficacy or intrinsic activity?

115 What is the most useful characteristic of physiological antagonism, i.e. antagonism by opposite action? Give examples of such antagon-

ists to the histamine induced bronchoconstriction.

116 With examples explain why partial agonists are also antagonists.

117 Which experimental criteria must a drug satisfy before it can be classified as a competitive antagonist?

118 What are the features of the log dose-response curves of an agonist in the presence of increasing concentrations of its competitive antagonist?

119 Which of the following drugs are competitive antagonists: suxamethonium, nicotine, hexamethonium, isoprenaline, ergotamine, neostigmine and atropine? Briefly state the mechanism of action of the other drugs.

120 To which agonists are the following drugs competitive antagonists: propranolol, chlorpromazine, cimetidine, spironolactone, naloxone and hyoscine.

121 What is the essential difference between competitive and non-competitive antagonists? State to which type most antagonists conform.

122 Which antagonists alter the shape of the log dose-response curve and why?

123 What is the relationship between potency values and affinity constants for agonists and receptor antagonists?

124 Which theories have been proposed to explain the relationship between drug–receptor interaction and ultimate pharmacological response?

125 If two agonists are equiactive, can one assume that they occupy the same number of receptors? Does the same conclusion apply when there is an equivalent response to an agonist in the absence and in the presence of a competitive antagonist?

126 What is the spare receptor hypothesis and how can it be demonstrated?