Pharmacology

Self-assessment Questions for Students

Rosemarie Einstein

Butterworths

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Dr A H Goodman of the Department of Surgery designed the computer programs used to store, update and retrieve the questions and the information associated with their past usage. With his help the work involved in the maintenance of the question bank has been greatly reduced and the selection of questions for inclusion in this book has been facilitated. The help and encouragement of Mrs J Saxon of the Tertiary Education Research Centre at the University of New South Wales is also gratefully acknowledged.

Introduction

Our Department of Pharmacology has been using objective question examinations for students in Medicine, Pharmacy, Science and Veterinary Science for the past six years. These examinations, short answer questions, assignments and practical classes all contribute to the students' final grades. The shortcomings of this type of examination are appreciated but the lack of alternative methods which provide rapid assessment of up to 1000 students at any one time leaves us no choice but to continue using objective question examinations. The student answer sheets are computer-marked at the Tertiary Education Research Unit, University of New South Wales. The computer output provides information relating to the examination performance of the students, including the percentage of students answering each question correctly and the coefficient of discrimination for each question. The latter gives some indication of the ability of the question to discriminate between good and poor students.

In order to reduce the problems associated with objective question examinations we have tried to build a large bank of questions. The bank is maintained and accessed by a series of computer programs which were designed for us by Dr A H Goodman of the Department of Surgery at the University of Sydney. Constant review of the bank includes storing the information relating to student performance for each question each time it is set, deleting questions which have become outdated or which are later found to be ambiguous, misleading, or otherwise unsatisfactory, and adding new questions.

We have allowed students free access to past examination papers, with the rationale that if they could learn the correct answers to all the questions in the bank they may have indeed mastered their pharmacology! The questions in this book have been selected from the bank and therefore reflect the content of lectures for our undergraduate courses in all faculties. Some of the questions are suitable only for particular faculties and some apply only to the local environment. There is, however, a large number which will provide a sample with which students may assess their progress. Every effort has been made to avoid undue duplication of subject matter and to ensure that questions are not ambiguous. We would welcome comments relating to these issues from all those using the book.

The book is primarily meant to be used some time after a period of study, to test understanding and retention of the learned material. To this end, the answers, obviously, have been included. We have consciously decided against including explanations of the answers — it is the responsibility of the student to consult his or her books or teachers for explanations. Finding out *why* an answer is true or false is part of the learning and reinforcing process.

Using this book

The questions in this book are of five different types. In increasing order of complexity these are:

TYPE 1 — **TRUE/FALSE**
Each question consists of a statement, indicate whether it is true or false.

TYPE 2 — **CORRECT OPTION**
Each question consists of a stem and up to five options or five sentences, only one of which is correct. Indicate the correct option.

TYPE 3 — **INCORRECT OPTION**
Same as Type 2, except the single incorrect option should be indicated.

TYPE 4 — **MULTIPLE CHOICE QUESTION (MCQ)**
Each question consists of a stem and up to five options or five sentences, a number of which are correct. Answer:

A if only (i), (ii) and (iii) are correct.
B if only (i) and (iii) are correct.
C if only (ii) and (iv) are correct.
D if only (iv) is correct.
E if all are correct.

TYPE 5 — **ASSERTION/REASON**
Each question consists of an assertion and a reason. Answer:

A if the assertion and the reason are true statements and the reason is the correct explanation of the assertion.
B if the assertion and the reason are true statements but the reason is not a correct explanation of the assertion.
C if the assertion is true, but the reason is a false statement.
D if the assertion is false, but the reason is a true statement.
E if both the assertion and the reason are false statements.

The answers to the questions in each chapter can be found at the end of that chapter. Those questions marked with "★" have been correctly answered by less than 60 per cent of students, often on more than one occasion. This result usually indicates that a question is difficult, or that it requires some thinking process or mathematical calculation that may be difficult under examination conditions. Those questions marked with a "V" have been set primarily for students of Veterinary Science and are not applicable for students in other faculties.

Questions for self-testing may be chosen either by working through an appropriate chapter or by reference to the keyword index at the back of the book. The index has been compiled from key-words as they appear in the questions, ie names of individual drugs or drug groups, naturally occurring active substances (hormones, transmitters, autacoids etc) and disease states.

August 1984 *Rosemarie Einstein*

Contents

1
General Principles of Pharmacology
Pharmacokinetics

TRUE / FALSE:

1.1 Tachyphylaxis is a form of resistance to the action of a drug.

1.2 Potentiation occurs when the combined effect of two drugs is less than the sum of their individual activities.

1.3 Alkaloids are no longer pharmacologically useful.

1.4 Drugs with different mechanisms of action may achieve the same effect.

1.5 All useful drugs have a clearly defined mechanism of action.

1.6 All registered drugs have a generic or non-proprietary name.

1.7 The chemical name for a drug is rarely the same as the non-proprietary name.

1.8 A single drug may have many trade names.

1.9 Areas of cell membranes with which drugs interact to produce their biological effect are called receptors.

1.10 Although drugs frequently exert their actions via specific macromolecular receptors, not all drug actions require such receptors.

1.11 All receptor sites are embedded in membranes.

1.12 Receptors for drug action may exhibit stereospecificity.

1.13 Receptors may be "down-regulated" by removal of endogenous inhibitors.

1.14* Multiple binding sites may interact in a co-operative manner to influence dose-response relationships.

1.15 Negative co-operativity results in very steep dose-response relationships.

1.16 The dissociation constant of a drug is independent of the lifetime of the drug-receptor complex.

1.17 Scatchard plots are used to determine the rate of drug action.

1.18 A curvilinear Scatchard plot indicates that a drug may exhibit co-operativity or bind to more than one site.

1.19 Ligand binding studies are essential for the development of new drugs.

1.20 A graph of the effect of a drug plotted against the logarithm of its dose is usually sigmoid in shape.

1.21 The quantal dose-response relationship provides a measure of the variation in doses needed to produce an all-or-none effect in a group of subjects.

1.22 A response does not necessarily follow the interaction of a drug with a binding site on a cell.

1.23 Logarithmic dose-response curves are sigmoidal in shape and are symmetrical about the point corresponding to 50% of the maximum response.

1.24 The negative logarithm of the molar concentration of an agonist drug, corresponding to the centre of symmetry of a log-dose response curve, is the measure of the potency of the agonist for the receptor.

1.25 The binding affinity of a drug is directly related to its efficacy of action.

1.26 The affinity of a drug for a receptor can be measured for both agonists and antagonists.

1.27 Agonist drugs which act on the same receptors have parallel log-dose response curves.

1.28 When conventional log dose-response curves are plotted to compare the results of LD_{50} determinations of two substances, the curve for the more toxic chemical will be on the right hand side.

1.29 Antagonist drugs are molecules which have affinity for the receptor but do not have the ability to stimulate the receptor.

1.30 Antagonist drugs have high intrinsic activity.

1.31 A drug which is described as a partial agonist can act as an antagonist.

1.32 Competitive antagonism may be overcome by increasing the dose of agonist.

1.33 Functional antagonism occurs when two agonist drugs, interacting through two independent receptor systems, cause effects which counteract each other.

1.34 The pA_2 value for atropine at a muscarinic receptor should be the same whether acetylcholine or muscarine is used as the agonist.

1.35-1.38

Drug W is a full agonist
Drug X is a competitive antagonist of drug W
Drug Y is a functional antagonist of drug W
Drug Z is a non-competitive antagonist of drug W

1.35 Drug Y interacts with a receptor system distinct from the receptor system of drug W.

1.36 The maximal effect obtained with drug W would decrease in the presence of increasing concentrations of drug X.

1.37 In the presence of drug Z, the slope of the dose-response curve to drug W would show a parallel shift to the right.

1.38 The maximum effect obtainable with drug W would decrease in the presence of increasing concentrations of drug Z.

1.39 Cell membranes have been shown to possess pores through which large molecules may enter cells.

1.40 The large size of ionized drug molecules inhibits their diffusion through cell membranes.

1.41 Drugs given orally should always be taken after meals.

1.42 The rate of absorption of an acidic drug from the stomach is enhanced by the co-administration of sodium bicarbonate.

1.43 Use of a depot preparation results in slow absorption.

1.44 Administration of a drug as a depot salt is the only effective method of increasing its half-life.

1.45 Absorption of drugs through mucous membranes is more effective than through skin.

The advantages of rectal administration are that:

1.46 an enteric coated dose form is unnecessary.

1.47 drugs can be given to unconscious patients.

1.48 drugs can be administered to vomiting patients.

Intravenous injections are advantageous because:

1.49 they are less likely to cause hypersensitivity reactions.

1.50 they can be given to an unconscious patient.

1.51 they give higher initial blood levels.

The rate of absorption of drugs through the intestinal wall:

1.52 varies directly with the area of absorption surface.

1.53 is reduced by peristalsis.

1.54 always depends on a positive concentration gradient between intestinal contents and plasma.

1.55* The distribution of thiopentone in the body is initially controlled by fat deposits.

1.56 Dangerous drug interactions may occur if one drug displaces another from protein binding sites.

1.57 Warfarin displaces phenylbutazone from its plasma protein binding sites.

1.58 Active transport mechanisms are responsible for most aspects of drug distribution in the body.

1.59 Binding of a drug to plasma proteins aids its transport into the central nervous system.

1.60 Plasma protein binding of drugs may serve as the means of transport of some drugs in the body.

1.61 Lipid solubility is the most important factor in influencing drug entry into the brain.

1.62 Drugs must be metabolized before they are excreted.

1.63 Oxidation of drugs *in vivo* is usually carried out by hepatic microsomal enzymes.

1.64 Conjugation with glycine is a significant method of drug biotransformation.

1.65 Metabolic reactions often involve conjugation which is then followed by oxidation.

1.66 Bio-oxidation is the most common method of drug metabolism.

Drug biotransformation:

1.67 occurs predominantly in the liver.

1.68 usually converts polar molecules to non-polar molecules.

1.69 may be responsible for the mutagenicity of certain drugs.

1.70 is responsible for the hepatotoxicity of paracetamol.

1.71 always utilizes energy from ATP.

1.72 usually increases the drug's water solubility.

1.73 The rate of urinary excretion of a strongly basic drug is enhanced by the co-administration of ammonium chloride.

1.74 The excretion of a weakly acidic drug may be decreased by decreasing urinary pH with ammonium chloride.

1.75 Excretion is the only method of terminating drug action.

1.76 Drug excretion in bile may result in its re-uptake.

1.77 Zero-order kinetics apply when the rate of absorption is a function of the amount of drug available for absorption.

1.78 The rate constant of elimination of a drug is equal to the sum of the rate constants of biotransformation and excretion.

1.79 When drugs are administered orally, the larger the dose, the more rapidly the maximum plasma level is obtained.

1.80 The volume of distribution of a drug is equal to the total amount of drug in the body divided by the concentration of drug in the plasma.

1.81 The volume of distribution of a drug cannot exceed the volume of total body water.

1.82* The volume of distribution of a drug can only exceed the volume of total body water for highly lipid-soluble drugs.

1.83 When a drug is bound to plasma proteins its apparent volume of distribution may be much greater than the total body water volume.

1.84 The area under the plasma concentration-time curve is a function of dose, volume of distribution and the rate of elimination.

1.85 The fraction of an oral dose absorbed can be calculated if the areas under the plasma level vs time curves for oral and intravenous doses are known.

1.86 In the equation to determine the plasma concentration of a drug at time t after i.v. administration, the number of exponential factors in the equation is equal to the number of compartments into which the drug is distributed.

1.87 The half-life of a drug is the time from administration until its maximum effect is reduced by half.

1.88 The half-life of a drug which is strongly protein-bound is liable to be shorter than that of a drug which is unbound.

1.89 The effect of a drug may still be evident long after all the drug has been excreted.

1.90 If a drug has a biological half-life of 6 hours, all its effects will have worn off after 24 hours.

1.91 If the clearances of drug A and drug B are the same but the distribution volume of drug A is greater than the distribution volume of drug B, then the half-life of elimination for drug A will be less than that for drug B.

1.92 Drugs which are highly lipid-soluble are less likely to give rise to problems of cumulative toxicity.

1.93 If the "first-pass" metabolism of a drug is extensive it will be necessary to prescribe a smaller oral dose to patients with liver disease.

1.94* For most drugs there is a well-defined range of plasma concentrations within which their therapeutic effects will occur.

If the plasma concentration of a drug is plotted against the time following the administration of a single oral dose:

1.95 the area under the curve will be independent of the rate of absorption.

1.96 a symmetrical bell-shaped curve would indicate that metabolism by the liver is important in the disposal of the drug.

1.97 the "half-life" of the plasma concentration could be calculated from the time taken to reach peak concentration.

1.98 the peak concentration will depend only on the rate and extent of absorption of the drug from the gastrointestinal tract.

After i.v. administration of a drug, pharmacokinetic data which fit a single compartment model can be used to calculate:

1.99* the absorption rate constant for the drug.

1.100 the volume of distribution.

1.101 the half-life of the drug.

1.102 the extent of absorption of the drug after oral administration.

If a patient is receiving a drug by continuous intravenous infusion:

1.103 increasing the rate of infusion reduces the time required to achieve a steady-state plasma level.

1.104 decreasing the rate of infusion decreases the steady-state plasma level.

1.105 The bioavailability of a drug formulation refers to the rate and extent of absorption of the drug from that formulation.

1.106 Clinical problems may arise from the variable bioavailability of warfarin.

1.107 Two tablets of phenylbutazone made by different manufacturers will always have the same bioavailability provided the dosage forms each contain 100mg of the pure drug.

1.108 Problems of bioavailability are most likely to arise with drugs which are poorly soluble.

1.109 The bioavailability of a drug is independent of other drugs administered concurrently.

1.110 The bioavailability of a drug is controlled in part by its lipid/water partition coefficient.

1.111 Drugs which are rapidly absorbed into body fat always have a short duration of action.

1.112 The more water-soluble a drug, the longer is its duration of action.

CORRECT OPTION:

1.113 The "therapeutic index" of a drug is:
- A. the ratio of the drug's potency to that of a standard drug
- B. a number, relating the potency to the toxicity of the drug
- C. the ratio of the lethal dose to the minimum dose which produces unacceptable side effects
- D. an expression of the severity of the undesirable effects produced by the drug
- E. a list of the diseases for which the drug is indicated.

1.114 The development of tolerance describes a situation where:
- A. a response of unusually large magnitude is produced by a normal dose
- B. the dose of a drug must be increased to maintain a given effect
- C. a patient experiences withdrawal symptoms if the drug is not given at regular intervals
- D. an unusual type of response is produced by a drug
- E. the patient is unable to tolerate a normal dose of a drug.

1.115 The intrinsic activity or efficacy of a drug is:
- A. a measure of its potency
- B. related to its maximal agonist effect
- C. related to its affinity for a receptor site
- D. restricted to describing antagonists
- E. the negative logarithm of the concentration producing half the maximum response.

1.116 Antagonists
- A. always bear an obvious structural relationship to agonists acting at the same receptor
- B. can only be discovered by random screening programmes
- C. are frequently active at more than one receptor site
- D. are invariably much larger molecules than agonists
- E. have a low affinity for the receptor and a high efficacy.

1.117 The pA_2 is:
- A. a measure of the potency of a competitive antagonist drug
- B. a measure of the potency of an agonist drug
- C. a measure of the intrinsic activity of an agonist drug
- D. a measure of the potency of a non-competitive antagonist drug.

1.118 Most quaternary nitrogen compounds do not penetrate the blood brain barrier because they:
- A. are very large molecules
- B. are negatively charged
- C. are poorly lipid soluble
- D. have hydrophilic groups
- E. do not have hydrophobic groups.

1.119* For optimal absorption after oral administration, a drug needs:
- A. enteric coating
- B. an ionized form
- C. acid lability
- D. water solubility.

1.120 Which of the following mechanisms is not involved in the biotransformation of drugs?
- A. conjugation
- B. oxidation
- C. hydrolysis
- D. esterification.

1.121 Biotransformation usually results in metabolites which, in comparison with the drug, have:
- A. greater biological activity
- B. greater water solubility
- C. lower molecular weight
- D. capacity for long storage in the body.

1.122 Which of the following enzymes is not important in drug biotransformation?
- A. mixed function oxidase
- B. cytochrome P450
- C. monoamine oxidase
- D. sulphonyl transferase
- E. prostaglandin dehydrogenase.

1.123* Which of the following require metabolism before they become pharmacologically active?
- A. cyclophosphamide
- B. isoniazid
- C. propantheline
- D. aspirin
- E. diazepam.

1.124 If a patient is receiving a drug by continuous intravenous infusion:
- A. 50% of the full clinical effect of the drug can be expected after a period equivalent to one half-life of the drug
- B. halving the concentration of the drug in the infused solution will reduce the half-life of elimination
- C. a steady state plasma level is achieved after a period equal to three to five half-lives of elimination
- D. none of the above.

1.125 The drug interaction of tetracycline and ferrous sulphate is most probably due to:
- A. displacement from plasma proteins
- B. inhibition of metabolism
- C. induction of metabolism
- D. decreased absorption from the gastrointestinal tract
- E. increased reabsorption from renal tubules.

INCORRECT OPTION:

1.126 Drug molecules may pass through cell membranes:
- A. by diffusion
- B. by reaction with a carrier molecule
- C. by influence of concentration gradient
- D. through pores, in the form of a metal complex.

1.127 Serum protein binding of a drug may affect:
- A. its rate of excretion
- B. toxicity of another drug given concurrently
- C. its route of administration
- D. passage into the cerebrospinal fluid.

1.128* Liver "mixed function oxidase" :
- A. It converts large doses of paracetamol to a hepatotoxic metabolite.
- B. It is inhibited by tyramine.
- C. Its metabolism of carbon tetrachloride may be prevented by proadifen.
- D. Its activity may be induced by barbiturates.
- E. It is inhibited by tranylcypromine.

MCQ:

1.129 When reliable absorption of a drug is desired over a prolonged period of time, the best administration procedure/s is/are:
- i. oral ingestion
- ii. intramuscular injection of the drug in suspension
- iii. intravenous injection of an insoluble form of the drug
- iv. subcutaneous implantation of a solid drug pellet.

ANSWERS:

1.1	T	1.23	T	1.45	T	1.67	T	1.89	T	1.111	F
1.2	F	1.24	T	1.46	T	1.68	F	1.90	F	1.112	F
1.3	F	1.25	F	1.47	T	1.69	T	1.91	F	1.113	B
1.4	T	1.26	T	1.48	T	1.70	T	1.92	F	1.114	B
1.5	F	1.27	T	1.49	F	1.71	F	1.93	T	1.115	B
1.6	T	1.28	F	1.50	T	1.72	T	1.94	F	1.116	C
1.7	T	1.29	T	1.51	T	1.73	T	1.95	T	1.117	A
1.8	T	1.30	F	1.52	T	1.74	T	1.96	F	1.118	C
1.9	T	1.31	T	1.53	F	1.75	F	1.97	F	1.119	D
1.10	T	1.32	T	1.54	F	1.76	T	1.98	F	1.120	D
1.11	F	1.33	T	1.55	F	1.77	F	1.99	F	1.121	B
1.12	T	1.34	T	1.56	T	1.78	T	1.100	T	1.122	E
1.13	F	1.35	T	1.57	F	1.79	F	1.101	T	1.123	A
1.14	T	1.36	F	1.58	F	1.80	T	1.102	F	1.124	C
1.15	F	1.37	F	1.59	F	1.81	F	1.103	F	1.125	D
1.16	F	1.38	T	1.60	T	1.82	F	1.104	F	1.126	D
1.17	F	1.39	F	1.61	T	1.83	T	1.105	T	1.127	C
1.18	T	1.40	F	1.62	F	1.84	T	1.106	T	1.128	B
1.19	F	1.41	F	1.63	T	1.85	T	1.107	T	1.129	C
1.20	T	1.42	F	1.64	T	1.86	T	1.108	F		
1.21	T	1.43	T	1.65	F	1.87	F	1.109	T		
1.22	T	1.44	F	1.66	T	1.88	F	1.110	F		

2
Molecular Pharmacology

TRUE / FALSE:

2.1 The activity of the majority of drug molecules can be predicted with certainty by examining conformational structure.

In a homologous series of physiologically active compounds:

2.2 activity changes geometrically in ascending the series.

2.3 a cut-off point occurs as molecular weight increases, after which activity sharply falls.

2.4 water solubility increases in ascending the series.

2.5 Positional isomers are molecules that differ in a position of a substituent, but still have the same chemical formulae.

2.6 Optical isomers differ only in their colour.

2.7 Bioisosteres are functional groups which can be used in a molecularly modified drug to replace a certain functional group in the original drug, so that the modified drug acquires anatgonist properties at the receptor site.

2.8 An important consideration for isosteric replacement in drug molecules is that the new drug molecule should posses the same total charge in order to interact with the same receptor site.

2.9 An acetyl substituent is necessary for a drug to have similar properties to acetylcholine.

2.10 Pharmacological activity in the homologous series of alkyl alcohols increases with the size of the alkyl group until a critical cut-off point is reached.

2.11 A drug which is ionized will not readily cross the blood brain barrier.

2.12 Steroids contain trans-fused cyclohexane rings held in the chair conformation.

2.13 Rotation about carbon-carbon double bonds is sufficiently rapid at body temperature so that cis and trans isomers have similar pharmacological activity.