

Clinical Pharmacology  
and Therapeutics:  
**Questions for  
Self Assessment**

THIRD  
EDITION



**Timothy GK Mant  
Lionel D Lewis  
James M Ritter  
Albert Ferro**

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**TIMOTHY GK MANT** BSc FFPM FRCP

Senior Medical Advisor, Quintiles, Guy's Drug Research Unit, and  
Visiting Professor, King's College London School of Medicine at Guys,  
King's and St Thomas' Hospitals, London, UK

**LIONEL D LEWIS** MA MB BCh MD FRCP

Professor of Medicine, Pharmacology and Toxicology at Dartmouth  
Medical School and the Dartmouth-Hitchcock Medical Center,  
Lebanon, New Hampshire, USA

**JAMES M RITTER** MA DPhil FRCP FMedSci FBPHARMACOLS

Professor of Clinical Pharmacology, King's College London School of  
Medicine at Guy's, King's and St Thomas' Hospitals, London, UK

**ALBERT FERRO** PhD FRCP FBPHARMACOLS

Reader in Clinical Pharmacology and Honorary Consultant  
Physician, King's College London School of Medicine at Guy's,  
King's and St Thomas' Hospitals, London, UK

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# INTRODUCTION

Multiple choice, extended matching, best of five and problem solving questions are now ubiquitous in medical graduate and postgraduate examinations. They provide a rapid method for testing a wide range of knowledge and marking is objective. The authors of this book, who are all practising physicians who have taught clinical pharmacology and therapeutics for many years, have based it on the fifth edition of *Textbook of Clinical Pharmacology and Therapeutics* not only to prepare students for their exams but also to emphasize the principles and facts that are the key to safe and effective prescribing.

The answers are related to the relevant section in *Textbook of Clinical Pharmacology and Therapeutics*, Fifth Edition. In addition there are brief explanatory annotations in the answer to each question.

Although this book can 'stand alone', we recommend that students will read a section of the main textbook and then reinforce and revise their knowledge by self testing using the self assessment book. At the end of the book is a practice examination of 50 'Best one correct answer of five' questions, the type currently most favoured in medical examinations, followed by five problem solving questions. This examination covers the spectrum of topics that may be encountered in a final MB (medical degree) examination or even in some postgraduate examinations (e.g. American Board of Clinical Pharmacology, Inc.). We suggest that students use this as a 'practice run' after finishing their revision of the subject as a whole. It is best to do it 'blind' at one sitting lasting not more than 60 minutes.

We thank the generations of students who have provided critical feedback and Val Brockwell for her word processing skills and patience.

Timothy Mant  
Lionel Lewis  
James Ritter  
Albert Ferro

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# GENERAL PRINCIPLES

## MULTIPLE CHOICE QUESTIONS

- 1 The following drugs exert their effects by binding to receptors and mimicking the effects of the endogenous ligand (i.e. are agonists):
  - a) Tamoxifen
  - b) Salbutamol
  - c) Morphine
  - d) Cetirizine
  - e) Lisinopril
- 2 The following drugs exert their principal effects by enzyme inhibition:
  - a) Pyridostigmine
  - b) Atropine
  - c) Amlodipine
  - d) Digoxin
  - e) Selegiline
- 3 The following drugs are reversible competitive antagonists:
  - a) Suxamethonium
  - b) Loratidine
  - c) Ranitidine
  - d) Phenoxybenzamine
  - e) Naloxone
- 4 The following drugs are partial agonists:
  - a) Isoprenaline
  - b) Morphine
  - c) Flumazenil
  - d) Buprenorphine
  - e) Oxprenolol



- 5** The following drugs cause their primary pharmacodynamic effect via non-receptor mediated mechanisms:
- a) Magnesium trisilicate
  - b) Mannitol
  - c) Methotrexate
  - d) Dimercaprol
  - e) Sumatriptan
- 6** The pharmacokinetic 'elimination half-life' of the following drugs mirrors their pharmacodynamic duration and intensity of action:
- a) Salbutamol
  - b) Phenelzine
  - c) Dobutamine
  - d) Omeprazole
  - e) Cyclophosphamide
- 7** The plasma clearance of a drug:
- a) Is the volume of plasma from which the drug is totally eliminated per unit time
  - b) Is equal to the administration rate divided by the steady state plasma concentration
  - c) Is a better measure of the efficiency of drug elimination from the body than elimination half-life
  - d) Does not include elimination by hepatic enzyme metabolism
  - e) May be affected by renal function (i.e. GFR)
- 8** For a drug that obeys first-order (linear) kinetics and fits a one-compartment model for elimination:
- a) Its rate of elimination (in mass units of drug/unit time) is proportional to its plasma concentration
  - b) Following cessation of an intravenous infusion the plasma concentration declines exponentially
  - c) The half-life is proportional to the dose
  - d) The half-life is unaffected by renal function (i.e. GFR)
  - e) The composition of drug products excreted is independent of the dose
- 9** The apparent volume of distribution:
- a) Can be greater than the total body volume
  - b) Is approximately 3 L for most drugs in adults
  - c) Is influenced by a drug's lipid solubility
  - d) A large value indicates that a drug will be efficiently eliminated by haemodialysis
  - e) Determines the peak plasma concentration after a single bolus intravenous dose

- 10 The following drugs have an elimination half-life of less than 4 hours in a healthy adult:
- Dopamine
  - Heparin
  - Amiodarone
  - Gentamicin
  - Diazepam
- 11 In repeated (chronic or multiple) dosing:
- If the dosing interval is much greater than the elimination half-life, little if any drug accumulation occurs
  - It takes approximately five half-lives to reach 50 per cent of the steady state concentration
  - If a drug is administered once every half-life once steady state is reached, the peak plasma concentration will be double the trough concentration
  - The use of a bolus loading dose reduces the time taken to reach steady state
  - In patients with renal impairment the dosing interval should be increased when prescribing gentamicin
- 12 The following drugs obey non-linear (dose-dependent) elimination pharmacokinetics:
- Acetylsalicylic acid (aspirin) overdose
  - Heparin
  - Phenytoin
  - Ethanol
  - Ceftazidime in therapeutic doses
- 13 The following drugs undergo significant enterohepatic circulation:
- Oestrogens
  - Atenolol
  - Rifampicin
  - Gentamicin
  - Levofloxacin
- 14 The oral bioavailability of a drug:
- Is a measure of the extent to which it enters the systemic circulation
  - May be influenced by changing the excipient after oral administration
  - Is defined as the ratio of the area under the plasma concentration time curve (AUC) following oral administration divided by that following intravenous administration
  - May be reduced by hepatic CYP450 induction
  - Two preparations of the same drug may have similar bioavailability but different peak concentrations ( $C_{max}$ )

- 15 The following are examples of prodrugs:
- Levodopa
  - Azathioprine
  - Penciclovir
  - Sulfasalazine
  - Enalapril
- 16 The following oral drugs do not require absorption from the gut to exert a therapeutic effect:
- Acarbose
  - Methionine
  - Orlistat
  - Olsalazine
  - Vancomycin
- 17 Drug absorption following oral administration:
- Is most commonly through passive diffusion
  - Occurs predominantly in the colon
  - Is usually complete within 90 minutes
  - Non-polar lipid-soluble drugs are absorbed more readily than polar water-soluble drugs
  - Peptides are well absorbed following oral administration
- 18 The following drugs are absorbed predominantly through active transport systems:
- Paracetamol (acetaminophen)
  - Phenytoin
  - Levodopa
  - Methyldopa
  - Lithium
- 19 The systemic bioavailability of the following oral drugs is increased if taken in the fasting state:
- Oxytetracycline
  - Amoxicillin
  - Levodopa
  - Acetylsalicylic acid/salicylates
  - Fluconazole
- 20 The following drugs are effectively administered via the sublingual route:
- Simvastatin
  - Carbamazepine
  - Ramipril
  - Buprenorphine
  - Glyceryl trinitrate

- 21 The following drugs are effectively administered by the rectal route to produce their systemic effect:
- Indometacin
  - Sulfasalazine
  - Metronidazole
  - Glycerin
  - Diazepam
- 22 The following drugs may be administered transcutaneously to produce their systemic therapeutic effect:
- Glyceryl trinitrate (GTN)
  - Estradiol
  - Lidocaine (lignocaine)
  - Fentanyl
  - Nicotine
- 23 In the case of an intramuscular injection of a drug:
- Rate of drug absorption is enhanced by exercise
  - Rate of drug absorption is greater from the deltoid injection site than the gluteus maximus site
  - If administered to the buttock should be in the upper outer quadrant
  - Should usually be no greater than a volume of 0.5 mL
  - Is an appropriate route of administration for the decanoate ester of fluphenazine
- 24 The following are commonly associated with phlebitis when given via the intravenous route:
- Potassium chloride
  - Hydrocortisone
  - Diazepam
  - 50 per cent glucose
  - 5 per cent glucose
- 25 The following are metabolized by enzymes in the hepatic smooth endoplasmic reticulum:
- Levodopa
  - Tyramine
  - Metoprolol
  - Suxamethonium
  - 6-Mercaptopurine
- 26 The following are substrates for CYP3A:
- Ciclosporin
  - Clarithromycin
  - Phenytoin
  - Adrenaline (epinephrine)
  - Warfarin

- 27** The following drugs undergo phase II metabolism by hepatic acetylation enzymes (*N*-acetyltransferases):
- a) Dapsone
  - b) Cyclosporin
  - c) Gentamicin
  - d) Isoniazid
  - e) Hydralazine
- 28** The following agents induce hepatic CYP450:
- a) Rifampicin
  - b) Carbamazepine
  - c) St John's wort
  - d) Phenobarbital
  - e) Penicillin
- 29** The following inhibit at least one of the hepatic CYP450 isoenzymes:
- a) Fluvoxamine
  - b) Grapefruit juice
  - c) Digoxin
  - d) Itraconazole
  - e) Ciprofloxacin
- 30** The following are subject to extensive presystemic (first-pass) metabolism:
- a) Metoprolol
  - b) Phenytoin
  - c) Ciprofloxacin
  - d) Morphine
  - e) Verapamil
- 31** The following decrease the rate of gastric emptying:
- a) Aspirin overdose
  - b) Migraine
  - c) Fluoxetine
  - d) Amitriptyline
  - e) Metoclopramide
- 32** Cardiac failure:
- a) Increases the bioavailability of oral thiazide diuretics
  - b) Increases the volume of distribution of lidocaine
  - c) Has little effect on the volume of distribution of furosemide
  - d) Decreases the elimination half-life of lidocaine
  - e) Decreases the elimination half-life of gentamicin

- 33 In severe renal failure:
- Gastric pH decreases
  - The 'therapeutic range' for phenytoin decreases
  - Drug distribution of famotidine to the brain is increased
  - Smaller maintenance doses of digoxin are required
  - Omeprazole should be avoided
- 34 The following statements concerning renal drug handling are correct:
- The kidneys receive approximately 20 per cent of the cardiac output
  - In healthy young adults approximately 130 mL/min of protein-free filtrate is formed at the glomeruli
  - Non-protein-bound drug of molecular weight  $<66\,000$  passes into the filtrate
  - Potentially saturable mechanisms for active secretion of both acids and bases exist in the proximal tubule
  - Low lipid solubility favours tubular reabsorption
- 35 The following drugs must be avoided in severe renal failure (glomerular filtration rate (GFR)  $<10$  mL/min):
- Prednisolone
  - Amoxicillin
  - Bumetanide
  - Metformin
  - Oxytetracycline
- 36 The following can reduce GFR:
- Naproxen
  - Ranitidine
  - Iodine-containing contrast media
  - Lisinopril
  - Amphotericin B
- 37 Monitoring plasma/serum drug concentrations of the following drugs is recognized as a valuable supplement to clinical monitoring:
- Carbimazole
  - Warfarin
  - Gentamicin
  - Lithium
  - Ciclosporin
- 38 In pregnancy:
- Most drugs cross the placenta by active transport
  - Ionized drugs cross the placenta more easily than un-ionized drugs
  - Drugs that reduce placental blood flow can reduce birth weight
  - The fetal blood-brain barrier is not developed until the second half of pregnancy
  - The human placenta metabolizes endogenous steroids

- 39** The following drugs are confirmed teratogens in humans:
- a) Ethanol (alcohol)
  - b) Warfarin
  - c) Isotretinoin
  - d) Paracetamol (acetaminophen)
  - e) Amoxicillin
- 40** During pregnancy:
- a) Gastric emptying and small intestinal motility are reduced
  - b) Blood volume increases
  - c) Plasma volume increases
  - d) Predominantly water-soluble drugs will have a larger apparent volume of distribution
  - e) Phenytoin metabolism is inhibited
- 41** During pregnancy:
- a) Renal plasma flow increases
  - b) GFR increases
  - c) Atenolol excretion increases
  - d) Lithium excretion increases
  - e) Gentamicin excretion increases
- 42** The following are considered safe during pregnancy:
- a) Salbutamol
  - b) Erythromycin
  - c) Levofloxacin
  - d) Tobramycin
  - e) Ribavirin
- 43** The following are appropriate in the management of benign dyspepsia in the second and third trimester of pregnancy:
- a) Low roughage diet
  - b) Avoidance of fresh fruit and vegetables
  - c) Small, frequent meals
  - d) Misoprostol
  - e) Omeprazole
- 44** The following drugs do not cross the placenta in significant amounts:
- a) Heparin
  - b) Warfarin
  - c) Corticosteroids
  - d) Sodium valproate
  - e) Pethidine

- 45 The use of phenytoin in pregnancy:
- Is absolutely contraindicated
  - Is associated with cleft lip and palate
  - The 'therapeutic' blood concentration of total drug is lower than in the non-pregnant state
  - Is associated with ataxia if an excessive dose is used
  - Requires oral vitamin D supplements
- 46 The following drugs are appropriate for managing severe hypertension diagnosed in early pregnancy in an asthmatic woman:
- Bendromethiazide
  - Atenolol
  - Labetalol
  - Lisinopril
  - Methyldopa
- 47 The following are absolutely contraindicated in pregnancy:
- Salbutamol
  - Corticosteroids
  - General anaesthesia
  - Quinine for malaria
  - Sucralfate
- 48 In neonates relative to adults:
- Gastric acid production is reduced
  - Fat content (as a percentage of body weight) is low
  - Plasma albumin concentration is low
  - The blood-brain barrier is more permeable
  - The GFR is reduced
- 49 The following drugs should be avoided during breastfeeding:
- Amiodarone
  - Carbamazepine
  - Ciprofloxacin
  - Cyclophosphamide
  - Ranitidine
- 50 The following drugs suppress lactation:
- Anthraquinones (e.g. senna)
  - Bromocriptine
  - Furosemide
  - Salbutamol
  - Metronidazole



- 51** The following properties of a drug facilitate its entry into breast milk:
- a) High lipid solubility
  - b) Un-ionized state at physiological pH
  - c) Low molecular weight
  - d) Weak base
  - e) Short half-life
- 52** The following are appropriate in the first-line management of acute severe asthma in a 5-year-old child:
- a) Nebulized beta<sub>2</sub> agonists
  - b) Systemic corticosteroids
  - c) Rectal diazepam
  - d) Systemic ipratropium
  - e) Systemic midazolam
- 53** A 'normal' man of 75 in comparison with a 'normal' man of 35:
- a) Is more likely to be on regular drug therapy
  - b) Is more prone to sedation with benzodiazepines
  - c) Has a higher endogenous production of creatinine
  - d) Has an increased liability to allergic drug reactions
  - e) Usually requires a lower dose of warfarin to achieve anticoagulation
- 54** The following drugs may precipitate acute retention of urine in the elderly:
- a) Gliclazide
  - b) Furosemide
  - c) Morphine
  - d) Amitriptyline
  - e) Trimethoprim
- 55** The half-life of the following is increased in the elderly:
- a) Gentamicin
  - b) Glibenclamide
  - c) Lithium
  - d) Morphine glucuronide
  - e) Diazepam
- 56** The following drugs should not be used in patients over 75 years old:
- a) Trandolapril
  - b) Finasteride
  - c) Streptokinase
  - d) Doxycycline
  - e) Fluoxetine

- 57 A woman of 75 is more likely to have the following adverse effects than a woman of 25:
- a) Confusion during treatment with cimetidine
  - b) Cholestatic jaundice following treatment with flucloxacillin
  - c) Gastrointestinal haemorrhage during treatment with ketorolac
  - d) Increased incidence of postural hypotension during doxazosin therapy
  - e) Increased risk of agranulocytosis during clozapine therapy
- 58 The following are 'type A' adverse reactions (i.e. a consequence of the drug's normal pharmacological effect):
- a) Propranolol and fatigue
  - b) Atorvastatin and hepatotoxicity
  - c) Naproxen and gastrointestinal haemorrhage
  - d) Cyclophosphamide and neutropenia
  - e) Diazepam and sedation
- 59 Stopping treatment with the following drugs may lead to adverse effects due to drug withdrawal:
- a) Prednisolone
  - b) Clonidine
  - c) Lorazepam
  - d) Metoprolol
  - e) Ergotamine
- 60 The following adverse reactions are associated with the drugs named:
- a) Oral contraception – gastrointestinal haemorrhage
  - b) Co-amoxiclav – acute liver failure
  - c) Cocaine – stroke
  - d) Thiazide diuretics – impotence
  - e) Prednisolone – osteomalacia
- 61 The following are examples of a type I hypersensitivity reaction:
- a) Penicillin-induced anaphylactic shock
  - b) Methyldopa-induced Coombs' positive haemolytic anaemia
  - c) Hydralazine-induced systemic lupus erythematosus (SLE)
  - d) Amiodarone-induced photosensitivity skin rashes
  - e) Sotalol-induced torsade de pointes
- 62 The following drugs are associated with erythema multiforme:
- a) Phenytoin
  - b) Cyclophosphamide
  - c) Salbutamol
  - d) Sevoflurane
  - e) Co-trimoxazole

- 63** The following drugs are recognized as causing thrombocytopenia:
- a) Aurothiomalate
  - b) Thiazides
  - c) Heparin
  - d) Mesalazine
  - e) Atenolol
- 64** The following combinations outside the body (e.g. in infusion bag) cause drug inactivation:
- a) Penicillin and hydrocortisone
  - b) Phenytoin and 5 per cent dextrose
  - c) Sodium bicarbonate and calcium chloride
  - d) Erythromycin and 0.9 per cent sodium chloride
  - e) Heparin and 5 per cent dextrose
- 65** Individuals who are 'slow acetylators' (i.e. have relatively low activities of hepatic *N*-acetyltransferase):
- a) Have prevalence of 5–10 per cent amongst the white population in the UK
  - b) Are more likely to develop agranulocytosis whilst being treated with clozapine
  - c) Are more likely to develop hepatotoxicity after a paracetamol overdose
  - d) Are more likely to develop a lupus-like syndrome during hydralazine therapy
  - e) Are more likely to develop peripheral neuropathy during isoniazid therapy
- 66** The following drugs can produce haemolysis in patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency:
- a) Dapsone
  - b) Probenecid
  - c) Primaquine
  - d) Co-trimoxazole
  - e) Ciprofloxacin
- 67** Drug-induced exacerbations of acute porphyria:
- a) Are usually precipitated by enzyme inhibitors (e.g. selegiline)
  - b) Are often precipitated by a single dose of drug
  - c) Are accompanied by increased urinary excretion of 5-aminolevulinic acid (ALA) and porphobilinogen
  - d) May be precipitated by ethanol
  - e) May be precipitated by rifampicin

- 68 Abnormal pseudocholinesterase:
- Is typically inherited as a Mendelian dominant condition
  - Results in malignant hyperthermia following exposure to suxamethonium
  - Causes warfarin resistance
  - Leads to prolonged paralysis following suxamethonium
  - Is associated with treatment failure with donepezil for Alzheimer's disease
- 69 Phase 1 studies (i.e. initial studies of drugs in humans involving an Investigational Medicinal Product) in the UK:
- Require authorization by the Medicines and Healthcare Products Regulatory Agency (MHRA)
  - The control group is usually the current drug of choice for the proposed indication
  - Always use the oral route of administration
  - Only commence after all animal studies have been completed
  - Are usually performed in patients who are asymptomatic with a terminal disease
- 70 The MHRA:
- Is an independent group of clinicians, clinical pharmacologists, toxicologists, pathologists and others who advise the drug licensing authority
  - Is financed directly by the pharmaceutical industry
  - Considers the quality, safety and efficacy of medicinal products
  - Considers the investigation, monitoring and response to adverse reactions once a drug has been licensed
  - Appoints the committees on ethical practice, which assess drug trials
- 71 The following adverse reactions should be reported to the MHRA using the yellow card system:
- A transient mild skin rash in a patient taking a new non-steroidal anti-inflammatory drug (NSAID) marked with a 'black triangle' in the *British National Formulary (BNF)*
  - Aggravation of asthma in a known asthmatic with the drug involved in question 'a' above
  - A convulsion following pertussis vaccination
  - Acute anaphylactic shock leading to death following intravenous benzylpenicillin
  - Fatal agranulocytosis associated with clozapine

- 72** The following licensed drugs are produced by insertion of human genes into bacterial, yeast or mammalian cell lines:
- a) Human insulin
  - b) Growth hormone
  - c) Factor VII
  - d) Erythropoietin
  - e) Interferon

**Answers: see pages 19–33**

## EXTENDED MATCHING QUESTIONS

### 73 PHARMACODYNAMICS

<b>A</b>	Omeprazole	<b>F</b>	Atenolol
<b>B</b>	Clopidogrel	<b>G</b>	Dobutamine
<b>C</b>	Morphine	<b>H</b>	Warfarin
<b>D</b>	Glucagon	<b>I</b>	Magnesium trisilicate
<b>E</b>	Fluoxetine	<b>J</b>	Insulin

Select the drug that causes the pharmacodynamic effect described below:

- 1 Prolongation of prothrombin time
- 2 Reduction in blood glucose
- 3 Reduction in exercise-induced increase in heart rate
- 4 Pupil constriction
- 5 Inhibition of gastric acid secretion

### 74 PHARMACOKINETICS

<b>A</b>	Prednisolone	<b>F</b>	Metoprolol
<b>B</b>	Amiodarone	<b>G</b>	Simvastatin
<b>C</b>	Carbamazepine	<b>H</b>	Paracetamol
<b>D</b>	Lithium	<b>I</b>	Gentamicin
<b>E</b>	Enalapril	<b>J</b>	Bendroflumethiazide

Choose the drug from the list above which is a good example for the pharmacokinetic characteristics listed below:

- 1 Absorption into the systemic circulation following oral administration is minimal
- 2 The mean elimination half-life is greater than 28 days in someone with normal hepatic and renal function
- 3 Is a prodrug which is hydrolysed to its active metabolite
- 4 Induces its own metabolism such that plasma concentrations may reduce significantly on repeated dosing
- 5 Undergoes active tubular reabsorption

**75 PHARMACOGENETICS**

<b>A</b>	Warfarin	<b>F</b>	Sildenafil
<b>B</b>	Digoxin	<b>G</b>	Suxamethonium
<b>C</b>	Omeprazole	<b>H</b>	Isoniazid
<b>D</b>	Cefuroxime	<b>I</b>	Heparin
<b>E</b>	Fluconazole	<b>J</b>	Codeine

Match the drug from the above list whose metabolism is most affected by the enzyme genetic polymorphism below:

- 1 CYP2D6
- 2 CYP2C9
- 3 *N*-Acetyltransferase
- 4 Pseudocholinesterase
- 5 CYP2C19

**76 ABSORPTION AND ROUTE OF ADMINISTRATION**

<b>A</b>	Digoxin tablets	<b>F</b>	Levodopa
<b>B</b>	Intravenous insulin	<b>G</b>	Prednisolone
<b>C</b>	Glyceryl trinitrate	<b>H</b>	Methotrexate
<b>D</b>	Aspirin preparations	<b>I</b>	Diltiazem preparations
<b>E</b>	Simvastatin preparations	<b>J</b>	Rectal diazepam

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Unsuitable for generic substitution
- 2 Bioavailability is 100 per cent
- 3 Prodrug
- 4 Sublingual administration circumvents extensive presystemic metabolism
- 5 Intrathecal injection is used in childhood leukaemia because of poor penetration of the blood–brain barrier

**77 DRUG METABOLISM**

<b>A</b>	Azathioprine	<b>F</b>	Rimonabant
<b>B</b>	Irinotecan	<b>G</b>	Midazolam
<b>C</b>	Clozapine	<b>H</b>	Amoxicillin
<b>D</b>	Dalteparin	<b>I</b>	Isoniazid
<b>E</b>	Phenylephrine	<b>J</b>	Warfarin

Choose the drug from the list above which is significantly affected by the enzyme below:

- 1 Monoamine oxidase
- 2 CYP1A2
- 3 CYP3A4
- 4 Uridine diphosphoglucuronyl transferase (UGT1A1)
- 5 Thiopurine methyltransferase (TPMT)

**78 RENAL ELIMINATION**

<b>A</b>	Clarithromycin	<b>F</b>	Lithium
<b>B</b>	Para-aminohippuric acid	<b>G</b>	Gentamicin
<b>C</b>	Probenecid	<b>H</b>	Senna
<b>D</b>	Salicylate	<b>I</b>	Thyroxine
<b>E</b>	Atorvastatin	<b>J</b>	Orlistat

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Depends mainly on renal elimination
- 2 Competes for organic anion transport (OAT)
- 3 Excretion is enhanced by high urinary pH
- 4 Shares a proximal tubular transporter with Na<sup>+</sup>
- 5 Is used to measure renal plasma flow

**79 RENAL TRACT**

<b>A</b>	Sildenafil	<b>F</b>	Acetazolamide
<b>B</b>	Finasteride	<b>G</b>	Bendroflumethiazide
<b>C</b>	Furosemide	<b>H</b>	Eplerenone
<b>D</b>	Oxybutinin	<b>I</b>	Desmopressin
<b>E</b>	Spironolactone	<b>J</b>	Tamsulosin

Link each of 1 to 5 below with the most appropriate drug from A to J:

- 1 Causes proximal renal tubular acidosis (RTA)
- 2 Oestrogen-related adverse effects
- 3 Blocks distal tubular Na<sup>+</sup>/Cl<sup>-</sup> reabsorption
- 4 Enhances ototoxicity of gentamicin
- 5 Adverse interaction with glyceryl trinitrate

**80 ADVERSE DRUG REACTIONS**

<b>A</b>	Gentamicin	<b>F</b>	Isoniazid
<b>B</b>	Amoxicillin	<b>G</b>	Spironolactone
<b>C</b>	Simvastatin	<b>H</b>	Clarithromycin
<b>D</b>	Prednisolone	<b>I</b>	Fluoxetine
<b>E</b>	Salbutamol	<b>J</b>	Flupentixol

For each adverse drug reaction match a likely causative drug:

- 1 Gynaecomastia
- 2 Osteoporosis
- 3 Myositis
- 4 SLE-like syndrome
- 5 Tardive dyskinesia



**81 MONOCLONAL ANTIBODIES**

<b>A</b>	Infliximab	<b>F</b>	Abciximab
<b>B</b>	Bevacizumab	<b>G</b>	Omalizumab
<b>C</b>	Basilixumab	<b>H</b>	Alemtuzumab
<b>D</b>	Anti-D (Rh) immunoglobulin	<b>I</b>	Rituximab
<b>E</b>	Natalizumab	<b>J</b>	Palivizumab

Match the monoclonal antibody with the mode of action described below:

- 1 Binds to respiratory syncytial virus
- 2 Anti IgE
- 3 Anti-tumour necrosis factor alpha (TNF- $\alpha$ )
- 4 Inhibition of vascular endothelial growth factor (VEGF)
- 5 Inhibition of glycoprotein IIb-IIIa

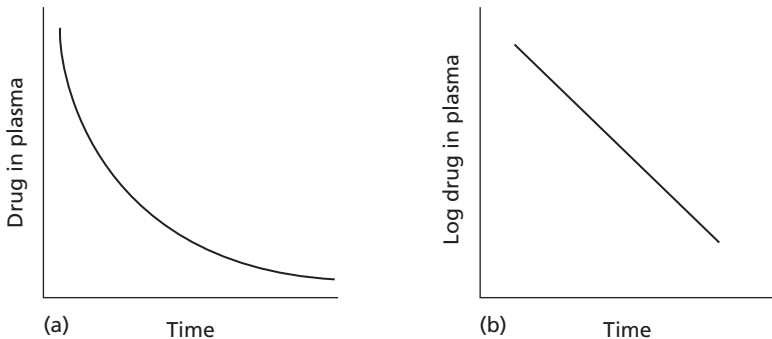
**ANSWERS: see pages 33–38**

## ANSWERS

## MCQ ANSWERS

- 1
  - a) False – Tamoxifen is an anti-oestrogen which binds to the oestrogen receptor in breast tissue and inhibits oestrogen action and is used in breast cancer
  - b) True – Salbutamol is a beta agonist. It is relatively selective for beta<sub>2</sub> effects (bronchodilation) but at higher doses beta<sub>1</sub> effects (tachycardia and tremor) also occur
  - c) True – Morphine mimics the endogenous encephalins
  - d) False – Cetirizine is an antihistamine (H<sub>1</sub> blocker)
  - e) False – Lisinopril is an angiotensin-converting enzyme (ACE) inhibitor
  
- 2
  - a) True – Pyridostigmine is an inhibitor of acetylcholinesterase and is used in myasthenia gravis
  - b) False – Atropine blocks muscarinic receptors
  - c) False – Amlodipine is a calcium channel blocker
  - d) True – Digoxin inhibits Na<sup>+</sup>/K<sup>+</sup> adenosine triphosphatase (ATPase)
  - e) True – Selegiline is a monoamine oxidase B (MAO-B) inhibitor used in Parkinson's disease
  
- 3
  - a) False – Suxamethonium is an agonist that causes a seemingly paradoxical inhibitory effect (neuromuscular blockade) by causing long-lasting depolarization of the neuromuscular junction
  - b) True – Loratidine is a histamine (H<sub>1</sub>) antagonist
  - c) True – Ranitidine is a competitive histamine (H<sub>2</sub>) antagonist
  - d) False – Phenoxybenzamine is an irreversible alpha-receptor antagonist
  - e) True – Naloxone is a competitive antagonist at the opiate mu-receptor
  
- 4
  - a) False
  - b) False
  - c) False
  - d) True – Buprenorphine is a partial agonist at the opiate mu-receptor
  - e) True – Oxprenolol is a partial agonist at the beta-adrenoceptor

- 5 a) True – Magnesium trisilicate is an antacid which neutralizes gastric acid  
 b) True – Mannitol is an osmotic diuretic  
 c) True – Methotrexate is a competitive inhibitor of dihydrofolate reductase and inhibits folate metabolism  
 d) True – Dimercaprol is a chelating agent used in heavy metal poisoning  
 e) False – Sumatriptan is a 5HT<sub>1D</sub> agonist used in migraine
- 6 a) True The magnitude of pharmacological effect usually depends directly on the concentration of drug (or active metabolites) in the vicinity of their receptors. However, some drugs bind to their target irreversibly so their effects outlast their presence at these sites (e.g. alkylating agents at DNA)  
 b) False  
 c) True  
 d) False  
 e) False
- 7 a) True Clearance and not half-life should be used as a measure of the efficiency of drug elimination  
 b) True  
 c) True  
 d) False  
 e) True
- 8 a) True Although the one-compartment model is an oversimplification, once absorption and distribution are complete many drugs do obey first-order elimination kinetics. See Fig. 1  
 b) True  
 c) False  
 d) False  
 e) True



**Fig. 1** One-compartment model. Plasma concentration-time curve following a bolus dose of drug plotted (a) arithmetically, or (b) semi-logarithmically. This drug fits a one-compartment model, i.e. its concentration falls exponentially with time.

- 9 a) True Volume of distribution = dose/ $C_0$ , where  $C_0$  is the plasma concentration at time 0 calculated by extrapolation of the log concentration versus time relationship back to zero  
 b) False  
 c) True

- d) False      following a bolus intravenous injection. 3L is the  
e) True        approximate total plasma volume in an adult
- 10 a) True      – Dopamine  $t_{1/2}$ , 2 minutes  
b) True      – Heparin  $t_{1/2}$ , 0.5–2.5 hours  
c) False     – Amiodarone  $t_{1/2}$ , mean 53 (range 26–107) days  
d) True      – Gentamicin  $t_{1/2}$ , 1.5–2 hours  
e) False     – Diazepam  $t_{1/2}$ , 20–50 hours
- 11 a) True      It takes approximately three half-lives to reach 87.5 per cent  
b) False     of steady state. After four half-lives it is 93.75 per cent and  
c) True      after five half-lives 96.9 per cent  
d) True  
e) True
- 12 a) True      Implications of non-linear elimination kinetics include: the  
b) True      time taken to eliminate 50 per cent of a dose increases with  
c) True      increasing dose, i.e. half-life increases with dose; once the  
d) True      drug elimination process is saturated, a relatively modest  
e) False     increase in dose dramatically increases the amount of drug  
                  in the body see *Textbook of Clinical Pharmacology and  
                  Therapeutics*, Chapter 3
- 13 a) True      Enterohepatic circulation is when a drug is excreted into  
b) False     the bile, reabsorbed from the intestine and returned via the  
c) True      portal system to the liver to be recycled  
d) False  
e) False
- 14 a) True      See *Textbook of Clinical Pharmacology and Therapeutics*,  
b) True      Chapter 4. Although the bioavailability of two preparations  
c) True      may be the same, the kinetics can be very different as seen  
d) True      in some immediate and slow-release drug formulations  
e) True
- 15 a) True      – Levodopa → dopamine  
b) True      – Azathioprine → 6-mercaptopurine  
c) True      – Penciclovir → aciclovir  
d) True      – Sulfasalazine → aminosalicylate + sulfapyridine  
e) True      – Enalapril → enalaprilat
- 16 a) True      – Acarbose is a competitive inhibitor of intestinal  
                   $\alpha$ -glucosidases  
b) False     – Methionine, an antidote to paracetamol poisoning, acts not  
                  in the gastrointestinal tract but predominantly in the liver  
                  where it repletes glutathione which inactivates the toxic  
                  paracetamol metabolite  
c) True      – Orlistat is used to reduce weight and is an inhibitor of  
                  gastrointestinal lipases and this impairs fat absorption

- d) True – Olsalazine delivers 5-aminosalicylate to the colon where it has a local action in inflammatory bowel disease
- e) True – Vancomycin kills toxin-producing *Clostridium difficile*, the cause of pseudomembranous colitis within the bowel
- 17 a) True Most oral drugs are absorbed by passive diffusion in the small bowel. In general low molecular weight, high lipid solubility and lack of charge encourage absorption. Most peptides are broken down enzymatically
- b) False
- c) False
- d) True
- e) False
- 18 a) False Active transport requires specific carrier-mediated energy-consuming mechanisms. Naturally occurring polar nutrients and aliments including sugars, amino acids and vitamins are absorbed by active or facilitated transport mechanisms. Drugs that are analogues of such molecules compete for uptake. Further examples include methotrexate and 5-fluorouracil
- b) False
- c) True
- d) True
- e) True
- 19 a) True Food and drink dilute the drug and can adsorb or otherwise compete with it. Transient increases in hepatic blood flow such as those that occur after a meal may result in greater availability of drug by reducing presystemic hepatic metabolism
- b) True
- c) False
- d) False
- e) False
- 20 a) False Sublingual administration can be an effective means of causing systemic effects, and has potential advantages over oral administration (i.e. when the drug is swallowed) for drugs with pronounced presystemic metabolism, providing direct and rapid access to the systemic circulation bypassing intestine and liver
- b) False
- c) False
- d) True
- e) True
- 21 a) True – Rectal indometacin administered at night is useful in reducing early morning stiffness in rheumatoid arthritis
- b) False – Rectal sulfasalazine is used for its local effect in inflammatory bowel disease
- c) True – Rectal metronidazole is well absorbed (and much less expensive than the intravenous preparation)
- d) False – Glycerin suppositories exert a local effect to stimulate defecation
- e) True – Rectal diazepam is used to control convulsions when venous access is difficult (as may be the case in children)
- 22 a) True – Transdermal GTN is used in ischaemic heart disease
- b) True – Transdermal estradiol is used for hormone replacement therapy in menopausal women
- c) False – Local lidocaine is used for its local anaesthetic action (e.g. for intravenous cannulation in children)

- d) True – Transcutaneous fentanyl may be administered as a patch for the treatment of chronic severe pain
- e) True – Nicotine is used to assist cigarette smokers to abstain
- 23**
- a) True – Exercise and local massage increase the rate of absorption
- b) True – Transport from the injection site is governed by muscle blood flow – deltoid > vastus lateralis > gluteus maximus
- c) True – This avoids the risk of sciatic nerve palsy
- d) False – Up to maximum of 5 mL is acceptable in the buttock of an adult
- e) True – This depot preparation is slowly hydrolysed in muscle to release active drug and is used to improve compliance in schizophrenic patients
- 24**
- a) True – Plus potentially fatal cardiotoxicity if rapid infusion
- b) False
- c) True – An oily emulsion (Diazemuls) reduces this complication
- d) True – Used in hypoglycaemic coma but 20 per cent dextrose usually preferable
- e) False
- 25**
- a) False – Levodopa is decarboxylated to dopamine in central neurons
- b) False – Tyramine is metabolized by monoamine oxidase (MAO) in intestine, liver, kidney and nervous tissue. MAO is a mitochondrial enzyme
- c) True – Metoprolol is extensively metabolized by the CYP450 (CYP2D6) enzyme family
- d) False – Suxamethonium is metabolized by plasma cholinesterase
- e) False – Purines (e.g. 6-mercaptopurine) are metabolized by thiopurine methyl transferase and xanthine oxidase which are non-microsomal enzymes
- 26**
- a) True – Ciclosporin is metabolized by the CYP3A family of isoenzymes
- b) True – Clarithromycin as well as being metabolized by CYP450 enzymes inhibits the metabolism of other drugs subject to CYP3A metabolism (e.g. warfarin, theophylline and terfenadine). Azithromycin does not inhibit CYP3A
- c) True – Phenytoin also induces several CYP450 enzymes
- d) False – Adrenaline is a catecholamine and is metabolized by catechol-O-methyltransferase which is present in the cytosol and MAO in mitochondria
- e) True – Warfarin has a narrow therapeutic index

- 27 a) True – Dapsone is used in leprosy and dermatitis herpetiformis  
b) False – Ciclosporin, an immunosuppressant, is metabolized by CYP3A  
c) False – Gentamicin is eliminated unchanged by the kidney  
d) True – Isoniazid is used to treat tuberculosis  
e) True – Hydralazine is a vasodilator used as an adjunct to other treatment for hypertension. When used alone it causes tachycardia and fluid retention. It can cause an SLE-like syndrome, which is more common in slow acetylators. An intravenous preparation is available to treat hypertensive crises in pregnancy
- 28 a) True – Rifampicin is a broad-spectrum antibiotic used in tuberculosis and Legionnaire's disease  
b) True – Carbamazepine autoinduces its metabolism and is an anticonvulsant  
c) True – St John's wort, a herbal remedy, may be purchased without a prescription. It is a potent, broad-spectrum CYP450 enzyme inducer  
d) True – Phenobarbital is an anticonvulsant  
e) False – Penicillin is predominantly eliminated unchanged in the urine

Drug interactions secondary to hepatic enzyme induction and inhibition are clinically significant when there is a close correlation between plasma concentration and effect, and a steep dose response curve. Regular use of ethanol induces CYP450 metabolism but has minimal effect on its own metabolism, which is predominantly via cytoplasmic alcohol dehydrogenase

- 29 a) True – Fluvoxamine, an antidepressant, is a selective serotonin reuptake inhibitor (SSRI) which inhibits the metabolism of theophylline and warfarin  
b) True – Grapefruit-containing products inhibit CYP3A predominantly in the intestine  
c) False – Digoxin is predominantly eliminated unchanged in the urine  
d) True – Itraconazole is an azole antifungal agent  
e) True – Ciprofloxacin is a fluoroquinolone antibacterial drug
- 30 a) True Presystemic metabolism occurs in the gastrointestinal mucosa and liver; presystemic (first-pass) metabolism  
b) False necessitates high oral doses in comparison with the  
c) False intravenous dose  
d) True  
e) True
- 31 a) True – Aspirin overdose decreases the rate of gastric emptying  
b) True

- c) True
  - d) True – Anticholinergic properties reduce gastro-intestinal motility
  - e) False – Metoclopramide accelerates gastric emptying
- 32**
- a) False – The absorption of thiazides is reduced
  - b) False – The volume of distribution of lidocaine is reduced probably because of decreased tissue perfusion
  - c) True – The distribution volume of furosemide is largely confined to the vascular compartment
  - d) False – Is prolonged predominantly due to decreased hepatic perfusion
  - e) False – Glomerular filtration is reduced in cardiac failure and hence the elimination half-life of gentamicin is prolonged (i.e. not decreased)
- 33**
- a) False – Gastric pH increases
  - b) True – The ratio of unbound:bound phenytoin rises in renal failure. It is the unbound drug which is active and the laboratory assay for phenytoin measures total blood concentration (bound and unbound)
  - c) True – The blood-brain barrier becomes functionally less of a barrier to drug distribution in severe renal failure. This may be the reason for the increased incidence of confusion associated with cimetidine and famotidine in renal failure
  - d) True
  - e) False
- 34**
- a) True
  - b) True
  - c) True
  - d) True
  - e) False
- The kidney is involved to some degree in the elimination of many drugs in the unchanged form and most drug metabolites in humans. High lipid solubility and the un-ionized state favour tubular reabsorption
- 35**
- a) False
  - b) False – But reduce dose; rashes more common
  - c) False – May need very high doses for any diuretic effect
  - d) True – Increased risk of lactic acidosis
  - e) True – Direct nephrotoxicity, anti-anabolic, increases blood urea
- 36**
- a) True
  - b) False
- NSAIDs cause salt and water retention and reduce renal blood flow by inhibition of prostacyclin and prostaglandin E<sub>2</sub> synthesis in patients with renal compromise. This disrupts autoregulation of renal blood flow and GFR thus preventing the normal physiological mechanism which



- ensures preferential perfusion of the functioning kidney.  
NSAIDs are less commonly associated with papillary necrosis or interstitial nephritis
- c) True – Radiographic contrast media cause a transient decrease in GFR. The mechanism is not completely understood
  - d) True – ACE inhibitors, although often effective in treating heart failure and hypertension in patients with renal disease, can impair renal function. They must be avoided in bilateral renal artery stenosis
  - e) True – Can cause acute tubular necrosis and renal tubular acidosis
- 37**
- a) False – Carbimazole is an antithyroid drug. The effective dose is determined by monitoring blood thyroid function tests. Carbimazole should be stopped promptly if there is clinical or laboratory evidence of neutropenia
  - b) False – Warfarin therapy is monitored by measurement of the prothrombin time (INR)
  - c) True – Gentamicin ‘peak’ concentrations (30 minutes after dose) correlate with efficacy, trough concentrations correlate with toxicity. Aminoglycosides are associated with ototoxicity and nephrotoxicity. Extended interval dosing for aminoglycosides uses nomograms of drug concentration related to time post dosing to guide further dosing
  - d) True – Insidious increases in serum lithium concentrations can lead to tremor, diarrhoea, gastrointestinal upsets, reduced conscious level and ultimately convulsions. Thyroid function should also be monitored
  - e) True – Not only does ciclosporin show marked interindividual variability but also compliance is a particular problem in children. Deterioration in renal function post transplant may reflect either graft rejection possibly associated with low ciclosporin concentrations or toxicity from excessive concentrations
- 38**
- a) False
  - b) False
  - c) True
  - d) True
  - e) True
- Most drugs cross the placenta (a cellular membrane) by passive diffusion down a concentration gradient. Lipid solubility enhances transport across membranes and drugs in the un-ionized state are more lipid soluble. The human placenta possesses multiple enzymes, including enzymes that metabolize endogenous compounds and drugs
- 39**
- a) True – The risk of having an abnormal baby is about 10 per cent in mothers drinking 30–60 mL ethanol per day, rising to 40 per cent in chronic alcoholics

- b) True – Warfarin has been associated with nasal hypoplasia and chondrodysplasia when given in the first trimester and with CNS abnormalities and haemorrhagic complications in later pregnancy. Neonatal haemorrhage is difficult to prevent because of the immature enzymes in fetal liver and low stores of vitamin K
- c) True – All retinoic acid derivatives are teratogens. Effective contraception must be used for at least one month before, during, and at least one month after oral treatment with any retinoic acid analogue or derivative
- d) False – The minor analgesic of choice in pregnancy
- e) False – Commonly used to treat urinary tract infection in pregnancy
- 40 a) True – This is of little consequence unless rapid drug absorption/action is required. Vomiting associated with pregnancy occasionally makes oral administration impractical
- b) True – Blood volume in pregnancy increases by one-third
- c) True – Plasma volume increases from 2.5 to 4 L at term and is disproportionate to the expansion in red cell mass so the haematocrit falls
- d) True – Oedema, which at least one-third of women experience during pregnancy, may add up to 8 L to the volume of extracellular water. For water-soluble drugs (which usually have a relatively small volume of distribution) this increases the volume of distribution
- e) False – Metabolism of drugs by the hepatocyte during pregnancy is increased
- 41 a) True Excretion of drugs via the kidney increases because renal plasma flow almost doubles and the GFR increases by
- b) True plasma flow almost doubles and the GFR increases by
- c) True two-thirds during pregnancy, see *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 9
- d) True
- e) True
- 42 a) True
- b) True
- c) False – Minimal experience, animal data discouraging
- d) False – The fetal VIIIth nerve is more sensitive to aminoglycoside toxicity
- e) False – Ribavirin inhibits a wide range of DNA and RNA viruses. It is used by inhalation to treat severe respiratory syncytial virus (RSV) bronchiolitis in children and is used in combination with interferon alfa to treat chronic hepatitis C infection. It is a very potent teratogen in animal models.

- Effective contraception must be ensured for four months after treatment in women and seven months after treatment in men. Condoms must be used if partner of male patient (ribavirin excreted in semen) is pregnant
- 43 a) False Non-drug treatment (reassurance, small frequent meals and advice on posture) should be pursued in the first instance  
b) False  
c) True  
d) False – Misoprostol, an analogue of prostaglandin E<sub>1</sub>, causes abortion  
e) True
- 44 a) True – This is also true for the low molecular weight heparins (which are often the anticoagulants of choice in pregnancy)  
b) False – Warfarin is a teratogen and is associated with a high incidence of haemorrhagic complications in late pregnancy  
c) False  
d) False  
e) False – Pethidine, which is commonly used as an analgesic during delivery, can cause apnoea of the newborn which is reversed with naloxone
- 45 a) False Epilepsy in pregnancy can lead to fetal and maternal morbidity/mortality through convulsions. Although all anticonvulsants are teratogenic, the risk of untreated epilepsy is greater to the mother and fetus than drug-induced teratogenicity. To counteract the risk of neural tube defects, adequate folate supplements are advised  
b) True  
c) True  
d) True  
e) False
- 46 a) False If treatment is initiated during pregnancy it is appropriate to use methyldopa which has the longest record of use and follow-up in children born to mothers following treatment. Beta blockers are contraindicated in asthma.  
b) False  
c) False  
d) False  
e) True ACE inhibitors are teratogens. Although not licensed for use in pregnancy, nifedipine appears effective and relatively well tolerated. See *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 9
- 47 a) False – Commonly used to treat asthma and occasionally premature labour  
b) False – Minimal problems when given by inhalation or in short courses (e.g. to help immature fetal lung) and although cleft palate and congenital cataract have been attributed to large systemic doses of corticosteroids the benefit of treatment usually outweighs the risk

- c) False – Although there is an increased risk of spontaneous abortion associated with general anaesthesia a causal link is unproven and in most circumstances failure to operate would have dramatically increased the risk to mother and fetus
- d) False – Falciparum malaria has a high mortality in pregnancy
- e) False – Sucralfate is not absorbed
- 48 a) True Neonates are not miniature adults in terms of drug handling because of differences in body constitution, drug absorption, distribution, metabolism, excretion and sensitivity to adverse reactions, see *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 10
- b) True
- c) True
- c) True
- d) True
- e) True
- 49 a) True – Significant concentration in breast milk and there is a theoretical risk from iodine release
- b) False – Minimal concentration in breast milk
- c) True – High concentration in breast milk, animal experiments suggest damage to growing joints
- d) True
- e) False
- 50 a) False – But may cause diarrhoea in infant
- b) True
- c) True
- d) False
- e) False – But gives milk an unpleasant taste
- 51 a) True The total dose of drug in breast milk ingested by the infant is usually too small to cause problems (with some notable exceptions, see Table 1). The infant should be monitored clinically if beta-adrenoceptor antagonists are prescribed to the mother. Milk is mildly acid, so weak bases accumulate in it
- b) True
- c) True
- d) True
- e) False
- 52 a) True
- b) True – A 5- to 10-day course of systemic corticosteroids is often sufficient
- c) False – Potentially fatal
- d) False
- e) False – Potentially fatal
- 53 a) True – See *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 11
- b) True
- c) False – One reason why plasma creatinine is a less reliable indicator of renal function in the elderly is that endogenous creatinine production is reduced

**Table 1** Some drugs to be avoided during breastfeeding

---

Amiodarone
Aspirin
Benzodiazepines
Chloramphenicol
Ciclosporin
Ciprofloxacin
Cocaine
Combined oral contraceptives
Cytotoxics
Ergotamine
Octreotide
Stimulant laxatives (senna)
Sulfonylureas
Thiazide diuretics
Vitamin A/retinoid analogues

---

- d) True
- e) True

- 54 a) False – Gliclazide, a short-acting sulfonylurea, is commonly prescribed to elderly diabetics whose blood glucose is inadequately controlled by diet alone
- b) True
  - c) True – Morphine increases bladder neck sphincter tone
  - d) True – Amitriptyline, a sedative tricyclic antidepressant, also has anticholinergic effects
  - e) False
- 55 a) True – Related to the decrease in GFR associated with ageing
- b) True – Related to the decrease in GFR associated with ageing
  - c) True – Related to the decrease in GFR associated with ageing
  - d) True – Related to the decrease in GFR associated with ageing reducing the clearance of the active morphine glucuronide
  - e) True – Due to the increase in volume of distribution and probably also reduced metabolism
- 56 a) False
- b) False – Finasteride is a specific inhibitor of the enzyme  $5\alpha$ -reductase which metabolizes testosterone into the more potent androgen, dihydrotestosterone
  - c) False

- d) False – Doxycycline is a unique tetracycline in that its pharmacokinetics are not affected by renal dysfunction
- e) False – Has fewer anticholinergic effects than most antidepressants
- 57 a) True
- b) True – Cholestatic jaundice may occur up to several weeks after treatment with flucloxacillin
- c) True
- d) True – Impairment of cardiovascular reflexes to erect posture in the elderly is exaggerated by alpha blockers
- e) True
- 58 a) True – See *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 12
- b) False
- c) True
- d) True
- e) True
- 59 a) True – Prolonged corticosteroid therapy leads to adrenal atrophy and insufficiency. Risks are minimized by the use of steroid cards, using systemic corticosteroids for the minimum period necessary and gradual withdrawal after prolonged therapy. Atrophy may persist for years after stopping corticosteroid therapy and may only be revealed during 'stress' (e.g. acute illness/surgery)
- b) True – Rebound hypertension
- c) True – Benzodiazepines cause psychological and physical addiction
- d) True
- e) False
- 60 a) False – Oral contraceptive use is associated with thromboembolism
- b) True
- c) True – Also associated with myocardial infarction and ischaemia to other organs
- d) True
- e) False – Corticosteroid therapy, if prolonged, is associated with osteoporosis. The use of antiepileptic drugs such as phenytoin and carbamazepine affect vitamin D metabolism and can lead to osteomalacia
- 61 a) True – Life-saving treatment is intramuscular adrenaline
- b) False – A type II reaction
- c) False – A type III reaction
- d) False – A type IV reaction
- e) False

- 62 a) True – Also associated with acne, coarse facies, hirsutism and toxic epidermal necrolysis  
b) False  
c) False  
d) False  
e) True – Usually due to the sulphamethoxazole component but may also be caused by trimethoprim
- 63 a) True – See *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 12  
b) True  
c) True  
d) True  
e) False
- 64 a) True – Inactivation of penicillin  
b) True – Precipitates  
c) True – Precipitates  
d) False  
e) False
- 65 a) False Approximately 45 per cent of the white population are slow acetylators. Examples of drugs acetylated include:  
b) False isoniazid, hydralazine, phenelzine, dapsone and  
c) False procainamide. The usual 'marker' is the monoacetyl  
d) True dapsone metabolite: dapsone ratio in the plasma  
e) True – Isoniazid-induced peripheral neuropathy can be prevented by prophylactic use of pyridoxine
- 66 a) True The gene for G6PD is located on the X chromosome. G6PD  
b) True deficiency is more common in people from Mediterranean  
c) True countries  
d) True  
e) True
- 67 a) False The acute porphyrias are due to hereditary enzyme defects  
b) True in haem biosynthesis and may be precipitated by many  
c) True drugs (see list in *BNF*), especially inducers of CYP450  
d) True enzymes  
e) True
- 68 a) False The usual response to a single intravenous dose of  
b) False suxamethonium is muscular paralysis which lasts for about  
c) False 6 minutes. The effect is brief due to hydrolysis of  
d) True suxamethonium by plasma pseudocholinesterase.  
e) False Approximately 1 in 2500 patients have abnormal  
pseudocholinesterase which may result in prolonged  
paralysis for 2 hours. Inheritance is Mendelian recessive

- 69 a) True  
 b) False – Placebo is the usual control  
 c) False  
 d) False  
 e) False – Phase 1 studies are usually performed in healthy male adults aged 18–35 years
- 70 a) False The MHRA is the regulatory review board of the UK who advise when certificates to perform clinical trials should be issued to pharmaceutical companies and advise, following review of all the data from a submission, on the granting of a product licence which will allow the company to market the drug  
 b) False  
 c) True  
 d) True  
 e) False
- 71 a) True See *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 12  
 b) True  
 c) True  
 d) True  
 e) True
- 72 a) True The production of human proteins using recombinant DNA/RNA technology not only produces large quantities of natural human proteins but also minimizes the risk of blood-borne viral infection such as hepatitis B and C and HIV  
 b) True  
 c) True  
 d) True  
 e) True

## EMQ ANSWERS

### 73 PHARMACODYNAMICS

Pharmacodynamics is the study of the effects of drugs on biological processes.

- 1 H Warfarin prolongs the prothrombin time and is the most commonly prescribed oral anticoagulant. It is a vitamin K antagonist. The onset of action is at least 48–72 hours after initiation of treatment following a loading dose. There is wide variability in drug response related to genetics, hepatic function, drug and alcohol interactions. Monitoring of treatment through measurement of INR (international normalized ratio) calculated from the prothrombin time is essential. Prolongation of INR predisposes to haemorrhage.
- 2 J Insulin controls the metabolic disposition of carbohydrate, fats and amino acids. Insulin is inactivated by gastrointestinal enzymes, hence administration is by injection or occasionally by inhalation. Excess insulin causes hypoglycaemia.
- 3 F Atenolol is one of the many beta-adrenoceptor blocking drugs available. Indications include hypertension and angina.



Beta-adrenoreceptor blockers are contraindicated in second- and third-degree heart block and asthma.

- 4 C Morphine, an opioid, narcotic analgesic causes pupillary constriction by stimulating  $\mu$ -receptors in the Edinger–Westphal nucleus in the mid-brain. Whilst this action is not of therapeutic importance it provides a useful diagnostic sign in narcotic overdose or recent exposure.
- 5 A Omeprazole inhibits gastric acid secretion by blockade of the  $H^+/K^+$  ATPase enzyme system of the gastric parietal cells. Omeprazole and other proton pump inhibitors are indicated in the management of peptic ulcers, dyspepsia and gastro-oesophageal reflux. In combination with antibacterial drugs proton pump inhibitors are used in the eradication of *Helicobacter pylori*.

#### 74 PHARMACOKINETICS

Pharmacokinetics is defined as the study of the time-course of drug absorption, distribution, metabolism and excretion.

- 1 I The absorption of gentamicin (and other aminoglycoside antibacterial drugs) following oral administration is minimal. Hence gentamicin is used by injection (intramuscular and intravenous) and topically.
- 2 B Amiodarone, an effective antidysrhythmic drug, is only slowly eliminated by the liver, with a mean elimination half-life of 53 days. Hence effects may continue for several months after dosing has ceased.
- 3 E Enalapril is hydrolysed to its active metabolite, enalaprilat, which is an ACE inhibitor.
- 4 C Carbamazepine, an antiepileptic, induces its own metabolism such that plasma concentrations reduce significantly on repeated dosing. It has an elimination half-life of 25–60 hours following a single dose, but approximately 10 hours after repeated dosing.
- 5 D Lithium undergoes active tubular reabsorption. It mimics sodium on the proximal tubular sodium ion reabsorption mechanism, hence co-administration of thiazides prolongs the half-life of lithium and predisposes to toxicity.

#### 75 PHARMACOGENETICS

Pharmacogenetics is the study of variation in drug responses under hereditary control.

- 1 J Approximately 70 polymorphic variants of CYP2D6 have been defined in humans. CYP2D6 enzyme is 'deficient' in about 7–10 per cent of the UK white population. Drugs affected include codeine (minimal analgesia as poor metabolizers convert little to morphine),

dextrometorphan, metoprolol, some SSRIs (e.g. fluoxetine) and some antipsychotics (e.g. haloperidol).

- 2 **A** Drugs metabolized by CYP2C9 are eliminated more slowly by poor metabolizers who are more susceptible to dose-related adverse drug reactions (ADRs), e.g. warfarin, losartan and sulphonylureas.
- 3 **H** Slow and rapid acetylator status are inherited in a simple Mendelian manner, rapid metabolism is autosomal dominant. Drugs that are *N*-acetylated include isoniazid, dapsone, procainamide and hydralazine.
- 4 **G** Pseudocholinesterase hydrolyses suxamethonium, a muscle relaxant used for short procedures such as intubation since muscle paralysis lasts only 3–6 minutes. There is an autosomal recessive enzyme variant (1:2500 of the population) which is associated with prolonged paralysis requiring artificial ventilation for 2 hours or longer after an intravenous dose. Heterozygotes are unaffected.
- 5 **C** CYP2C19 polymorphism affects metabolism of some proton pump inhibitors e.g. omeprazole and lansoprazole. Poor metabolizers obtain greater acid suppression and improved healing rates. Other substrates for CYP2C19 include certain tricyclic and SSR1 antidepressants and R-warfarin. Warfarin is primarily a CYP2C9 substrate.

## **76 ABSORPTION AND ROUTE OF ADMINISTRATION**

Drug absorption, and hence the route by which a particular drug may usefully be administered, is largely determined by the rate and extent of penetration of biological phospholipid membranes.

- 1 **I** Generic substitution seldom causes clinical problems but slow-release preparations of diltiazem, a calcium channel blocker, are an exception.
- 2 **B** When a drug is administered intravenously its bioavailability is by definition 100 per cent.
- 3 **F** Levodopa (unlike dopamine) can enter nerve terminals in the basal ganglia where it undergoes decarboxylation to form dopamine, partially correcting the nigrostriatal dopamine deficiency present in Parkinson's disease.
- 4 **C** Glyceryl trinitrate is used most commonly to relieve and prevent anginal pain.
- 5 **H** Intrathecal injection predisposes to neurotoxicity. This route should never be used without expert training.

**77 DRUG METABOLISM**

Drug metabolism is one of the primary mechanisms by which drugs are inactivated. However, drug metabolism in certain cases leads to increased drug activity, e.g. activation of prodrugs.

- 1 E Phenylephrine, an indirectly acting sympathomimetic, may cause a hypertensive crisis if taken by a patient on an MAO inhibitor.
- 2 C Clozapine is metabolized by CYP1A2, which is inhibited by fluvoxamine (SSRI antidepressant).
- 3 G Midazolam, a short-acting benzodiazepine, is often used as a 'probe' in studies to determine if a drug induces or inhibits CYP3A4 metabolism.
- 4 B Patients with Gilbert's disease have unconjugated hyperbilirubinaemia caused by an inherited deficiency of UGT1A1. Fasting and oestrogens may aggravate jaundice. Gilbert's disease is almost always irrelevant to drug metabolism with the exception of the active metabolite of irinotecan (used in metastatic colon cancer), whose toxicity is increased in Gilbert's disease.
- 5 A 6-Mercaptopurine (6-MP) is the active metabolite of azathioprine. Bone marrow suppression is more likely in those deficient in thiopurine methyltransferase (0.3 per cent of white population).

**78 RENAL ELIMINATION**

The kidneys are involved in the elimination of virtually every drug or drug metabolite.

- 1 G Gentamicin, an aminoglycoside antibacterial drug with a low therapeutic index, is predominantly eliminated via the kidney.
- 2 C Probenecid competes for the proximal tubule active secretion of organic anions hence reduces the tubular secretion of penicillin and methotrexate.
- 3 D Urinary alkalinization enhances the excretion of salicylate reducing toxicity after salicylate/ aspirin overdose.
- 4 F Hence salt depletion which causes increased proximal tubular sodium ion reabsorption causes lithium toxicity unless the dose of lithium is reduced.
- 5 B Para-aminohippuric acid is excreted so efficiently that it is completely extracted from the renal plasma in a single pass through the kidney.

**79 RENAL TRACT**

- 1 F Acetazolamide is a carbonic anhydrase inhibitor that reduces aqueous humour production which is beneficial in glaucoma. It is a weak

diuretic and has a specific role in treating epilepsy associated with menstruation.

- 2 E Spironolactone's active metabolite, canrenone, is an aldosterone antagonist, which also acts on sex hormone receptors and can cause gynaecomastia, menstrual disorders and testicular atrophy.
- 3 G Bendroflumethiazide blocks tubular  $\text{Na}^+/\text{Cl}^-$  reabsorption.
- 4 C Furosemide and other loop diuretics enhance aminoglycoside ototoxicity through their action on  $\text{Na}^+/\text{K}^+/\text{2Cl}^-$  co-transport in the inner ear.
- 5 A Sildenafil inhibits phosphodiesterase V that inactivates cGMP; glyceryl trinitrate activates guanylate cyclase and the combination can cause severe hypotension.

## **80 ADVERSE DRUG REACTIONS**

Adverse drug reactions are unwanted effects caused by normal therapeutic doses of drugs.

- 1 G Spironolactone acts as a potassium-sparing diuretic through its antagonism of aldosterone, but also acts on progesterone and androgen receptors.
- 2 D Osteoporosis is an important adverse effect with chronic use of prednisolone and all other glucocorticosteroids (diabetes is another).
- 3 C Myositis is a dose-related adverse effect associated with statins and fibrates.
- 4 F SLE-like syndrome is associated with isoniazid, procainamide, hydralazine, chlorpromazine and anticonvulsants. It resembles SLE together with a positive antinuclear factor test. It is dose related. These drugs may act as haptens, combining with DNA and forming antigens. The symptoms resolve (sometimes slowly) on drug withdrawal.
- 5 J Tardive dyskinesia is a troublesome adverse effect associated predominantly with 'traditional'  $\text{D}_2$ -blocking antipsychotic drugs, which follows months or years of continued treatment.

## **81 MONOCLONAL ANTIBODIES**

Monoclonal antibodies are highly specific antibodies derived from one class of cells which recognize one antigen. Receptor affinity is high and toxicity is likely to be due to exaggerated pharmacological action or hypersensitivity.

- 1 J Palivizumab (Synagis<sup>®</sup>) is used in 'at-risk' infants to prevent serious lower respiratory-tract disease caused by RSV. At-risk infants includes those with serious congenital heart disease.

- 2 G** Omalizumab (Xolair<sup>®</sup>) binds to IgE and can be used as additional therapy in asthmatics with proven IgE sensitivity to inhaled allergens whose asthma is inadequately controlled by high-dose glucocorticosteroids (systemic and inhaled); optimal bronchodilator therapy (short- and long-acting beta-2 agonists plus anticholinergics) plus oral leukotriene antagonists.
- 3 A** Infliximab (Remicade<sup>®</sup>) inhibits TNF activity and is used in rheumatoid arthritis and psoriatic arthritis in adults who have failed to respond to at least two other disease-modifying agents (e.g. penicillamine and methotrexate). It can also be used in inflammatory bowel disease.
- 4 B** Bevacizumab (Avastin<sup>®</sup>) inhibits VEGF. It is a first-line treatment for metastatic colorectal cancer in combination with 5 fluorouracil plus folinic acid plus irinotecan (FOLFIRI).
- 5 F** Abciximab (ReoPro<sup>®</sup>) binds to platelet IIb/IIIa receptors blocking fibrinogen binding. It is used as an adjunct to heparin and aspirin in high-risk patients undergoing percutaneous coronary intervention. It can be used once only to avoid thrombocytopenia.

# NERVOUS SYSTEM

## MULTIPLE CHOICE QUESTIONS

- 82 Benzodiazepines:
- a) Potentiate the sedative effects of alcohol
  - b) Should only be used as hypnotics for a maximum of 2–4 weeks
  - c) Suppress rapid eye movement (REM) sleep
  - d) Act by binding to the gamma-aminobutyric acid (GABA) receptor–chloride channel complex and facilitate the opening of the channel in the presence of GABA
  - e) Are anxiolytic
- 83 Benzodiazepine dependence and withdrawal syndrome:
- a) Benzodiazepine withdrawal symptoms should be treated with buspirone
  - b) Fits can occur in the first week after withdrawal
  - c) The full withdrawal picture usually appears after an interval of 3–8 weeks
  - d) Perceptual distortions are characteristic
  - e) Shorter-acting benzodiazepines are less likely to cause dependence and should be substituted for long-acting benzodiazepines when withdrawing a patient from benzodiazepines
- 84 Diazepam:
- a) Has a half-life of less than 20 hours
  - b) Can cause anterograde amnesia
  - c) Is effective in terminating acute dystonia caused by metoclopramide
  - d) Never causes fatal overdose
  - e) The major site of metabolism is the liver
- 85 Temazepam:
- a) Has a shorter half-life than diazepam
  - b) Potentiates the effects of alcohol
  - c) Causes no 'hangover' effect 10 hours post dosing
  - d) Is not addictive
  - e) Is more potent than lorazepam

- 86** Clomethiazole (chlormethiazole):
- a) Is not absorbed orally
  - b) Has a half-life of approximately 10 hours
  - c) In cirrhosis the bioavailability is increased about 10-fold
  - d) High doses cause cardiovascular and respiratory depression
  - e) Is antagonized by ethanol
- 87** Promethazine:
- a) Is a GABA agonist
  - b) Is available without prescription
  - c) Causes dry mouth, constipation and reduced sweating
  - d) Liver failure is an absolute contraindication
  - e) May cause hallucinations
- 88** Zopiclone:
- a) Is an ultra short-acting benzodiazepine
  - b) Is the hypnotic of choice in a breastfeeding mother
  - c) Is a more effective anticonvulsant than clonazepam
  - d) Is associated with drug dependence
  - e) Can cause confusion
- 89** The following drugs may mimic some of the common clinical features of schizophrenia:
- a) Levodopa
  - b) Salbutamol
  - c) LSD
  - d) Diamorphine
  - e) Methylendioxyethylamphetamine (MDMA, ecstasy)
- 90** Blockade of central  $D_2$  receptors:
- a) Parallels the clinical efficacy of the conventional antipsychotic drugs such as chlorpromazine and haloperidol
  - b) Induces extrapyramidal effects
  - c) Repeated administration of  $D_2$  antagonists causes a reduction in  $D_2$  agonist sensitivity due to an increase in abundance of these receptors
  - d) Repeated administration of  $D_2$  antagonists may lead to tardive dyskinesia
  - e) Causes a decrease in cardiac output
- 91** Adverse effects associated with phenothiazines include:
- a) Dry mouth
  - b) Blurred vision
  - c) Postural hypotension
  - d) Impaired temperature control
  - e) Jaundice

- 92 Chlorpromazine:
- a) Is the first-line treatment for malignant neuroleptic syndrome
  - b) Has a low volume of distribution (approx. 100 mL/kg)
  - c) Is predominantly eliminated via the kidneys as unchanged chlorpromazine
  - d) Of the chlorpromazine in plasma, 90–95 per cent is bound to plasma proteins
  - e) Usually once-daily administration is adequate
- 93 Flupentixol:
- a) Is particularly effective in mania
  - b) May be given once every 2–4 weeks via the intramuscular route for chronic schizophrenia
  - c) Is less sedating than chlorpromazine
  - d) Is more prone than chlorpromazine to produce extrapyramidal toxicity
  - e) Should not be used in patients with porphyria
- 94 Clozapine:
- a) Has weak D<sub>2</sub>-blocking activity
  - b) Is effective in up to 60 per cent of patients who have not responded to phenothiazines
  - c) Is effective against negative as well as positive symptoms
  - d) Rarely causes tardive dyskinesia
  - e) Causes blood dyscrasias more commonly than most antipsychotics
- 95 Newer atypical drugs such as olanzapine and risperidone:
- a) Are less effective than traditional antipsychotic drugs against the negative symptoms of schizophrenia
  - b) Are associated with weight loss
  - c) Bind irreversibly to D<sub>2</sub> receptors
  - d) Are associated with an increased incidence of stroke in elderly patients with dementia
  - e) Are virtually free from extrapyramidal side-effects at standard doses
- 96 The following drugs raise synaptic and/or total brain monoamines:
- a) Cocaine
  - b) Amitriptyline
  - c) Imipramine
  - d) Phenelzine
  - e) Amphetamine



**97** Tricyclic antidepressants:

- a) Are more effective in endogenous rather than reactive depression
- b) Are particularly effective when the depression is associated with psychomotor and physiological changes
- c) Onset of therapeutic action is approximately two weeks after starting therapy
- d) Are effective in the management of panic disorder
- e) Are used for the treatment of nocturnal enuresis in children

**98** Antidepressants with sedative properties include:

- a) Amitriptyline
- b) Dosulepin
- c) Citalopram
- d) Paroxetine
- e) Sertraline

**99** The following are consistent with tricyclic antidepressant overdose:

- a) Dilated pupils
- b) Hyperreflexia
- c) Sinus tachycardia
- d) Widened QRS on the ECG
- e) Convulsions

**100** Amitriptyline:

- a) Is highly lipid soluble
- b) Is highly protein bound
- c) Has a low volume of distribution (approx. 100 mL/kg body weight)
- d) Blocks uptake of monoamines into cerebral and other neurons
- e) Delays gastric emptying

**101** Fluvoxamine:

- a) Inhibits monoamine oxidase (MAO)
- b) Is a powerful anticholinergic agent
- c) Is less sedative than trazodone
- d) Inhibits a CYP450 isoenzyme
- e) During therapy the blood count should be monitored weekly

**102** Fluoxetine:

- a) Selectively blocks neuronal uptake of noradrenaline
- b) Is more cardiotoxic than imipramine
- c) Is less sedative than amitriptyline
- d) Is associated with nausea and dyspepsia
- e) Has a short elimination half-life of 1–2 hours

**103** Phenelzine:

- a) Is a reversible selective inhibitor of MAO-B
- b) Onset of therapeutic effect is usually within one week
- c) Is ineffective if used alone in the treatment of depression
- d) Is sometimes effective in reducing hypochondriacal and hysterical symptoms
- e) Is more likely to cause a hypertensive crisis when an indirectly acting sympathomimetic (e.g. ephedrine) is given concurrently rather than a directly acting sympathomimetic (e.g. adrenaline combined with local anaesthetic)

**104** Moclobemide:

- a) Is a reversible selective inhibitor of MAO-A
- b) Is effective adjunct therapy in Parkinson's disease
- c) Has a longer duration of MAO inhibition compared to phenelzine after stopping therapy
- d) Causes dry mouth in over 50 per cent of patients
- e) Is less likely than phenelzine to cause a food (tyramine) interaction

**105** The following foodstuffs can cause a hypertensive/hyperthermic reaction during non-selective MAO inhibitor therapy:

- a) Cheese
- b) Yoghurt
- c) Beer
- d) Marmite
- e) Grouse

**106** Lithium toxicity can be precipitated by:

- a) Sodium depletion
- b) Thiazide therapy
- c) Angiotensin-converting enzyme (ACE) inhibitors
- d) Non-steroidal anti-inflammatory drugs (NSAIDs)
- e) Atenolol

**107** Tricyclic antidepressant therapy should not be started within 14 days of therapy with:

- a) Citalopram
- b) Isocarboxazid
- c) Tranylcypromine
- d) Moclobemide
- e) St John's wort

- 108** Muscarinic antagonists (e.g. procyclidine):
- a) Are predominantly used in parkinsonism caused by antipsychotic drugs
  - b) Are least effective in the treatment of tremor
  - c) Are ineffective in the management of post-encephalitic parkinsonism
  - d) Must not be used with levodopa
  - e) May cause confusion in the elderly
- 109** The following enhance central dopaminergic activity:
- a) Inhibition of MAO-B
  - b) Bromocriptine
  - c) Apomorphine
  - d) Haloperidol
  - e) Intravenous dopamine
- 110** Levodopa:
- a) Can enter nerve terminals
  - b) Is oxidized by MAO to form dopamine
  - c) Is antagonized by ropinirole
  - d) Metabolism is reduced by entacapone
  - e) May cause dystonic reactions
- 111** Levodopa:
- a) Is the amino acid precursor of dopamine
  - b) Improves bradykinesia and rigidity more than tremor
  - c) Levodopa therapy should be initiated with a loading dose
  - d) Should be taken on an empty stomach
  - e) Involuntary movements and psychiatric complications are common unwanted effects
- 112** Bromocriptine:
- a) Stimulates release of endogenous dopamine
  - b) Stimulates postsynaptic D<sub>2</sub> receptors
  - c) Should not be prescribed until there is inadequate response to levodopa
  - d) Has an antiemetic action
  - e) Inhibits the release of prolactin from the pituitary
- 113** Selegiline:
- a) Selectively inhibits MAO-B
  - b) The most common adverse effect is postural hypotension
  - c) Is principally eliminated unchanged in the urine
  - d) Cannot be prescribed concurrently with levodopa
  - e) Cannot be prescribed concurrently with amantadine

- 114** The following drugs reduce spasticity in patients with upper motor neuron lesions:
- Donepezil
  - Riluzole
  - Diazepam
  - Baclofen
  - Dantrolene
- 115** Tardive dyskinesia:
- Occurs in about 15 per cent of patients treated with phenothiazines for over 2 years
  - Stopping treatment results in slow improvement in approximately 40 per cent of patients
  - Dyskinesia may initially worsen after discontinuing treatment
  - Consists of rapid involuntary movements of the limbs
  - Is treated with botulinum toxin A
- 116** In myasthenia gravis:
- Therapy is usually initiated with neostigmine
  - Thymectomy may be beneficial
  - Corticosteroids and azathioprine reduce circulating T cells
  - There is increased sensitivity to atenolol
  - Corticosteroids can worsen or improve weakness
- 117** Severe weakness in a patient with myasthenia gravis may be potentiated by:
- Spontaneous deterioration in the natural history of the disease
  - Excessive anticholinesterase drug
  - Acute infection
  - Aminoglycosides
  - Fluoxetine
- 118** In Alzheimer's disease:
- Donepezil can slow down the progression of mild and moderate Alzheimer's disease
  - Rivastigmine acts through reversible inhibition of acetylcholinesterase
  - Adverse effects associated with donepezil, rivastigmine and galantamine include nausea, vomiting and diarrhoea
  - Overdose with donepezil is likely to be associated with tachycardia
  - Associated depression may be treated with a selective serotonin reuptake inhibitor

- 119 The following drugs are effective in partial seizures with or without secondary generalized tonic clonic seizures:
- a) Carbamazepine
  - b) Valproate
  - c) Topiramate
  - d) Lamotrigine
  - e) Ethosuximide
- 120 The following adverse effects are associated with sodium valproate therapy:
- a) Tremor
  - b) Nausea, vomiting and abdominal pain
  - c) Ventricular tachycardia
  - d) Thrombocytosis
  - e) Hair loss (temporary)
- 121 The following are recognized adverse effects associated with phenytoin therapy:
- a) Ataxia
  - b) Dysarthria
  - c) Acne
  - d) Hyperkalaemia
  - e) Macrocytic anaemia
- 122 The pharmacokinetics of phenytoin are characterized by:
- a) Wide interindividual variation
  - b) Less than 10 per cent systemic bioavailability if taken by mouth with food
  - c) Two populations – fast and slow acetylators
  - d) The half-life is not affected by dose
  - e) Once-daily dosing is adequate
- 123 Carbamazepine:
- a) Inhibits GABA transaminase
  - b) Inhibits its own metabolism
  - c) Is effective in temporal lobe epilepsy
  - d) Inhibits the metabolism of warfarin
  - e) Modified-release tablets significantly lessen the incidence of dose-related side-effects
- 124 The following adverse effects are associated with carbamazepine therapy:
- a) Trigeminal neuralgia
  - b) Sedation
  - c) Dizziness
  - d) Diplopia
  - e) Hyponatraemia

- 125 Sodium valproate:
- a) Is a dopamine antagonist
  - b) Is indicated in tonic-clonic epilepsy
  - c) Blood concentration should be monitored frequently during treatment
  - d) Rarely causes hepatic necrosis
  - e) Is safe in pregnancy
- 126 Vigabatrin:
- a) Is a structural analogue of GABA
  - b) Increases the brain concentration of GABA
  - c) Can cause visual field defects
  - d) May cause hallucinations and paranoia
  - e) Is excreted unchanged in bile
- 127 The following antiepileptics induce the metabolism of oestrogen and can lead to unwanted pregnancies in women using oral contraception:
- a) Carbamazepine
  - b) Phenytoin
  - c) Sodium valproate
  - d) Phenobarbital
  - e) Lamotrigine
- 128 An 18-year-old man is admitted to casualty in status epilepticus. There is a history of three previous unexplained blackouts in the last year. The following are appropriate:
- a) Intravenous lorazepam
  - b) Intramuscular phenytoin
  - c) Measurement of blood glucose
  - d) Administration of 24 per cent oxygen
  - e) Once the acute episode is over oral gabapentin should be commenced
- 129 Febrile convulsions:
- a) Approximately 3 per cent of children have at least one febrile convulsion
  - b) A prolonged convulsion can usually be terminated with rectal diazepam
  - c) Paracetamol is contraindicated in children who have febrile convulsions
  - d) Regular prophylaxis with phenobarbital reduces the likelihood of adult epilepsy
  - e) Children with recurrent febrile convulsions should take prophylactic penicillin

- 130** In acute migraine the following are correct:
- a) Paracetamol NSAID or aspirin is usually the treatment of choice
  - b) Metoclopramide may be effective due to its dopamine agonist action
  - c) Ergotamine may be given by the rectal route
  - d) Sumatriptan probably works through its 5HT<sub>1D</sub> agonist properties
  - e) Pizotifen is effective when given by intramuscular injection during the acute episode
- 131** Sumatriptan:
- a) Has a greater bioavailability after subcutaneous injection than oral administration
  - b) Is contraindicated in patients with ischaemic heart disease
  - c) Causes a significant, but transient, pressor response
  - d) Should not be combined with ergotamine
  - e) Metabolism is inhibited by paracetamol
- 132** The following are used in the prophylaxis of migraine:
- a) Rizatriptan
  - b) Ergotamine
  - c) Pizotifen
  - d) Propranolol
  - e) Methysergide
- 133** In comparison to halothane, sevoflurane:
- a) Is associated with more rapid recovery
  - b) Is more likely to cause hepatic necrosis
  - c) Is less likely to cause ventricular dysrhythmias
  - d) Is more extensively metabolized by the liver
  - e) Is more expensive
- 134** Fentanyl:
- a) Has powerful analgesic properties
  - b) Is a powerful muscle relaxant
  - c) Acts within 1–2 minutes following intravenous administration
  - d) Undergoes rapid metabolism by non-specific blood and tissue esterases
  - e) To avoid excessive dosage in obese patients dose may need to be calculated on the basis of ideal body weight
- 135** Nitrous oxide:
- a) Is a powerful muscle relaxant
  - b) Is predominantly excreted by exhalation
  - c) During recovery transient hypoxia may occur in patients with respiratory disease
  - d) Increases blood pressure and heart rate
  - e) Is antagonized by naloxone

- 136 Propofol in comparison to thiopental sodium:
- Cannot be used for induction of anaesthesia
  - Has a longer elimination half-life
  - Has no active metabolites
  - Is less irritant
  - Produces a more rapid 'clear headed' recovery
- 137 The following agents may be used as premedication for anaesthesia:
- Hyoscine
  - Temazepam
  - Morphine
  - Neostigmine
  - Ketamine
- 138 Atracurium:
- Is a non-depolarizing muscle relaxant
  - Has histamine-blocking properties
  - May be used as a continuous infusion in intensive care to facilitate intermittent positive pressure ventilation
  - Is metabolized in the liver
  - Patients with reduced renal function show reduced elimination and prolonged neuromuscular blockade
- 139 The following would be suitable for postoperative analgesia in a patient with severe chronic obstructive airways disease with CO<sub>2</sub> retention who has had an abdominoperineal resection:
- Intramuscular morphine
  - Epidural block with bupivacaine
  - Rectal diclofenac
  - Intramuscular diclofenac
  - Oral oxycodone
- 140 The following are indicated in the management of malignant hyperthermia due to volatile anaesthetics or suxamethonium:
- Discontinuation of anaesthetic
  - 100 per cent oxygen
  - Intravenous dantrolene
  - Correction of acidosis and hyperkalaemia
  - Cooling



**141** Lidocaine, a local anaesthetic:

- a) Prevents the rapid inflow of sodium ions which is the ionic basis of the action potential
- b) Causes vasoconstriction
- c) Is not absorbed from the urethra
- d) Can be combined with adrenaline for digital 'ring' blocks
- e) Has a shorter duration of action than bupivacaine

**142** The following drugs are correctly paired with their putative site(s) of action:

- a) NSAIDs – at the site of injury, by interfering with the chemical mediators involved in nociception
- b) Paracetamol – peripheral inhibition of cyclo-oxygenase
- c) Lidocaine – block of transmission in peripheral nerves
- d) Opioids – modification of transmission at the dorsal horn
- e) Opioids – interference with central appreciation of pain and inhibition of emotional concomitants

**143** Aspirin:

- a) Inhibits cyclo-oxygenase irreversibly
- b) Produces its major analgesic and anti-inflammatory effects by inhibition of prostaglandin E<sub>2</sub> and prostacyclin biosynthesis
- c) Impairs colour vision
- d) Acts on the hypothalamus to reduce body temperature
- e) Chronic use is associated with iron-deficiency anaemia

**144** Adverse effects associated with salicylates include:

- a) Claudication
- b) Bronchoconstriction
- c) Systemic lupus erythematosus
- d) Hepatitis
- e) Reye's syndrome

**145** Ibuprofen:

- a) Is a reversible cyclo-oxygenase inhibitor
- b) Has analgesic properties
- c) Has antipyretic properties
- d) Has anti-inflammatory properties
- e) Can cause renal impairment

**146** Nefopam:

- a) Is associated with gastrointestinal haemorrhage
- b) Causes miosis
- c) Causes more respiratory depression than morphine
- d) Potentiates the dysrhythmogenic effect of halothane anaesthesia
- e) Is contraindicated in epilepsy

147 Co-codamol contains:

- a) Aspirin
- b) Paracetamol
- c) Dextropropoxyphene
- d) Caffeine
- e) Promethazine

148 Morphine:

- a) Acts as an agonist at opioid receptors (especially  $\mu$ ) in the brain and spinal cord
- b) Causes pupillary constriction by stimulation of the Edinger–Westphal nucleus in the mid-brain
- c) Acts as an antihistamine
- d) Is subject to presystemic metabolism
- e) Stimulates the chemoreceptor trigger zone

149 The following are particularly sensitive to the pharmacological actions of morphine:

- a) Young children
- b) The elderly
- c) Patients with hepatic failure
- d) Patients with renal failure
- e) Patients with hyperthyroidism

150 Morphine causes:

- a) Diarrhoea
- b) Increased intrabiliary pressure
- c) Histamine release
- d) Reduced sensitivity of the respiratory centre to carbon dioxide
- e) Vasoconstriction

151 Pethidine:

- a) Is more potent than morphine
- b) Does not cause respiratory depression
- c) Always causes pupillary constriction at analgesic doses
- d) Suppresses cough at analgesic doses
- e) Reduces the activity of the pregnant term uterus

152 Codeine:

- a) Is a metabolite of morphine
- b) Has a plasma half-life of approximately 12 hours
- c) Its effects are antagonized by naloxone
- d) Is used as a cough suppressant
- e) Causes constipation

**153** Buprenorphine:

- a) Is a partial agonist on opioid receptors
- b) Occupies a much larger fraction of opioid receptors to produce its analgesic effect than does morphine
- c) Should only be used to treat acute pain
- d) Is subject to prescription requirements under the Misuse of Drugs Act
- e) May be administered sublingually

**154** Naloxone:

- a) Binds to opioid  $\mu$  receptors
- b) Acts as a partial opioid agonist
- c) Has little effect on a healthy person who has not taken opioid drugs
- d) Has an elimination half-life of approximately 12 hours
- e) Is contraindicated in young children

**Answers:** see pages 55–66

## EXTENDED MATCHING QUESTIONS

### 155 CENTRALLY ACTIVE DRUGS

<b>A</b>	Temazepam	<b>F</b>	Orphenadrine
<b>B</b>	Lithium	<b>G</b>	Sumatriptan
<b>C</b>	Citalopram	<b>H</b>	Aripiprazole
<b>D</b>	Haloperidol	<b>I</b>	Gabapentin
<b>E</b>	Pizotifen	<b>J</b>	Valproate

For each clinical scenario below, suggest the most appropriate therapy:

- 1 Acute migraine in a 20-year-old woman, which is unresponsive to paracetamol, ibuprofen and metoclopramide
- 2 A 40-year-old man with troublesome myoclonic jerks
- 3 A 70-year-old man with schizophrenia, who has developed incapacitating tardive dyskinesia on his maintenance therapy of oral chlorpromazine
- 4 A 40-year-old man with endogenous depression
- 5 Severe disabling insomnia

### 156 DRUG-INDUCED MOVEMENT DISORDERS

<b>A</b>	Interferon beta	<b>F</b>	Esmolol
<b>B</b>	Ciprofloxacin	<b>G</b>	Prednisolone
<b>C</b>	Salbutamol	<b>H</b>	Pioglitazone
<b>D</b>	Doxazosin	<b>I</b>	Phenytoin
<b>E</b>	Gentamicin	<b>J</b>	Ranitidine

Select the drug from the list above that is most likely to be the cause of the effect below:

- 1 Tremor
- 2 'Cerebellar' ataxia
- 3 Vestibular toxicity causing loss of balance
- 4 Proximal myopathy
- 5 Tenosynovitis

**157 TREATMENT OF MOVEMENT DISORDERS AND DEMENTIA**

- |          |                 |          |             |
|----------|-----------------|----------|-------------|
| <b>A</b> | Botulinum toxin | <b>F</b> | Zopiclone   |
| <b>B</b> | Procyclidine    | <b>G</b> | Ropinirole  |
| <b>C</b> | Donepezil       | <b>H</b> | Buspirone   |
| <b>D</b> | Phenelzine      | <b>I</b> | Thiamine    |
| <b>E</b> | Lamotrigine     | <b>J</b> | Neostigmine |

Select the drug from the above list which is licensed for the indication below:

- 1 Idiopathic Parkinson's disease
- 2 Hemifacial spasm
- 3 Myasthenia
- 4 Fluphenazine-induced dystonia
- 5 Alzheimer's disease

**158 ANALGESICS/PAIN**

- |          |             |          |                |
|----------|-------------|----------|----------------|
| <b>A</b> | Fentanyl    | <b>F</b> | Indometacin    |
| <b>B</b> | Aspirin     | <b>G</b> | Morphine       |
| <b>C</b> | Nefopam     | <b>H</b> | Paracetamol    |
| <b>D</b> | Allopurinol | <b>I</b> | Metoclopramide |
| <b>E</b> | Pregabalin  | <b>J</b> | Ephedrine      |

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Mild analgesic suitable for children
- 2 Suitable for acute gout
- 3 Used by injection for patient-controlled self-administration
- 4 Overdose causes tinnitus
- 5 Can be administered as transdermal patch

**ANSWERS: see pages 66–68**

## ANSWERS

## MCQ ANSWERS

- 82 a) True Benzodiazepines, whilst being much safer than the  
 b) True barbiturates, still have the problems of dependence,  
 c) True potentiation of alcohol, respiratory depression in overdose  
 d) True and suppressing REM sleep  
 e) True
- 83 a) False – Buspirone is a non-benzodiazepine anxiolytic drug. It does  
 not have marked hypnotic, anticonvulsant or muscle  
 relaxant properties. It does not alleviate benzodiazepine  
 withdrawal symptoms  
 b) True  
 c) False – The full withdrawal picture usually appears after an  
 interval of 3–8 days  
 d) True  
 e) False – It is common practice to substitute shorter-acting with  
 longer-acting benzodiazepines (e.g. temazepam to  
 diazepam) to assist withdrawal
- 84 a) False – Up to 50 hours, the active desmethyl metabolite has a half-  
 life of 36–200 hours  
 b) True  
 c) True  
 d) False – Usually in combination with alcohol or other drugs  
 e) True
- 85 a) True – 5–6 hours in comparison with 20–50 hours  
 b) True – This combination is a cause of fatal overdose as well as  
 disinhibited behaviour which may lead to crime or road  
 traffic accidents  
 c) False – Patients must be warned not to drive or operate heavy  
 machinery if affected  
 d) False – Temazepam is a controlled drug  
 e) False
- 86 a) False – Absorption is rapid with peak plasma levels being  
 obtained at 60 minutes. Clomethiazole undergoes extensive  
 first-pass metabolism so oral bioavailability is only  
 approximately 15 per cent  
 b) False – The half-life is 50 minutes. The short half-life reduces the  
 risk of hangover, ataxia and confusion the next day  
 c) True – This results from decreased first-pass metabolism

- d) True – Fatalities have occurred because of poorly supervised intravenous infusions. Constant rate infusions lead to accumulation
- e) False – It potentiates the effects of alcohol although it may be used to treat acute alcohol withdrawal
- 87** a) False – Promethazine is an H<sub>1</sub> antihistamine
- b) True
- c) True – Antimuscarinic effects
- d) True – May cause coma
- e) True
- 88** a) False Zopiclone is a non-benzodiazepine hypnotic which enhances GABA activity. In addition to sedation adverse effects include bitter, metallic taste, anorexia, nausea and vomiting, visual hallucinations, amnesia, aggression and agitation
- b) False
- c) False
- d) True
- e) True
- 89** a) True Occasionally drug-induced hallucinations/psychosis may be mistaken for schizophrenia. The hypothesis that chronic cannabis use and LSD can cause schizophrenia is unproven
- b) False
- c) True
- d) False
- e) True
- 90** a) True Prolonged use of D<sub>2</sub> receptor blockers is associated with the onset of tardive dyskinesia which may involve structural brain damage and is often irreversible
- b) True
- c) False
- d) True
- e) False
- 91** a) True – Anticholinergic
- b) True – Anticholinergic
- c) True – Peripheral alpha-adrenoceptor blockade
- d) True – Hypothermia in cold weather, hyperthermia in hot weather
- e) True – Jaundice occurs in 0.5 per cent of patients taking chlorpromazine. It is due to intrahepatic cholestasis and is a hypersensitivity phenomenon associated with eosinophilia
- 92** a) False – Antipsychotic drugs may cause malignant neuroleptic syndrome. This rare syndrome (hyperthermia, varying conscious level, rigidity and autonomic dysfunction) may be treated with dantrolene or bromocriptine
- b) False – Volume of distribution is large, approximately 22 L/kg
- c) False – Metabolism predominantly by hepatic microsomes. Over 70 metabolites have been identified
- d) True
- e) True

- 93 a) False Depot intramuscular preparations such as flupentixol  
b) True decanoate are valuable in the management of  
c) True schizophrenia for maintenance therapy to ensure  
d) True compliance which is often poor in such patients  
e) True
- 94 a) True Clozapine is an 'atypical antipsychotic'. The term is used  
b) True imprecisely but generally covers those antipsychotic drugs  
c) True whose principal pharmacological effect is not D<sub>2</sub> blockade  
d) True and are rarely associated with extrapyramidal side-effects  
e) True – Neutropenia or agranulocytosis develops in up to 3 per  
cent of patients taking clozapine for 1 year. Although  
dystonias and tardive dyskinesias are rare, clozapine is  
associated with fits in 3–4 per cent of patients and postural  
hypotension (particularly after the first dose)
- 95 a) False In comparison to the conventional antipsychotics where  
b) False potency is closely related to D<sub>2</sub> receptor blockade, atypical  
c) False antipsychotics bind less tightly to D<sub>2</sub> receptors and have  
d) True additional pharmacological activity which varies with the  
e) True drug. Efficacy against negative symptoms as well as fewer  
extrapyramidal side-effects are characteristic. These may be  
the result of the transient ('hit and run') binding to D<sub>2</sub>  
receptors. May also block D<sub>4</sub> and 5HT<sub>2</sub> receptors
- 96 a) True Tricyclic drugs of the amitriptyline type raise synaptic  
b) True stores of NA and 5HT and are antidepressant. MAO  
c) True inhibitors which increase total brain NA and 5HT are also  
d) True antidepressant. Amphetamine and cocaine raise synaptic  
e) True NA and alter mood but are not antidepressant
- 97 a) True See *Textbook of Clinical Pharmacology and Therapeutics*,  
b) True Chapter 20. Although clinical experience is most  
c) True extensive with the tricyclic antidepressants, the side-effect  
d) True profile of selective serotonin reuptake inhibitors (SSRIs) is  
e) True usually less troublesome and these drugs are safer in  
overdose
- 98 a) True The less sedative tricyclic and related antidepressants  
b) True include desipramine, imipramine, lofepramine and  
c) False nortriptyline. Protriptyline is a stimulant. The more  
d) False sedative drugs are preferred for agitated and anxious  
e) False patients, whilst the less sedative are preferred in  
withdrawn patients. Citalopram, paroxetine and  
sertraline are SSRIs. SSRIs are less sedating than most  
tricyclic antidepressants. Insomnia occurs in some  
patients on SSRIs



- 99 a) True Tricyclic antidepressant overdoses are commonly fatal.  
b) True Patients may die from cardiac dysrhythmias, convulsions or  
c) True direct CNS depression leading to respiratory arrest/  
d) True asphyxia. See *Textbook of Clinical Pharmacology and*  
e) True *Therapeutics*, Chapter 54
- 100 a) True Amitriptyline is a sedative tricyclic antidepressant which is  
b) True usually administered as a single nocte dose  
c) False  
d) True  
e) True
- 101 a) False – Fluvoxamine is an SSRI  
b) False  
c) True  
d) True – Fluvoxamine inhibits CYP1A2 and therefore decreases the  
metabolism of theophylline and warfarin. Both these drugs  
have a narrow therapeutic index hence their concomitant  
administration with fluvoxamine should be avoided if  
possible  
e) False
- 102 a) False Fluoxetine is an SSRI. It is safer in overdose and causes  
b) False fewer antimuscarinic side-effects than the tricyclic  
c) True antidepressants. The most common adverse effects related  
d) True to SSRIs are nausea, dyspepsia, diarrhoea, dry mouth,  
e) False headache, insomnia and dizziness. Sweating, erectile  
dysfunction and delayed orgasm are well-recognized  
associations
- 103 a) False Phenelzine (and isocarboxazid and tranylcypromine) are  
b) False irreversible non-selective MAO inhibitors  
c) False  
d) True  
e) True – Adrenaline is metabolized by catechol-*O*-methyltransferase
- 104 a) True – Moclobemide is a reversible, competitive, selective MAO-A  
inhibitor  
b) False – Selegiline, an MAO-B inhibitor, is used in Parkinson's disease  
c) False  
d) False – No anticholinergic action (cf. tricyclic antidepressants)  
e) True
- 105 a) True Patients on MAO inhibitors should be given a treatment  
b) True card which lists necessary precautions. Interactions with  
c) True foodstuffs, many proprietary preparations and prescribed  
d) True drugs may cause a hypertensive crisis. Phenotolamine  
e) True and/or labetalol are effective treatment for such a reaction

- 106 a) True Lithium salts have a narrow therapeutic index. Lithium concentrations may rise insidiously and once adverse effects such as tremor, ataxia, dysarthria and nystagmus develop treatment must be stopped whilst the serum lithium (avoid lithium heparin tubes to collect plasma) is measured urgently
- b) True
- c) True
- d) True
- e) False
- 107 a) False – Selective serotonin reuptake inhibitor
- b) True – Irreversible non-selective MAO inhibitor
- c) True – Irreversible non-selective MAO inhibitor
- d) False – Reversible selective MAO inhibitor
- e) False – St John's wort is a herbal remedy which is popular for self-treatment of depression. It is a potent CYP450 enzyme inducer
- 108 a) True Muscarinic antagonists are effective in the treatment of parkinsonian tremor and to a lesser extent rigidity. They have minimal effects on bradykinesia. Although more commonly prescribed to counteract antipsychotic drug-induced parkinsonism they may be used alone in idiopathic parkinsonism and postencephalitic parkinsonism if tremor is the predominant symptom
- b) False
- c) False
- d) False
- e) True
- 109 a) True Parkinsonism arises because of deficient dopaminergic transmission. Bromocriptine and apomorphine are dopamine receptor agonists. Acetylcholine is antagonistic to dopamine within the striatum
- b) True
- c) True
- d) False
- e) False
- 110 a) True Levodopa (unlike dopamine) can enter nerve terminals in the basal ganglia where it undergoes decarboxylation to form dopamine
- b) False
- c) False
- d) True – Entacapone is a catechol-*O*-methyltransferase inhibitor
- e) True
- 111 a) True The dose of levodopa is titrated upwards, balancing efficacy against adverse effects. Nausea and vomiting are reduced by the addition of a dopa decarboxylase inhibitor and taking the drug after food
- b) True
- c) False
- d) False
- e) True
- 112 a) False Bromocriptine may be used as an initial treatment in Parkinson's disease, particularly in younger patients (<70 years) or as an adjunct with levodopa–dopa decarboxylase combinations in patients with severe motor fluctuations. There is great inter-individual variation in its efficacy. Ropinirole is another dopamine D<sub>2</sub> receptor agonist
- b) True
- c) False
- d) False
- e) True

- 113 a) True Selegiline, an MAO-B inhibitor, may slow disease  
b) False progression in idiopathic Parkinson's disease. It usually  
c) False allows dose reduction and prolongs the duration of action of  
d) False levodopa. Oral selegiline is well absorbed (100 per cent) and  
e) False extensively metabolized in the liver. Rarely hypertension has  
been reported. Amantadine (which stimulates release of  
endogenous dopamine) potentiates its anti-Parkinson effects
- 114 a) False Donepezil is used for Alzheimer's disease. Riluzole is used  
b) False in motor neuron disease. Treatment of spasticity is seldom  
c) True very effective, but physiotherapy or limited surgical release  
d) True procedures have some place. The drugs used to reduce  
e) True spasticity have considerable limitations. Diazepam is  
sedative, baclofen is less sedative at equi-effective doses  
but can cause vertigo, nausea and hypotension. Intrathecal  
baclofen is currently being evaluated. Dantrolene is less  
useful for spasticity as it markedly reduces muscle power.  
It is used in the management of neuroleptic malignant  
syndrome and malignant hyperthermia
- 115 a) True Tardive dyskinesia is thought to result from the  
b) True development of 'denervation hypersensitivity' in  
c) True dopaminergic postsynaptic receptors of the nigrostriatal  
d) False pathway following chronic receptor blockade by  
e) False neuroleptics. It is therefore due to a relative preponderance of  
dopaminergic effects. Botulinum toxin A is one of the  
neurotoxins produced by *Clostridium botulinum* and is used to  
treat blepharospasm, certain other dystonias and dynamic  
equinus foot deformities due to spasticity in ambulant  
paediatric cerebral palsy patients. It blocks the release of  
acetylcholine at the neuromuscular junction and is given by  
local intramuscular injection. This is a specialist field!
- 116 a) True Myasthenia gravis is a syndrome of increased muscle  
b) True fatigability and weakness of striated muscle and results  
c) True from an autoimmune process with antibodies to nicotinic  
d) False acetylcholine receptors  
e) True
- 117 a) True Clinically the distinction between a deficiency (myasthenic  
b) True crisis) or an excess (cholinergic crisis) may be difficult and  
c) True improvement with an injection of the very short-acting  
d) True anticholinesterase edrophonium is diagnostic of  
e) False myasthenic crisis. Because of its short duration of action,  
any deterioration of a cholinergic crisis is unlikely to have  
serious consequences although facilities for artificial  
ventilation must be available. NB: cholinesterase inhibitors  
cause pupillary constriction

- 118 a) True Acetylcholinesterase-inhibiting drugs can slow down the  
 b) True progression of mild and moderate Alzheimer's disease, but  
 c) True the benefit is small and only temporary. Memantine, an  
 d) False NMDA receptor antagonist, inhibits glutamate transmission  
 e) True and is licensed for moderate to severe dementia in  
 Alzheimer's disease
- 119 a) True See Table 2 for choice of drug in various forms of seizure.  
 b) True Topiramate has been associated with acute myopia with  
 c) True secondary angle-closure glaucoma  
 d) True  
 e) False

**Table 2** Choice of drug in various forms of seizure

Form of seizure	First line	Second line
Partial seizures $\pm$ secondary generalized tonic clonic seizures	Valproate Carbamazepine Lamotrigine	Phenytoin Topiramate Tiagabine
Generalized seizures		
Primary (tonic clonic)	Valproate Lamotrigine	Carbamazepine Topiramate Phenytoin
Absence seizures	Ethosuximide Valproate	Lamotrigine Clobazam / Clonazepam
Myoclonic jerks	Valproate	Lamotrigine Clobazam / Clonazepam

Note: Other antiepileptics not listed above may be useful. Refer to National Institute for Health and Clinical Excellence (NICE) guidelines.

- 120 a) True Tremor, ataxia and incoordination are dose related. The  
 b) True gastrointestinal effects can be reduced by the use of an  
 c) False enteric coated formulation  
 d) False  
 e) True
- 121 a) True High blood concentrations of phenytoin produce a  
 b) True cerebellar syndrome, involuntary movements and sedation.  
 c) True Macrocytic anaemia which responds to folate is common.  
 d) False Rashes, fever, hepatitis, gum hypertrophy, hirsutism and  
 e) True lymphadenopathy are all well-recognized adverse effects  
 of phenytoin
- 122 a) True Age, body weight, sex and, in particular, saturable  
 b) False metabolism which is under polygenic control, contribute to  
 c) False the wide variation in handling of phenytoin  
 d) False  
 e) True

- 123 a) False      In addition to its effectiveness in many forms of epilepsy  
b) False      except absence seizures, carbamazepine is effective in  
c) True        trigeminal neuralgia. It induces its own metabolism, hence  
d) False      the half-life after a single dose is 25–60 hours, but on  
e) True        chronic dosing this falls to 10 hours
- 124 a) False      Carbamazepine commonly causes adverse effects but these  
b) True        are seldom severe. They are particularly troublesome early  
c) True        in treatment and may resolve without alteration of dose  
d) True        which is probably related to the induction of its own  
e) True        metabolism, although pharmacodynamic tolerance is also a  
                  factor. Carbamazepine therapy should be initiated at a low  
                  dose and titrated upwards slowly depending on response.  
                  Hyponatraemia is caused by stimulation of antidiuretic  
                  hormone secretion
- 125 a) False      Sodium valproate is effective against several forms of  
b) True        epilepsy. Adverse effects most commonly involve the  
c) False      alimentary system. These include nausea, vomiting and  
d) True        abdominal pain (which may be reduced by enteric coated  
e) False      tablets). Use in pregnancy is associated with increased  
                  neural tube defects. To reduce the risk of neural tube  
                  defects, folate supplements are advised before and during  
                  pregnancy in women on antiepileptic drugs
- 126 a) True        Vigabatrin is reserved for the treatment of epilepsy  
b) True        unsatisfactorily controlled by more established drugs. It is  
c) True        associated with visual field defects. Onset of symptoms  
d) True        varies from one month to several years after starting  
e) False      treatment. Unlike most anticonvulsants it is not metabolized  
                  by the liver and is excreted unchanged by the kidney
- 127 a) True        Women on long-term enzyme-inducing drugs who are  
b) True        unable to use an alternative reliable method of contraception  
c) False      should use an oral contraceptive containing at least 50 µg  
d) True        ethinylestradiol under expert family planning supervision.  
e) False      Enzyme induction is also the basis of anticonvulsant  
                  osteomalacia (extremely rare) due to reduced serum  
                  25-hydroxycholecalciferol
- 128 a) True        Status epilepticus is a medical emergency with a mortality  
b) False      of about 10 per cent. Rapid suppression of seizure activity  
c) True        can usually be achieved with intravenous lorazepam.  
d) False      False teeth should be removed, an airway established  
e) False      and oxygen (60 per cent) administered as soon as possible
- 129 a) True        Uncomplicated febrile seizures have an excellent  
b) True        prognosis. It is usual to reduce fever using paracetamol,

- c) False removal of clothing, tepid sponging and fanning  
d) False  
e) False
- 130** a) True Oral aspirin, NSAID or paracetamol is effective in the  
b) False treatment of the headache of acute migraine in nearly  
c) True 75 per cent of patients. During a migraine attack, gastric stasis  
d) True occurs, hence the popularity of a combination of aspirin or  
e) False paracetamol with metoclopramide (a dopamine antagonist)  
which enhances gastric emptying as well as counteracting  
the nausea common in migraine. The value of ergotamine  
is very limited. There is a risk of peripheral vasospasm
- 131** a) True Sumatriptan is a selective agonist of 5HT<sub>1D</sub> receptors,  
b) True which are found predominantly in the cranial circulation.  
c) True Prepacked dosage vials are available for subcutaneous  
d) True self-injection. Sumatriptan is only 14 per cent available  
e) False after oral administration. A nasal spray is also available.  
The half-life is 2 hours. Headache recurs after a single dose  
in 30–40 per cent of patients
- 132** a) False Pizotifen is given at night as its principal adverse effect  
b) False is drowsiness. It also increases appetite and causes  
c) True weight gain. Beta blockers potentiate the peripheral  
d) True vasoconstriction caused by ergotamine and these drugs  
e) True should not be given concurrently. Ergotamine must not be  
used for prophylaxis. Methysergide has 5HT<sub>2</sub> antagonist  
activity with partial 5HT agonist activity. It should only be  
used under specialist hospital supervision. Retroperitoneal  
fibrosis may lead to renal failure
- 133** a) True Halothane is a potent anaesthetic but weak analgesic. It has  
b) False a low therapeutic index. In many centres in the UK  
c) True sevoflurane is the inhalation anaesthetic of first choice  
d) False  
e) True
- 134** a) True Fentanyl is a synthetic opioid and is commonly used as an  
b) False analgesic supplement. Its short duration of action (peak  
c) True effect 20–30 minutes) is explained by redistribution from  
d) False the brain. The half-life is 2–4 hours. It undergoes hepatic  
e) True metabolism
- 135** a) False Nitrous oxide is commonly combined with volatile  
b) True anaesthetics for its analgesic properties. Premixed nitrous  
c) True oxide and oxygen mixtures are used in obstetric practice  
d) False and by ambulance drivers  
e) False

- 136 a) False Thiopental sodium, an ultra short-acting barbiturate, is used primarily as an induction agent. Propofol is used for induction, maintenance of anaesthesia and sedation in intensive care units  
b) False  
c) True  
d) True  
e) True
- 137 a) True The chief aim of premedication is to allay anxiety in the patient awaiting surgery. Inadequate premedication may lead to the administration of larger doses of anaesthetic than would otherwise have been required, resulting in delayed recovery. Neostigmine, an anticholinesterase, may be used at the end of a procedure to reverse non-depolarizing muscle relaxants such as tubocurarine. Ketamine is a parenteral anaesthetic which has a wide therapeutic index. Although it is a potent analgesic and sedative it can cause vivid unpleasant hallucinations which may recur for months. It increases muscle tone and blood pressure. It is useful in major disasters for rapid, safe anaesthesia of trapped casualties to carry out procedures such as amputation  
b) True  
c) True  
d) False  
e) False
- 138 a) True Atracurium has a rapid onset of action. It occasionally causes histamine release leading to flushing of the face and chest, hypotension and rarely bronchospasm. Continuous infusion is popular in intensive care. It is inactivated spontaneously in the plasma, which is a valuable property in hepatic and renal failure  
b) False  
c) True  
d) False  
e) False
- 139 a) False Opioids may cause fatal respiratory depression. Even epidural opioids can cause respiratory depression and in this situation epidural 'local' anaesthesia and intramuscular NSAIDs are preferred  
b) True  
c) False  
d) True  
e) False
- 140 a) True Malignant hyperthermia is a rare but potentially lethal complication of anaesthesia. It consists of a rapid increase in body temperature accompanied by tachycardia and generalized muscle spasm. Severe acidosis and hyperkalaemia occur. Dantrolene reverses the muscle spasm  
b) True  
c) True  
d) True  
e) True
- 141 a) True Small unmyelinated fibres are depressed first, hence the order of loss of function is pain, temperature, touch, proprioception and motor function. Lidocaine does not affect vascular smooth muscle but is available with adrenaline, a vasoconstrictor which prolongs its local effect. This combination may cause vasospasm and severe digital ischaemia if used for a 'ring' block, hence the combination is contraindicated in this situation. Bupivacaine is a

- long-acting local anaesthetic which is often used for peripheral nerve, plexus, epidural and spinal anaesthesia. Toxicity includes cardiac dysrhythmias
- 142** a) True  
b) False  
c) True  
d) True  
e) True
- Paracetamol probably produces its analgesic effect by central inhibition of cyclo-oxygenase. It is antipyretic but not anti-inflammatory
- 143** a) True  
b) True  
c) False  
d) True  
e) True
- Gastric irritation is reduced by taking aspirin after food
- 144** a) False  
b) True  
c) False  
d) True  
e) True
- The commonest adverse effect associated with salicylates is dyspepsia. Chronic blood loss from the stomach may be asymptomatic. Salicylism which is associated with high blood concentrations, consists of tinnitus, deafness, nausea, vomiting and occasionally abdominal pain and flushing
- 145** a) True  
b) True  
c) True  
d) True  
e) True
- Ibuprofen is an NSAID which is available without prescription. The side-effects are those of all the NSAIDs, of which gastrointestinal irritation is the most common. Selective inhibitors of cyclo-oxygenase 2 (COX 2), e.g. celecoxib, may improve gastrointestinal tolerance, but are associated with an increased incidence of cardiovascular events
- 146** a) False  
b) False  
c) False  
d) True  
e) True
- Nefopam is chemically and pharmacologically unrelated to opioids and NSAIDs. It is used for moderately severe pain. It can cause fatal hypertension if prescribed during or within two weeks of cessation of non-selective MAO inhibitor treatment
- 147** a) False  
b) True  
c) False  
d) False  
e) False
- Co-codamol, a compound analgesic of codeine phosphate and paracetamol, is widely prescribed. If the codeine content/tablet is 8 mg it is available without prescription. When taking a drug history one must be aware that many over-the-counter remedies contain a surprising mixture of pharmacologically active agents, although sometimes in almost 'homeopathic' quantities
- 148** a) True  
b) True  
c) False  
d) True  
e) True
- The most important use of morphine is pain relief. It is of particular value in palliative care. The use of oral modified-release preparations allows twice-daily dosing whereas if the standard solution is used it needs to be given every 4 hours
- 149** a) True  
b) True
- Patients with decreased respiratory reserve and myxoedema are also more sensitive



- c) True  
d) True  
e) False
- 150 a) False Morphine increases smooth muscle tone throughout the gastrointestinal tract and in addition reduces peristalsis through an action on the receptors in the ganglion plexus in the gut wall which results in constipation. Diamorphine is diacetylmorphine. Its actions are similar to those of morphine but is more potent as an analgesic when given by injection. It is more soluble than morphine. Diamorphine and 6-acetylmorphine enter the brain more rapidly than morphine  
b) True  
c) True  
d) True  
e) False
- 151 a) False Pethidine causes similar respiratory depression and vomiting to morphine, but does not release histamine or suppress cough and only uncommonly produces pupillary constriction to the same extent as morphine  
b) False  
c) False  
d) False  
e) False
- 152 a) False Morphine is a metabolite of codeine. Codeine is used as an analgesic, cough suppressant and antidiarrhoeal agent. The plasma half-life is 3–4 hours. It is metabolized by CYP2D6. It is less effective in patients deficient in CYP2D6  
b) False  
c) True  
d) True  
e) True
- 153 a) True In common with other partial agonists buprenorphine occupies a much larger fraction of the receptors to produce its analgesic effect than does a full agonist. Consequently it can precipitate pain and cause withdrawal symptoms in patients who have received other opioids and relatively much larger doses of naloxone are required to displace it from receptors in overdose compared to a full agonist  
b) True  
c) False  
d) True  
e) True
- 154 a) True Naloxone is a pure competitive antagonist. It has a half-life of 1 hour which is less than many opioids  
b) False  
c) True  
d) False  
e) False

**EMQ ANSWERS****155 CENTRALLY ACTIVE DRUGS**

- 1 G Sumatriptan is a 5HT<sub>1</sub> antagonist. Sumatriptan can be given by mouth, subcutaneous injection or as a nasal spray during a migraine attack. Sumatriptan and other 5HT<sub>1</sub> agonists (rizatriptan and zolmitriptan) can cause vasoconstriction in coronary and pulmonary vascular beds.

- 2 J Valproate is the first-choice anticonvulsant for myoclonic jerks. It is effective against many forms of epilepsy.
- 3 H Tardive dyskinesias follow months or years of conventional ( $D_2$  blocking) antipsychotic treatment. Anticholinergics aggravate symptoms. The  $D_2$  blocker should be stopped, but structural changes (possible increased sensitivity of presynaptic dopamine receptors) occur and may be irreversible. An atypical antipsychotic (e.g. aripiprazole) may help alleviate the symptoms and should help maintain control of the schizophrenia.
- 4 C An SSRI such as citalopram is usually effective in depression and much safer in overdose than a tricyclic antidepressant (e.g. imipramine).
- 5 A A short-acting benzodiazepine such as temazepam is the treatment of choice for severe disabling insomnia.

### **156 DRUG-INDUCED MOVEMENT DISORDERS**

- 1 C Salbutamol, a  $\beta_2$  agonist, commonly causes a dose-related tremor. Other drug causes include caffeine, thyroxine, SSRIs (e.g. fluoxetine), valproate, lithium and withdrawal from alcohol and benzodiazepines.
- 2 I Phenytoin, an antiepileptic, causes dose-related ataxia with cerebellar signs including nystagmus (as does alcohol intoxication).
- 3 E Aminoglycosides, e.g. gentamicin, cause 8th nerve damage, which can affect hearing and balance. 8th nerve toxicity correlates with trough drug blood levels.
- 4 G The commonest drug causes of proximal myopathy are chronic corticosteroid therapy and alcoholism.
- 5 B Tendon damage including rupture has been associated with fluoroquinolone (e.g. ciprofloxacin) therapy. Elderly patients and those on concurrent corticosteroids are most at risk.

### **157 TREATMENT OF MOVEMENT DISORDERS AND DEMENTIA**

- 1 G Ropinirole is a dopamine receptor agonist which is often used as initial treatment in younger (<70 years) patients with parkinsonism.
- 2 A Botulinum toxin (A and B) is a neurotoxin. It irreversibly blocks the release of acetylcholine at the neuromuscular junction. It is often used in cosmetic clinics.
- 3 J Neostigmine and pyridostigmine are cholinesterase inhibitors.
- 4 B Procyclidine is an antimuscarinic of value in treating antipsychotic drug-induced acute dystonias.
- 5 C Donepezil has a limited effect on slowing the speed of progression of Alzheimer's disease.

**158 ANALGESICS/PAIN**

- 1 **H** Paracetamol is a mild analgesic and antipyretic which, unlike aspirin, is not associated with Reye's syndrome. Therapeutic doses are extremely well tolerated but overdose can be fatal usually through hepatic failure.
- 2 **F** Indometacin, an NSAID, is effective in acute gout.
- 3 **G** Patient-controlled analgesia using morphine is especially valuable in the management of post-operative visceral pain.
- 4 **B** Aspirin overdose is associated with tinnitus.
- 5 **A** Fentanyl, a potent synthetic opioid, is available as a transdermal patch which can provide analgesia for up to 72 hours.

## MUSCULOSKELETAL SYSTEM

### MULTIPLE CHOICE QUESTIONS

- 159 Gold salts when used in the treatment of progressive rheumatoid arthritis:
- Are usually administered daily by intravenous injection
  - If effective, benefit should be observed after the first week of treatment
  - Produce objective improvement in about 75 per cent of patients
  - Can cause skin rashes which can necessitate treatment cessation
  - If they cause stomatitis this may be due to neutropenia
- 160 Penicillamine is used in the management of:
- Rheumatoid arthritis
  - Systemic lupus erythematosus (SLE)
  - Wilson's disease
  - Cystinuria
  - Lead poisoning
- 161 Adverse effects associated with penicillamine include:
- Thrombocytopenia
  - Leucopenia
  - Immune complex glomerulonephritis
  - Loss of taste
  - Myasthenia gravis
- 162 Etanercept:
- Is a humanized monoclonal antibody against tumour necrosis factor alpha (TNF- $\alpha$ )
  - Can cause life-threatening hypersensitivity reactions
  - Has a half-life of 5–13 days
  - Can cause pancytopenia
  - Is rarely associated with a demyelinating syndrome

- 163** The following are likely to be effective in the treatment of an acute episode of gout:
- a) Indometacin
  - b) Naproxen
  - c) Alendronate
  - d) Probenecid
  - e) Colchicine
- 164** The following may cause hyperuricaemia:
- a) Sulfipyrazone
  - b) Cytosine arabinoside when treating acute leukaemia
  - c) Bendromethiazide
  - d) Low-dose aspirin
  - e) Bezafibrate
- 165** Allopurinol:
- a) Inhibits xanthine oxidase
  - b) May precipitate acute gout
  - c) Is contraindicated in renal failure
  - d) Should not be prescribed with a non-steroidal anti-inflammatory drug (NSAID)
  - e) Blocks the metabolic inactivation of suxamethonium
- 166** In a patient with osteoarthritis:
- a) Physical exercise and weight loss can be helpful
  - b) NSAIDs are contraindicated
  - c) Gold therapy reverses the pathophysiology of the disease
  - d) Symptoms are exacerbated by bisphosphonates, e.g. alendronate
  - e) Raloxifene may slow disease progression
- 167** Indometacin causes the following adverse effects:
- a) Biochemical hepatitis
  - b) Spuriously increased serum creatinine
  - c) Hypokalaemia
  - d) Exacerbates cardiac failure
  - e) Antagonizes the antihypertensive effects of angiotensin-converting enzyme (ACE) inhibitors

**Answers: see pages 72–73**

**EXTENDED MATCHING QUESTIONS****168 ARTHRITIS**

- |          |                 |          |                    |
|----------|-----------------|----------|--------------------|
| <b>A</b> | Colchicine      | <b>F</b> | Methylprednisolone |
| <b>B</b> | Azathioprine    | <b>G</b> | Hydroxychloroquine |
| <b>C</b> | Allopurinol     | <b>H</b> | Naproxen           |
| <b>D</b> | Gold injections | <b>I</b> | D-penicillamine    |
| <b>E</b> | Methotrexate    | <b>J</b> | Etanercept         |

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Chronic use can cause cirrhosis
- 2 Used before commencing chemotherapy of leukaemia
- 3 Licensed for severe ankylosing spondylitis inadequately responsive to conventional therapy
- 4 Intra-articular injection in rheumatoid arthritis
- 5 Used in familial Mediterranean fever

**ANSWERS:** see pages 73–74

## ANSWERS

## MCQ ANSWERS

- 159 a) False Gold (as sodium aurothiomalate) is usually administered  
 b) False as weekly intramuscular injections or by mouth daily.  
 c) True Benefit is not anticipated for at least six weeks. Blood  
 d) True dyscrasias and glomerular injury (nephrotic syndrome)  
 e) True occur and monitoring of blood counts and urine is  
 performed monthly. Rashes may progress to  
 exfoliation
- 160 a) True Penicillamine, a breakdown product of penicillin, is given  
 b) False by mouth. In rheumatoid arthritis clinical improvement is  
 c) True anticipated only after 6–12 weeks. It is contraindicated in  
 d) True SLE. Apart from its immunosuppressive action, it also  
 e) True chelates certain heavy metals (Cu, Pb, etc.)
- 161 a) True The toxicity of penicillamine is such that it should only be  
 b) True used by clinicians with experience of the drug and with  
 c) True meticulous patient monitoring  
 d) True  
 e) True
- 162 a) False – Etanercept is a recombinant protein that has two soluble  
 TNF receptors joined to an Fc fragment; this is in contrast  
 to infliximab, a humanized murine monoclonal against  
 TNF- $\alpha$  used in Crohn's disease. Both are licensed for the  
 treatment of adult rheumatoid arthritis  
 b) True – Like all proteins it can cause hypersensitivity reactions  
 c) True – It has a long half-life in plasma and is administered every  
 two weeks  
 d) True – It can cause bone marrow suppression (all lineages) and  
 sepsis  
 e) True – Rarely, demyelinating syndromes like multiple sclerosis  
 have been reported with its use
- 163 a) True Acute gout is treated by anti-inflammatory analgesic  
 b) True agents. Colchicine is an alternative in those unable to  
 c) False tolerate NSAIDs but commonly causes diarrhoea.  
 d) False Alendronate is a bisphosphonate used in the  
 e) True management of Paget's disease. Bisphosphonates  
 are also used to treat hypercalcaemia of pregnancy. They  
 may be used in the prevention of postmenopausal  
 osteoporosis

- 164** a) False Uric acid is the end product of purine metabolism in humans, and gives rise to problems because of its limited solubility.  
 b) True  
 c) True Cytosine arabinoside causes massive cell death and increased uric acid production. Diuretics, low-dose salicylates and pyrazinamide inhibit tubular excretion of uric acid  
 d) True  
 e) False
- 165** a) True Allopurinol is used as long-term medication to treat patients with recurrent gout. By inhibiting xanthine oxidase it decreases uric acid production. It potentiates azathioprine by blocking inactivation of its active metabolite 6-mercaptopurine  
 b) True  
 c) False  
 d) False  
 e) False
- 166** a) True  
 b) False – NSAIDs are probably one of the most widely used treatments although paracetamol, because of its superior tolerance in the elderly, should be tried first  
 c) False  
 d) False  
 e) False – Raloxifene is used in the treatment and prevention of postmenopausal osteoporosis
- 167** a) True – Can cause transaminitis  
 b) False – Reduces glomerular filtration rate (GFR) and truly causes an increase in serum creatinine by diminishing vasodilatory prostaglandins in the renal bed  
 c) False – Reduces renal potassium excretion thus leads to hyperkalaemia  
 d) True – Reduces Na excretion leading to increased fluid retention and fluid overload  
 e) True

**EMQ ANSWERS****168 ARTHRITIS**

- 1 E** Methotrexate is one of the most frequently used disease-modifying antirheumatic drugs (DMARDs) in rheumatoid arthritis. Myelosuppression is another potentially fatal adverse effect.
- 2 C** As well as being used in the prophylaxis of gout, allopurinol is used before commencing chemotherapy of rapidly dividing malignancies where killing a large number of tumour cells increases nucleic acid breakdown so increasing production of urate which can precipitate in the renal tract. Allopurinol prevents this (xanthine is much more water soluble than urate).
- 3 J** Inhibitors of TNF can reactivate latent tuberculosis as can corticosteroids and other immunosuppressants.



- 4 F** Intra-articular corticosteroids, e.g. methylprednisolone, are valuable to reduce pain, increase mobility and reduce deformity in one or a few joints in a rheumatoid arthritis flare.
- 5 A** Colchicine, in addition to its use in the treatment and prophylaxis of gout, is also effective in the treatment of familial Mediterranean fever.

# CARDIOVASCULAR SYSTEM

## MULTIPLE CHOICE QUESTIONS

- 169 The following are modifiable risk factors for the genesis of atheromatous plaque:
- a) Smoking
  - b) Obesity
  - c) Dyslipidaemia
  - d) Glucose intolerance
  - e) Hypertension
- 170 Colestyramine:
- a) Causes a fall in plasma cholesterol
  - b) Increases fecal excretion of bile acids
  - c) Reduces absorption of folic acid
  - d) Causes diarrhoea in diabetic autonomic neuropathy
  - e) Reduces pruritus in incomplete biliary obstruction
- 171 Bezafibrate:
- a) Lowers plasma triglyceride
  - b) Is ineffective post cholecystectomy
  - c) Inhibits lipoprotein lipase
  - d) Is indicated in alcohol-induced hyperlipidaemia
  - e) Potentiates the effects of warfarin
- 172 Simvastatin, an HMG-CoA (3-hydroxy-3-methyl-glutaryl-CoA) reductase inhibitor:
- a) Lowers low-density lipoprotein (LDL) cholesterol
  - b) Is particularly useful in heterozygous familial hypercholesterolaemia
  - c) Acts locally on HMG-CoA reductase in the intestine
  - d) Is associated with myositis/myopathy
  - e) Is ineffective if prescribed with ezetimibe

- 173** The following can cause hypertension:
- a) Corticosteroid therapy
  - b) Oral contraception
  - c) Alcohol withdrawal
  - d) Amphetamines
  - e) Ergotamine
- 174** Thiazide diuretics when used in the management of uncomplicated essential hypertension:
- a) Reduce the risk of stroke
  - b) Are natriuretic
  - c) Potassium supplements are usually required
  - d) Reduce plasma renin
  - e) Are associated with impotence
- 175** Beta-adrenoceptor antagonists:
- a) Are indicated in patients with stable heart failure
  - b) Prolong life in survivors of myocardial infarction
  - c) Improve performance of sprinters
  - d) The antihypertensive effect is antagonized by non-steroidal anti-inflammatory drugs (NSAIDs)
  - e) May cause life-threatening bronchospasm in asthmatics
- 176** The following drugs when used as monotherapy in the management of hypertension are likely to be less effective in Afro-Caribbean than in white patients:
- a) Atenolol
  - b) Enalapril
  - c) Bendroflumethiazide
  - d) Amlodipine
  - e) Diltiazem
- 177** Ramipril, an angiotensin-converting enzyme (ACE) inhibitor:
- a) Reduces concentrations of angiotensin II
  - b) Increases concentrations of bradykinin
  - c) Increases noradrenaline release from sympathetic nerve terminals
  - d) Increases aldosterone secretion
  - e) Causes hypokalaemia
- 178** Irbesartan (an angiotensin-11 receptor antagonist) is contraindicated in:
- a) Left ventricular failure
  - b) Asthma
  - c) Bilateral renal artery stenosis
  - d) Pregnancy
  - e) Diabetic nephropathy

- 179** Nifedipine, a dihydropyridine calcium channel blocker:
- Dilates veins more than arteries
  - Can be combined with beta blockers in the management of hypertension
  - Increases plasma calcium concentration
  - Is contraindicated in asthma
  - Raises the plasma concentration of cholesterol
- 180** Nifedipine in comparison to verapamil is more likely to:
- Worsen angina
  - Cause ankle swelling unresponsive to diuretics
  - Have negative inotropic effects
  - Cause flushing and headache
  - Cause constipation
- 181** Doxazosin:
- Is a selective reversible  $\alpha_1$  receptor antagonist
  - Should always be prescribed with a beta blocker to prevent reflex tachycardia
  - Is associated with first-dose hypotension
  - Reduces plasma LDL/high-density lipoprotein (HDL) cholesterol ratio
  - Can cause urinary incontinence in women with pre-existing pelvic pathology
- 182** Sodium nitroprusside:
- Is administered by intravenous infusion
  - Prolonged administration can lead to cyanide poisoning
  - Has a half-life of about one week
  - Reduces cardiac 'pre-load'
  - Reduces cardiac 'afterload'
- 183** Methyldopa:
- Causes central  $\alpha_2$  agonist effects
  - Causes drowsiness and fatigue
  - Pyrexia is an adverse effect
  - Is associated with Coombs'-positive haemolytic anaemia
  - A single missed dose can cause profound rebound hypertension
- 184** The following hypotensive combinations are rational when a single drug has not been effective in treating essential hypertension:
- Thiazide and candesartan
  - Thiazide and ramipril in an asthmatic
  - Amiloride and ramipril in an asthmatic who has gout
  - Nifedipine and verapamil in a man who has had thiazide-induced impotence, second-degree heart block and captopril-induced rash
  - Ramipril and doxazosin in a man with prostatism

- 185** The following drug effects have been correctly paired with the named drug:
- a) Hydralazine – drug-induced systemic lupus erythematosus (SLE)
  - b) Minoxidil – hirsutism
  - c) Captopril – first-dose hypotension
  - d) Atenolol – tremor
  - e) Candesartan – cough
- 186** Management of acute ST elevation myocardial infarction (STEMI) should usually include:
- a) 24 per cent oxygen
  - b) Intravenous opiate with an antiemetic
  - c) Aspirin
  - d) Some measure to open the coronary artery (e.g. angioplasty)
  - e) Lidocaine (lignocaine)
- 187** The management of unstable angina usually includes:
- a) Aspirin
  - b) Glycerol trinitrate (GTN)
  - c) Low molecular weight heparin
  - d) Salbutamol
  - e) Beta-adrenoceptor antagonist
- 188** GTN:
- a) Relaxes vascular smooth muscle
  - b) Is associated with tolerance more commonly with transdermal GTN patches than sublingual GTN
  - c) Is volatile
  - d) Is more selective for arteriolar than for venous smooth muscle
  - e) May relieve the pain of oesophageal spasm
- 189** Beta-adrenoceptor antagonists:
- a) Increase cardiac tissue cyclic adenosine monophosphate (cAMP)
  - b) Competitively antagonize the  $\beta$  receptor-mediated effects of adrenaline and noradrenaline
  - c) Non-competitively antagonize several of the actions of thyroxine
  - d) Decrease peripheral vascular resistance
  - e) Reduce renin secretion
- 190** The following drugs may reduce the risk of recurrence or death post myocardial infarction:
- a) Aspirin
  - b) Beta blockers
  - c) Dexfenfluramine
  - d) Sildenafil
  - e) Statins

- 191 Verapamil is used:
- a) For prophylaxis of angina
  - b) To treat hypertension
  - c) To treat ventricular tachycardia
  - d) To prevent cerebral vasospasm following subarachnoid haemorrhage
  - e) To treat left ventricular failure
- 192 A calcium channel blocker such as amlodipine or nifedipine is preferred to a beta blocker such as atenolol to treat hypertension and angina in patients who also have:
- a) Chronic bronchitis
  - b) Peripheral vascular disease
  - c) Heart block
  - d) Diabetes
  - e) Anxiety
- 193 Aspirin:
- a) Reduces the risk of stroke in patients with transient ischaemic attacks
  - b) Predisposes to peptic ulceration
  - c) Irreversibly inhibits fatty acid cyclo-oxygenase
  - d) Has no effect on bleeding time
  - e) Needs to be given twice daily to prevent platelet cyclo-oxygenase resynthesis within the dose interval
- 194 Streptokinase:
- a) Is derived from streptococci
  - b) Reduces the acute mortality of myocardial infarction only if administered within 4 hours of the onset of chest pain
  - c) Is contraindicated if the patient is taking regular NSAID therapy
  - d) Is administered by intravenous infusion
  - e) Should not be given to patients over the age of 60 years
- 195 Alteplase:
- a) Is a prodrug that liberates streptokinase
  - b) Heparin must not be administered within 24 hours of alteplase infusion
  - c) Should only be administered if pulmonary artery pressure can be measured
  - d) Is indicated in the treatment of pulmonary embolism
  - e) Is contraindicated if aspirin has been administered in the last 24 hours

- 196** The following are relative contraindications to the use of streptokinase in acute myocardial infarction:
- a) Therapy with streptokinase from 5 days to 12 months previously
  - b) Stroke due to cerebral thrombosis in the last six months
  - c) Concurrent hormone replacement therapy for menopausal symptoms
  - d) Pulmonary disease with cavitation
  - e) Penicillin allergy
- 197** Unfractionated heparin:
- a) Binds to antithrombin III
  - b) Inhibits the action of thrombin
  - c) Is monitored in the laboratory by measurement of activated partial thromboplastin time (APTT)
  - d) Is less effective in patients with inherited or acquired deficiency of antithrombin III
  - e) Is reversed by protamine sulphate
- 198** Low molecular weight heparin (LMWH) prophylaxis to prevent deep vein thrombosis/pulmonary embolism in major surgery:
- a) Must be started one week before surgery
  - b) Is via twice-daily intramuscular injection
  - c) Is more likely to be of value in an obese man of 50 than in a slim man of 30
  - d) Unfractionated heparin should be substituted for LMWH in renal failure
  - e) Concomitant antibiotics are contraindicated
- 199** The following are recognized adverse effects of unfractionated heparin therapy:
- a) Osteoporosis
  - b) Alopecia
  - c) Thrombocytopenia
  - d) Diarrhoea
  - e) Fetal cleft palate
- 200** The following statements are correct:
- a) Thrombocytopenia is more commonly associated with unfractionated heparin than LMWH
  - b) LMWH is eliminated solely by renal excretion
  - c) Neither heparin nor LMWH cross the placenta
  - d) Fondaparinux selectively binds and inhibits factor Xa
  - e) Hirudin is a direct thrombin inhibitor

- 201** Warfarin:
- a) Prevents the hepatic synthesis of the vitamin K-dependent coagulation factors II, VII, IX and X
  - b) Is structurally closely related to vitamin K
  - c) Should initially be given as a subcutaneous loading dose
  - d) During life-threatening bleeding can be reversed by vitamin K and fresh frozen plasma
  - e) Anticoagulant effect is monitored by measurement of the prothrombin time/international normalized ratio (INR)
- 202** The following are relative or absolute contraindications to warfarin therapy:
- a) First trimester of pregnancy
  - b) Prosthetic heart valves
  - c) Space-occupying CNS lesion
  - d) Concurrent digoxin therapy
  - e) Glucose 6-phosphate dehydrogenase (G6PD) deficiency
- 203** The following inhibit the metabolism of warfarin:
- a) Cimetidine
  - b) Fluvoxamine
  - c) St John's wort
  - d) Carbamazepine
  - e) Smoking
- 204** The following inhibit platelet activation and/or aggregation:
- a) Warfarin
  - b) Heparin
  - c) Thromboxane A<sub>2</sub>
  - d) Prostacyclin (epoprostenol)
  - e) Dipyridamole
- 205** Clopidogrel:
- a) Is a direct inhibitor of glycoprotein IIb and IIIa
  - b) The antiplatelet effect lasts the life of the platelet
  - c) Is usually given by intravenous bolus in acute coronary syndrome
  - d) Is a prodrug, requiring conversion in the liver to its active metabolite
  - e) Prolongs the QTc (QT interval on the ECG corrected for heart rate) predisposing to ventricular tachycardia
- 206** Prostacyclin (epoprostenol):
- a) Relaxes pulmonary and systemic vasculature
  - b) Is the principal endogenous prostaglandin of large- and medium-sized blood vessels
  - c) Is an effective anticoagulant
  - d) Is contraindicated in haemodialysis
  - e) Increases diastolic pressure



- 207** The principal beneficial effect in heart failure of the following drugs is to reduce preload (left ventricular filling pressure):
- Digoxin
  - Furosemide
  - Dobutamine
  - GTN
  - Sodium nitroprusside
- 208** The following drugs at standard therapeutic doses aggravate heart failure:
- Imatinib (a tyrosine kinase inhibitor)
  - Verapamil
  - Daunorubicin
  - Ibuprofen
  - Bendroflumethiazide
- 209** In acute pulmonary oedema the following are usually appropriate:
- Sublingual nifedipine
  - Lie the patient supine
  - Oxygen
  - Intravenous loop diuretic
  - Intravenous morphine
- 210** Intravenous furosemide:
- Causes natriuresis
  - Causes kaliuresis
  - Has an indirect vasodilator effect
  - Diuresis begins 10–20 minutes after an intravenous dose
  - High doses are ototoxic
- 211** ACE inhibitors:
- Are positive inotropes
  - Increase afterload
  - Increase preload
  - May cause cough
  - Should be given parenterally in acute heart failure
- 212** The following statements concerning drugs in heart failure are correct:
- The combination of furosemide (a loop diuretic) and ramipril (an ACE inhibitor) should be avoided
  - Candesartan (an angiotensin-II receptor antagonist) is generally better tolerated than captopril (an ACE inhibitor)
  - Beta blockers are contraindicated in heart failure
  - The combination of loop diuretic, ACE inhibitor and spironolactone must always be avoided because of the risk of hyperkalaemia
  - The combination of hydralazine and nitrates is of demonstrated efficacy in African-origin patients

- 213** Dobutamine:
- Is a sympathomimetic amine
  - Is predominantly a  $\beta_1$ -receptor agonist
  - Increases blood pressure via vasoconstriction
  - Should not be given at the same time as loop diuretics
  - Increases myocardial oxygen consumption
- 214** The following drugs can cause sinus tachycardia:
- Esmolol
  - Theophylline
  - Ephedrine
  - Amphetamine
  - Verapamil
- 215** Lidocaine:
- Is a class 1b agent that blocks cardiac  $\text{Na}^+$  channels, reducing the rate of rise of the cardiac action potential and increasing the effective refractory period
  - Is epileptogenic
  - Is a positive inotrope
  - Is usually administered as an intravenous bolus followed by infusion
  - Is the drug of first choice for supraventricular tachycardia
- 216** The following drugs prolong the QT interval and/or cause torsades de pointes:
- Erythromycin
  - Pimozide
  - Foscarnet
  - Tacrolimus
  - Disopyramide
- 217** Amiodarone:
- Is effective in resistant atrial fibrillation or flutter
  - Is effective in preventing recurrent ventricular fibrillation
  - Is contraindicated in Wolff–Parkinson–White (WPW) syndrome
  - May be given intravenously via a central line
  - Prolongs the QT interval
- 218** The following adverse effects are associated with amiodarone:
- Visual disturbances (e.g. coloured halos)
  - Hyperthyroidism
  - Hypothyroidism
  - Pulmonary fibrosis
  - Photosensitivity

**219** Amiodarone:

- a) Is highly lipid soluble
- b) Has an apparent volume of distribution of approximately 5000 L
- c) Is predominantly eliminated by the kidney
- d) Accumulates in the heart
- e) Has a half-life of 3 weeks

**220** Sotalol:

- a) Is effective in supraventricular and ventricular dysrhythmias
- b) Is not effective when given by mouth
- c) The dose should be reduced in renal impairment
- d) May cause torsade de pointes
- e) Is a less potent negative inotrope than amiodarone

**221** Intravenous verapamil:

- a) May terminate supraventricular tachycardia
- b) Must not be given to patients receiving beta blockers
- c) Reduces digoxin excretion
- d) One must delay DC cardioversion at least 2 hours after a dose
- e) Shortens the PR interval on the ECG

**222** Adenosine:

- a) Is used to terminate ventricular tachycardia
- b) Is contraindicated in regular broad complex tachycardia
- c) Dilates bronchial smooth muscle
- d) Is associated with chest pain
- e) Circulatory effects last 20–30 seconds

**223** Digoxin:

- a) Reduces the ventricular rate in atrial fibrillation
- b) Is contraindicated in second-degree heart block
- c) Is the treatment of choice in atrial fibrillation in a patient with WPW syndrome
- d) Induced dysrhythmias may be terminated by magnesium
- e) 80 per cent of administered digoxin is excreted unchanged in the bile

**224** A 70-year-old woman has recurrent, symptomatic ventricular tachycardia following an acute myocardial infarction in spite of DC conversion and lidocaine. The following may be effective:

- a) Amiodarone
- b) Atropine
- c) Verapamil
- d) Adenosine
- e) Isoprenaline

- 225** The following are indications for transvenous pacing:
- a) Asymptomatic sinus bradycardia post inferior myocardial infarction
  - b) First-degree heart block post inferior myocardial infarction
  - c) A heart rate of 34 bpm at rest in an athlete with second-degree (Mobitz type 1) heart block
  - d) Asymptomatic congenital complete heart block
  - e) Blackouts associated with bradycardia in sick sinus syndrome
- 226** The following dysrhythmias are correctly paired with their first-line treatment:
- a) Ventricular fibrillation – synchronized DC cardioversion
  - b) Ventricular fibrillation – unsynchronized DC cardioversion
  - c) Ventricular tachycardia post myocardial infarction – esmolol
  - d) Rapid chronic (established) atrial fibrillation – flecainide
  - e) Drug-induced torsade de pointes – disopyramide

**Answers: see pages 89–97**

## EXTENDED MATCHING QUESTIONS

### 227 ATHEROMA AND THROMBOSIS

- |          |                             |          |                              |
|----------|-----------------------------|----------|------------------------------|
| <b>A</b> | Simvastatin                 | <b>F</b> | Fenofibrate                  |
| <b>B</b> | Recombinant hirudin         | <b>G</b> | Warfarin                     |
| <b>C</b> | Tranexamic acid             | <b>H</b> | Colestyramine                |
| <b>D</b> | Epoprostenol (prostacyclin) | <b>I</b> | Tissue plasminogen activator |
| <b>E</b> | Estradiol                   | <b>J</b> | Ezetimibe                    |

Link each of 1 to 5 below with the most appropriate item from A to J:

- Useful combined with a statin
- Inhibition of platelet aggregation during haemodialysis
- Lowers serum triglyceride and cholesterol concentrations
- Causes malabsorption of fat-soluble vitamins
- Myalgia

### 228 HYPERTENSION

- |          |            |          |                     |
|----------|------------|----------|---------------------|
| <b>A</b> | Labetalol  | <b>F</b> | Spironolactone      |
| <b>B</b> | Minoxidil  | <b>G</b> | Candesartan         |
| <b>C</b> | Doxazosin  | <b>H</b> | Trandolapril        |
| <b>D</b> | Methyldopa | <b>I</b> | Bendroflumethiazide |
| <b>E</b> | Atenolol   | <b>J</b> | Amlodipine          |

Select the drug from the list above most appropriate to prescribe to the patients described below. In each patient the current blood pressure is above 'target'.

- A 40-year-old Afro-Caribbean man who has poorly controlled hypertension having stopped bendroflumethiazide, which caused impotence
- A 70-year-old white man who takes losartan and amlodipine and who has symptoms from prostatic hyperplasia
- A 50-year-old hypertensive man who has hyperaldosteronism due to bilateral adrenal hyperplasia who is currently on no therapy
- A 50-year-old white man who has type II diabetes and asthma. He currently takes gliclazide, simvastatin and inhaled beclomethasone. He was on trandolapril, but this was associated with a troublesome cough
- A 50-year-old Afro-Caribbean woman who developed marked lower limb oedema on amlodipine

**229 ISCHAEMIC HEART DISEASE**

- |          |                              |          |                   |
|----------|------------------------------|----------|-------------------|
| <b>A</b> | Ramipril                     | <b>F</b> | Nifedipine        |
| <b>B</b> | Warfarin                     | <b>G</b> | Verapamil         |
| <b>C</b> | Tissue plasminogen activator | <b>H</b> | Nicorandil        |
| <b>D</b> | Glyceryl trinitrate          | <b>I</b> | Simvastatin       |
| <b>E</b> | Magnesium                    | <b>J</b> | None of the above |

Which of the above drugs is useful in each of the following clinical situations?

- 1 Acute treatment of an angina attack in a 65-year-old man with ischaemic chest pain following exertion
- 2 Acute treatment of anterior ST-elevation myocardial infarction in a previously healthy 60-year-old man
- 3 Long-term treatment of left ventricular dysfunction in a 65-year-old woman post myocardial infarction
- 4 Long-term prevention of cardiac events in an asymptomatic 67-year-old woman with a 10-year history of type 2 diabetes and a total cholesterol of 5.0 mmol/L
- 5 Prevention of angina in a 78-year-old man with widespread diffuse coronary artery disease, not amenable to percutaneous coronary intervention or surgery, who is having troublesome exertional angina despite combination treatment with a long-acting nitrate, beta blocker and calcium antagonist

**230 ANTICOAGULANTS AND ANTIPLATELET DRUGS**

- |          |                         |          |   |
|----------|-------------------------|----------|---|
| <b>A</b> | Aspirin                 | <b>G</b> | Aspirin + clopidogrel                           |
| <b>B</b> | Warfarin                | <b>H</b> | Aspirin + dipyridamole                          |
| <b>C</b> | Intravenous heparin     | <b>I</b> | Aspirin + clopidogrel + subcutaneous enoxaparin |
| <b>D</b> | Subcutaneous enoxaparin | <b>J</b> | Clopidogrel + dipyridamole                      |
| <b>E</b> | Dipyridamole            |          |   |
| <b>F</b> | Clopidogrel             |          |   |

Which drug or drug combination is appropriate for each of the following scenarios?

- 1 Treatment of a 68-year-old man with known ischaemic heart disease, admitted to hospital with unstable angina
- 2 Treatment of a 65-year-old woman, known to have mitral stenosis secondary to childhood rheumatic fever, who is otherwise well and presents with a two-week history of atrial fibrillation
- 3 Immediate treatment of a 30-year-old man, normally well, who presents with a suspected deep vein thrombosis following a long-haul flight
- 4 Immediate treatment of a 70-year-old woman, known to have pancreatic carcinoma and renal impairment (creatinine 300  $\mu\text{mol/L}$ ), who presents with a suspected deep vein thrombosis
- 5 Treatment of a 55-year-old man with known stable angina pectoris, on beta blocker treatment, who is allergic to aspirin

**231 HEART FAILURE**

<b>A</b>	Daunorubicin	<b>F</b>	Glyceryl trinitrate
<b>B</b>	Infliximab	<b>G</b>	Ibuprofen
<b>C</b>	Amlodipine	<b>H</b>	Verapamil
<b>D</b>	Digoxin	<b>I</b>	Amiloride
<b>E</b>	Bisoprolol	<b>J</b>	Furosemide

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Improves survival in stable heart failure
- 2 Positive inotrope
- 3 Contraindicated in heart failure because a strong negative inotrope
- 4 Causes hypokalaemia
- 5 Cardiotoxic

**232 CARDIAC DYSRHYTHMIAS**

<b>A</b>	Intravenous adenosine	<b>F</b>	Intravenous digoxin
<b>B</b>	Intravenous lidocaine	<b>G</b>	Intravenous verapamil
<b>C</b>	Oral disopyramide	<b>H</b>	Oral mexiletine
<b>D</b>	Direct current cardioversion	<b>I</b>	Intravenous atropine
<b>E</b>	Oral sotalol	<b>J</b>	None of the above

Which of the above is appropriate for each clinical situation below?

- 1 Prevention of paroxysmal atrial fibrillation in an otherwise well 60-year-old man
- 2 Treatment of supraventricular tachycardia in a 28-year-old woman, otherwise well, where vagal manoeuvres have failed
- 3 Treatment of symptomatic supraventricular tachycardia in a 22-year-old woman with brittle asthma, where vagal manoeuvres have failed
- 4 Treatment of symptomatic sinus bradycardia (rate 35/minute) in a 62-year-old man with an acute inferior myocardial infarction
- 5 Treatment of frequent asymptomatic ventricular ectopic beats in a 65-year-old man with an acute anterior myocardial infarction

**ANSWERS: see pages 97–100**

**ANSWERS****MCQ ANSWERS**

- 169 a) True      Atheroma is the commonest cause of ischaemic heart disease, stroke and peripheral vascular disease  
b) True  
c) True  
d) True  
e) True
- 170 a) True      The anion-exchange resins colestyramine and colestipol are not absorbed into the systemic circulation and bind bile acids in the gut lumen inhibiting reabsorption of bile salts and cholesterol. They have been almost completely superseded by statins in the management of hypercholesterolaemia. Colestyramine causes malabsorption of fat-soluble vitamins, and is used to treat pruritus in patients with incomplete biliary obstruction. Side-effects include flatulence, constipation and nausea  
b) True  
c) False  
d) False  
e) True
- 171 a) True      The fibrates stimulate lipoprotein lipase and reduce plasma triglyceride. They also tend to reduce LDL cholesterol and to raise HDL cholesterol. They can cause myositis which is more common in alcoholics, patients with impaired renal function and in patients on concurrent HMG-CoA reductase inhibitors (statins). Other adverse effects include nausea and abdominal discomfort  
b) False  
c) False  
d) False  
e) True
- 172 a) True      HMG-CoA reductase is the rate-limiting step in cholesterol biosynthesis from acetate. HMG-CoA reductase inhibitors are ineffective in rare patients with homozygous familial hypercholesterolaemia as they cannot make LDL receptors.  
b) True  
c) False  
d) True  
e) False      – Ezetimibe is used in combination with diet and statins for severe hypercholesterolaemia or when statins are contraindicated
- 173 a) True      Although hypertension is usually 'essential' (i.e. idiopathic), the possibility of secondary hypertension must always be considered. Equally important is the confirmation or rejection of persistent hypertension by repeated measures (blood pressure is very variable) and the identification of other treatable risk factors such as diabetes, smoking, hypercholesterolaemia and obesity  
b) True  
c) True  
d) True  
e) True
- 174 a) True      Thiazide diuretics (e.g. bendroflumethiazide) remain a logical first choice for treating older patients and  
b) True



- c) False Afro-Caribbean patients with mild hypertension unless  
d) False contraindicated by some co-existent disease, and are also  
e) True valuable in patients with more severe hypertension in  
combination with other therapy
- 175 a) True The relatively cardioselective  $\beta$ -adrenoreceptor antagonists,  
b) True atenolol and metoprolol, are no longer used as first-line  
c) False treatment of hypertension in the UK. They are particularly  
d) True valuable in patients with additional pathology, such as  
e) True angina or heart failure (e.g. metoprolol, carvedilol), or who  
have survived a myocardial infarction. Atenolol is a polar  
drug and undergoes renal elimination whilst metoprolol is  
non-polar and is metabolized by CYP450 2D6
- 176 a) True Afro-Caribbean patients are less likely to have high  
b) True circulating renin levels, hence beta blockers and ACE  
c) False inhibitors are less likely to be effective. This difference  
d) False is statistical and based on large populations. Both ACE  
e) False inhibitors and beta blockers can be effective in individual  
Afro-Caribbean patients but a thiazide or calcium channel  
antagonist is usually the antihypertensive of first choice
- 177 a) True ACE inhibitors inhibit the conversion of inactive angiotensin  
b) True I to active angiotensin II, a powerful vasoconstrictor, and also  
c) False inhibit the breakdown of the vasodilator peptides such as  
d) False bradykinin. ACE inhibitors are of particular value in  
e) False treating diabetic hypertensive patients as they significantly  
slow down the progressive renal impairment typical in  
these patients
- 178 a) False Angiotensin-II receptor antagonists, unlike ACE inhibitors, do  
b) False not inhibit the breakdown of bradykinin, hence dry cough is  
c) True a much less common adverse effect. In bilateral renal artery  
d) True stenosis glomerular filtration is dependant on angiotensin-II-  
e) False mediated efferent arteriolar vasoconstriction
- 179 a) False Nifedipine is used in the management of Raynaud's  
b) True syndrome, hypertension and angina. Modified-release tablets  
c) False are preferred. Amlodipine is a once-daily calcium channel  
d) False blocker with similar pharmacodynamic properties  
e) False
- 180 a) True Nifedipine, unlike verapamil, has little effect on the  
b) True conducting system of the heart. It can worsen angina due to  
c) False a reflex tachycardia whilst verapamil causes a bradycardia.  
d) True Both drugs are effective arterial dilators. Verapamil is a much  
e) False more potent negative inotrope and has a greater inhibitory  
effect on intestinal peristalsis

- 181 a) True Non-specific alpha blockers such as phenoxybenzamine  
b) False cause profound postural hypotension and reflex tachycardia.  
c) True Doxazosin does not block presynaptic  $\alpha_2$  receptors that are  
d) True normally stimulated by released noradrenaline and which  
e) True inhibit further transmitter release. This is a negative  
feedback pathway hence there is little reflex tachycardia  
with doxazosin although first-dose hypotension is a  
problem; therefore start with a low dose, usually at night
- 182 a) True Sodium nitroprusside is valuable in treating hypertensive  
b) True encephalopathy and in the management of certain types of  
c) False 'shock' when it is combined with positive inotropes.  
d) True Continuous blood pressure monitoring is essential as it  
e) True causes profound hypotension. It has a half-life of less than  
10 minutes
- 183 a) True Although generally safe and not contraindicated in asthma  
b) True and pregnancy, methyldopa is often poorly tolerated. The  
c) True dose should be slowly titrated upwards. Drowsiness and  
d) True fatigue may be intolerable when used chronically. It is a well  
e) False recognized (but uncommon) cause of drug fever and  
Coombs'-positive haemolytic anaemia
- 184 a) True Diuretics worsen symptoms of bladder neck obstruction,  
b) True whereas  $\alpha_1$  antagonists improve such symptoms as well as  
c) False synergizing with ACE inhibitors  
d) False  
e) True
- 185 a) True – More common in slow acetylators  
b) True – Fluid retention is also a problem  
c) True – Worse if on diuretics  
d) False – May reduce tremor  
e) False – First-dose hypotension can occur so use same precautions  
as with an ACE inhibitor
- 186 a) False The highest concentration of oxygen available should be  
b) True used unless there is coincident pulmonary disease with  $\text{CO}_2$   
c) True retention. Aspirin and opening the occluded artery (either  
d) True with thrombolytic therapy or angioplasty) have an additive  
e) False beneficial effect on reduction of infarct size and  
improvement in survival. There is evidence of some benefit  
from early treatment with ACE inhibitors post infarction in  
patients with left ventricular dysfunction
- 187 a) True Patients with unstable angina require urgent admission,  
b) True urgent antiplatelet therapy (aspirin and clopidogrel) plus

- c) True antithrombotic therapy (usually low molecular weight  
d) False heparin). GTN (usually by infusion in this indication) is often  
e) True effective in relieving pain, but does not significantly alter  
outcome
- 188** a) True GTN is generally best used as acute prophylaxis (i.e.  
b) True immediately before undertaking strenuous activity). The  
c) True spray has a longer 'shelf-life' but is more expensive than the  
d) False sublingual GTN. GTN is subject to extensive presystemic  
e) True metabolism if swallowed. Longer-acting oral nitrates (e.g.  
isosorbide mononitrate) are effective as regular  
prophylactic therapy
- 189** a) False Beta blockers slow the heart, are negatively inotropic (but  
b) True metoprolol, bisoprolol, carvedilol and nebivolol may be of  
c) True value in stable heart failure) and reduce arterial blood  
d) False pressure, are antidysrhythmic, increase peripheral vascular  
e) True resistance, reduce plasma renin activity and predispose to  
bronchoconstriction
- 190** a) True Modifiable risk factors should be sought and attended to.  
b) True Stopping smoking is particularly important. ACE inhibitors  
c) False are recommended for patients with left ventricular  
d) False dysfunction  
e) True
- 191** a) True In addition to hypertension and angina, verapamil is used to  
b) True treat supraventricular tachycardia. Nimodipine helps  
c) False prevent cerebral vasospasm and nifedipine is used in  
d) False Raynaud's syndrome  
e) False
- 192** a) True The commonest side-effects of nifedipine and amlodipine are  
b) True flushing and headache. They have no significant effect on the  
c) True conduction system of the heart  
d) True  
e) False
- 193** a) True Thromboxane (TX) A<sub>2</sub> is the main cyclo-oxygenase product  
b) True of activated platelets and is proaggregatory and a  
c) True vasoconstrictor  
d) False  
e) False
- 194** a) True Streptokinase combines with plasminogen to form an  
b) False activator complex that converts remaining free plasminogen  
c) False to plasmin which dissolves fibrin. The potential benefit  
d) True lessens with delay but the value of treatment within 24 hours  
e) False is well established

- 195 a) False – Alteplase is a direct-acting plasminogen activator  
b) False – Immediate heparin following alteplase is necessary to prevent re-occlusion  
c) False  
d) True – Also indicated in acute myocardial infarction and acute ischaemic stroke (under specialist neurologists)  
e) False
- 196 a) True Immune reactions are important with streptokinase and its prodrug anistreplase. It seems unlikely that mild infections such as sore throats reduce its efficacy. ‘Recent’ dental extraction is considered a contraindication  
b) True  
c) False  
d) True  
e) False
- 197 a) True Unfractionated heparin binds to antithrombin III, the naturally occurring inhibitor of thrombin and of the other serine proteases (factors IXa, Xa and XIa), enormously potentiating its inhibitory action  
b) True  
c) True  
d) True  
e) True
- 198 a) False Prophylactic once-daily subcutaneous LMWH reduces the risk of thromboembolism associated with major surgery.  
b) False Laboratory monitoring of coagulation is not necessary in routine clinical use. The benefit normally outweighs the increased risk of bleeding in major orthopaedic surgery  
c) True  
d) True  
e) False
- 199 a) True The commonest adverse effect is bleeding. This can be treated by stopping the infusion (if relevant), local compression, protamine sulphate and, if severe and continues in spite of the above, fresh frozen plasma  
b) True  
c) True  
d) False  
e) False
- 200 a) True LMWH is preferred to heparin unless renal failure is present  
b) True  
c) True  
d) True – Fondaparinux, a synthetic pentasaccharide, has been shown to be superior to unfractionated heparin or LMWH for thromboprophylaxis in some studies  
e) True
- 201 a) True Warfarin is the most commonly prescribed oral anticoagulant. It usually takes at least 3 days to achieve adequate anticoagulation. If more rapid action is required intravenous heparin and oral warfarin are used until the INR is in the usual therapeutic range (2–3 for most indications)  
b) True  
c) False  
d) True  
e) True – Heparin only influences the INR if the APTT is >2.5 times the control. The laboratory can allow for this by the *in vitro* addition of protamine

- 202 a) True      Other contraindications include active bleeding, blood dyscrasias with haemorrhagic diatheses, dissecting aneurysm of the aorta and recent CNS surgery. Aspirin and warfarin should not be used together routinely, although trials of low-dose combination therapy are in progress  
b) False  
c) True  
d) False  
e) False
- 203 a) True      Warfarin has a narrow therapeutic range and steep dose–response curve. It is metabolized by CYP450.  
b) True  
c) False      Cimetidine, an H<sub>2</sub> blocker used to reduce gastric acid production, and fluvoxamine, a selective serotonin reuptake inhibitor (SSRI) antidepressant, both inhibit CYP450.  
d) False      St John’s wort, carbamazepine and smoking induce CYP450. The INR must be monitored to reduce both the risk of bleeding and inadequate anticoagulation  
e) False
- 204 a) False      Thromboxane A<sub>2</sub> is synthesized by activated platelets and acts on platelet receptors to cause further activation and propagation of the aggregate. It also acts on vascular smooth muscle to cause vasoconstriction. Heparin inhibits thrombin, which is a platelet agonist, as well as causing coagulation  
b) True  
c) False  
d) True  
e) True
- 205 a) False      Clopidogrel is combined with aspirin to treat patients with acute coronary syndrome/myocardial infarction and following percutaneous coronary intervention with stent placement. It may be substituted for aspirin in other indications as an antiplatelet drug if aspirin is poorly tolerated  
b) True  
c) False  
d) True  
e) False
- 206 a) True      Prostacyclin may be used to prevent coagulation in extracorporeal circuits. It causes flushing, headache, reduced diastolic pressure, increased pulse pressure and usually a reflex tachycardia. Occasionally vagally mediated bradycardia and hypotension occur  
b) True  
c) True  
d) False  
e) False
- 207 a) False      The major influences on preload are blood volume and capacitance vessel tone  
b) True  
c) False  
d) True  
e) False
- 208 a) True      Negative inotropes, direct cardiac toxins (e.g. daunorubicin) and drugs that cause salt retention (e.g. NSAIDs) aggravate heart failure. Excessive tachycardia does not allow sufficient time for the ventricle to fill in diastole  
b) True  
c) True  
d) True  
e) False
- 209 a) False      In addition to helping relieve the acute anxiety and discomfort associated with acute pulmonary oedema, opioids  
b) False

- c) True dilate capacitance vessels  
d) True  
e) True
- 210 a) True Loop diuretics inhibit  $\text{Na}^+/\text{K}^+/\text{2Cl}^-$  co-transport in the thick ascending limb of Henle's loop  
b) True  
c) True  
d) True  
e) True
- 211 a) False ACE inhibitors and angiotensin-II antagonists act as arterial and venous vasodilators in cardiac failure, prolonging survival  
b) False  
c) False  
d) True  
e) False
- 212 a) False Spironolactone can cause life-threatening hyperkalaemia, however if renal function is not appreciably impaired and serum potassium monitored, the addition of spironolactone to the loop diuretic/ACE inhibitor combination is usually beneficial. Although beta blockers are negative inotropes, several trials have shown that careful addition of beta blockers to other treatments (e.g. ACE inhibitors) improve survival  
b) True  
c) False  
d) False  
e) True
- 213 a) True Dobutamine is a positive inotrope used predominantly in cardiogenic shock. Hypovolaemia must be corrected before its use  
b) True  
c) False  
d) False  
e) True
- 214 a) False The management of sinus tachycardia is directed to the underlying cause (e.g. pain, anxiety, left ventricular failure, asthma, thyrotoxicosis) and iatrogenic factors. Of calcium antagonists, verapamil causes bradycardia, dihydropyridines can cause reflex tachycardia, and diltiazem seldom causes appreciable changes in heart rate. Esmolol is a beta blocker with a very short duration of action  
b) True  
c) True  
d) True  
e) False
- 215 a) True Lidocaine has a narrow therapeutic index but is used for the treatment of ventricular tachycardia and fibrillation (post DC cardioversion). It is also used as a local anaesthetic  
b) True  
c) False  
d) True  
e) False
- 216 a) True A prolonged QT interval predisposes to torsade de pointes, a form of ventricular tachycardia  
b) True  
c) True – Used for cytomegalovirus (CMV) retinitis and patients with acquired immunodeficiency syndrome (AIDS)

- d) True – An immunosuppressant whose adverse effects include cardiomyopathy
- e) True
- 217 a) True Amiodarone, a class III agent, is highly effective in both  
b) True supraventricular and ventricular arrhythmias. It is not a  
c) False negative inotrope in contrast to most antidysrhythmic  
d) True agents  
e) True
- 218 a) True Adverse effects are many and varied and are common  
b) True when plasma amiodarone concentration exceeds 2.5 mg/L.  
c) True Most are reversible on stopping treatment, but this is not true  
d) True of pulmonary fibrosis  
e) True
- 219 a) True Amiodarone is highly protein bound and is slowly excreted  
b) True by the liver. Antidysrhythmic activity may persist for several  
c) False months after stopping treatment  
d) True  
e) True
- 220 a) True Sotalol is a  $\beta$ -adrenoreceptor antagonist (class II) with  
b) False additional class III antidysrhythmic activity  
c) True  
d) True  
e) False
- 221 a) True Verapamil slows intracardiac conduction affecting in  
b) True particular the atrioventricular (AV) node but also the  
c) True sinoatrial (SA) node. It is a potent negative inotrope. It  
d) False should be avoided in WPW as it can increase conduction  
e) False through an accessory pathway
- 222 a) False Adenosine is used to terminate supraventricular tachycardia  
b) False (SVT). It is particularly useful diagnostically in patients with  
c) False regular broad complex tachycardia which is suspected of  
d) True being SVT with aberrant conduction. If adenosine terminates  
e) True the bradycardia the AV node is involved
- 223 a) True The main use of digoxin as an antidysrhythmic is to control  
b) True the ventricular rate (and hence improve cardiac output) in  
c) False patients with atrial fibrillation. Drugs causing hypokalaemia  
d) True aggravate digoxin toxicity  
e) False
- 224 a) True Isoprenaline, a beta agonist, is likely to be dysrhythmogenic  
b) False and will increase myocardial oxygen consumption.

- c) False Verapamil is a potent negative inotrope and is only effective  
 d) False in SVT  
 e) False
- 225 a) False Bradycardia and first-degree heart block are common post  
 b) False inferior myocardial infarction. If the bradycardia causes  
 c) False symptoms 0.6 mg atropine intravenously is usually effective  
 d) False  
 e) True
- 226 a) False If causing immediate cardiovascular embarrassment, DC  
 b) True cardioversion is indicated in ventricular tachycardia.  
 c) False Otherwise, if intravenous lidocaine is ineffective, or oral  
 d) False prophylaxis is required, amiodarone may be used.  
 e) False Intravenous magnesium sulphate has been recommended  
 for torsades de pointes. It also has a major role in eclampsia  
 for the prevention of recurrent seizures

## EMQ ANSWERS

**227 ATHEROMA AND THROMBOSIS**

- 1 J Ezetimibe blocks cholesterol absorption and is useful when combined with a statin. (Specialists sometimes combine fibrates with statins but this is not routine as there is an increased risk of adverse effects.)
- 2 D Epoprostenol (prostacyclin) is used to inhibit platelet aggregation during haemodialysis. It can also be used in primary pulmonary hypertension.
- 3 F Fenofibrate, bezafibrate and gemfibrozil are used mainly for patients with mixed dyslipidaemia with severely raised triglycerides, especially if they are poorly responsive to statins.
- 4 H Colestyramine used to be combined with a statin but has been rendered largely obsolete by ezetimibe because of its inconvenience and adverse effects. Colestyramine is indicated for pruritus associated with partial biliary obstruction and primary biliary cirrhosis, diarrhoea associated with Crohn's disease, ileal resection, vagotomy, diabetic vagal neuropathy and radiation.
- 5 A Simvastatin is very well tolerated but myalgia is its most common adverse effect (see *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 27).



**228 HYPERTENSION**

See *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 28.

- 1 J Thiazide diuretics are associated with erectile dysfunction which is reversible on stopping the thiazide. Calcium channel blockers (e.g. amlodipine) and thiazide diuretics are the antihypertensives of first choice in Afro-Caribbean patients.
- 2 C Doxazosin has postsynaptic  $\alpha_1$ -blocking activity and is an effective hypotensive agent. First-dose hypotension is a potential problem. It relaxes smooth muscle in benign prostatic hyperplasia improving flow rate and reducing obstructive symptoms.
- 3 F Spironolactone competes with aldosterone for its intracellular receptors. Its indications include Conn's syndrome, secondary hyperaldosteronism in ascites and resistant, low renin hypertension. Hyperkalaemia is a potential problem, particularly if on another potassium-sparing drug (e.g. an ACE inhibitor such as trandolapril), or if there is renal impairment.
- 4 G Candesartan is an angiotensin II blocker. Unlike ACE inhibitors it does not inhibit the breakdown of bradykinin, the likely cause of an ACE inhibitor-induced cough.
- 5 I Although not sinister, ankle oedema is a troublesome adverse effect of calcium channel blockers (less common with verapamil). Thiazides are often effective in Afro-Caribbean patients. Metabolic adverse effects include hypokalaemia, hyperglycaemia, hypercalcaemia and hyperuricaemia.

**229 ISCHAEMIC HEART DISEASE**

- 1 D Sublingual GTN is an effective and convenient acute treatment for angina.
- 2 C Recombinant tissue plasminogen activator (alteplase) is an effective thrombolytic.
- 3 A Long-term use of ACE inhibitors (e.g. ramipril) post myocardial infarction in patients with left ventricular dysfunction prevents cardiac remodelling and subsequent worsening of heart failure.
- 4 I Numerous large studies have shown statins to be beneficial in reducing future cardiac events in this situation.
- 5 H Nicorandil combines activation of the potassium  $K_{ATP}$  channel with vasodilator (nitric oxide donor) actions.

**230 ANTICOAGULANTS AND ANTIPLATELET DRUGS**

- 1 I Aspirin + clopidogrel + subcutaneous enoxaparin (an LMWH) approximately halves the likelihood of myocardial infarction in patients with acute coronary syndrome.
- 2 B Warfarin would reduce the risk of stroke in this patient with mitral stenosis and atrial fibrillation.
- 3 D Subcutaneous enoxaparin is an effective and convenient (once-daily subcutaneous injection) acute treatment in suspected deep vein thrombosis.
- 4 C Unfractionated heparin has been replaced by LMWH for most indications but remains important in patients with impaired or rapidly changing renal function.
- 5 F Clopidogrel is an inactive prodrug that is converted in the liver to an active metabolite that binds to and irreversibly inhibits platelet ADP receptors, thereby inhibiting platelet aggregation and arterial thrombotic disease.

**231 HEART FAILURE**

Heart failure occurs when the heart fails to deliver adequate oxygenated blood to the tissues during exercise, or in severe cases, at rest.

- 1 E Bisoprolol, and other  $\beta$ -adrenoreceptor antagonists, although negative inotropes can improve survival in heart failure, if the dose is titrated carefully. This improvement is probably through antagonism of counter-regulatory sympathetic activation.
- 2 D Digoxin inhibits  $\text{Na}^+/\text{K}^+$  ATPase causing an increase in intracellular  $\text{Ca}^{2+}$  which results in a positive inotropic effect, although its main value is in reducing ventricular rate in rapid atrial fibrillation.
- 3 H Verapamil is a strong negative inotrope.
- 4 J Furosemide, a loop diuretic, causes hypokalaemia which predisposes to dysrhythmias.
- 5 A Daunorubicin, ethanol, imatinib, gefitinib and trastuzumab are cardiac toxins.

**232 CARDIAC DYSRHYTHMIAS**

- 1 E Sotalol is a  $\beta$ -adrenoreceptor antagonist which additionally has substantial class III activity.
- 2 A Intravenous adenosine is used to terminate SVT. Adenosine  $\text{A}_1$  receptors block AV nodal conduction.

- 3 G** Intravenous verapamil is used to terminate SVT in patients who are not haemodynamically compromised if adenosine is contraindicated. Verapamil is a calcium channel blocker.
- 4 I** Atropine, a selective antagonist of acetylcholine at muscarinic receptors, accelerates the heart rate by inhibiting vagal tone.
- 5 J** Asymptomatic ventricular ectopic beats post anterior myocardial infarction do not require any drug therapy. Trials of anti-dysrhythmic drugs in this situation have shown that they are more likely to increase mortality.

## RESPIRATORY SYSTEM

### MULTIPLE CHOICE QUESTIONS

- 233 The following should be administered to an otherwise healthy 27-year-old male with acute severe asthma:
- Intravenous midazolam
  - Nebulized salbutamol
  - Intravenous glucocorticosteroids
  - Nebulized salmeterol
  - Continuous high percentage oxygen ( $FiO_2$  35–40 per cent)
- 234  $\beta_2$  agonists (e.g. salbutamol, terbutaline, salmeterol):
- Relax bronchial smooth muscle
  - Inhibit release of mast cell and other inflammatory mediators
  - Reduce heart rate
  - Cause pulmonary vasoconstriction
  - Decrease intracellular cyclic adenosine monophosphate (cAMP)
- 235 Pharmacodynamic properties of salmeterol include:
- Tremor
  - Exacerbation of atrial dysrhythmias
  - Hyperkalaemia
  - Prolonged pharmacodynamic effects allowing twice-daily dosing
  - Seizures
- 236 Omalizumab:
- Is contraindicated in patients with IgE-mediated sensitivity to inhaled allergen
  - Is used to treat severe acute attacks
  - Is administered by subcutaneous injection
  - Inhibits warfarin metabolism via CYP 2C9
  - Cannot be used in children

237 Ipratropium bromide:

- a) Is administered intravenously
- b) Causes bronchodilatation because of its antagonistic effects at the cholinergic  $M_2/M_3$  receptors
- c) Has a more rapid onset of bronchodilatation than  $\beta_2$  agonists
- d) Has a bitter taste
- e) May precipitate glaucoma in high doses

238 Adverse effects associated with the use of theophylline include:

- a) Cardiac dysrhythmias
- b) Convulsions
- c) Oral candidiasis
- d) Headache
- e) Nausea and vomiting

239 In acute severe asthma hydrocortisone:

- a) Is usually given via the intravenous route
- b) Subjective improvement following steroid administration takes 30–60 minutes
- c) Is contraindicated in growing children
- d) Is contraindicated in pregnancy
- e) Should not be administered until at least two doses of nebulized salbutamol have been administered without significant evidence of sustained bronchodilatation

240 Administration of fluticasone via a metered dose inhaler:

- a) Allows reduction in the maintenance dose of oral prednisolone in chronic asthma
- b) More of the dose is swallowed than enters the lungs
- c) Does not cause hypothalamo-pituitary-adrenal suppression at a dose of 2000  $\mu\text{g}/\text{day}$
- d) Has a lower systemic bioavailability than beclomethasone
- e) In children, causes reversible inhibition of long bone growth at high doses

241 Inhaled sodium cromoglicate:

- a) Is effective in alleviating an acute episode of allergic asthma
- b) Has no benefit in preventing exercise-induced bronchospasm
- c) Prevents antigen–antibody combination
- d) Inhibits mediator release from mast cells
- e) Causes cardiac dysrhythmias by prolonging the QTc

- 242 Montelukast:
- a) Is a competitive antagonist at the Cys LT<sub>1</sub> receptor
  - b) Can be given orally
  - c) Is usually taken once daily at bedtime
  - d) May be associated with Churg–Strauss syndrome
  - e) Is not beneficial to patients with antigen-induced asthma
- 243 The following drugs can produce pulmonary fibrosis:
- a) Methotrexate
  - b) Bleomycin
  - c) Busulphan
  - d) Lisinopril
  - e) Amiodarone
- 244 Pulmonary eosinophilia is caused by the following drugs:
- a) Methysergide
  - b) Aspirin
  - c) Nitrofurantoin
  - d) Carmustine (BCNU)
  - e) Sulfasalazine
- 245 The following agents if given to an asthmatic are likely to cause catastrophic bronchospasm:
- a) Carvedilol
  - b) Losartan
  - c) Adenosine
  - d) Lidocaine (lignocaine)
  - e) Bethanecol
- 246 The following drugs are used as ‘standard of care’ when treating a patient with type II (hypoxic–hypercapnic) respiratory failure:
- a) 35 per cent oxygen
  - b) Doxapram
  - c) Salbutamol
  - d) Methylprednisolone
  - e) Dantrolene

Answers: see pages 105–107

## EXTENDED MATCHING QUESTIONS

### 247 RESPIRATORY DRUGS – MECHANISM OF ACTION

<b>A</b>	Salbutamol	<b>F</b>	Sodium cromoglicate
<b>B</b>	Salmeterol	<b>G</b>	Theophylline
<b>C</b>	Tiotropium	<b>H</b>	Omalizumab
<b>D</b>	Methylprednisolone	<b>I</b>	Cetirizine
<b>E</b>	Montelukast	<b>J</b>	Zafirlukast

Select the drug whose mechanism of action is described below:

- 1 Inhibits transcription of proinflammatory cytokines
- 2 Binds to the Fc portion of IgE
- 3 Inhibits H<sub>1</sub> but not H<sub>2</sub> receptors
- 4 Modulates the firing of respiratory C fibres
- 5 Competitively inhibits M<sub>2</sub> and M<sub>3</sub> muscarinic receptors

### 248 RESPIRATORY DRUGS – ADVERSE EFFECTS

<b>A</b>	Terbutaline	<b>F</b>	Nedocromil
<b>B</b>	Formoterol	<b>G</b>	Theophylline
<b>C</b>	Azithromycin	<b>H</b>	Omalizumab
<b>D</b>	Dexamethasone	<b>I</b>	Loratadine
<b>E</b>	Montelukast	<b>J</b>	Codeine

Select the drugs most frequently associated with the adverse effects described below:

- 1 Seizures
- 2 Apnoea
- 3 QTc prolongation
- 4 Hypertension
- 5 Anaphylaxis

**ANSWERS: see page 108**

## ANSWERS

## MCQ ANSWERS

- 233 a) False Never give anxiolytics/sedatives in acute asthma.  
 b) True Intravenous fluids are administered to correct/prevent dehydration. Antibiotics are administered if there is history/signs of infection. Refractory cases require an intravenous short-acting beta<sub>2</sub> agonist (salbutamol) or as a last resort theophylline. If these are inadequate, intermittent positive pressure ventilation is required. Nebulized salmeterol is not available and its onset of bronchodilation is too slow to be used acutely  
 c) True  
 d) False  
 e) True
- 234 a) True Beta<sub>2</sub> agonists stimulate the β<sub>2</sub> receptor which via linked G-proteins increases adenylyl cyclase activity and increases intracellular cAMP. They cause a tachycardia and vasodilatation  
 b) True  
 c) False  
 d) False  
 e) False
- 235 a) True Beta<sub>2</sub> agonists are generally well tolerated when given by inhalation. Salmeterol, a long-acting beta<sub>2</sub> agonist, is inhaled twice daily and reduces the need for shorter-acting agents and possibly the dose of inhaled corticosteroids.  
 b) True  
 c) False  
 d) True  
 e) False Beta<sub>2</sub> agonists cause hypokalaemia
- 236 a) False Omalizumab is a recombinant humanized IgG<sub>1</sub> monoclonal anti-IgE antibody. It is used in paediatric patients (12 or older) who have allergic/atopic asthma refractory to maximal regular therapy. If there is no improvement in 16 weeks it should be discontinued, see NICE guidelines 2007  
 b) False  
 c) True  
 d) False  
 e) False
- 237 a) False Inhaled antimuscarinic drugs such as ipratropium and tiotropium (long acting once daily) are effective as acute and maintenance bronchodilator therapy in asthma. Their action is slower in onset than that of beta<sub>2</sub> agonists. High doses usually via a nebulizer may precipitate acute glaucoma or urinary retention  
 b) True  
 c) False  
 d) True  
 e) True
- 238 a) True Theophylline has a narrow therapeutic index and its pharmacokinetics show considerable interindividual variation. Because of hepatic metabolism it is prone to a number of drug–drug interactions which may lead to toxicity (see Table 3). Its main side-effects are gastrointestinal, cardiovascular and CNS  
 b) True  
 c) False  
 d) True  
 e) True



**Table 3** Factors influencing theophylline clearance

Factors decreasing theophylline clearance and suggested initial dose* adjustment (assuming normal dose is 100%)	Factors increasing theophylline clearance and suggested initial dose* adjustment (assuming normal dose is 100%)
Congestive cardiac failure (40%)	Hyperthyroidism (150%)
Hepatic disease, cirrhosis (40%)	Marijuana (150%)
Neonates (60%)	Smoking (150%)
Pneumonia (70%)	Charcoal barbecued meat (130%)
Old age (80%)	
Drugs	Drugs
Azole-antifungals (e.g. ketoconazole etc.) (50%)	Carbamazepine (150%)
Cimetidine (50%)	Phenytoin (150%)
Fluoroquinolones (e.g. ciprofloxacin) (50%)	Rifampicin (150%)
Chloramphenicol (75%)	High protein, low carbohydrate diet (150%)
Erythromycin (75%)	Ethanol (chronic) (120%)
Flu vaccine and interferon (75%)	
Propranolol (70%)	

\*Subsequent dose adjustment to be made in the light of plasma concentration monitoring, which should be carried out more frequently in the circumstances listed. The suggested adjustments are obviously very approximate, and depend on the extent of exposure to the various agents.

- 239 a) True      Objective improvement does not occur until 6 hours and is  
b) False      maximal 13 hours after the start of intravenous glucocorti-  
c) False      costeroid treatment in asthma. This delay is due to the  
d) False      pharmacodynamics of glucocorticoids which work via  
e) False      modifying transcription of certain genes and thus affecting  
their protein synthesis. They should be administered early  
in acute asthma
- 240 a) True      Systemic adverse events are rarely significant with inhaled  
b) True      glucocorticoids unless the dose exceeds e.g. 1000  $\mu\text{g}$  of  
c) False      fluticasone or its equivalent. They are invaluable in the  
d) False      prophylaxis of asthma and have been shown to reduce  
e) True      asthma deaths and exacerbations in patients with chronic  
obstructive pulmonary disease (COPD)
- 241 a) False      Sodium cromoglicate is administered by inhalation of a  
b) False      powder. Used prophylactically it can prevent type I and  
c) False      type III allergic reactions and exercise-induced asthma.

- d) True It is very safe although approximately 1:10 000 experience a cough or hoarseness  
e) False
- 242 a) True It is a potent, oral, once-daily inhibitor of cysteinyl  
b) True leukotrienes at the Cys LT<sub>1</sub> receptor. Thus its main action is  
c) True to antagonize the potent proinflammatory effects of  
d) True leukotrienes. It causes about a 5–10 per cent increase in  
e) False baseline FEV<sub>1</sub> but this takes about 1 hour to manifest. About  
5 per cent of patients develop a reversible transaminitis
- 243 a) True Several cytotoxics, particularly if given with or following  
b) True radiation, cause a severe pulmonary fibrosis that may not  
c) True be reversible. Angiotensin-converting enzyme (ACE)  
d) False inhibitors – but not the angiotensin II receptor blockers  
e) True (ARBs) are associated with a dose-dependent chronic dry  
cough thought to be related to bradykinin accumulation
- 244 a) False Methysergide causes retroperitoneal fibrosis. Aspirin  
b) True (and nitrofurantoin, imipramine, isoniazid, penicillins,  
c) True sulfonamides and streptomycin) has been associated with  
d) False pulmonary eosinophilia. Carmustine causes pulmonary  
e) True fibrosis
- 245 a) True – Carvedilol is a non-selective beta blocker whose  
indications include hypertension, angina and, as adjunct  
to other agents, symptomatic chronic heart failure. The  
initial dose for this indication is a quarter of the other  
indications  
b) False  
c) True – Adenosine causes bronchoconstriction by stimulating  
adenosine receptors  
d) False  
e) True – Bethanecol and carbachol are acetylcholine analogues and  
increase cholinergic (parasympathetic) tone
- 246 a) False – Use low FiO<sub>2</sub> (e.g. 22–24 per cent) and titrate upwards  
based on blood gas response/clinical response  
b) False – Analeptics are no longer used unless mechanical  
ventilation is unavailable or contraindicated  
c) True  
d) True  
e) False – Dantrolene is a muscle relaxant; this would worsen  
respiratory failure

## EMQ ANSWERS

**247 RESPIRATORY DRUGS – MECHANISM OF ACTION**

- 1 D** Corticosteroids bind to its receptor in the cytoplasm, which then moves to the nucleus where it binds to DNA suppressing the transcription of certain genes such as interleukins and tumour necrosis factor (TNF) and enhancing transcription of beta<sub>2</sub> receptors, ACE and other anti-inflammatory entities.
- 2 H** Omalizumab binds to the Fc receptor portion of IgE and blocks IgE, interacting with its receptor on inflammatory cells and reduces circulating IgE concentrations.
- 3 I** Second-generation antihistamines are competitive antagonists at the H<sub>1</sub> receptor without significant binding to other receptors including the gastric H<sub>2</sub>, muscarinic and serotonin receptors.
- 4 F** Sodium cromoglicate – whose precise anti-inflammatory mechanism is not clearly defined modulates the firing of cough C fibres.
- 5 C** Tiotropium is a competitive antagonist at respiratory muscarinic receptors and blocks parasympathetic effects on bronchiolar smooth muscle.

**248 RESPIRATORY DRUGS – ADVERSE EFFECTS**

- 1 G** Theophylline adverse effects are usually dose (concentration) dependent with mainly gastrointestinal disturbances at low toxic concentrations, then CVS (dysrhythmias etc.) at moderately toxic concentrations and CNS stimulation at high toxic concentrations.
- 2 J** Opiates are  $\mu$  agonists and directly suppress the respiratory centre, leading to apnoea.
- 3 B** Formoterol like other long-acting beta<sub>2</sub> agonists prolongs QTc and can also cause hypokalaemia which can exacerbate QTc prolongation.
- 4 D** Corticosteroids in anti-inflammatory systemic doses cause an increase in vascular resistance and sodium retention which both lead to an increase in blood pressure.
- 5 H** Omalizumab is a recombinant humanized monoclonal antibody to IgE, but as with all monoclonals can cause severe acute and delayed anaphylactic reactions. (It has a long terminal elimination half-life of approximately 21 days.)

## ALIMENTARY SYSTEM

### MULTIPLE CHOICE QUESTIONS

- 249 The following stimulate gastric acid secretion:
- Vagal stimulation
  - Gastrin
  - Acetylcholine stimulation of the  $M_1$  receptor
  - Histamine stimulation of the  $H_2$  receptor
  - Increased intracellular cyclic adenosine monophosphate (cAMP)
- 250 Prostaglandin  $E_2$ :
- Is the principal prostaglandin synthesized in the stomach
  - Stimulates gastric acid secretion
  - Causes vasoconstriction of submucosal blood vessels
  - Biosynthesis is inhibited by aspirin
  - Biosynthesis is inhibited by rectal indometacin
- 251 *Helicobacter pylori*:
- Is strongly linked to the development of carcinoma of the colon
  - Is a bacterium that is strongly linked to the development and recurrence of peptic ulcer disease
  - Is usually found in the gastric antrum
  - Is uncommon in asymptomatic patients
  - Colonization of the stomach is inhibited by corticosteroids
- 252 The following accelerate healing in gastric ulcers:
- Diclofenac
  - Stopping smoking
  - Corticosteroids
  - Ranitidine
  - Sucralfate

- 253 Antacids:
- Large doses heal gastric ulcers more frequently than duodenal ulcers
  - Standard doses reduce gastric acidity for approximately 4 hours
  - Magnesium salts tend to cause diarrhoea
  - Aluminium salts tend to cause a diuresis
  - Magnesium and aluminium salts reduce the rate and extent of absorption of phenytoin
- 254 Cimetidine therapy is associated with:
- Transient increase in serum prolactin
  - Irreversible gynaecomastia
  - Mental confusion in the elderly
  - Asystole after rapid intravenous injection
  - Reversible rise in serum creatinine
- 255 Eradication of *H. pylori* following a positive breath test is recommended in the following situations:
- Duodenal ulcer
  - Gastric ulcer
  - Patients requiring long-term proton pump inhibitor treatment
  - Severe gastritis
  - Mucosa-associated lymphoid tissue lymphoma
- 256 In comparison to cimetidine, ranitidine:
- Does not bind to androgen receptors
  - Is less likely to cause gynaecomastia
  - Penetrates the blood–brain barrier to a lesser extent
  - Is not available for parenteral use
  - Has a lower affinity for CYP450
- 257 Omeprazole:
- Is an irreversible inhibitor of the hydrogen/potassium adenosine triphosphatase locus of the gastric parietal cell
  - Reduces gastric acid secretion
  - Is the drug of choice in Zollinger–Ellison syndrome
  - Has a plasma half-life of approximately 1 hour
  - Requires dose reduction in renal failure
- 258 Omeprazole enhances the effects of the following drugs through inhibition of drug metabolism:
- Atenolol
  - Amoxicillin
  - Captopril
  - Warfarin
  - Phenytoin

- 259 Problems associated with proton pump inhibitors include:
- a) Masking symptoms of gastric cancer
  - b) Diarrhoea, nausea and vomiting
  - c) Increased risk of gastrointestinal infection
  - d) Headache
  - e) Prolonged QT interval on ECG
- 260 Misoprostol:
- a) Is a synthetic analogue of prostaglandin E
  - b) Inhibits cyclo-oxygenase
  - c) Causes vasodilatation in the submucosa
  - d) Is rapidly and nearly completely absorbed
  - e) Is contraindicated in pregnancy
- 261 Bismuth chelate (tripotassium dicitratobismuthate):
- a) Precipitates at acid pH
  - b) Stimulates mucus production
  - c) Has a direct toxic effect on *H. pylori*
  - d) Causes pale stools
  - e) Causes nausea
- 262 Sucralfate:
- a) Requires systemic absorption for anti-ulcer activity
  - b) Contains aluminium
  - c) Is effective in healing gastric ulcers
  - d) Is contraindicated in pregnancy
  - e) Is associated with constipation
- 263 The following drugs are used to prevent motion sickness:
- a) Hyoscine
  - b) Promethazine
  - c) Cinnarizine
  - d) Metoclopramide
  - e) Chlorpromazine
- 264 Cyclizine:
- a) Is a dopamine receptor antagonist
  - b) Is effective in morphine-induced vomiting
  - c) Is a proven teratogen
  - d) Causes dry mouth
  - e) Causes drowsiness

**265** Metoclopramide:

- a) Is most effective in centrally mediated vomiting
- b) Is ineffective in drug-induced nausea
- c) Increases the rate of gastric emptying
- d) Should be avoided for 3–4 days following gastrointestinal surgery
- e) High doses block 5HT<sub>3</sub> receptors

**266** Ondansetron:

- a) Is a phenothiazine
- b) Is not absorbed after oral administration
- c) Is effective in preventing nausea and vomiting due to cancer chemotherapy and radiotherapy
- d) Is ineffective in ciplastin-induced nausea
- e) 1 per cent of patients have dystonic reactions

**267** In ulcerative colitis:

- a) Intravenous hydrocortisone is of proven value in the treatment of acute colitis
- b) Oral corticosteroids are first line for maintenance treatment
- c) Localized rectal disease often responds to prednisolone enemas/suppositories
- d) In severe colitis codeine should be used
- e) Fibre is contraindicated

**268** Sulfasalazine:

- a) Is a prodrug
- b) Is used for maintenance treatment of ulcerative colitis
- c) Is effective in small bowel Crohn's disease
- d) Should be avoided in glucose 6-phosphate dehydrogenase (G6PD) deficiency
- e) Should be avoided in salicylate hypersensitivity

**269** Adverse effects associated with sulfasalazine include:

- a) Blood dyscrasias
- b) Oligospermia
- c) Stevens–Johnson syndrome
- d) Systemic lupus erythematosus (SLE)-like syndrome
- e) Hepatitis

**270** Mesalazine:

- a) Is a prodrug consisting of a dimer of two 5-aminosalicylic acid molecules
- b) Dissolves at the pH found in the terminal ileum and colon
- c) Is contraindicated in sulphonamide hypersensitivity
- d) Is associated with oligospermia
- e) Is associated with interstitial nephritis

- 271 Infliximab:
- a) Inhibits tumour necrosis factor (TNF)
  - b) Can only be administered on one occasion due to antibody production
  - c) Is licensed for management of irritable bowel syndrome
  - d) Can be used for maintenance therapy in Crohn's disease and ulcerative colitis
  - e) Should not be used in a patient who has been treated with corticosteroids within the previous 12 months
- 272 The following drugs cause constipation:
- a) Amiodarone
  - b) Amitriptyline
  - c) Amoxicillin
  - d) Misoprostol
  - e) Metformin
- 273 Lactulose:
- a) Is a chemical stimulant to the colon
  - b) Produces its effect 10–12 hours after an oral dose
  - c) Requires colonic bacteria for activity
  - d) Should not be administered concurrently with bran
  - e) Is contraindicated in liver failure
- 274 Loperamide:
- a) Decreases intestinal transit time
  - b) Increases bulk of gut contents
  - c) Requires systemic absorption for activity on the bowel
  - d) Causes pupil constriction
  - e) Causes hypersalivation
- 275 Treatment of hepatic encephalopathy includes:
- a) Dietary protein restriction
  - b) Emptying the lower bowel
  - c) Oral lactulose
  - d) Prophylactic vitamin K
  - e) Oral methionine
- 276 The emergency drug therapy of portal hypertension and oesophageal varices may include:
- a) Terlipressin
  - b) Chenodeoxycholic acid
  - c) Calcitonin
  - d) Octreotide
  - e) Isoprenaline



**277** The following drugs are associated with cholestatic jaundice/hepatitis:

- a) Ondansetron
- b) Methotrexate
- c) Synthetic oestrogens
- d) Chlorpromazine
- e) Rifampicin

**278** The following are licensed in the UK for the management of obesity:

- a) Orlistat
- b) Sibutramine
- c) Thiazide diuretics
- d) Pizotifen
- e) Dexamphetamine

**279** Rimonabant:

- a) Inhibits insulin secretion
- b) Systemic absorption is minimal
- c) Has been associated with pulmonary hypertension
- d) Is contraindicated in, and may cause, depression
- e) Is metabolized by CYP3A4

**Answers: see pages 116–120**

**EXTENDED MATCHING QUESTIONS****280 ALIMENTARY SYSTEM**

- |          |                    |          |                                  |
|----------|--------------------|----------|----------------------------------|
| <b>A</b> | Gemcitabine        | <b>F</b> | Ondansetron                      |
| <b>B</b> | Capecitabine       | <b>G</b> | Olsalazine                       |
| <b>C</b> | Etoposide          | <b>H</b> | Lansoprazole                     |
| <b>D</b> | Adefovir dipivoxil | <b>I</b> | Mebeverine                       |
| <b>E</b> | Loperamide         | <b>J</b> | Ribavarin and peginterferon alfa |

Match the drug from the list above with the mode of action/indication below:

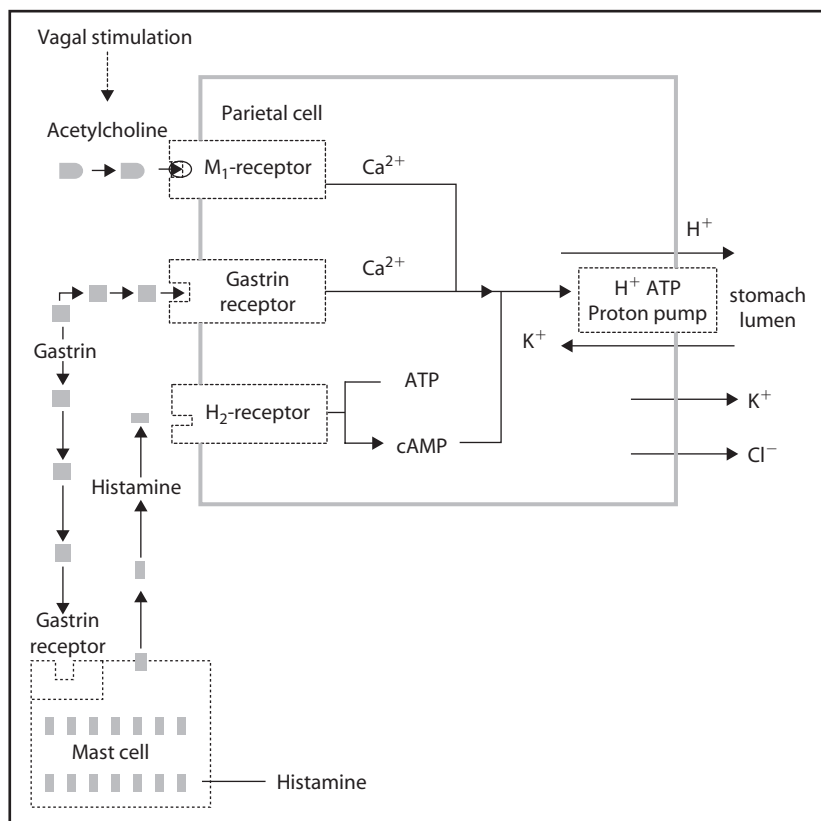
- 1 Serotonin (5HT<sub>3</sub>) receptor blockade
- 2 Symptomatic treatment of acute diarrhoea
- 3 Maintenance of remission of ulcerative colitis
- 4 Chemotherapy for patients with advanced or metastatic adenocarcinoma of the pancreas
- 5 Chronic hepatitis C

**ANSWERS: see page 121**

## ANSWERS

## MCQ ANSWERS

- 249 a) True    See Fig. 2  
 b) True  
 c) True  
 d) True  
 e) True



**Fig. 2** Mechanisms regulating hydrochloric acid secretion. Ca<sup>2+</sup>, calcium; ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate; K<sup>+</sup>, potassium; Cl<sup>-</sup>, chloride

- 250 a) True Prostaglandin E<sub>2</sub> is an important gastroprotective mediator.  
b) False It inhibits secretion of acid, promotes secretion of protective  
c) False mucus and causes vasodilation of submucosal blood  
d) True vessels  
e) True
- 251 a) False *Helicobacter pylori* is strongly linked to the development  
b) True and recurrence of duodenal ulcer. Possible linkage to  
c) True gastric carcinoma is under investigation  
d) False  
e) False
- 252 a) False – Non-steroidal anti-inflammatory drug (NSAID),  
ulcerogenic  
b) True – More effective in preventing recurrence of duodenal ulcers  
than H<sub>2</sub> blockers  
c) False – Ulcerogenic  
d) True – H<sub>2</sub> blocker  
e) True
- 253 a) False Antacids are available without prescription and produce  
b) False prompt but transient pain relief in patients with peptic  
c) True ulceration. Aluminium salts cause constipation  
d) False  
e) True
- 254 a) True Chronic cimetidine therapy causes reversible  
b) False gynaecomastia in 0.1–0.2 per cent of patients. It is  
c) True generally well tolerated. Cimetidine blocks the tubular  
d) True secretion of creatinine  
e) True
- 255 a) True Eradication should be confirmed, preferably by urea breath  
b) True test at a minimum of four weeks post treatment  
c) True  
d) True  
e) True
- 256 a) True All the H<sub>2</sub>-receptor blockers currently available in the UK are  
b) True effective in peptic ulceration and are well tolerated. There  
c) True is most experience with cimetidine and ranitidine  
d) False  
e) True
- 257 a) True Omeprazole, a proton pump inhibitor, is effective in  
b) True reducing gastric acid secretion and in spite of its short half-life  
c) True only has to be administered once daily since it acts  
d) True irreversibly  
e) False

- 258 a) False For drugs such as phenytoin and warfarin which have a narrow therapeutic index this is clinically significant  
b) False  
c) False  
d) True  
e) True
- 259 a) True There are currently five proton pump inhibitors licensed in the UK: esomeprazole, omeprazole, lansoprazole, pantoprazole and rabeprazole  
b) True  
c) True  
d) True  
e) False
- 260 a) True Misoprostol inhibits gastric acid secretion, causes vasodilatation in the submucosa and stimulates production of protective mucus. It contracts uterine muscle and causes abortion  
b) False  
c) True  
d) True  
e) True
- 261 a) True Several studies show bismuth chelate to be as active as cimetidine in the healing of duodenal and gastric ulcers after 4–8 weeks of treatment. It is, however, associated with frequent minor adverse effects. Ranitidine bismuth chelate can be substituted for a proton pump inhibitor as part of ‘triple therapy’ for the eradication of *H. pylori*  
b) True  
c) True  
d) False  
e) True
- 262 a) False Sucralfate, a basic aluminium salt, becomes a sticky adherent paste in the presence of acid which retains antacid efficacy and apparently coats the floor of ulcer craters  
b) True  
c) True  
d) False  
e) True
- 263 a) True – Muscarinic antagonist; NB: anticholinergic side-effects  
b) True – H<sub>1</sub> blocker minor antimuscarinic action  
c) True – H<sub>1</sub> blocker minor antimuscarinic action  
d) False – Dopamine receptor antagonist  
e) False – Chlorpromazine is not used for motion sickness
- 264 a) False Cyclizine is an H<sub>1</sub> blocker with additional antimuscarinic actions. Its indications are nausea, vomiting, vertigo, motion sickness and labyrinthine disorders  
b) True  
c) False  
d) True  
e) True
- 265 a) False – Relatively ineffective in motion sickness and other forms of centrally mediated vomiting  
b) False  
c) True – Increases the rate of absorption of oral drugs  
d) True  
e) True – Effective in some patients in preventing cisplatin-induced nausea and vomiting

- 266 a) False – Ondansetron is a highly selective 5HT<sub>3</sub>-receptor antagonist  
b) False – Is used orally, rectally and intravenously  
c) True  
d) False  
e) False – Causes constipation
- 267 a) True – Correction of dehydration, nutritional and electrolyte imbalance are life-saving  
b) False – Because of side-effects  
c) True – Some systemic absorption may occur  
d) False – May precipitate paralytic ileus and megacolon  
e) False – A high-fibre diet and bulk-forming drugs are useful in adjusting faecal consistency
- 268 a) True – Broken down to 5-aminosalicylate and sulfapyridine  
b) True  
c) False  
d) True  
e) True
- 269 a) True Adverse effects are more common in slow acetylators. Any  
b) True patient who is receiving aminosalicylates must be advised  
c) True to report unexplained bleeding, bruising, purpura or  
d) True malaise  
e) True
- 270 a) False – This describes olsalazine  
b) True  
c) False – But is contraindicated in salicylate hypersensitivity  
d) False  
e) True – Contraindicated in renal impairment
- 271 a) True Infliximab, a monoclonal antibody which inhibits TNF, is  
b) False licensed for the management of severe active Crohn's  
c) False disease and moderate to severe ulcerative colitis in patients  
d) True who are refractory to or intolerant of corticosteroids and  
e) False conventional immunosuppressants
- 272 a) True The cause of any change in bowel habit should be  
b) True determined before laxatives are used  
c) False  
d) False  
e) False
- 273 a) False Lactulose is a disaccharide which is broken down in the  
b) False colon by bacteria to unabsorbed organic anions which  
c) True retain fluid in the gut lumen  
d) False  
e) False

- 274 a) False See *Textbook of Clinical Pharmacology and Therapeutics*,  
b) False Chapter 34. Loperamide rarely causes CNS effects.  
c) False However, co-administration with quinidine, a known  
d) False inhibitor of the P-glycoprotein transmembrane pump, is  
e) False associated with respiratory depression independent of  
changes in plasma concentration indicating increased  
CNS penetration
- 275 a) True See *Textbook of Clinical Pharmacology and Therapeutics*,  
b) True Chapter 34. Prophylactic broad-spectrum intravenous  
c) True antibiotics are commonly used, especially if there is  
d) True evidence of infection (e.g. spontaneous peritonitis).  
e) True Intravenous acetylcysteine is also used but its precise  
value is yet to be fully confirmed
- 276 a) True See *Textbook of Clinical Pharmacology and Therapeutics*,  
b) False Chapter 34. Terlipressin is a derivative of vasopressin  
c) False (antidiuretic hormone). Octreotide is an analogue of  
d) True somatostatin  
e) False
- 277 a) False – Usually mild and asymptomatic increase in transaminases  
b) False – Hepatic fibrosis/cirrhosis  
c) True – Rare now that low-dose oestrogens are more commonly  
prescribed  
d) True – Associated with fever, abdominal pain and pruritus  
e) True – Usually transient
- 278 a) True – A lipase inhibitor. Adverse effects include rectal leakage  
and oily faeces  
b) True – Sibutramine inhibits the reuptake of noradrenaline and  
serotonin. It is not licensed for use for longer than 1 year  
c) False – Transient weight loss secondary to fluid loss  
d) False – Inhibits 5HT<sub>2</sub> receptors, increases appetite and causes  
weight gain  
e) False – Although dexamphetamine decreases appetite, it has  
considerable abuse potential. This and adverse effects  
which include insomnia, restlessness, convulsions,  
tachycardia, hypertension severely limits its use to  
specialist treatment of narcolepsy and attention deficit  
disorder
- 279 a) False Rimonabant is an oral, selective, cannabinoid CB1 receptor  
b) False antagonist which is used as an adjunct to diet to achieve  
c) False weight loss. It is not licensed for use for longer than 2 years  
d) True  
e) True

## EMQ ANSWERS

**280 ALIMENTARY SYSTEM**

- 1 **F** Ondansetron is a 5HT<sub>3</sub> antagonist which is very effective in the prevention and treatment of acute nausea and vomiting secondary to cytotoxic chemotherapy and radiotherapy as well as following abdominal surgery.
- 2 **E** Loperamide is an effective, well-tolerated antidiarrhoeal agent. It is an opioid that does not, under normal circumstances, cross the blood–brain barrier.
- 3 **G** Olsalazine is a prodrug consisting of a dimer of two 5-aminosalicylic acid (5ASA) molecules linked by an azo bond. The azo bond is cleaved by colonic bacteria liberating 5ASA to the colon. In common with other aminosalicylates, olsalazine helps maintain remission in ulcerative colitis.
- 4 **A** Gemcitabine is an option for first-line chemotherapy for patients with advanced or metastatic adenocarcinoma of the pancreas.
- 5 **J** Ribavarin and peginterferon alfa are used in combination to treat chronic hepatitis C.



## ENDOCRINE SYSTEM

### MULTIPLE CHOICE QUESTIONS

- 281 In young, insulin-dependent diabetic (type 1 diabetic) patients:
- a) There is good evidence that improved diabetic control reduces the incidence of microvascular complications
  - b) Blood glucose monitoring should be performed at home
  - c) Inhaled insulin should be tried before subcutaneous insulin
  - d) The dietary carbohydrate content should be 45–55 per cent of total calories
  - e) A fibre-rich diet reduces peak plasma glucose after meals and reduces insulin requirements
- 282 Recombinant human insulin in diabetes mellitus:
- a) Never produces allergic reactions
  - b) The effective dose may be less than animal insulin
  - c) Patients are less aware of hypoglycaemia
  - d) Should not be given intravenously
  - e) Is not of any value in type 2 diabetes mellitus
- 283 A 17-year-old woman is admitted comatose with diabetic ketoacidosis. The following is accepted as 'standard of care':
- a) Administer 500 mL of 0.9 per cent saline in the first 2 hours
  - b) Bladder catheterization
  - c) Administer subcutaneous insulin 0.1 unit/kg/hour
  - d) Administer 8.4 per cent sodium bicarbonate intravenously if the arterial pH is between 7.2 and 7.3
  - e) Aspiration of the stomach

284 Sulphonylureas:

- a) Are used in obese diabetics who show a tendency to ketosis
- b) Improve symptoms of polyuria and polydipsia
- c) Have been proven to reduce the vascular complications of type 2 diabetics
- d) Require functioning beta cells for a hypoglycaemic effect
- e) Are usually administered once daily at bed time

285 Gliclazide:

- a) Should never be combined with acarbose
- b) Can be safely prescribed concomitantly with an angiotensin-converting enzyme (ACE) inhibitor
- c) Hypoglycaemia can be reversed by intramuscular glucagon
- d) Should not be prescribed concurrently with metformin
- e) Stimulates appetite

286 Metformin, a biguanide:

- a) May cause lactic acidosis
- b) Is particularly useful in alcoholic diabetic patients
- c) Causes hypoglycaemia in non-diabetic patients
- d) Should be discontinued before major elective surgery
- e) Causes anorexia and weight loss

287 'Glitazones' (e.g. pioglitazone and rosiglitazone):

- a) Are indicated in type 1 diabetes
- b) Bind to peroxisome proliferating activator receptor  $\gamma$  (PPAR  $\gamma$ ), a nuclear receptor found mainly in adipocytes and also in hepatocytes and myocytes
- c) Have a rapid onset of action and should be taken shortly before each main meal
- d) Reduce peripheral insulin resistance
- e) Are associated with weight gain and fluid retention

288 Carbimazole:

- a) Decreases thyroid hormone synthesis
- b) Inhibits the peripheral conversion of  $T_4$  to the more active  $T_3$
- c) Should be stopped immediately if a rash develops
- d) Has an active metabolite
- e) Is associated with neutropenia

289 In a thyroid crisis with hyperpyrexia, tachycardia, vomiting, dehydration and shock the following are usually indicated:

- a) Metaraminol
- b) Propranolol
- c) Intravenous saline
- d) Glucocorticoids
- e) Aspirin

- 290** The following may cause hypercalcaemia:
- Cinacalcet
  - Calcitonin
  - Bisphosphonates
  - Alfacalcidol (1 $\alpha$ -hydroxycholecalciferol)
  - Thiazide diuretics
- 291** Disodium etidronate is used:
- Orally because it has high oral bioavailability
  - In Paget's disease
  - In hypercalcaemia of malignancy
  - With calcium carbonate in established vertebral osteoporosis
  - To inhibit bone resorption and formation
- 292** Glucocorticoids:
- Reduce circulating numbers of eosinophils by inducing apoptosis
  - Reduce circulating numbers of T lymphocytes
  - Increase circulating numbers of neutrophils
  - Increase circulating numbers of platelets
  - Increase the transcription of proteins such as tumour necrosis factor (TNF), interleukin 1 (IL-1) and granulocyte colony-stimulating factor (G-CSF)
- 293** Rapid withdrawal after prolonged prednisolone administration can cause:
- Acute adrenal insufficiency
  - Malaise
  - Hypercalciuria
  - Arthralgia
  - Fever
- 294** Chronic administration of corticosteroids (iatrogenic Cushing's syndrome) results in:
- Increased susceptibility to opportunistic infection
  - Hyperkalaemia
  - Hypertension
  - Posterior capsular cataracts
  - Proximal myopathy
- 295** Oral corticosteroid (e.g. prednisolone) therapy is indicated in:
- Fibrosing alveolitis
  - Temporal arteritis
  - Viral meningitis
  - Diabetes insipidus
  - Idiopathic thrombocytopenic purpura

- 296 The risk of thromboembolic disease associated with use of the combined oral contraceptive is increased in women:
- Over 35 years of age
  - Who smoke
  - Who have been using oral contraceptives continuously for 5 years or more
  - Who take St John's wort
  - Who have known protein C or protein S deficiency
- 297 Adverse effects associated with the combined oral contraceptive include:
- Aggravation of asthma
  - Stroke in women with migraine
  - Nephrotic syndrome
  - Peripheral neuropathy
  - Budd–Chiari syndrome
- 298 The following are indications to stop the oral contraceptive immediately (pending investigation and treatment):
- Haemoptysis
  - Jaundice
  - Concurrent rifabutin therapy
  - First (unexplained) epileptic seizure
  - Severe unilateral calf pain
- 299 Post-coital contraception consisting of levonorgestrel given within 72 hours of unprotected intercourse:
- Has a failure rate of less than 10 per cent
  - Is less effective than having a copper intrauterine device (IUD) inserted within 5 days of unprotected sexual intercourse
  - If vomiting occurs within 3 hours of ingestion, that dose should be repeated
  - Asthma is a contraindication
  - The next menstrual bleed may be early or late
- 300 Bromocriptine:
- Stimulates lactation
  - Is used to treat hyperprolactinaemia
  - Is a dopamine D<sub>2</sub> receptor agonist
  - Commonly causes diarrhoea
  - Is effective in reducing symptoms of the syndrome of inappropriate antidiuretic hormone (ADH) secretion

- 301** There is reliable evidence that giving oestrogen for several years starting at the menopause to a woman with an intact uterus:
- a) Reduces risk of osteoporosis
  - b) Reduces risk of coronary artery disease
  - c) Reduces age-related decline in cognitive function
  - d) Increases risk of stroke
  - e) Increases risk of breast cancer
- 302** Octreotide:
- a) Is a synthetic peptide with a molecular weight of 10 000
  - b) Is effective in reducing symptoms of carcinoid syndrome
  - c) Is effective in treating diarrhoea states induced by irinotecan cancer chemotherapy
  - d) Commonly causes hyperglycaemia
  - e) Is effective in the acute treatment of bleeding from oesophageal varices
- 303** Clomifene:
- a) Is an oestrogen receptor agonist
  - b) Is used in infertility treatment
  - c) Reduces follicle-stimulating hormone/luteinizing hormone (FSH/LH) secretion
  - d) Causes multiple births
  - e) Can cause acute psychotic reactions
- 304** The following may help alleviate symptoms associated with prostatic hyperplasia:
- a) Clonidine
  - b) Tamsulosin
  - c) Doxazosin
  - d) Cyproterone acetate
  - e) Finasteride
- 305** Sildenafil:
- a) Is administered by intracavernosal injection
  - b) Inhibits prostaglandin E<sub>1</sub>
  - c) Inhibits type V phosphodiesterase
  - d) Potentiates the action of organic nitrates
  - e) May cause headaches, flushing, nasal congestion and disturbances of colour vision

**Answers: see pages 129–132**

## EXTENDED MATCHING QUESTIONS

### 306 DIABETES MELLITUS

- |          |                     |          |                |
|----------|---------------------|----------|----------------|
| <b>A</b> | Bendroflumethiazide | <b>F</b> | Gliclazide     |
| <b>B</b> | Inhaled insulin     | <b>G</b> | Pioglitazone   |
| <b>C</b> | Glucagon            | <b>H</b> | Orlistat       |
| <b>D</b> | Insulin glargine    | <b>I</b> | Insulin lispro |
| <b>E</b> | Acarbose            | <b>J</b> | Metformin      |

Link each of 1 to 5 below with the most appropriate item from A to J:

- Lactic acidosis
- Rapid hypoglycaemic effect
- Useful in treatment of hypoglycaemia in a comatose patient
- Action on a nuclear receptor
- Depolarizes pancreatic islet beta cells

### 307 THYROID

- |          |                   |          |                                     |
|----------|-------------------|----------|-------------------------------------|
| <b>A</b> | Salbutamol        | <b>F</b> | <sup>131</sup> I                    |
| <b>B</b> | Carbimazole       | <b>G</b> | Thyroxine                           |
| <b>C</b> | Lithium           | <b>H</b> | Lugol's iodine                      |
| <b>D</b> | Imatinib          | <b>I</b> | Thyrotropin-releasing hormone (TRH) |
| <b>E</b> | Tri-iodothyronine | <b>J</b> | Amiodarone                          |

Link each of 1 to 5 below with the most appropriate item from A to J:

- Rapid onset of thyroid action
- Its principal metabolite inhibits peroxidase in the thyroid
- Preparation for surgery on a toxic goitre
- Treatment of thyroid carcinoma
- Associated with goitre, hypo- or hyper-thyroidism

### 308 CALCIUM METABOLISM

- |          |                    |          |                   |
|----------|--------------------|----------|-------------------|
| <b>A</b> | Calcitonin         | <b>F</b> | Calcium carbonate |
| <b>B</b> | Alfacalcidol       | <b>G</b> | Zinc sulphate     |
| <b>C</b> | Strontium ranelate | <b>H</b> | Calciferol        |
| <b>D</b> | Cinacalcet         | <b>I</b> | Teriparatide      |
| <b>E</b> | Risedronate        | <b>J</b> | Chlortalidone     |

Link each of 1 to 5 below with the most appropriate item from A to J:

- Indicated in renal osteodystrophy
- Phosphate-binding agent
- Prevention and treatment of osteoporosis
- Enhances signalling through the calcium-sensing receptor
- May raise the serum calcium, glucose and urate whilst lowering the serum potassium

**309 ADRENAL**

<b>A</b>	Metyrapone	<b>F</b>	Aldosterone
<b>B</b>	Fludrocortisone	<b>G</b>	Isoprenaline
<b>C</b>	Dexamethasone	<b>H</b>	Phenoxybenzamine
<b>D</b>	Adrenaline	<b>I</b>	Dipivefrine
<b>E</b>	Aliskiren	<b>J</b>	Spirolactone

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Helpful in controlling symptoms of Cushing's disease
- 2 Reduces cerebral oedema associated with brain tumour
- 3 Used therapeutically for its mineralocorticoid action
- 4 Irreversible alpha receptor antagonist
- 5 The main adrenal mineralocorticoid

**310 PITUITARY**

<b>A</b>	Octreotide	<b>F</b>	Demeclocycline
<b>B</b>	Atosiban	<b>G</b>	Pegvisomant
<b>C</b>	Goserelin	<b>H</b>	Tetracosactide
<b>D</b>	Somatropin	<b>I</b>	L-Arginine
<b>E</b>	Desmopressin	<b>J</b>	Prolactin

Link each of 1 to 5 below with the most appropriate item from A to J:

- 1 Long-acting somatostatin analogue
- 2 Downregulates FSH/LH release
- 3 Stimulation test to exclude Addison's disease
- 4 Growth hormone receptor antagonist
- 5 Treatment of syndrome of inappropriate antidiuretic hormone secretion (SIADH)

**ANSWERS: see pages 133–134**

## ANSWERS

## MCQ ANSWERS

- 281 a) True In insulin-dependent diabetes mellitus (IDDM), in addition to tight diabetic control which can usually be achieved by education and insulin two or three times daily plus diet, there must be regular screening for microvascular complications. Laser therapy of early proliferative retinopathy prevents blindness  
 b) True  
 c) False  
 d) True  
 e) True
- 282 a) False – But are much less common than with animal insulin  
 b) True – Possibly due to fewer blocking antibodies  
 c) False – Initial fears unfounded following double-blind studies  
 d) False  
 e) False – If target glucose values in type 2 diabetes mellitus are not achieved with diet and oral glucose-lowering-agents, insulin is used
- 283 a) False – 1.5–2 L over the first 2 hours  
 b) True – Helps in accurate monitoring of urine output. A central venous pressure line also aids fluid management  
 c) False – Give intravenous short-acting insulin via syringe pump  
 d) False – May worsen intracellular and cerebrospinal acidemia  
 e) True – Gastric stasis is common and inhalation of vomit can be fatal. Insertion of a cuffed endotracheal tube may be necessary before nasogastric aspiration depending on the patient's level of consciousness
- 284 a) False  
 b) True  
 c) False – Early and effective treatment of hypertension does reduce the macro- and microvascular complications of diabetes  
 d) True – Increase plasma insulin concentrations  
 e) False – Most commonly as a single dose with breakfast
- 285 a) False Acarbose is a reversible competitive inhibitor of intestinal alpha-glucoside hydrolases and delays the absorption of starch and sucrose, but does not affect the absorption of ingested glucose  
 b) True  
 c) True – A useful alternative to intravenous glucose if the patient is unable to take glucose orally and venous access is impractical (e.g. in the home) or unavailable  
 d) False  
 e) True – cf. metformin



- 286 a) True Metformin is particularly useful in obese patients with  
b) False non-insulin-dependent (type 2) diabetes mellitus  
c) False uncontrolled by diet and a sulphonylurea.  
d) True Lactic acidosis is the most sinister adverse effect and  
e) True has a high mortality. Metformin is contraindicated in  
renal/hepatic/cardiac failure because of the increased  
risk of lactic acidosis
- 287 a) False The 'glitazones' reduce peripheral insulin resistance  
b) True leading to a reduction in blood glucose concentration.  
c) False Whilst use of 'glitazones' lowers HbA<sub>1c</sub> (glycated  
d) True haemoglobin) in type 2 diabetes mellitus patients  
e) True inadequately controlled on diet ± other oral  
hypoglycaemic drugs, an effect on mortality or diabetic  
complications is currently unproven. There is a possible  
increased risk of cardiac failure associated with 'glitazones'  
in diabetic patients
- 288 a) True  
b) False – In contrast to propylthiouracil and beta blockers  
c) False – Pruritus and rashes are common. They may be treated with  
antihistamines or propylthiouracil substituted for the  
carbimazole if symptoms are significant  
d) True – Methimazole, which is responsible for the therapeutic action  
e) True – Potentially life-threatening/fatal
- 289 a) False A thyroid crisis requires emergency treatment with  
b) True intravenous fluids, propranolol, hydrocortisone, oral  
c) True iodine and propylthiouracil or carbimazole  
d) True  
e) False
- 290 a) False Hypercalcaemia may be a life-threatening emergency.  
b) False General management includes rehydration and  
c) False maintenance of hydration with physiological saline.  
d) True Cinacalcet sensitizes calcium-sensing receptors and is used  
e) True in secondary hyperparathyroidism. Calcitonin and  
bisphosphonates reduce the plasma calcium.  
Glucocorticoids reduce plasma calcium in sarcoidosis
- 291 a) False Is given intravenously or orally in spite of poor systemic  
b) True bioavailability (1–5 per cent). It is generally well tolerated  
c) True  
d) True  
e) True
- 292 a) True Glucocorticoids reduce transcription of many  
b) True proinflammatory genes and induce the transcription of  
c) True others, e.g. lipocortin which inhibits phospholipase

- d) True  $A_2$  and consequently inhibits the formation of several proinflammatory mediators. The anti-inflammatory action takes 6–8 hours to manifest after dosing
- e) False – Glucocorticosteroids inhibit the transcription of proinflammatory cytokines such as TNF, IL-1, etc.
- 293 a) True Even in patients who have been successfully weaned from  
b) True chronic steroid therapy, an acute stress (e.g. trauma,  
c) False surgery, infection) may precipitate an acute adrenal crisis  
d) True  
e) True
- 294 a) True – For example fungal infections and tuberculosis – may  
reactivate old tuberculous lesions  
b) False – Hypokalaemia (aldosterone-like effect)  
c) True  
d) True – In addition local application of steroids to the eye  
predisposes to infection  
e) True
- 295 a) True – Not curative but delays deterioration in some patients  
b) True – May prevent irreversible loss of vision  
c) False  
d) False  
e) True
- 296 a) True The combined oral contraceptive should be stopped four  
b) True weeks before major elective surgery  
c) True  
d) False – St John's wort is likely to induce metabolism of steroids,  
reducing their efficacy and side-effect risks  
e) True – Such patients have a high risk of thromboembolism because  
the lack of these proteins produces a procoagulable state
- 297 a) False The overall acceptability of the combined pill is 80 per cent;  
b) True minor side-effects can often be controlled by a change in  
c) False preparation  
d) False  
e) True
- 298 a) True Other indications to stop the combined oral contraceptive  
b) True immediately include sudden severe chest pain, sudden  
c) False unilateral calf pain, serious neurological effects, hepatitis,  
d) True hepatomegaly, severe depression and hypertension  
e) True
- 299 a) True Urgent medical attention is necessary if lower abdominal  
b) True pain occurs, as it could signify an ectopic pregnancy.  
c) True Mifepristone, a progesterone antagonist, is an unlicensed  
d) False alternative post-coital contraceptive  
e) True

- 300 a) False – Suppresses lactation  
b) True  
c) True  
d) False – The commonest adverse effects are nausea and constipation and orthostatic hypotension  
e) False – Fluid restriction and demeclocycline is usually effective
- 301 a) True Hormone replacement therapy (HRT) using small doses of oestrogen (with progesterone if uterus intact) alleviates menopausal symptoms such as vaginal atrophy and vasomotor instability  
b) False  
c) False  
d) True  
e) True
- 302 a) False – It is a synthetic octapeptide of eight amino acids, molecular weight approx. 900  
b) True  
c) True  
d) True – It antagonizes insulin release  
e) True
- 303 a) False – It is an anti-oestrogen  
b) True  
c) False – It blocks oestrogen receptors in the hypothalamus, feedback inhibition of FSH/LH is reduced and FSH/LH secretion increases  
d) True  
e) True
- 304 a) False – A central  $\alpha_2$  and imidazoline agonist that is useful for menopausal vasomotor symptoms  
b) True – Selective alpha blocker  
c) True – Selective alpha blocker  
d) False – An anti-androgen used in the treatment of severe hypersexuality and sexual deviation in the male. It may be used as an adjunct in inoperable prostate cancer  
e) True – Finasteride inhibits  $5\alpha$ -reductase, reducing prostate size. Adverse effects include decreased libido and impotence
- 305 a) False Sildenafil, a phosphodiesterase type 5 inhibitor, is used for the treatment of erectile dysfunction. It is taken by mouth approximately 1 hour before sexual activity. Concomitant nitrates are contraindicated  
b) False  
c) True  
d) True  
e) True

## EMQ ANSWERS

**306 DIABETES MELLITUS**

- 1 J Metformin is the drug of choice in overweight diabetic patients in whom diet is inadequate. It should be avoided in patients with renal impairment due to the risk of lactic acidosis.
- 2 I Insulin lispro has a more rapid and shorter duration of hypoglycaemic action than natural insulin.
- 3 C Glucagon, via stimulation of adenylyl cyclase, stimulates glycogen breakdown and gluconeogenesis.
- 4 G Pioglitazone binds to PPAR  $\gamma$ , a nuclear receptor.
- 5 F Gliclazide, a sulphonylurea, depolarizes pancreatic islet beta cells, thereby stimulating insulin secretion.

**307 THYROID**

- 1 E Tri-iodothyronine ( $T_3$ ) is more potent and has a more rapid onset of action than thyroxine ( $T_4$ ).
- 2 B Methimazole, the principal metabolite of carbimazole, inhibits peroxidase in the thyroid. Granulocytopenia is a severe adverse drug effect.
- 3 H Lugol's iodine is useful for suppressing thyroid activity prior to the thyroidectomy.
- 4 F  $^{131}\text{I}$  is used to treat thyrotoxicosis (from Graves' disease or toxic nodular goitre) and is also used in high dose for thyroid carcinoma as it can be taken up by metastases and thus deliver radiotherapy locally to the tumour.
- 5 J Several drugs cause goitre, including lithium and imatinib, but amiodarone is unusual in being associated not only with goitre but also with either underactive or overactive thyroid.

**308 CALCIUM METABOLISM**

- 1 B Calciferol (regular vitamin D) is not effective in patients with renal failure because it needs to be hydroxylated in the kidney. Such patients require preparations such as alfacalcidol or calcitriol.
- 2 F Calcium carbonate and aluminium hydroxide are used as phosphate-binding agents in the management of hyperphosphataemia in renal failure.
- 3 E Risedronate and other bisphosphonates are used for the prevention and treatment of osteoporosis.

- 4 D Cinacalcet enhances signalling through the calcium-sensing receptor reducing parathyroid hormone. It is licensed for the treatment of secondary hyperparathyroidism in dialysis patients with renal failure and in parathyroid carcinoma to reduce serum calcium concentration.
- 5 J Chlorthalidone and the related thiazide diuretics are associated with the following metabolic consequences: hypokalaemia, hypomagnesaemia, hyponatraemia, hypercalcaemia, hypochlorhaemic alkalosis, hyperuricaemia and hyperglycaemia.

### 309 ADRENAL

- 1 A Metyrapone is a competitive inhibitor of  $11\beta$ -hydroxylation in the adrenal cortex.
- 2 C Dexamethasone is used relatively short term (as a diagnostic test, or to treat cerebral oedema).
- 3 B Fludrocortisone may be combined with hydrocortisone since hydrocortisone alone may not possess sufficient mineralocorticoid activity for complete replacement in patients with adrenal insufficiency.
- 4 H Phenoxybenzamine is an irreversible alpha-receptor antagonist indicated in hypertensive episodes in phaeochromocytoma, and to prepare patients with phaeochromocytoma for surgery.
- 5 F Aldosterone has no glucocorticoid activity, but is 1000 times more active than hydrocortisone as a mineralocorticoid. Its effects can be blocked by spironolactone.

### 310 PITUITARY

- 1 A Octreotide is a long-acting somatostatin analogue used for the relief of symptoms related to neuroendocrine (particularly carcinoid) tumours and acromegaly. It is also used (unlicensed) in the management of variceal bleeding.
- 2 C Goserelin is an analogue of gonadotrophin-releasing hormone. It initially stimulates the release of FSH/LH, but then downregulates this response (usually after two weeks) effectively leading to medical orchidectomy/ovariectomy.
- 3 H Tetracosactide is a synthetic analogue of adrenocorticotrophic hormone (ACTH).
- 4 G Pegvisomant is a genetically modified analogue of human growth hormone, which acts as an antagonist to growth hormone.
- 5 F First-line treatment of SIADH is to restrict fluid intake. Demeclocycline blocks ADH action on the kidney and may be used in addition.

## SELECTIVE TOXICITY

### MULTIPLE CHOICE QUESTIONS

- 311 The following antibacterial drugs inhibit folic acid biosynthesis:
- a) Amoxicillin
  - b) Aztreonam
  - c) Levofloxacin
  - d) Trimethoprim
  - e) Sulfonamides
- 312 The following infections have been paired with appropriate antibacterial therapy:
- a) Acute otitis media – amoxicillin
  - b) Acute epiglottitis in children – cefotaxime/ceftriaxone or chloramphenicol
  - c) Legionnaire's disease – erythromycin and rifampicin
  - d) Acute cystitis arising outside hospital in adults – trimethoprim
  - e) Antibiotic-associated pseudomembranous colitis – oral vancomycin
- 313 The following antibacterial drug combinations are of accepted benefit in the treatment of the stated infection:
- a) Amoxicillin and cefadroxil for lower urinary tract infection in severely ill patients
  - b) Phenoxymethylpenicillin and tetracycline for acute osteomyelitis in a child under 5 years
  - c) Isoniazid, rifampicin, pyrazinamide and ethambutol in the initial treatment for pulmonary tuberculosis (TB)
  - d) Erythromycin and tetracycline for septicaemia
  - e) Metronidazole and nitrofurantoin for non-specific urethritis

- 314** The following anti-infective drugs are suitable as prophylaxis in the stated conditions:
- a) Co-amoxiclav – human and animal bites
  - b) Ciprofloxacin – close adult contacts of meningococcal disease
  - c) Flucloxacillin – prevention of a secondary case of diphtheria
  - d) Erythromycin – whooping cough contact in an unvaccinated child under 1 year old
  - e) Aciclovir – close contacts of patients with herpes labialis
- 315** Benzylpenicillin:
- a) Is inactivated in gastric acid
  - b) Is effective in meningococcal infections
  - c) Has a half-life of 24 hours
  - d) Is less susceptible than flucloxacillin to beta-lactamase-producing strains of staphylococci
  - e) Approximately 1 in 500 injections cause anaphylactic shock
- 316** Amoxicillin:
- a) Unlike benzylpenicillin is not susceptible to beta-lactamases
  - b) Is effective against many strains of *Haemophilus influenzae*
  - c) Is ineffective in most cases of community-acquired urinary tract infections
  - d) Drug-related skin rashes may appear after dosing has stopped
  - e) Drug-related skin rashes are more common in patients with infectious mononucleosis
- 317** The following drugs are effective in staphylococcal infections:
- a) Ampicillin
  - b) Co-amoxiclav
  - c) Fusidic acid
  - d) Flucloxacillin
  - e) Metronidazole
- 318** Cefuroxime:
- a) Has activity against streptococci
  - b) Has no activity against Gram-negative organisms
  - c) Plasma concentrations should be monitored to avoid toxicity
  - d) Is principally renally eliminated
  - e) Has approximately 5–10 per cent cross-sensitivity for allergic reactions with benzylpenicillin

- 319 Gentamicin, an aminoglycoside:
- Is effective in pneumococcal pneumonia
  - Is poorly absorbed from the gut
  - Has an elimination half-life of approximately 12 hours if renal function is normal
  - Cerebrospinal fluid (CSF) penetration is poor
  - Causes irreversible eighth nerve damage
- 320 Chloramphenicol is usually effective in:
- Pulmonary tuberculosis
  - Epiglottitis
  - Typhoid
  - Bacterial meningitis
  - Bacterial conjunctivitis
- 321 Uses of clarithromycin include:
- Mycoplasma pneumoniae*
  - Legionnaire's disease
  - Campylobacter* enteritis
  - Non-specific urethritis
  - Meningococcal meningitis
- 322 Erythromycin:
- Is poorly absorbed when given by mouth
  - Has a shorter half-life than azithromycin
  - The most common adverse effect is headache
  - Inhibits CYP450 enzymes
  - Cannot be prescribed with amoxicillin
- 323 Tetracyclines are used to treat:
- Infections caused by *Clostridium difficile*
  - Lyme disease
  - Acne vulgaris
  - Systemic lupus erythematosus
  - Non-specific urethritis
- 324 Metronidazole is used to treat:
- Trichomonal infections
  - Amoebic dysentery
  - Giardiasis
  - Tetanus
  - Gas gangrene



- 325** Ciprofloxacin:
- a) Is a drug of first choice in *Streptococcus pneumoniae* infections
  - b) Is effective in *Pseudomonas* infections
  - c) Should be avoided in children
  - d) Should be avoided in epileptics
  - e) Is ineffective if administered orally
- 326** Isoniazid:
- a) Undergoes acetylation (by *N*-acetyltransferase) in the liver
  - b) Is used for only the initial two months of the recommended six-month anti-TB regimen in the UK
  - c) Is readily absorbed from the gut
  - d) Does not diffuse into the CSF
  - e) Is contraindicated in children under the age of 10 years
- 327** Adverse effects associated with rifampicin include:
- a) Hepatitis and cholestatic jaundice
  - b) Peripheral neuropathy
  - c) Convulsions
  - d) Influenza-like symptoms
  - e) Pink/red urine and tears
- 328** Rifampicin accelerates the CYP450-mediated metabolism of:
- a) Corticosteroids
  - b) Warfarin
  - c) Streptomycin
  - d) Digoxin
  - e) Oestrogen
- 329** The following adverse effects are correctly paired with a causative antituberculous drug:
- a) Peripheral neuropathy – isoniazid
  - b) Ototoxicity – rifampicin
  - c) Hyperuricaemia – pyrazinamide
  - d) Retrobulbar neuritis – ethambutol
  - e) Hepatotoxicity – streptomycin
- 330** Dapsone:
- a) Is used in the treatment of amoebiasis
  - b) Is indicated in multibacillary leprosy
  - c) Is used in the treatment of dermatitis herpetiformis
  - d) Is acetylated in the liver
  - e) Has cross-sensitivity with sulfonamides

- 331** Amphotericin:
- a) Is effective in local *Candida* spp. infections
  - b) Is effective in systemic *Candida* spp. infections
  - c) Is nephrotoxic
  - d) Causes hypokalaemia
  - e) Is ineffective in cryptococcosis
- 332** The following antifungal agents have been paired correctly with an appropriate indication:
- a) Nystatin – oral *Candida* infections
  - b) Voriconazole – invasive aspergillosis
  - c) Flucytosine – tinea pedis
  - d) Clotrimazole – intertrigo
  - e) Miconazole – cold sores
- 333** Voriconazole:
- a) Is available and effective as oral and intravenous therapy
  - b) Is active against *Aspergillus*
  - c) Inhibits cortisol biosynthesis
  - d) Inhibits CYP3A
  - e) Gastrointestinal absorption is reduced by omeprazole
- 334** Fluconazole:
- a) Oral absorption is minimal unless taken on an empty stomach
  - b) Presystemic metabolism is extensive
  - c) Penetrates the central nervous system well
  - d) Is excreted 80 per cent by the kidney
  - e) Causes gynaecomastia
- 335** Terbinafine:
- a) Is indicated in dermatophyte nail infections
  - b) A topical preparation is indicated in ringworm infection (e.g. tinea pedis/cruris)
  - c) A single dose is usually effective
  - d) Is a potent CYP450 enzyme inducer
  - e) May exacerbate psoriasis
- 336** Aciclovir:
- a) Inhibits viral DNA polymerase
  - b) Is indicated in herpetic keratitis
  - c) Should be avoided if possible in pregnancy
  - d) Is indicated in herpetic meningoencephalitis
  - e) Is ineffective in chicken pox

- 337** Foscarnet:
- a) Is indicated in cytomegalovirus (CMV) retinitis in acquired immune deficiency syndrome (AIDS) patients
  - b) Aciclovir-resistant herpes simplex virus infections
  - c) Is nephrotoxic
  - d) Causes fits
  - e) Is usually administered by mouth or topically
- 338** Ribavarin:
- a) Is indicated in CMV retinitis in AIDS patients
  - b) Inhibits viral RNA methyltransferase
  - c) Must be taken up into cells and phosphorylated to be effective
  - d) Can be administered via aerosol inhalation to treat bronchiolitis
  - e) Is combined with interferon alfa in the treatment of hepatitis C
- 339** The following are used in the prophylaxis or treatment of influenza:
- a) Amantadine
  - b) Palivizumab
  - c) Entecavir
  - d) Oseltamivir
  - e) Zanamivir
- 340** Adverse effects associated with the interferons include:
- a) Hypocalcaemia
  - b) Inhibition of spermatogenesis
  - c) Renal tubular acidosis
  - d) Lymphopenia
  - e) Influenza-like symptoms
- 341** One or more of the interferons are indicated in:
- a) Herpes simplex encephalitis
  - b) Chronic hepatitis B infection
  - c) Chronic hepatitis C infection
  - d) Hairy cell leukaemia
  - e) CMV retinitis
- 342** Which of the following antiretroviral drug combinations is accepted first-line therapy for patients with human immunodeficiency virus (HIV) infection?
- a) Zidovudine (AZT) plus 2,3-dideoxycytidine (ddC)
  - b) AZT + lamivudine + lopinavir/ritonavir
  - c) Ritonavir + amprenavir + enfuvirtide
  - d) AZT + lamivudine + nevirapine
  - e) AZT + stavudine (d4T) + enfuvirtide

- 343** Properties of HIV protease inhibitors include:
- Cause hypertriglyceridaemia and truncal fat redistribution
  - Are most effective of the antiretrovirals at reducing plasma HIV RNA copy number
  - Oral bioavailability is consistent and >95 per cent
  - Cause many drug–drug interactions due to inhibition of CYP3A
  - HIV resistance to one agent in the class usually means cross-resistance to others
- 344** The following are used to treat *Pneumocystis carinii* pneumonia (PCP) in patients with HIV infection:
- Aztreonam
  - Intravenous co-trimoxazole
  - Rifabutin
  - Pentamidine
  - Glucocorticosteroids if the arterial  $PO_2$  is less than 60 mmHg
- 345** Quinine sulfate:
- Is the drug of choice in chloroquine-resistant falciparum malaria
  - Is available for intravenous and oral use
  - Is effective in eradicating the hepatic parasites in *Plasmodium vivax* malaria
  - Is contraindicated in renal failure
  - Large therapeutic doses cause tinnitus
- 346** The following adverse effects are paired with the correct causative antimalarial drug:
- Acneiform eruption – chloroquine
  - Stevens–Johnson syndrome – quinine
  - Psychosis – mefloquine
  - Prolongation of QTc – proguanil
  - Haemolytic anaemia – primaquine
- 347** The following infections have been paired with appropriate drug therapy:
- Trypanosoma gambiense* (African sleeping sickness), early stages – pentamidine and suramin
  - Giardia lamblia* – metronidazole
  - Taenia saginata* (a tapeworm) – emetine
  - Strongyloides stercoralis* (threadworm) – mebendazole
  - Toxocara canis* – pyraquantal

- 348** The following anticancer drugs are considered highly emetogenic:
- a) Cyclophosphamide
  - b) Methotrexate
  - c) 5-Fluorouracil
  - d) Interleukin 2
  - e) Cisplatin
- 349** The following cytotoxic drugs may be associated with profound and prolonged myelosuppression:
- a) Chlorambucil
  - b) Melphalan
  - c) 1,3-bis (2 chloroethyl)-1-nitroso-urea (BCNU)
  - d) Bleomycin
  - e) Vincristine
- 350** During cancer chemotherapy:
- a) Infection is the commonest life-threatening complication
  - b) Infection is often acquired from the patient's own gut flora
  - c) If infection occurs, pyrexia is usually absent
  - d) Men and women must be strongly advised to avoid conception
  - e) There is a danger of inducing second malignancies
- 351** Cyclophosphamide:
- a) Is normally used in combination with other cytotoxic agents
  - b) Is an alkylating agent
  - c) Causes granulocytopenia
  - d) Causes nausea and vomiting
  - e) Causes alopecia
- 352** Methotrexate:
- a) Inhibits dihydrofolate reductase which synthesises tetrahydrofolate from dihydrofolate
  - b) The toxicity of high doses can be reduced by giving folinic acid 24 hours after the methotrexate
  - c) Is primarily excreted in the bile
  - d) Chronic treatment can cause cirrhosis
  - e) Is the first-line treatment for choriocarcinoma
- 353** The following cytotoxic drugs are paired with a characteristic adverse effect:
- a) Etoposide – peripheral neuropathy
  - b) Paclitaxel – alopecia
  - c) Daunorubicin – cardiomyopathy
  - d) Irinotecan – diarrhoea
  - e) 6-Mercaptopurine – pulmonary fibrosis

- 354** During cisplatin therapy:
- a) Pretreatment hydration is mandatory
  - b) Pretreatment with dexamethasone and a 5HT<sub>3</sub> antagonist (e.g. ondansetron) reduces the nausea and vomiting
  - c) Visual disturbances are common
  - d) Magnesium supplements are usually given
  - e) Nephrotoxicity is dose related and dose limiting
- 355** Paclitaxel (a taxane):
- a) May be used alone or in combination for a broad range of epitheloid tumours and lymphomas
  - b) Inhibits purine synthesis
  - c) Causes sensory neuropathies
  - d) Requires glucocorticosteroid premedication to minimize acute hypersensitivity reactions
  - e) Is not associated with myelosuppression
- 356** Recombinant human erythropoietin is used to treat:
- a) Iron-deficient anaemia when iron is malabsorbed
  - b) Sickle cell anaemia
  - c) Anaemia of chronic renal failure
  - d) AZT-related anaemia
  - e) Clozapine-induced agranulocytosis
- 357** Filgrastim (human granulocyte colony-stimulating factor):
- a) Is usually administered by subcutaneous injection
  - b) Causes immediate transient neutropenia
  - c) Is used in myeloid leukaemia
  - d) Stimulates proliferation and differentiation of myeloid progenitor cells
  - e) Causes bone pain
- 358** Lopinavir, an HIV-protease inhibitor, is associated with the following:
- a) Lipodystrophy syndrome
  - b) Hyperglycaemia
  - c) Peripheral neuropathy
  - d) Lactic acidosis
  - e) Inhibition of metabolism of rifabutin

**Answers: see pages 147–154**

## EXTENDED MATCHING QUESTIONS

### 359 ANTIBACTERIAL DRUGS

- |          |                               |          |                            |
|----------|-------------------------------|----------|----------------------------|
| <b>A</b> | Oral vancomycin               | <b>F</b> | Rifampicin                 |
| <b>B</b> | Trimethoprim                  | <b>G</b> | Ciprofloxacin              |
| <b>C</b> | Flucloxacillin + fusidic acid | <b>H</b> | Gentamicin + metronidazole |
| <b>D</b> | Clarithromycin                | <b>I</b> | Neomycin                   |
| <b>E</b> | Doxycycline                   | <b>J</b> | Amoxicillin                |

Which antibacterial drug or drug combination from the list above is the most appropriate choice for the infection scenarios listed below?

- 1 Lyme disease
- 2 Invasive salmonellosis
- 3 Antibiotic-associated colitis (pseudomembranous colitis)
- 4 Peritonitis in a patient allergic to cephalosporins
- 5 Uncomplicated community-acquired pneumonia in a penicillin-allergic patient

### 360 ANTIBACTERIAL DRUGS

- |          |                                     |          |                                    |
|----------|-------------------------------------|----------|------------------------------------|
| <b>A</b> | Cefuroxime and clarithromycin       | <b>F</b> | Ciprofloxacin                      |
| <b>B</b> | Benzylpenicillin and flucloxacillin | <b>G</b> | Erythromycin and rifampicin        |
| <b>C</b> | Benzylpenicillin and gentamicin     | <b>H</b> | Flucloxacillin and sodium fusidate |
| <b>D</b> | Ceftriaxone                         | <b>I</b> | Teicoplanin                        |
| <b>E</b> | Cefuroxime and metronidazole        | <b>J</b> | Trimethoprim                       |

From the above list, choose the most appropriate antibiotic regime for each of the following clinical situations:

- 1 A 35-year-old man severely ill with community-acquired pneumonia
- 2 A 40-year-old man with acute septic arthritis in his knee caused by *Staphylococcus aureus*
- 3 A 25-year-old woman with suspected bacterial meningitis
- 4 Suspected bacterial endocarditis following dental extraction in a 65-year-old man with mitral valve prolapse
- 5 A 38-year-old woman allergic to beta-lactam antibiotics with pyelonephritis

**361 HIV**

<b>A</b>	Azatanavir	<b>F</b>	Enfuvirtide
<b>B</b>	Rimantidine	<b>G</b>	Raltegravir
<b>C</b>	Efavirenz	<b>H</b>	Adefovir
<b>D</b>	Zidovudine (ZDV)	<b>I</b>	Ganciclovir
<b>E</b>	Zanamivir	<b>J</b>	Foscarnet

Match the correct drug with its pharmacodynamic effect (either on the HIV virus or the human host)

- 1 Competitive inhibition of the HIV reverse transcriptase
- 2 Inhibition of HIV entry into T cells
- 3 Non-competitive inhibition of HIV reverse transcriptase
- 4 Inhibition of HIV protease
- 5 Competitive inhibition of HIV integrase

**362 HIV**

<b>A</b>	Lopinavir	<b>F</b>	Maraviroc
<b>B</b>	Lamivudine	<b>G</b>	Abacavir
<b>C</b>	Nevirapine	<b>H</b>	Tenofovir
<b>D</b>	ZDV	<b>I</b>	Ganciclovir
<b>E</b>	Didanosine	<b>J</b>	Foscarnet

Match the drug with the correct property/side-effect defined below:

- 1 Active against HIV and CMV
- 2 Causes macrocytic anaemia with reticulocytopenia
- 3 Potent inhibitor of CYP3A and P-gp (ABCB1)
- 4 Does not require activation to a nucleotide
- 5 Oral bioavailability increased ('boosted') by ritonavir

**363 MALARIA AND PARASITIC INFECTIONS**

<b>A</b>	Atovaquone + proguanil	<b>F</b>	Mebendazole
<b>B</b>	Quinine	<b>G</b>	Diethylcarbamazine
<b>C</b>	Primaquine	<b>H</b>	Ivermectin
<b>D</b>	Artemisinin derivatives	<b>I</b>	Pentamidine
<b>E</b>	Niclosamide	<b>J</b>	Metronidazole

Select a drug/drug combination from the list above most appropriate for the indication below:

- 1 Acute falciparum malaria in a country with widespread chloroquine resistance (e.g. Ghana) where parenteral therapy is required
- 2 Malaria prophylaxis for a European tourist in Ghana
- 3 Eradication of hepatic forms of *P. vivax*
- 4 Threadworm infection in a 3-year-old child
- 5 Giardiasis



**364 CANCER**

<b>A</b>	Imatinib	<b>F</b>	Capecitabine
<b>B</b>	Oxaliplatin	<b>G</b>	Gemcitabine
<b>C</b>	Irinotecan	<b>H</b>	Gefitinib
<b>D</b>	Rituximab	<b>I</b>	Docetaxel
<b>E</b>	Trastuzumab	<b>J</b>	Bevacizumab

Match the drug with its correct molecular target:

- 1 BCR-Abl kinase
- 2 DNA Topoisomerase I
- 3 HER2/NEU (epidermal growth factor receptor-2 (EGFR-2))
- 4 Vascular endothelial growth factor (VEGF)
- 5 Epidermal growth factor receptor–tyrosine kinase (EGFR-TK)

**365 CANCER**

<b>A</b>	Dasatinib	<b>F</b>	Vincristine
<b>B</b>	Cisplatin	<b>G</b>	Doxorubicin
<b>C</b>	Fludarabine	<b>H</b>	Sorafenib
<b>D</b>	Interleukin 2	<b>I</b>	Paclitaxel
<b>E</b>	Interferon	<b>J</b>	Panimumomab

Match the drug with the correct common and serious adverse effect:

- 1 Hypothyroidism
- 2 Cerebellar ataxia
- 3 Acute renal tubular necrosis
- 4 Adult respiratory distress syndrome (non-cardiogenic pulmonary oedema)
- 5 Hypertension

**ANSWERS:** see pages 154–158

## ANSWERS

## MCQ ANSWERS

- 311 a) False – Inhibits bacterial cell wall peptidoglycan cross-linking  
 b) False – Inhibits bacterial cell wall peptidoglycan cross-linking  
 c) False – Inhibit bacterial DNA gyrase (a bacterial DNA topoisomerase)  
 d) True  
 e) True
- 312 a) True – When bacterial commonly caused by group A streptococci  
 b) True – Caused by *H. influenzae*  
 c) True  
 d) True  
 e) True – Caused by colonization of the colon with *Clostridium difficile*. Alternative oral metronidazole (NB: stop causative antibiotic)
- 313 a) False – Intravenous gentamicin and cefuroxime  
 b) False – Caused commonly by *H. influenzae* or *Staphylococcus aureus* – amoxicillin and flucloxacillin is usually a satisfactory combination  
 c) True – Reduces the risk of TB resistance  
 d) False – Choice depends on clinical conditions, a beta-lactam and an aminoglycoside is a common bacteriocidal combination used for septicaemia  
 e) False – Single agent is effective (e.g. tetracycline or erythromycin)
- 314 a) True  
 b) True  
 c) False – Erythromycin  
 d) True  
 e) False – See *Textbook of Clinical Pharmacology and Therapeutics*, Chapters 43 and 45
- 315 a) True – Whilst phenoxymethylpenicillin (penicillin V) is stable in gastric acid and is administered orally  
 b) True  
 c) False – Short half-life of approximately 30 minutes  
 d) False  
 e) False – 1 in 100 000
- 316 a) False Amoxicillin is an extended-range penicillin used for chest infections, otitis media, urinary tract infection, biliary infections and prevention of bacterial endocarditis. Rashes are common and there is an especially high incidence in infectious mononucleosis and lymphatic leukaemia  
 b) True  
 c) False  
 d) True  
 e) True

- 317 a) False – Susceptible to beta-lactamases  
b) True – A combination of amoxicillin with clavulanic acid (a beta-lactamase inhibitor)  
c) True  
d) True  
e) False – Metronidazole is effective in anaerobic and protozoal infections. It is used as a part of triple therapy to eradicate *Helicobacter pylori*
- 318 a) True Cefuroxime combines lactamase stability with activity  
b) False against streptococci, staphylococci, *H. influenzae* and  
c) False *Escherichia coli*  
d) True  
e) True
- 319 a) False Aminoglycosides are used particularly in serious infections  
b) True such as septicaemia, usually in combination with a beta-  
c) False lactam (e.g. a penicillin). Blood concentration monitoring is  
d) True mandatory to avoid toxicity. The half-life is approximately  
e) True 2 hours if renal function is normal
- 320 a) False Chloramphenicol has a broad spectrum and penetrates  
b) True tissues exceptionally well. Its widespread use in  
c) True developing countries has led to some resistance. Its major  
d) True disadvantage is a 1:40 000 incidence of aplastic anaemia  
e) True (which can be irreversible)
- 321 a) True Macrolide antibiotics (erythromycin, clarithromycin and  
b) True azithromycin), are useful alternatives to penicillin in  
c) True penicillin-allergic patients (with the notable exception of  
d) True meningitis) and are also effective against several unusual  
e) False bacteria. Clarithromycin and azithromycin are given twice  
and once daily, respectively, unlike erythromycin which is  
given four times daily. They cause fewer gastrointestinal  
side-effects and show better tissue penetration (particularly  
azithromycin)
- 322 a) False – Well absorbed  
b) True – Erythromycin, 1–1.5 hours; azithromycin, 40–60 hours  
c) False – Gastrointestinal effects are most common  
d) True – Causes accumulation of theophylline, warfarin and  
atorvastatin  
e) False – They can be co-prescribed in e.g. community-acquired  
pneumonia
- 323 a) False Oral absorption of tetracyclines is reduced by food (except  
b) True doxycycline). They must be avoided in renal impairment  
c) True (except doxycycline)  
d) False  
e) True

- 324 a) True Metronidazole has high activity against protozoa and anaerobic bacteria. It is widely used prophylactically before abdominal surgery when the rectal route is often suitable  
b) True  
c) True  
d) False  
e) True – Often in conjunction with clindamycin
- 325 a) False Oral bioavailability of the 4-fluoroquinolones is good and they offer an oral alternative to parenteral aminoglycosides and anti-pseudomonal penicillins for the treatment of pseudomonal infection. Quinolones cause arthropathy in young animals and can cause convulsions. Photosensitivity also occurs  
b) True  
c) True  
d) True  
e) False
- 326 a) True The recommended regimen for ‘unsupervised treatment’ of pulmonary TB in the UK for a patient at low risk of poor compliance is isoniazid, rifampicin, ethambutol and pyrazinamide for two months followed by rifampicin and isoniazid for a further four months. Specialist advice should be sought for immunocompromised patients  
b) False  
c) True  
d) False  
e) False
- 327 a) True Serious liver damage is uncommon but minor histological changes and rises in aminotransferase are common and in the absence of jaundice are not an indication for stopping treatment  
b) False  
c) False  
d) True  
e) True
- 328 a) True In women using the contraceptive pill, an alternative method of contraception should be provided. Streptomycin and digoxin are primarily cleared from the body by renal elimination  
b) True  
c) False  
d) False  
e) True
- 329 a) True – Use prophylactic pyridoxine in diabetics, alcoholics and the malnourished – more common in slow acetylators  
b) False – Occurs with streptomycin  
c) True – May precipitate gout  
d) True – Regular questioning for visual symptoms and baseline assessment of visual acuity are essential. There must be further visual examination if symptoms develop  
e) False – Occurs with isoniazid, rifampicin and pyrazinamide
- 330 a) False Dapsone is a sulfonamide derivative which is a competitive inhibitor of dihydropteroate (folate) synthetase, thereby inhibiting dihydrofolic acid production. Clofazimine and rifampicin are also used to treat leprosy  
b) True  
c) True  
d) True  
e) True

- 331 a) True Amphotericin is a broad-spectrum antifungal although  
b) True *Aspergillus* spp. are usually resistant. It is administered  
c) True topically (lozenges), orally (suspension) or intravenously.  
d) True Thrombophlebitis is a common problem when used  
e) False intravenously. Intravenous lipid formulations are less  
nephrotoxic but more expensive
- 332 a) True – NB: bitter taste  
b) True – Alone or with flucytosine. Amphotericin is nephrotoxic  
c) False – Used with amphotericin for systemic candidiasis and  
cryptococcosis  
d) True – Powder suitable  
e) False – Cold sores are due to the virus herpes simplex
- 333 a) True  
b) True – Voriconazole is a potent broad-spectrum triazole antifungal  
active against *Candida* and *Aspergillus*  
c) True – Inhibits enzymes involved in cortisol and testosterone  
synthesis  
d) True – Inhibits the metabolism of many drugs which are  
metabolized by CYP3A  
e) False – The absorption of fluconazole and voriconazole is not  
significantly reduced by agents which increase gastric pH  
(H<sub>2</sub> blockers or proton pump inhibitors)
- 334 a) False Fluconazole is a potent and broad-spectrum antifungal  
b) False drug. It may be used for local or systemic infections as well  
c) True as prophylaxis in neutropenic patients. Adverse effects are  
d) True gastrointestinal, erythema multiforme and hepatitis  
e) False
- 335 a) True Terbinafine is available only as an oral preparation. It is  
b) False used to treat ringworm or dermatophyte infections of the  
c) False nails. It is usually given for 2–6 weeks (longer for nail bed  
d) False infections)  
e) True
- 336 a) True Aciclovir is a potent and selective inhibitor of herpes virus  
b) True DNA polymerase. It may be administered as an ointment  
c) True (e.g. in herpetic keratitis), orally (as in shingles) or by  
d) True intravenous infusion as in encephalitis  
e) False
- 337 a) True Foscarnet is a nucleotide analogue that inhibits viral DNA  
b) True polymerase and thus DNA synthesis. It is administered as  
c) True an intravenous infusion in both immunocompetent and

- d) True immunosuppressed patients  
e) False
- 338 a) False – Ganciclovir  
b) True – NB: Ribavirin is a potent teratogen  
c) True  
d) True  
e) True
- 339 a) True – Also used in Parkinson's disease  
b) False – Monoclonal antibody used in prevention of respiratory syncytial virus (RSV) infection in at-risk children  
c) False – Entecavir is used to treat chronic hepatitis B infection  
d) True – Oral administration  
e) True – By inhalation only
- 340 a) False – Associated with foscarnet  
b) False – Associated with ganciclovir which is indicated in severe CMV infection in immunocompromised patients  
c) False – Associated with amphotericin  
d) True  
e) True
- 341 a) False Interferons are glycoproteins secreted by cells infected with viruses or foreign double-stranded DNA. They are  
b) True with viruses or foreign double-stranded DNA. They are  
c) True non-antigenic and species specific. Interferon alfa is  
d) True combined with ribavirin for the treatment of hepatitis C.  
e) False Interferon beta is licensed for the treatment of multiple sclerosis
- 342 a) False Triple therapy: two nucleoside reverse transcriptase inhibitors  
b) True plus HIV protease inhibitor or plus a non-nucleoside reverse  
c) False transcriptase inhibitor is accepted first-line therapy. See  
d) True *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 46  
e) False – AZT + d4T antagonistic *in vitro* at least. Not used clinically
- 343 a) True Saquinavir, ritonavir, indinavir, lopinavir, amprenavir,  
b) True atazanavir, tripanavir and nelfinavir are anti-HIV protease  
c) False inhibitors  
d) True  
e) True
- 344 a) False High-dose co-trimoxazole is first-line standard treatment  
b) True for PCP in patients with HIV infection. After recovery,  
c) False secondary prophylaxis with oral co-trimoxazole is usual.  
d) True Rifabutin is indicated for prophylaxis of *Mycobacterium*  
e) True *avium intracellulare* infections in HIV patients with low CD4 count

- 345 a) True – If resistance is not a possibility, chloroquine may be used  
b) True  
c) False – Primaquine  
d) False  
e) True – Cinchonism, which also includes deafness, headache, nausea and visual disturbance
- 346 a) True – Other chloroquine side-effects include convulsions, visual disturbances, depigmentation and hair loss. It is very toxic in overdose  
b) False – Recognized with pyrimethamine with sulfadoxine  
c) True – Also potentiates the bradycardic effect of beta blockers  
d) False  
e) True – In glucose 6-phosphate dehydrogenase-deficient patients
- 347 a) True  
b) True  
c) False – A single dose of praziquantel is curative  
d) True – Pyrantel is also effective  
e) False – Diethylcarbamazine, in addition corticosteroids may be needed to treat allergic reactions to dying larvae
- 348 a) True Nausea and vomiting are often the principal immediate toxic effects associated with cytotoxic chemotherapy. To avoid tissue necrosis, another immediate effect, expert attention to vascular access is mandatory  
b) False  
c) False  
d) False  
e) True
- 349 a) True There are two patterns of bone marrow recovery after suppression: rapid and delayed. The use of haematopoietic growth factors, e.g. erythropoietin, G-CSF is a major advance in supportive care. Vincristine and bleomycin seldom cause myelosuppression. Vincristine is associated with peripheral or autonomic neuropathy. It is very irritant and must never be given into the intrathecal space. Extravasation from a vein causes profound local ulceration  
b) True  
c) True  
d) False  
e) False
- 350 a) True Broad-spectrum antibacterial treatment must be started empirically in febrile neutropenic patients without waiting for culture results. The effect on fertility and the risk of future fetal abnormalities are very variable. Alkylating agents are particularly harmful. Successful pregnancies are not unusual in women at least six months after completion of chemotherapy. Sperm and oocyte storage should be considered  
b) True  
c) False  
d) True  
e) True
- 351 a) True Cyclophosphamide is used as part of combination chemotherapy for various lymphomas and leukaemias and in myeloma. It is similarly used in treating certain  
b) True  
c) True

- d) True      solid tumours (e.g. breast cancer, small cell lung cancer).  
e) True      In cytotoxic doses it is usually given by intravenous injection
- 352 a) True  
b) True  
c) False    – Contraindicated in significant renal impairment, excreted primarily in the urine  
d) True  
e) True
- 353 a) False    – Peripheral neuropathy is common with vincristine  
b) True    – Etoposide, a topoisomerase II inhibitor, is particularly active in small cell lung cancer  
c) True  
d) True    – Irinotecan is a topoisomerase I inhibitor  
e) False    – Pulmonary fibrosis is associated with busulfan or bleomycin therapy
- 354 a) True    Cisplatin is of value in metastatic germ cell cancers  
b) True    (seminoma and teratoma). Carboplatin is widely used  
c) False    in advanced ovarian cancer and lung cancer (especially  
d) True    in small cell lung cancer). It is generally better tolerated  
e) True    than cisplatin; however it is more myelosuppressive.  
Oxaliplatin is used in metastatic colorectal cancer in  
combination with fluorouracil and folinic acid.  
Neurotoxicity is dose limiting
- 355 a) True    Paclitaxel was derived from the bark of the Pacific yew  
b) False    tree. It antagonizes the depolymerization of microtubules,  
c) True    halting mitosis. The affected cells undergo apoptosis.  
d) True    Hypersensitivity reactions, bone marrow suppression,  
e) False    myalgia, arthralgia, nausea and vomiting and alopecia are  
also associated adverse effects
- 356 a) False    – Use parenteral iron. Erythropoietin treatment will  
precipitate iron deficiency and generally supplemental iron  
should be prescribed concomitantly with erythropoietin  
b) False  
c) True  
d) True  
e) False
- 357 a) True    – Often self-administered  
b) True  
c) False    – Increases proliferation of the malignant clone  
d) True  
e) True    – Also myalgia, fever, splenomegaly, thrombocytopenia and  
abnormal hepatic transaminases



- 358 a) True – Fat redistribution, insulin resistance and dyslipidaemia  
b) True  
c) True  
d) False – Associated with nucleoside reverse transcriptase inhibitors  
e) True – Via inhibition of CYP3A, increasing the risk of rifabutin toxicity

**EMQ ANSWERS****359 ANTIBACTERIAL DRUGS**

- 1 E Lyme disease: doxycycline.  
2 G Invasive salmonellosis: ciprofloxacin or cefotaxime.  
3 A Antibiotic-associated colitis (pseudomembranous colitis): oral metronidazole or oral vancomycin.  
4 H Peritonitis in a patient allergic to cephalosporins: gentamicin + metronidazole.  
5 D Uncomplicated community-acquired pneumonia in a penicillin-allergic patient: clarithromycin

**360 ANTIBACTERIAL DRUGS**

- 1 A Severe community-acquired pneumonia: cefuroxime and clarithromycin (add flucloxacillin if staphylococcal infection suspected).  
2 H Acute septic arthritis: flucloxacillin and sodium fusidate.  
3 D Suspected bacterial meningitis in a 25-year-old woman: ceftriaxone.  
4 C Bacterial endocarditis following dental extraction: benzylpenicillin and gentamicin.  
5 F Pyelonephritis (beta-lactam allergic): ciprofloxacin.

**361 HIV**

- 1 D Zidovudine (ZDV, AZT) undergoes intracellular anabolic phosphorylation to its triphosphate anabolite (ZDV-TP) which acts as a competitive inhibitor to endogenous nucleotides for the HIV-reverse transcriptase. ZDV-TP similarly competitively inhibits the mitochondrial DNA polymerase gamma. ZDV is used as one of the component drugs in highly active anti-retroviral therapy (HAART). Other compounds in this group called the nucleoside reverse transcriptase inhibitors

(NRTIs) include lamivudine (3TC), stavudine (d4T), ddI, emtricitabine and abacavir. The commonest toxicities of ZDV are fatigue, anaemia and gastrointestinal upset.

- 2 F Enfuvirtide is a peptide which blocks the interaction between the HIV gp41 protein and the host cell membrane by binding to a hydrophobic groove in the N36 region of gp41. Due to its unique mechanism of action, enfuvirtide is active against HIV which has developed resistance to HAART. It is given by intravenous injection and its main side-effects are infusion reactions, lymphadenopathy, flu-like syndrome and eosinophilia.
- 3 C Efavirenz is a non-nucleoside (non-competitive) HIV reverse transcriptase (HIV-RT) inhibitor (NNRTI) which binds to an allosteric (non-catalytic) site on HIV-RT, inhibiting its function. Other drugs in this class are nevirapine and delavirdine. They are synergistic with NRTIs against HIV-RT. They should not be used as monotherapy as viral resistance develops quickly and are thus a component of HAART. The main side-effects are gastrointestinal upsets, lipodystrophy, arthralgia, myalgia and complex drug-drug interactions due to modulation of CYP450.
- 4 A Azatanavir is a competitive inhibitor of the HIV protease and inhibits the cleavage of HIV pre-proteins into active HIV proteins. It is one of a class of HIV protease inhibitors that is most potent in inhibiting HIV replication. Other agents in the class include amprenavir (fosamprenavir), ritonavir, indinavir, lopinavir, nelfinavir, saquinavir and tripanavir. These agents form part of HAART. Side-effects include gastrointestinal upset, fatigue, lipodystrophy, hyperglycaemia-hypertriglyceridaemia and drug-drug interactions by inhibiting CYP3A.
- 5 G Raltegravir. This is a competitive inhibitor of the insertion of HIV DNA into the host genome of the enzyme HIV integrase. It is also termed a strandtransfer inhibitor. It is administered orally on a twice-daily basis and is only to be used in patients who have resistance to standard HAART combinations. Common toxicities are diarrhoea, nausea, headaches and myositis.

### 362 HIV

- 1 J Foscarnet is a pyrophosphate analogue which is a non-competitive inhibitor of CMV DNA polymerase and HIV-RT. It thus can inhibit replication of both viruses. It is primarily used to treat CMV infections. It is administered systemically and its main side-effects are nephrotoxicity, CNS irritability, hypocalcaemia and hypomagnesaemia.
- 2 D Zidovudine (ZDV, AZT) undergoes intracellular anabolic phosphorylation to its triphosphate anabolite (ZDV-TP) which acts as a competitive inhibitor to endogenous nucleotides for the HIV-RT. ZDV-TP similarly competitively inhibits the mitochondrial DNA polymerase gamma.

The anaemia it causes is macrocytic (with normal B<sub>12</sub> and folate) and impaired erythroid precursor development manifested as reticulocytopenia. Aplastic anaemia can be observed, as can suppression of the myeloid lineages (neutropenia). This effect is dose-dependent and minimized by treatment with erythropoietin.

- 3 G Ritonavir is one of the least potent HIV-protease inhibitors used to treat HIV. One of its ancillary properties is that it is a potent inhibitor of CYP3A (gastrointestinal and hepatic) and the drug efflux protein in the gastrointestinal tract P-glycoprotein (MDR-1/ABC-B1). By inhibiting the function of both these proteins low-dose ritonavir is used in combination with other agents in this drug class (e.g. lopinavir) to enhance their bioavailability. This is termed 'boosted' lopinavir therapy.
- 4 H Tenofovir is the first nucleotide (as distinct from nucleoside – a non-phosphorylated purine or pyrimidine) reverse transcriptase inhibitor and is used in combination with NRTIs. It is a derivative of adenosine monophosphate, but lacks the ribose ring. It undergoes further sequential phosphorylation to the diphosphate and then the triphosphate which is a competitive inhibitor of HIV-RT.
- 5 A Lopinavir – see explanation for answer 3 G above.

### 363 MALARIA AND PARASITIC INFECTIONS

- 1 B Quinine sulphate is the drug of choice for treating an acute attack of falciparum malaria where the parasite is likely to be chloroquine resistant.
- 2 A Atovaquone and proguanil is a recommended prophylactic antimalarial for a visit to Ghana (high risk of malaria, widespread chloroquine resistance).
- 3 C Primaquine is used after standard chloroquine therapy to eradicate hepatic forms of *P. vivax* and *P. malariae*.
- 4 F Mebendazole is appropriate for treating threadworm infection in those over 2 years. It is also effective in roundworm, whipworm and hookworm infections. Piperazine may be used in threadworm and roundworm infections from the age of three months.
- 5 J Metronidazole is the treatment of choice for giardiasis and acute invasive amoebic dysentery.

### 364 CANCER

- 1 A Imatinib is the first in class oral targeted therapy for Philadelphia chromosome-positive chronic myeloid leukaemia (CML). It is an ATP mimetic and binds to the ATP site of the BCR-Abl fusion protein and acts as a competitive inhibitor of this kinase enzyme in the leukaemic cells.

- 2 C Irinotecan is a compound of the camptothecin family. It is an inhibitor of the DNA topoisomerase I which locks the DNA in the cleavable complex, preventing replication. Its metabolite SN-38 is the most active moiety at inhibiting DNA topoisomerase.
- 3 E Trastuzumab is a humanized monoclonal antibody that binds to the extracellular non-ligand-binding domain of HER2/NEU (EGFR-2) with a  $K_d$  in the nanomolar range. This target is overexpressed on a number of neoplastic cells, especially breast cancers and prevents signal transduction and proliferation.
- 4 J Bevacizumab is a humanized monoclonal antibody that binds to VEGF A, B and C, preventing their subsequent interaction with the VEGF receptor on new vessel walls in the tumour neovasculature and thus preventing tumour angiogenesis. It has activity in colon, lung and renal cell carcinoma.
- 5 H Gefitinib is the first in class oral EGFR-targeted therapy. It is an ATP mimetic and inhibits the tyrosine kinase found on the EGF receptor, which autophosphorylates the receptor and thus yields signal transduction and cellular proliferation. Inhibition of this signalling leads to apoptosis and cell death. Many epithelial tumours overexpress this receptor – lung, head and neck and breast cancer.

### 365 CANCER

- 1 E Interferon is used in cancer therapy in high doses to treat metastatic renal carcinoma and melanoma. Common side-effects include fatigue, a flu-like syndrome, memory impairment, hyperglycaemia, bone marrow suppression and hypothyroidism.
- 2 C Fludarabine is used in combination therapy for acute leukaemias. It commonly causes neurotoxicity which includes a reversible cerebellar syndrome. This is similar to the toxicity caused by cytarabine (cytosine arabinoside). Other common toxicities include haematopoietic suppression.
- 3 B Clinically available platinum compounds (cisplatin, carboplatin and oxaliplatin) are active as part of combination chemotherapy in many solid tumours. Cisplatin and carboplatin commonly produce renal tubular dysfunction which may lead to tubular necrosis, which is cumulative and may in some cases be only partially reversible. Oxaliplatin causes least nephrotoxicity. Hydration, electrolyte replacement and diuresis minimize the platinum compound tubular toxicity, which is a direct concentration-dependent toxic effect on tubular cells.
- 4 D Interleukin 2 is used to treat metastatic melanoma and renal carcinoma. It stimulates the immune response against tumour cells. Interleukin 2 itself and the other cytokines that it releases produce a

pulmonary capillary leak syndrome and acute respiratory distress syndrome (ARDS), which is reversible but may require ventilatory support.

- 5 H** Sorafenib is effective in treating advanced renal cell carcinoma and inhibits Raf kinase and the VEGFR tyrosine kinase. Almost all the agents which target VEGF or the VEGF tyrosine kinase inhibitor can produce hypertension in patients who were previously normotensive or exacerbate hypertension in patients with high blood pressure. The mechanism of this effect is unclear. Treatment with calcium channel blockers and/or ACE inhibitors can ameliorate this side-effect.

# CLINICAL IMMUNOPHARMACOLOGY

## MULTIPLE CHOICE QUESTIONS

- 366** Glucocorticosteroids inhibit:
- a) Platelet thromboxane A<sub>2</sub> synthesis
  - b) Histamine release
  - c) Leukotriene C<sub>4</sub> and D<sub>4</sub> synthesis
  - d) Arachidonic acid metabolism
  - e) Transcription of tumour necrosis factor (TNF) and interleukin 6 (IL-6)
- 367** The following agents are used to prevent or treat graft-versus-host disease:
- a) Methylprednisolone
  - b) Ciclosporin
  - c) Mycophenolate mofetil
  - d) Tacrolimus
  - e) Infliximab
- 368** Adverse effects associated with ciclosporin include:
- a) Reduced glomerular filtration pressure leading to nephrotoxicity
  - b) Gingival hyperplasia
  - c) Alopecia
  - d) Tremor
  - e) Hypokalaemia
- 369** Administration of basiliximab (IL-2 receptor blocking antibody) may cause the following side-effects:
- a) Hypotension
  - b) Delayed, severe dyspnoea and wheezing
  - c) Fever and chills
  - d) Aseptic meningitis
  - e) Cardiomyopathy

- 370 Mycophenolate mofetil:
- a) Is a prodrug
  - b) Inhibits inosine monophosphate dehydrogenase, impairing *de novo* purine synthesis in T and B cells
  - c) Is given intravenously
  - d) Causes leukopenia
  - e) Is used as adjunct therapy in solid organ transplantation and is more effective than azathioprine
- 371 Natalizumab is indicated in the treatment of refractory:
- a) Rheumatoid arthritis
  - b) Eczema
  - c) Asthma
  - d) Multiple sclerosis
  - e) Acute solid organ transplant rejection
- 372 The following agents inhibit the metabolism of ciclosporin:
- a) Diltiazem
  - b) Itraconazole
  - c) Cimetidine
  - d) Rifampicin
  - e) Gentamicin
- 373 The following are indicated in the management of acute anaphylactic shock following a bee sting out of hospital and without monitoring facilities:
- a) Intramuscular adrenaline (epinephrine) (0.5–1 mL, 1 in 1000)
  - b) Intravenous adrenaline (epinephrine) (10 mL, 1 in 10000)
  - c) Intravenous hydrocortisone
  - d) Intravenous chlorpheniramine
  - e) Oxygen
- 374 Azathioprine:
- a) Is metabolized to 6-mercaptopurine
  - b) Inhibits delayed hypersensitivity (cell-mediated immunity) and those aspects of inflammation that require cell division
  - c) Is administered by continuous infusion
  - d) Causes neutropenia and thrombocytopenia
  - e) Concurrent allopurinol increases the clearance of azathioprine

- 375 Cyclophosphamide is used as an immunosuppressive in the following diseases:
- Pneumoconiosis (silicosis)
  - Autoimmune haemolytic anaemia
  - Nephrotic syndrome with minimal microscopic glomerular changes
  - Nephritis due to systemic lupus erythematosus
  - Wegener's granulomatosis
- 376 Fexofenadine:
- Is a competitive antagonist at the H<sub>1</sub> receptor
  - Is used as a sedative in children
  - Is effective treatment for motion sickness
  - Is used prophylactically in hayfever
  - Plasma concentrations when very high can lead to prolonged QTc and torsades de pointes
- 377 The following are successfully used in the management of allergic rhinitis (hayfever):
- Oral H<sub>3</sub> receptor antagonists
  - Desensitization with a mix of grass pollen, cat dander and house dust mite
  - Nasal sodium cromoglicate
  - Nasal terbutaline
  - Nasal budesonide
- 378 Annual immunization with influenza vaccine is strongly recommended for individuals aged over six months with the following conditions:
- Immunosuppression because of prolonged corticosteroid treatment
  - Diabetes mellitus requiring insulin or oral hypoglycaemic drugs
  - Patients with chronic lung disease
  - Human immunodeficiency virus (HIV) infection
  - Chronic renal disease

Answers: see pages 163–165



## EXTENDED MATCHING QUESTIONS

### 379 CLINICAL IMMUNOPHARMACOLOGY

- |          |                    |          |              |
|----------|--------------------|----------|--------------|
| <b>A</b> | Tacrolimus         | <b>F</b> | Natalizumab  |
| <b>B</b> | Mycophenolate      | <b>G</b> | Etanercept   |
| <b>C</b> | Muromonab          | <b>H</b> | Basilixumab  |
| <b>D</b> | Prednisolone       | <b>I</b> | Azathioprine |
| <b>E</b> | Aldesleukin (IL-2) | <b>J</b> | Methotrexate |

Match a drug from the list above which corresponds most closely to the statement below:

- 1 An anti-IL-2 receptor antibody
- 2 Toxicity can be reduced by 'folinic acid rescue'
- 3 A calcineurin inhibitor that is more potent than ciclosporin
- 4 An anti- $\alpha_4\beta_3$  integrin monoclonal antibody used in patients with progressive multiple sclerosis
- 5 Used in metastatic renal cell carcinoma

### 380 CLINICAL IMMUNOPHARMACOLOGY

- |          |                       |          |                       |
|----------|-----------------------|----------|-----------------------|
| <b>A</b> | Nedocromil            | <b>F</b> | Sirolimus             |
| <b>B</b> | 6-Mercaptopurine      | <b>G</b> | Ciclosporin           |
| <b>C</b> | Natalizumab           | <b>H</b> | Methylprednisolone    |
| <b>D</b> | Fexofenadine          | <b>I</b> | Mycophenolate mofetil |
| <b>E</b> | Meningococcal vaccine | <b>J</b> | Basilixumab           |

Match the single agent most correctly linked with each of the following pharmacodynamic effects:

- 1 Gingival hyperplasia
- 2 Inhibition of mammalian target of rapamycin (mTOR)
- 3 Hypokalaemia
- 4 Thrombocytopenia
- 5 Binds to the  $\alpha_4\beta_3$  integrin

**ANSWERS:** see pages 165–166

## ANSWERS

## MCQ ANSWERS

- 366 a) False      Glucocorticosteroids reduce the transcription of  
 b) True          proinflammatory mediators (e.g. TNF, IL-6) and inhibit  
 c) True          type I, II, III and IV hypersensitivity reactions. They are the  
 d) True          most widely used immunosuppressive agents. They inhibit  
 e) True          eicosanoid synthesis from arachidonic acid in nucleated  
                      cells by increasing the production of lipocortin, an inhibitor  
                      of phospholipase A<sub>2</sub> (PLA<sub>2</sub>)
- 367 a) True  
 b) True          – Specific T lymphocyte suppressor, primarily against T  
                      helper cells  
 c) True          – Need regular blood counts  
 d) True          – Is neurotoxic and nephrotoxic  
 e) True          – Monoclonal antibody which binds TNF and prevents its  
                      action
- 368 a) True          – Also may cause hypertension. Nephrotoxicity may be  
                      reduced by concurrent calcium channel blockade  
 b) True  
 c) False          – Hirsutism  
 d) True          – May be an early sign of toxic plasma concentrations  
 e) False          – Causes hyperkalaemia
- 369 a) True          – Any murine/humanized monoclonal antibody when given  
                      to humans may cause anaphylaxis  
 b) True          – Manifestation of a delayed hypersensitivity reaction  
 c) True  
 d) False          – Intravenous human normal immunoglobulin (HNIG) in  
                      high dose can cause this  
 e) False
- 370 a) True          – It is a prodrug ester of mycophenolic acid; the latter under-  
                      goes hepatic glucuronidation to an inactive metabolite  
 b) True          – Blocks purine synthesis in proliferating lymphocytes and  
                      may reduce production of proinflammatory cytokines  
 c) False          – Is given orally. Antacids decrease its absorption. Also  
                      causes gastrointestinal side-effects  
 d) True  
 e) True
- 371 a) False          Natalizumab is an anti- $\alpha_4\beta_3$  integrin monoclonal antibody.  
 b) False          It inhibits the migration/trafficking of leukocytes into the

- c) False CNS. Its use in severe progressive multiple sclerosis was temporarily suspended due to an association with progressive multifocal leukoencephalopathy (PML)
- d) True
- e) False
- 372 a) True CYP3A4 inhibitors block ciclosporin (and tacrolimus) metabolism, increasing the risk of toxicity if the dose of immunosuppressant is not reduced
- b) True
- c) True
- d) False – Rifampicin (and all rifamycins) induce CYP3A4, reducing ciclosporin blood concentrations for the same dose
- e) False – But gentamicin potentiates the nephrotoxicity of ciclosporin
- 373 a) True – Life saving
- b) False – May induce ventricular fibrillation
- c) True – But takes 4–6 hours to be of benefit
- d) False – The use of intravenous antihistamines here is controversial
- e) True – If hypotensive, intravenous fluids may also be of value and may be available in an ambulance
- 374 a) True Azathioprine is an antimetabolite and thus most effective on proliferating cells. It is administered by mouth and metabolized to its active moiety – 6-mercaptopurine. It is used as an adjunct to prevent transplant rejection and also in the treatment of autoimmune diseases such as systemic lupus erythematosus and chronic active hepatitis. Owing to its potential toxicity (bone marrow) it is usually reserved for situations in which corticosteroids alone are inadequate
- b) True
- c) False
- d) True
- e) False
- 375 a) False Cyclophosphamide, in addition to its use as a cytotoxic cancer drug, is particularly valuable in aggressive autoimmune diseases inhibiting lymphocyte proliferation
- b) False
- c) True
- d) True
- e) True
- 376 a) True
- b) False – Fexofenadine, cetirizine and loratadine are ‘non-sedative’ antihistamines
- c) False
- d) True
- e) False – Fexofenadine is the non-cardiotoxic metabolite of terfenadine
- 377 a) False Avoidance of allergens is ideal but rarely practical. With the exception of oral H<sub>1</sub> blockers, local therapy is preferred. If indicated, desensitization therapy with a single allergen is acceptable, but the risk of anaphylaxis is high and it should only be undertaken in specialist allergy clinics
- b) False
- c) True
- d) False
- e) True

- 378 a) True Influenza viruses are constantly changing their antigenic structure. Current influenza vaccines are grown in chick embryos and are contraindicated in those with hypersensitivity to eggs
- b) True
- c) True
- d) True
- e) True

## EMQ ANSWERS

### 379 CLINICAL IMMUNOPHARMACOLOGY

- 1 H Basiliximab is an anti-IL-2 receptor antibody which inhibits IL-2-mediated T-cell activation and is used in the management of organ transplant rejection.
- 2 J Methotrexate resembles folic acid and competes with it at the active site of dihydrofolate reductase. Consequently methotrexate blocks nucleic acid synthesis. It is used as an immunosuppressant and anticancer drug. Folinic acid circumvents the block and can minimize bone marrow and gut toxicity, whilst maintaining efficacy if administered at a set time after methotrexate administration.
- 3 A Tacrolimus is often used in patients who are refractory to ciclosporin. Wide interindividual variation exists in its pharmacokinetics. It is metabolized by CYP3A4. It may cause more neurotoxicity and nephrotoxicity than ciclosporin. Therapeutic monitoring of trough drug concentrations is useful.
- 4 F Natalizumab inhibits leukocyte migration into the CNS and is licensed for use in highly active multiple sclerosis. There is an association with opportunistic infection including (rarely) PML.
- 5 E Aldesleukin (recombinant IL-2) is licensed for metastatic renal cell carcinoma.

### 380 CLINICAL IMMUNOPHARMACOLOGY

- 1 G Ciclosporin causes gingival hyperplasia in 4–16 per cent of recipients. It is reversible and appears more common in paediatric patients. Few drugs cause this side-effect and others include phenytoin and nifedipine.
- 2 F Sirolimus (also known as rapamycin) binds to the mammalian target of Rapamycin (mTOR) and inhibits mTOR-mediated mitogenic signal transduction.
- 3 H Methylprednisolone and most synthetic glucocorticosteroids cause hypokalaemia as they have some mineralocorticoid action and thus promote potassium loss via the kidney.

- 4 B** 6-Mercaptopurine causes bone marrow suppression, especially thrombocytopenia, but also neutropenia.
- 5 C** Natalizumab binds to the endothelial cell adhesion molecule  $\alpha_4\beta_3$  integrin. Thus it impairs migration of inflammatory cells, especially lymphocytes, from the vascular space into the tissues. It is used in progressive multiple sclerosis.

## THE SKIN AND THE EYE

### MULTIPLE CHOICE QUESTIONS

- 381** Acne vulgaris:
- a) Can be effectively treated with topical benzoyl peroxide
  - b) May be precipitated by oral methylprednisolone
  - c) Is caused by propionibacteria
  - d) Cold tar treatment reduces the severity of lesions
  - e) Can be exacerbated by oral aciclovir
- 382** Isotretinoin:
- a) Is a synthetic vitamin D analogue
  - b) The usual course of treatment is two weeks
  - c) Is teratogenic
  - d) Causes hirsutism
  - e) Is eliminated from the body over a period of weeks
- 383** The following are effective in the management of eczema:
- a) Topical betamethasone
  - b) Topical alpha-tocopherol
  - c) Dithranol
  - d) Calcipotriol
  - e) Emulsifying ointment
- 384** Local application of the following are of benefit in the management of psoriasis:
- a) Adepalene
  - b) Salicylic acid
  - c) Psoralens
  - d) Dithranol
  - e) Calcipotriol

- 385** The following may be effective in the management of severe psoriasis:
- a) Weekly methotrexate
  - b) Erythromycin
  - c) Efalizumab
  - d) Nateglinide
  - e) Acitretin
- 386** The following drugs are recognized causes of Stevens–Johnson syndrome:
- a) Co-trimoxazole
  - b) Amoxicillin
  - c) L-Thyroxine
  - d) Phenytoin
  - e) Lamotrigine
- 387** The following infections/infestations are paired with their appropriate treatment:
- a) Candida vulvovaginitis – topical ketoconazole
  - b) Fungal nail infections – oral griseofulvin
  - c) Tinea corporis – topical clotrimazole
  - d) Initial or recurrent genital herpes simplex – oral aciclovir
  - e) Scabies – topical malathion
- 388** Administration of the following eye drops/ointments can produce the correctly paired systemic effects:
- a) Carteolol – bradycardia
  - b) Aciclovir – alopecia
  - c) Gentamicin – renal tubular necrosis
  - d) Prednisolone – hypercalcaemia
  - e) Pilocarpine – dry mouth
- 389** Dilatation of the pupil (mydriasis) is produced by:
- a) Cyclopentolate
  - b) Dorzolamide
  - c) Atropine
  - d) Phenylephrine
  - e) Ketorolac
- 390** In the treatment of open angle glaucoma the following drugs are effective:
- a) Acetazolamide
  - b) Chlorpheniramine
  - c) Dexamethasone
  - d) Latanoprost
  - e) Timolol

- 391** The following treatments have been correctly paired with their licensed indication in ophthalmology:
- a) Aciclovir – cytomegalovirus (CMV) retinitis
  - b) Ranizumab – age-related macular degeneration
  - c) Ciprofloxacin – corneal ulceration
  - d) Fusidic acid – hypersensitivity reactions
  - e) Travoprost – open angle glaucoma

**Answers: see pages 171–172**



## EXTENDED MATCHING QUESTIONS

### 392 DRUGS AND THE SKIN

- |          |                    |          |                      |
|----------|--------------------|----------|----------------------|
| <b>A</b> | Calcipotriol       | <b>F</b> | Methotrexate         |
| <b>B</b> | Lindane 1 per cent | <b>G</b> | Prednisolone         |
| <b>C</b> | Terbinafine        | <b>H</b> | Retinoic acid        |
| <b>D</b> | Clotrimazole       | <b>I</b> | Topical minoxidil    |
| <b>E</b> | Topical aciclovir  | <b>J</b> | Low-dose doxycycline |

Match the most appropriate drug from the list above with the indication below:

- 1 Topical treatment for acne
- 2 Topical treatment for psoriasis
- 3 Systemic treatment for refractory psoriasis
- 4 Tinea pedis
- 5 Fungal nail infection

### 393 DRUGS AND THE EYE

- |          |               |          |             |
|----------|---------------|----------|-------------|
| <b>A</b> | Tropicamide   | <b>F</b> | Ganciclovir |
| <b>B</b> | Mannitol      | <b>G</b> | Pilocarpine |
| <b>C</b> | Fusidic acid  | <b>H</b> | Timolol     |
| <b>D</b> | Betamethasone | <b>I</b> | Rifampicin  |
| <b>E</b> | Aciclovir     | <b>J</b> | Verteporfin |

Match the indication/effect from the list below with the most appropriate drug:

- 1 Causes miosis
- 2 CMV retinitis
- 3 Acute glaucoma
- 4 Short-duration mydriatic
- 5 Discolours soft contact lenses

**ANSWERS: see page 173**

## ANSWERS

## MCQ ANSWERS

- 381** a) True Acne vulgaris occurs in at least 90 per cent of adolescents.  
 b) True The topical use of peeling agents such as benzoyl peroxide  
 c) True or azelaic acid or topical retinoids on a regular basis is  
 d) False usually all that is necessary. In more severe cases oral  
 e) False antibacterial drugs are beneficial and if this is ineffective  
 oral isotretinoin may be considered by specialists
- 382** a) False Isotretinoin is a vitamin A analogue. It is prescribed under  
 b) False hospital supervision usually for at least four months. There is  
 c) True a persistent risk of teratogenicity for at least one month after  
 d) False stopping oral therapy. Co-pyrindiol (cyproterone acetate, an  
 e) True anti-androgen with ethinylestradiol) is useful in women  
 whose acne is refractory to antibiotics/topical treatments and  
 who also wish to receive oral contraception. There is an  
 increased risk of thromboembolism
- 383** a) True In mild wet eczema, the topical use of drying agents such  
 b) False as lotions of aluminium acetate or calamine are useful.  
 c) False When the lesions are dry and scaly the use of emollients  
 d) False (e.g. E45) combined with a keratolytic is beneficial.  
 e) True Topical corticosteroids are often required both in 'wet' and  
 'dry' eczema. Nocturnal pruritus may be relieved by  
 sedative antihistamines
- 384** a) False – Adapalene is a topical retinoid-like drug used in mild to  
 moderate acne  
 b) True – Enhances rate of loss of surface scale  
 c) False – PUVA (photochemotherapy using an oral psoralen with  
 long-wave ultraviolet radiation) is an effective treatment  
 for psoriasis  
 d) True – Irritates normal skin  
 e) True – Does not irritate normal skin
- 385** a) True – Folic acid reduces the possibility of toxicity  
 b) False – Sometimes useful in acne  
 c) True – Inhibits T-cell activation  
 d) False – Used in type 2 diabetes in combination with metformin  
 e) True – An oral retinoid
- 386** a) True All sulfonamides and beta-lactam antibacterials can cause  
 b) True this syndrome  
 c) False

- d) True
- e) True
- 387 a) True – With unusual/recurrent skin infections consider diabetes mellitus or immunosuppression. Antibiotic therapy, diabetes mellitus and immunosuppression are risk factors
  - b) True
  - c) True
  - d) True
  - e) True
- 388 a) True – Intraocular administered doses avoid hepatic first-pass metabolism and can lead to bradycardia
  - b) False
  - c) False – Not enough absorbed to cause systemic toxicity
  - d) False
  - e) True – With high doses enough can be absorbed to produce systemic anticholinergic effects
- 389 a) True – Muscarinic ( $M_3$  in the eye) receptor antagonist blocks action of sphincter muscle of the iris
  - b) False – Topical carbonic anhydrase inhibitor
  - c) True – Muscarinic ( $M_3$  in the eye) receptor antagonist blocks action of sphincter muscle of the iris
  - d) True – Stimulates  $\alpha_1$  adrenoreceptors constricting the radial muscle of the iris
  - e) False – Non-steroidal anti-inflammatory drug (NSAID) used in eye drops for prophylaxis and reduction of inflammation following ocular surgery
- 390 a) True – Carbonic anhydrase inhibitor given systemically reduces production of the aqueous humour
  - b) False – First-generation antihistamine which will dilate the pupil (due to its anticholinergic properties), worsening glaucoma
  - c) False – Steroids can exacerbate glaucoma in certain genetically predisposed patients
  - d) True – Prostaglandin  $F_{2\alpha}$  analogue lowers intraocular pressure by increasing uveoscleral flow
  - e) True – Beta-adrenergic antagonist reduces secretion/formation of aqueous humour
- 391 a) False – Aciclovir is indicated for herpes simplex infection
  - b) True – Blocks vascular endothelial growth factor (VEGF)
  - c) True
  - d) False – Useful for staphylococcal infections
  - e) True – Prostaglandin analogue which increases uveoscleral flow

## EMQ ANSWERS

**392 DRUGS AND THE SKIN**

- 1 H The topical use of keratolytic agents such as benzoyl peroxide or retinoic acid on a regular basis in conjunction with systemic antibiotic therapy is successful in most patients with acne.
- 2 A Calcipotriol, a vitamin D analogue, is effective topically in psoriasis.
- 3 F Immunosuppressants such as ciclosporin or methotrexate are sometimes required in refractory psoriasis.
- 4 D Topical clotrimazole is effective in fungal skin infections.
- 5 C Terbinafine is the treatment of choice for fungal nail infections.

**393 DRUGS AND THE EYE**

- 1 G Pilocarpine, a cholinergic agonist, constricts the pupil and is used in simple glaucoma topically.
- 2 F Ganciclovir (foscarnet is an alternative) can be used via the intravenous/intraocular route to treat CMV retinitis.
- 3 B Acute glaucoma is a medical emergency. Intravenous mannitol, an osmotic diuretic, shifts water from intracellular and transcellular compartments (including the eye) into plasma and promotes fluid loss via diuresis. In addition a carbonic anhydrase inhibitor (intravenous acetazolamide or topical dorzolamide) may be required.
- 4 A Tropicamide is a convenient short-acting topical mydriatic frequently used to assist examination of the fundus.
- 5 I Rifampicin discolours urine, saliva, tears and other body secretions orange-red.

# CLINICAL TOXICOLOGY

## MULTIPLE CHOICE QUESTIONS

- 394 Methadone:
- a) Has the potential to cause dependence
  - b) Can only be prescribed to registered addicts by doctors with a special licence
  - c) Is usually administered as an elixir
  - d) Depresses the cough centre
  - e) Effects are reversed by naloxone
- 395 The following are clinical signs consistent with heroin (diamorphine) intoxication:
- a) Hypertension
  - b) Rapid respiratory rate
  - c) Hypothermia
  - d) Pinpoint pupils
  - e) Slurred speech
- 396 Features of the opioid withdrawal syndrome include:
- a) Yawning
  - b) Rhinorrhoea
  - c) Mydriasis
  - d) Diarrhoea
  - e) Tremor
- 397 Specific causes of death which are positively related to smoking include:
- a) Ischaemic heart disease
  - b) Cancer of the oesophagus
  - c) Emphysema
  - d) Aortic aneurysm
  - e) Cancer of the tongue

- 398** There is an increased rate of metabolism of the following drugs in smokers:
- a) Diazepam
  - b) Phenytoin
  - c) Ethanol
  - d) Warfarin
  - e) Theophylline
- 399** Ethyl alcohol (ethanol):
- a) The majority of oral ethanol is absorbed from the small intestine
  - b) Ethanol delays gastric emptying
  - c) 95 per cent of ingested ethanol is metabolized
  - d) Ethanol elimination demonstrates first-order kinetics
  - e) Is second to heroin as the most important drug of dependence in Western Europe
- 400** Cardiovascular complications associated with alcohol consumption include:
- a) Atrial fibrillation
  - b) Buerger's disease
  - c) Cardiomyopathy
  - d) Coronary artery disease
  - e) Peripheral vascular disease
- 401** Delirium tremens:
- a) Occurs in approximately 60 per cent of patients withdrawing from alcohol
  - b) Has a mortality of 5–10 per cent
  - c) Benzodiazepines are contraindicated
  - d) Thiamine should be administered parenterally
  - e) Phenytoin should be administered prophylactically to prevent convulsions
- 402** Chronic use of anabolic steroids is associated with:
- a) Pancreatitis
  - b) Ototoxicity
  - c) Hepatic tumours
  - d) Cardiomyopathy
  - e) Peripheral neuropathy

- 403** 3,4-Methylenedioxy-*N*-methylamphetamine (MDMA or ecstasy):
- Has agonist properties at the 5HT<sub>2</sub> receptor
  - Has mixed hallucinogenic and stimulant properties
  - Occasionally causes hyperpyrexia
  - In chronic use has been associated with increased impulsivity and impaired memory
  - Chronic usage may cause irreversible degeneration of serotonergic nerves
- 404** The combination of coma, dilated pupils, hyperreflexia and tachycardia is consistent with overdose of the following drugs when taken alone:
- Co-dydramol
  - Dosulepin
  - Aspirin
  - Amitriptyline
  - Lorazepam
- 405** The following suspected overdoses are indications for emergency measurement of drug concentration:
- Iron
  - Methanol
  - Amitriptyline
  - Temazepam
  - Salicylates
- 406** The following poisons/drugs have been correctly paired with an appropriate antidote/specific measure:
- Paracetamol – acetylcysteine
  - Iron – desferrioxamine
  - Codeine – naloxone
  - Organophosphorus insecticides – dicobalt edetate
  - Methanol – ethanol
- 407** An 18-year-old woman is admitted 4 hours after taking 50 paracetamol and 50 × 300 mg aspirin tablets. The following statements are correct:
- She is likely to be in a grade IV coma
  - Stomach washout is indicated
  - Acetylcysteine should be administered
  - Blood gases are likely to show a mixed metabolic acidosis/respiratory alkalosis
  - If petechiae and subconjunctival haemorrhages are present, fresh frozen plasma should be administered immediately

---

**408** The following are confirmed aphrodisiacs:

- a) Ginseng
- b) Oysters
- c) Extract of rhino horn
- d) Passion fruit
- e) Vitamin E

**Answers: see pages 179–182**



## EXTENDED MATCHING QUESTIONS

### 409 CLINICAL MANIFESTATIONS OF DRUG OVERDOSE

- |          |                |          |            |
|----------|----------------|----------|------------|
| <b>A</b> | Amitriptyline  | <b>F</b> | Iron       |
| <b>B</b> | Simvastatin    | <b>G</b> | Aspirin    |
| <b>C</b> | Lithium        | <b>H</b> | Methadone  |
| <b>D</b> | MDMA (ecstasy) | <b>I</b> | Atenolol   |
| <b>E</b> | Temazepam      | <b>J</b> | Nifedipine |

Choose the drug overdose from the list above which is most likely to present with the symptoms/signs listed below:

- 1 Coma, hypotension, flaccidity
- 2 Coma, pinpoint pupils, hypoventilation
- 3 Coma, dilated pupils, hyperreflexia, tachycardia
- 4 Restlessness, hypertonia, hyperreflexia, pyrexia
- 5 Tinnitus, overbreathing, pyrexia, sweating, flushing, usually alert

### 410 ANTIDOTES/OTHER SPECIFIC MEASURES IN THE MANAGEMENT OF POISONING

- |          |                   |          |  |
|----------|-------------------|----------|--|
| <b>A</b> | Acetylcysteine    | <b>G</b> | Calcium chloride   |
| <b>B</b> | Desferrioxamine   | <b>H</b> | Flumazenil   |
| <b>C</b> | Ethanol           | <b>I</b> | Urinary alkalisation   |
| <b>D</b> | Dimercaprol (BAL) | <b>J</b> | Oxygen, intravenous sodium nitrite followed by intravenous sodium thiosulphate |
| <b>E</b> | Naloxone          |          |  |
| <b>F</b> | Pralidoxime       |          |  |

Match the most appropriate antidote/other specific measure from the above list to treat a clinically significant overdose with the agent listed below:

- 1 Aspirin
- 2 Paracetamol
- 3 Methanol
- 4 Iron
- 5 Cyanide

**ANSWERS:** see pages 182–183

## ANSWERS

## MCQ ANSWERS

- 394 a) True      Methadone elixir/mixture is the mainstay of many drug addiction clinics. It has a long half-life of 15–55 hours and it is very difficult to administer these oral formulations as an injection. Doctors should report cases of drug misuse to their regional or national drug misuse data base or centre (see BNF)
- b) False
- c) True
- d) True
- e) True
- 395 a) False      Initially intravenous heroin produces an intense euphoria for several seconds (often accompanied by nausea/vomiting). Many chronic users often claim the only effect is remission from abstinence symptoms
- b) False
- c) True
- d) True
- e) True
- 396 a) True      Withdrawal symptoms generally start at the time the next dose would usually be given and their intensity is related to the usual dose. For heroin, symptoms usually reach a maximum at 36–72 hours and gradually subside over the next 5–10 days. Lofexidine, an  $\alpha_2$  antagonist, alleviates many of the withdrawal symptoms. Loperamide helps reduce the diarrhoea
- b) True
- c) True
- d) True
- e) True
- 397 a) True      In the UK, in men under 70 years, the ratio of death rate among cigarette smokers to non-smokers is 2:1. To assist smokers to give up, nicotine chewing gum, patches, sublingual tablets and spray are available. Varenicline, a selective nicotine receptor partial agonist, and bupropion, an antidepressant, have been introduced as adjuncts to smoking cessation. Bupropion is contraindicated in patients with a history of seizures or of eating disorders
- b) True
- c) True
- d) True
- e) True
- 398 a) False      In addition to pharmacokinetic differences, smokers may exhibit altered pharmacodynamic responses (e.g. smokers show less CNS depression after a standard dose of diazepam than non-smokers)
- b) False
- c) False
- d) False
- e) True
- 399 a) True      It has been estimated that the incidence of alcoholism in North America and Western Europe is nearly 5 per cent of the population. Ethanol is a weak inducer of its own metabolism but is a more potent inducer of the metabolism of drugs whose principal metabolic process is via CYP450 particularly CYP2E1 and differences in rate of ethanol metabolism are principally genetic
- b) True
- c) True
- d) False
- e) False

- 400 a) True  
b) False – Associated with smoking  
c) True  
d) False – Associated with smoking  
e) False – Associated with smoking
- 401 a) False – <10 per cent  
b) True  
c) False – Clormethiazole and benzodiazepines (long half-life) are suitable sedatives  
d) True – To avoid precipitation of acute thiamine deficiency when intravenous dextrose/oral carbohydrates are administered  
e) False
- 402 a) False Anabolic steroids are abused by athletes to build up muscle tissue  
b) False  
c) True  
d) True  
e) False
- 403 a) True MDMA is widely abused for its stimulant and hallucinogenic properties. It is metabolized by CYP2D6, which it inhibits for up to two weeks following a single dose. It is occasionally associated with hyperpyrexia, hyponatremia, rhabdomyolysis and coma  
b) True  
c) True  
d) True  
e) True
- 404 a) False A meticulous, rapid but thorough clinical examination is essential not only to exclude other causes of coma or behaviour, but also because the symptoms and signs may be characteristic of certain poisons (see Table 4)  
b) True  
c) False  
d) True  
e) False
- 405 a) True – See Table 5  
b) True  
c) False  
d) False  
e) True
- 406 a) True – See Table 6  
b) True  
c) True  
d) False  
e) True
- 407 a) False Paracetamol and salicylate overdoses only very rarely cause coma acutely. Acetylcysteine is a potentially life-saving antidote in paracetamol overdose  
b) False  
c) True  
d) True  
e) False

**Table 4** Clinical manifestations of some common poisons

Symptoms/signs of acute overdose	Common poisons
Coma, hypotension, flaccidity	Benzodiazepines and other hypnosedatives, alcohol
Coma, pinpoint pupils, hypoventilation	Opioids
Coma, dilated pupils, hyperreflexia, tachycardia	Tricyclic antidepressants, phenothiazines; other drugs with anticholinergic properties
Restlessness, hypertonia, hyper-reflexia, pyrexia	Amphetamines, MDMA, anticholinergic agents
Convulsions	Tricyclic antidepressants, phenothiazines, carbon monoxide, monoamine oxidase inhibitors, mefenamic acid, theophylline, hypoglycaemic agents, lithium, cyanide
Tinnitus, overbreathing, pyrexia, sweating, flushing, usually alert	Salicylates
Burns in mouth, dysphagia, abdominal pain	Corrosives, caustics, paraquat

**Table 5** Common indications for emergency measurement of drug concentration

Suspected overdose	Effect on management
Paracetamol	Administration of antidotes – acetylcysteine or methionine
Iron	Administration of antidote – desferrioxamine
Methanol/ethylene glycol	Administration of antidote – ethanol or fomepizole with or without dialysis
Lithium	Dialysis
Salicylates	Simple rehydration or urinary alkalinisation or dialysis
Theophylline	Necessity for ITU admission

- 408** a) False      The authors recommend champagne!  
 b) False  
 c) False  
 d) False  
 e) False

**Table 6** Antidotes and other specific measures

Overdose drug	Antidote/other specific measures
Paracetamol	Acetylcysteine i.v. Methionine p.o.
Iron	Desferrioxamine
Cyanide	Oxygen, amyl nitrate (inhalation), dicobalt edetate i.v., sodium nitrite i.v. followed by sodium thiosulphate i.v.
Benzodiazepines	Flumazenil i.v.
Beta-blockers	Atropine Isoprenaline Glucagon
Carbon monoxide	Oxygen Hyperbaric oxygen
Methanol/ethylene glycol	Ethanol, fomepizole
Lead (inorganic)	Sodium EDTA i.v. Penicillamine p.o. Dimercaptosuccinic acid (DMSA) i.v. or p.o.
Mercury	Dimercaptopropane sulphonate (DMPS) Dimercaptosuccinic acid (DMSA) Dimercaprol Penicillamine
Opioids	Naloxone
Organophosphorus insecticides	Atropine, pralidoxime
Digoxin	Digoxin-specific FAB antibody fragments
Calcium-channel blockers	Calcium chloride or gluconate i.v.
Insulin	20% dextrose i.v. Glucagon i.v. or i.m.

Note: DMSA, DMPS and 4-methyl-pyrazole are not licensed in the UK.

## EMQ ANSWERS

### 409 CLINICAL MANIFESTATIONS OF DRUG OVERDOSE

- E** Coma, hypotension and flaccidity are characteristic of a significant benzodiazepine or ethanol overdose (remember to smell the breath).
- H** Coma, pinpoint pupil and hypoventilation are characteristic of opioid overdose.
- A** Coma, dilated pupils, hyperreflexia and tachycardia are characteristic of poisoning by drugs with anticholinergic properties. Tricyclic antidepressants can also cause dysrhythmias and convulsions.

- 4 D Other features of ecstasy (MDMA) poisoning may include: delirium, convulsions, ventricular dysrhythmias, rhabdomyolysis, disseminated intravascular coagulation and adult respiratory distress syndrome.
- 5 G Unless comatose (rare and indicates very severe or mixed overdose) patients who have taken a salicylate overdose present feeling very unwell with tinnitus, hyperventilating, feeling hot and sweaty.

#### **410 ANTIDOTES/OTHER SPECIFIC MEASURES IN THE MANAGEMENT OF POISONING**

- 1 I Urinary alkalinisation accelerates the urinary elimination of weak acids such as aspirin.
- 2 A Acetylcysteine is a potentially life-saving antidote in paracetamol poisoning. It may also be of value in carbon tetrachloride poisoning (unproven).
- 3 C Ethanol saturates alcohol dehydrogenase, thus blocking the conversion of methanol to the toxic formaldehyde which causes metabolic acidosis and ocular toxicity and occasionally leads to convulsions, renal failure and death. Fomepizole is a potent inhibitor of alcohol dehydrogenase. Unlike ethanol it is not sedative and has more predictable pharmacokinetics but it is not as readily available and is expensive.
- 4 B Desferrioxamine should be given intravenously to patients with a serum iron greater than  $500\mu\text{g}/100\text{mL}$  or who have hypotension, severe lethargy, coma or convulsions.
- 5 J Antidotes for cyanide poisoning include nitrites (inhaled amyl nitrite and intravenous sodium nitrite), intravenous sodium thiosulphate and intravenous dicobalt edetate. Oxygen must also be administered.

## PRACTICE EXAMINATION

### BEST OF FIVES

- 1 Individuals who are slow acetylators (i.e. have a relatively low activity of hepatic *N*-acetyltransferase):
  - A Have a prevalence of 15–20 per cent in European caucasians
  - B Are more likely to develop thrombocytopenia, nephrotic syndrome and rash during gold treatment
  - C Are more likely to develop hepatotoxicity following halothane anaesthesia
  - D Are more likely to develop antinuclear antibodies during hydralazine therapy
  - E Are more likely to develop agranulocytosis during clozapine therapy
- 2 Which of the following has the shortest elimination half-life?
  - A Naloxone
  - B Morphine
  - C Methadone
  - D Fentanyl
  - E Remifentanyl
- 3 Estimation of plasma/serum drug concentrations are most useful in optimizing the therapeutic dose required of:
  - A Warfarin
  - B Omeprazole
  - C Salbutamol
  - D Olanzapine
  - E Ciclosporin

- 4 Digoxin has a half-life of approximately 40 hours if renal function is normal. How long will it take to reach >90 per cent of the steady state plasma concentration?
- A 2 days
  - B 7 days
  - C 10 days
  - D 14 days
  - E 18 days
- 5 A 60-year-old epileptic woman who has been on the same dose of phenytoin for 20 years develops cerebellar ataxia with nystagmus. Her other medication consists of folic acid, hormone replacement therapy (HRT) and furosemide prescribed by the GP for ankle swelling and mild hypertension. She is referred to A&E. Routine investigations reveal an elevated plasma creatinine, normal plasma potassium and calcium, hypoalbuminaemia and proteinuria. The phenytoin concentration is 15 mg/L (therapeutic reference range 10–20 mg/L). A diagnosis of nephrotic syndrome is made and the cerebellar signs are attributed to phenytoin toxicity. Which of the following is likely to be correct?
- A A raised plasma creatinine interferes with the phenytoin assay, making it unreliable
  - B Furosemide interferes with the blood–brain barrier, making it more permeable to phenytoin
  - C Concurrent oestrogen (in the HRT) increases the CNS toxicity of phenytoin
  - D The unbound phenytoin (free phenytoin) fraction is 20 per cent rather than 10 per cent
  - E The cerebellar signs are more likely to be related to a cerebrovascular event
- 6 Which of the following drugs need *not* be avoided or only used at a reduced dose in renal failure?
- A Prednisolone
  - B Netilmicin (an aminoglycoside)
  - C Metformin
  - D Methotrexate
  - E Tinzaparin (a low molecular weight heparin, LMWH)
- 7 Which of the following drugs is more likely to cause hyperkalaemia than hypokalaemia in a patient with diabetes and estimated glomerular filtration rate (eGFR) within the ‘normal’ reference range?
- A Amphotericin
  - B Prednisolone
  - C LMWH
  - D Salmeterol
  - E Insulin



- 8 It is rational and advised therapeutic practice to commence treatment with the following drug using a loading dose if a rapid onset of action is required:
- A Clozapine
  - B Zolmitriptan
  - C Amiodarone
  - D Levodopa
  - E Doxazosin
- 9 Which of the following drugs is contraindicated if there is a history of acute porphyria?
- A Quinine
  - B Atenolol
  - C Oral contraceptive
  - D Heparin
  - E Amoxicillin
- 10 A 20-year-old man is diagnosed to have acute schizophrenia. Which of the following is an appropriate first-line treatment?
- A Intravenous (i.v.) haloperidol
  - B Intramuscular flupentixol
  - C Oral olanzapine
  - D Oral procyclidine
  - E Oral fluoxetine
- 11 Which of the following agents if taken in overdose by a depressed patient is most likely to result in a fatal outcome?
- A Amitriptyline
  - B Fluoxetine
  - C Fluvoxamine
  - D Paroxetine
  - E Citalopram
- 12 Which of the following drugs is likely to increase the plasma lithium concentration if co-prescribed to a patient on chronic lithium therapy?
- A St John's wort
  - B Ibuprofen
  - C Phenytoin
  - D Haloperidol
  - E Sertraline

- 13 Which of the following is least likely to have an adverse drug interaction with phenelzine (a monoamine oxidase (MAO) inhibitor)?
- A Levodopa
  - B Ropinirole
  - C Tolcapone
  - D Propofol
  - E Pseudoephedrine
- 14 Which of the following antiepileptic drugs is associated with visual field defects?
- A Valproate
  - B Carbamazepine
  - C Lamotrigine
  - D Vigabatrin
  - E Tiagabine
- 15 Which of the following is the most effective in the management of absence seizures?
- A Carbamazepine
  - B Topiramate
  - C Clobazam
  - D Phenytoin
  - E Ethosuximide
- 16 Which drug in the following list has an analgesic effect which is *not* mediated wholly or partly by binding to opioid receptors?
- A Codeine
  - B Tramadol
  - C Dextropropoxyphene
  - D Nefopam
  - E Buprenorphine
- 17 Carbidopa when combined with levodopa:
- A Inhibits the intracerebral metabolism of levodopa
  - B Reduces nausea and postural hypotension by permitting a lower dose of levodopa
  - C Cannot be prescribed with concomitant warfarin
  - D Delays the onset of improvement in bradykinesia
  - E Abolishes the 'on-off' phenomenon

- 18** Which of the following drugs blocks reuptake of 5-hydroxytryptamine (serotonin)?
- A** Buspirone
  - B** Pizotifen
  - C** Granisetron
  - D** Paroxetine
  - E** Sumatriptan
- 19** Which of the following is most suitable for migraine prophylaxis in an otherwise healthy 30-year-old woman?
- A** Ergotamine
  - B** Paracetamol
  - C** Propranolol
  - D** Carbamazepine
  - E** Sumatriptan
- 20** The following is suitable for treatment of acute dystonia as a result of metoclopramide treatment:
- A** Prochlorperazine intravenously
  - B** Benzhexol orally
  - C** Levodopa subcutaneously
  - D** Bromocriptine sublingually
  - E** Risperidone intramuscularly
- 21** A 65-year-old man undergoes an orthopaedic procedure. He spends an hour in the recovery room before being returned to the ward. You are called to see him and on examination note that he is drowsy, has shallow breathing, a slow pulse and pinpoint pupils. The notes show an uneventful anaesthetic using an inhalational agent, muscle relaxant and fentanyl. In the recovery room he was breathing normally and was awake, but because of pain was initially given intravenous morphine and then intramuscular morphine before being returned to the ward. Your course of action is:
- A** Call the resuscitation team
  - B** Give i.v. atropine
  - C** Give i.v. neostigmine
  - D** Give i.v. flumazenil
  - E** Give i.v. naloxone

- 22 A 38-year-old man with hypertension experiences a first ever attack of acute pain, redness and tenderness in the left first metatarsophalangeal joint ('podagra'). His medication is furosemide, calcium carbonate and irbesartan. Serum uric acid is 0.78 mmol/L (upper limit of normal for men 0.48 mmol/L). Which of the following is most appropriate pharmacotherapy?
- A Paracetamol
  - B Aspirin
  - C Probenecid
  - D Allopurinol
  - E Diclofenac
- 23 An 80-year-old man is taking digoxin and warfarin because of longstanding atrial fibrillation. He has an indwelling urinary catheter *in situ*, whilst awaiting a prostatectomy. At his pre-operation assessment he has a ventricular rate of 120/minute. The house officer doubles his daily digoxin dose and the operation is delayed one week. One week later he returns with nausea, vomiting, diarrhoea, abdominal pain, confusion, delirium and visual disturbances. The most likely cause of his current symptoms is:
- A Viral infection
  - B Hyperkalaemia
  - C Excessive prolongation of prothrombin time
  - D Digoxin toxicity
  - E Urinary tract infection
- 24 Which of the following drugs is most effective in converting a patient with atrial fibrillation into sinus rhythm?
- A Digoxin
  - B Amiodarone
  - C Atenolol
  - D Lidocaine
  - E Diltiazem

- 25 A 78-year-old man is admitted with deterioration of chronic heart failure. He is house-bound and has had three similar admissions in the past nine months. There is a history of ischaemic heart disease. His medication comprises furosemide, ramipril in full dose, valsartan, spironolactone, simvastatin and aspirin. He is dyspnoeic on minimal exertion, looks unwell, pulse 100/min regular, BP 90/70 mmHg, jugular venous pressure (JVP) is at 4 cm, gallop rhythm, chest clear, pretibial oedema. ECG shows sinus rhythm, an old inferior infarct and poor anterior R wave progression. Serum urea 15 mmol/L, creatinine 90  $\mu$ mol/L,  $\text{Na}^+$  140,  $\text{K}^+$  4.6. Which of the following would be most appropriate?
- A Morphine
  - B Hydralazine and isosorbide mononitrate
  - C Digoxin
  - D Carvedilol
  - E Metolazone
- 26 A 46-year-old businessman of Caribbean origin is found to have a total serum cholesterol concentration of 6.2 mmol/L, high-density lipoprotein (HDL) of 0.7 mmol/L and triglycerides of 9.4 mmol/L. He drinks no alcohol (ethanol) during the week but admits to eight pints of lager and up to one bottle of rum at weekends. Other chemistries are notable only for a serum glutamic oxaloacetic transaminase (SGOT) level of 72 (upper limit of normal = 42 u/L) and gamma glutamyl transferase (GGT) level of 128 (upper limit of normal = 51 u/L). Which of the following is correct?
- A The low HDL can be explained by his alcohol intake
  - B He is at risk of pancreatitis
  - C A fibrate is indicated in the first instance because of mixed dyslipidaemia
  - D Ezetimibe would increase his low-density lipoprotein (LDL)
  - E Eicosapentaenoic acid is indicated to lower his total cholesterol
- 27 An otherwise healthy 78-year-old man is found to have a blood pressure (BP) of 168/80 at a routine check, and similar pressures are confirmed on three separate occasions despite adhering to dietary advice. Investigations including an ECG and creatinine/electrolytes are normal. Which of the following is the most appropriate next step in management?
- A A 2-D echo should be obtained
  - B Since his diastolic BP is normal he should be reassured
  - C Doxazosin therapy should be initiated
  - D Ramipril therapy should be initiated
  - E Amlodipine therapy should be initiated

- 28 A 20-year-old woman who is 15 weeks pregnant is admitted feverish and dehydrated with acute severe asthma associated with a community-acquired pneumonia. She has a history of angioedema following a cephalosporin. Which of the following is *not* appropriate therapy?
- A Rehydration with intravenous crystalloid
  - B High inspired oxygen concentration ( $FiO_2$  of 40 per cent)
  - C Nebulized salbutamol
  - D Intravenous hydrocortisone
  - E Intravenous gentamicin
- 29 Which drug combination is recommended for chronic hepatitis C infection?
- A Pegylated interferon alfa and lamivudine
  - B Pegylated interferon alfa and adefovir dipivoxil
  - C Pegylated interferon alfa and ribavirin
  - D Adefovir and lamivudine
  - E Oseltamivir and zanamivir
- 30 A 60-year-old woman has ulcerative colitis resistant to aminosalicylates and topical corticosteroids. It is decided to treat her with systemic corticosteroids. Which of the following is *not* a likely complication of the treatment?
- A Osteoporosis
  - B Weight loss
  - C Diabetes
  - D Hypertension
  - E Mood changes
- 31 Which of the following is suitable for immediate treatment of an 18-year-old woman presenting with weight loss, tachycardia and a goitre?
- A Verapamil
  - B  $^{131}$ Iodine
  - C Carbamazepine
  - D Atenolol
  - E L-Thyroxine

- 32 A 62-year-old woman with type 2 diabetes, hypertension, renal impairment (creatinine  $146\ \mu\text{mol/L}$ ) and mild congestive cardiac failure has poor diabetic control ( $\text{HbA}_{1c} = 10.5$  per cent), despite treatment with maximum doses of a sulfonylurea. Her body mass index (BMI) is 26. Which of the following would be most appropriate pharmacotherapy?
- A Substitute insulin for the sulfonylurea
  - B Add rosiglitazone
  - C Add bisoprolol
  - D Add rimonibant
  - E Add metformin
- 33 An asymptomatic 46-year-old Indian woman is found to have an elevated serum calcium ( $2.80\ \text{mmol/L}$ , corrected) at a 'well-woman' screening clinic. Other chemistries are normal, in particular phosphate is  $0.8\ \text{mmol/L}$  (normal range  $0.8\text{--}1.45$ ), and parathormone (PTH) is  $5.4\ \text{pmol/L}$  (normal range  $<0.9\text{--}5.4$ ). She has a sedentary occupation in a northern UK city. Which of the following would be most suitable management?
- A Alfacalcidol
  - B Sevelamer
  - C Teriparatide
  - D Watchful waiting (monitoring serum calcium)
  - E Surgical exploration of the parathyroids
- 34 A 24-year-old beautician has a history of chronic fatigue since an attack of infectious mononucleosis when aged 20. Her fatigue has become progressively worse. Her periods are painful, heavy and irregular. Her BP is  $116/62$  (supine) and  $92/52$  (standing). Serum  $\text{Na}^+$  is  $132$ ,  $\text{K}^+$   $5.5$ , creatinine  $60\ \mu\text{mol/L}$ . Which of the following would be most appropriate management?
- A Lifelong fludrocortisone
  - B Cognitive behavioural therapy
  - C A course of aciclovir
  - D A single dose of tetracosactide for diagnosis
  - E Estradiol

- 35 A 28-year-old woman is admitted with suspected urinary sepsis (temperature 40.2°C, BP 84/50, pulse 128). She had a massive haemorrhage following the birth of her only child when she was aged 24; since then she has had no periods. Her partner says that she has been progressively listless and depressed for at least two years. There is left loin tenderness and she has no pubic or axillary hair. Which of the following would be most appropriate?
- A Amoxicillin (p.o.)
  - B Hydrocortisone (i.v.)
  - C Pelvic examination
  - D Human menopausal gonadotrophin (follicle-stimulating hormone (FSH) + luteinizing hormone (LH))
  - E Triiodothyronine (i.v.)
- 36 A 56-year-old man with progressive, chronic renal impairment is awaiting renal replacement therapy. His treatment includes calcium carbonate tablets, furosemide, irbesartan and amlodipine. He is admitted severely unwell with a BP of 40 by palpation, pulse 112. An ECG shows a broad complex tachycardia with no P waves. Serum  $\text{Ca}^{2+}$  is 2.3 mmol/L,  $\text{PO}_4$  1.7 mmol/L, creatinine 785  $\mu\text{mol/L}$ ,  $\text{Na}^+$  142 mmol/L,  $\text{K}^+$  7.4 mmol/L. Which of the following would be appropriate management?
- A Amiodarone (i.v.)
  - B Digoxin (i.v.)
  - C Calcium gluconate (i.v.)
  - D Transvenous cardiac pacing
  - E Colestyramine
- 37 Which of the following is the systemic treatment of choice for female hirsutism?
- A Tamoxifen
  - B Ethinylestradiol
  - C Norethisterone
  - D Cyproterone
  - E Finasteride
- 38 A history of which of the following is a contraindication to short-term HRT to prevent menopausal vasomotor symptoms and menopausal vaginitis?
- A Depression
  - B Breast cancer
  - C Hysterectomy
  - D Chronic bronchitis
  - E Eczema



- 39 Which of the following antibacterials is most suitable for treatment of a lower urinary tract infection in a 28-year-old woman who is 10 weeks pregnant?
- A Amoxicillin
  - B Trimethoprim
  - C Tetracycline
  - D Erythromycin
  - E Flucloxacillin
- 40 A patient presents fully conscious with acute falciparum malaria following a visit to Nigeria. Which of the following treatments is most appropriate?
- A Chloroquine
  - B Proguanil and atovaquone
  - C Primaquine
  - D Pyrimethamine
  - E Hydroxychloroquine
- 41 Which of the following drugs causes the most significant inhibition of metabolism of rifabutin?
- A Zidovudine
  - B Ritonavir
  - C Enfuvirtide
  - D Nevirapine
  - E St John's wort
- 42 A 42-year-old woman has widely disseminated colon cancer. Her main symptom is pain from a spinal crush fracture, incompletely suppressed by oral morphine. She is also troubled by constipation, nausea and occasional vomiting. Which of the following is true?
- A Fentanyl patches would not cause nausea at analgesic doses
  - B Cisplatin prolongs survival
  - C Radiotherapy to the primary with adjunctive chemotherapy is the treatment mainstay
  - D Biopsy of the fractured vertebra is indicated
  - E Intercostal nerve block should be arranged
- 43 Which of the following drugs used in cancer chemotherapy is most likely to be associated with cerebellar dysfunction?
- A Cytosine arabinoside (cytarabine)
  - B Cyclophosphamide
  - C Mitoxantrone
  - D Bleomycin
  - E Vincristine

- 44 Which of the following cytotoxic drugs is least likely to cause emesis during chemotherapy?
- A Cisplatin
  - B Dacarbazine
  - C Doxorubicin
  - D Mustine
  - E Vincristine
- 45 A 25-year-old woman suffers a bee sting and within a few minutes she notices a blotchy rash appearing on her body. She is taken to A&E where her BP is 90/60 mmHg. The most appropriate immediate therapy would be:
- A Oral antihistamine (chlorphenamine 4 mg)
  - B Intravenous adrenaline (10 mL of 1:10 000)
  - C Intravenous steroid (hydrocortisone 200 mg)
  - D Intramuscular adrenaline (0.5 mL of 1:1000)
  - E Inhaled salbutamol via nebulizer
- 46 Which of the following is most effective as a topical agent for a candida infection of the skin?
- A Griseofulvin
  - B Beclometasone
  - C Aciclovir
  - D Amphotericin
  - E Nystatin
- 47 Which of the following is suitable for initial treatment of acute glaucoma?
- A Timolol
  - B Pilocarpine
  - C Mannitol
  - D Tropicamide
  - E Latanoprost
- 48 Which of the following is the antidote of first choice in the treatment of potentially fatal paracetamol overdose?
- A Methionine
  - B Acetylcysteine
  - C Naloxone
  - D Dicobalt edetate
  - E Flumazenil

- 49** Which of the following 'overdoses' is most commonly associated with respiratory alkalosis, but when more severe a metabolic acidosis?
- A** Methanol
  - B** Lead
  - C** Paracetamol
  - D** Salicylate
  - E** Codeine
- 50** The following is most suitable for thromboembolic prophylaxis in a patient with a left ventricular aneurysm following a myocardial infarction three months ago:
- A** Intravenous heparin
  - B** Subcutaneous enoxaparin
  - C** Oral warfarin
  - D** Oral aspirin
  - E** Oral aspirin + clopidogrel

**Answers: see pages 202–207**

## PROBLEM SOLVING QUESTIONS

### PROBLEM 1 A PATIENT WITH TYPE 2 DIABETES WHO PRESENTS WITH CONGESTIVE CARDIAC FAILURE

#### Question 51

A 61-year-old woman with type 2 diabetes presents to her GP with two months progressive fatigue, effort dyspnoea and ankle swelling. She is obese and has been controlled with diet alone since diabetes was diagnosed at age 58. Her BP is 142/92 and there are signs of congestive cardiac failure. An echocardiogram confirms poor left ventricular function with a large area of anterior hypokinesia. Fasting blood glucose is 10.2 mmol/L and HbA<sub>1c</sub> 9.2 per cent, total cholesterol 4.8 mmol/L, HDL 0.9 mmol/L and triglyceride 1.2 mmol/L; creatinine is 92 µmol/L, serum electrolytes are normal. Management would appropriately include:

- A Referral for cardiac catheterization
- B Clopidogrel
- C Ramipril
- D Furosemide
- E Rosiglitazone

#### Question 52

Initially she improves on treatment with metformin, simvastatin, valsartan and aspirin but two weeks later she is brought to hospital, severely ill. She is pale and shocked with a systolic BP of 76, an ECG shows Q waves in I, AVL, V1–3 and non-specific T wave changes. Urinalysis shows 1<sup>+</sup> ketones, 3<sup>+</sup> glucose, arterial blood gas (ABG) shows a pH of 6.9, oxygen saturation is 94 per cent breathing air, her temperature is 37°C, haemoglobin 12.0, white cell count 9000 with a normal differential, C reactive protein (CRP) <5, creatine kinase (CK) = 450 u/L (normal range 24–170), glucose 18.6 mmol/L. Plausible differential diagnoses include:

- A Acute gastrointestinal blood loss
- B Diabetic ketoacidosis
- C Lactic acidosis
- D Non-ST elevation myocardial infarction (NSTEMI)
- E Acute rhabdomyolysis

#### Question 53

Management on the ITU would appropriately include:

- A Discontinuation of metformin
- B Intravenous infusion of adrenaline
- C Hyperbaric O<sub>2</sub>
- D Intravenous insulin
- E Intravenous pantoprazole

**PROBLEM 2 CARPAL TUNNEL SYNDROME****Question 54**

A 43-year-old vegetarian woman presents with symptoms of carpal tunnel syndrome (right worse than left). There is a family history of type 1 diabetes. Her heart rate is 52 and she has several large patches of vitiligo. Investigations include total serum cholesterol 7.2 mmol/L, HDL 1.2 mmol/L, triglycerides 0.8 mmol/L, CK 150 u/L (normal range 24–170), haemoglobin 11.6 with macrocytic red cells present on the film. Immediate management should include:

- A Vitamin B12 injection
- B Surgical referral for right wrist decompression
- C Triiodothyronine
- D Simvastatin
- E Measurement of serum thyrotropin (TSH)

**Question 55**

Serum vitamin B12 comes back as 160 ng/L (normal range 150–750) and intrinsic factor antibodies are positive. She improves initially with appropriate therapy but one month later develops symptoms of classical angina. Her heart rate is 72 and regular and the examination otherwise unremarkable. An ECG is normal. Management should include:

- A Bone marrow examination
- B Atenolol
- C Measurement of serum thyrotropin
- D Simvastatin
- E Cardiological referral

**Question 56**

Walking home from the consultation with her GP she becomes acutely unwell with chest pain and palpitations. She is taken by ambulance to the emergency department. Her BP is 126/68. An ECG shows heart rate of 96 and is otherwise normal except for some non-specific T wave changes. Immediate management should include:

- A Ciclosporin
- B Thrombolysis
- C Aspirin (300 mg p.o.)
- D Carbimazole
- E Beta blockade

**PROBLEM 3 LOSS OF BLOOD PRESSURE CONTROL****Question 57**

A 67-year-old man was diagnosed with essential hypertension aged 52 at which time investigations were normal. He was treated with amlodipine and atenolol with good control until the most recent three readings of around 160/100 over the past three months. He is otherwise well in himself but is awaiting orthopaedic assessment because of osteoarthritis in his left hip. His only other regular medication is naproxen for hip pain. He has 2<sup>+</sup> ankle oedema but no other signs of congestive heart failure. Serum creatinine is 320  $\mu\text{mol/L}$ . Serum cholesterol is 4.6 mmol/L, urine protein 2<sup>+</sup>. Immediate management should include:

- A Substitution of atenolol with an angiotensin-converting enzyme (ACE) inhibitor
- B Discontinuation of amlodipine
- C Substitution of regular paracetamol for naproxen
- D Renal ultrasound
- E Measurement of random renin and aldosterone

**Question 58**

Following appropriate changes to his medication, his BP improves to around 150/95 and his serum creatinine falls to 280  $\mu\text{mol/L}$ . Pain in his hip becomes more troublesome. A magnetic resonance angiogram of the renal arteries shows irregularities of both renal arteries. Irbesartan is commenced.

- A This may protect residual renal function
- B This may precipitate acute renal failure
- C A statin is indicated
- D Low-dose aspirin is contraindicated
- E Codeine could usefully be prescribed

**Question 59**

His BP improves to around 130/80 as does the pain in his hip, but he becomes constipated and his ankle swelling persists.

- A Watchful waiting and dietary advice are appropriate
- B Hip replacement is contraindicated
- C Angioplasty of renal arteries is indicated
- D Substitution of modified release verapamil for amlodipine is indicated to improve ankle swelling
- E Senna may be useful

**PROBLEM 4 DEEP VEIN THROMBOSIS IN PREGNANCY****Question 60**

A 28-year-old woman develops a deep vein thrombosis in week 34 of her first pregnancy.

- A LMWH is contraindicated because it crosses the placenta
- B Warfarin should be started only after delivery
- C Breastfeeding will be contraindicated
- D Vaginal delivery is contraindicated
- E Antiplatelet therapy with aspirin is indicated

**Question 61**

Two days following delivery she becomes acutely short of breath. BP is 104/64, respiratory rate 24; pulse 128 irregular, there is a gallop rhythm, oxygen saturation is 88 per cent, an ECG confirms atrial fibrillation.

- A Computerized tomography (CT) pulmonary angiogram is appropriate
- B Post-partum cardiomyopathy is the probable underlying diagnosis
- C Digoxin is appropriate
- D Serum thyrotropin should be measured
- E DC cardioversion is indicated

**Question 62**

Following discharge:

- A Warfarin is indicated
- B Oral contraception is contraindicated in the long term
- C Electrophysiological mapping of pre-excitation pathways should be undertaken
- D Anticoagulation should be life-long
- E Residual effort dyspnoea could be due to pulmonary hypertension

**PROBLEM 5 CHILD WITH HEADACHE, VOMITING, FEVER AND NECK STIFFNESS****Question 63**

A 4-year-old child presents to A&E complaining of a 6-hour history of gradually increasing and severe headache and vomiting. On examination, she has a temperature of 38.5°C, and marked neck stiffness, but no rash is present. Fundoscopy proves impossible due to severe photophobia. Initial management should include:

- A Immediate lumbar puncture
- B Oral co-amoxiclav
- C CT head scan
- D Intravenous ceftriaxone
- E Antibiotics should not be started until a lumbar puncture has been performed and cerebrospinal fluid sent for bacteriological analysis

**Question 64**

A CT head scan reveals no evidence of raised pressure, and is otherwise unremarkable. A subsequent lumbar puncture reveals a purulent meningitis, with high neutrophil count, raised protein and depressed glucose levels. Microscopy reveals the presence of *Haemophilus influenzae*, and this is confirmed on subsequent culture to be *H. influenzae* type b. Further management should include:

- A Ceftriaxone for 5 days
- B Ceftriaxone for 10 days
- C Amoxicillin for 10 days
- D Metronidazole
- E Rifampicin

**Question 65**

She makes a good recovery. However, soon after the antibiotic is stopped, she develops watery diarrhoea associated with abdominal pain. Two days later, she has fever and bloody diarrhoea (frequency 20 times per day). Appropriate management should now include:

- A Restarting the original antibiotic
- B Intravenous vancomycin
- C Oral metronidazole
- D Intravenous fluid replacement
- E Corticosteroid therapy

**Answers: see pages 208–210**



**ANSWERS****ANSWERS TO 'BEST OF FIVES'**

- 1 D Rapid acetylator status has a prevalence of 45–50 per cent in European caucasians. Individuals who are 'rapid acetylators' are more likely to develop peripheral neuropathy during isoniazid therapy.
- 2 E Remifentanyl has an elimination half-life of 5–7 minutes, naloxone 30–80 minutes, morphine 90–120 minutes, fentanyl 2–4 hours, methadone 15–55 hours. If naloxone is used to reverse opioid agonist effects, repeat dose/doses/infusion may be necessary to outlast the opioid effect, with the exception of remifentanyl (and possibly alfentanil which has a half-life of 40–140 minutes).
- 3 E Ciclosporin is a potent immunosuppressant which is of particular value in organ transplantation. It has little effect on the bone marrow, but is nephrotoxic. There is considerable interindividual variability in its pharmacokinetics.
- 4 B If a constant dose of a drug is administered at intervals less than its half-life, the average concentration will rise to a plateau (see *Textbook of Clinical Pharmacology and Therapeutics*, Chapter 3, Figure 3.3). After one half-life (in the case of digoxin 40 hours), the plasma concentration will be 50 per cent of the plateau (steady state concentration) after two half-lives 75 per cent, three half-lives 87.5 per cent and after four half-lives 93.75 per cent;  $4 \times 40$  hours = 6.6 days.
- 5 D Hypoalbuminaemia will result in an increased ratio of unbound:bound (i.e. active:inactive) phenytoin in plasma. Therapeutic drug monitoring assays routinely measure total plasma drug and do not differentiate between bound and unbound drug. Hence in conditions where hypoalbuminaemia exists (e.g. nephrotic syndrome and pregnancy) the usual therapeutic concentration range is inappropriate. In severe renal failure endogenous substances that accumulate due to renal failure may also displace drugs from protein-binding sites.
- 6 A Prednisolone metabolic clearance is not significantly altered in renal dysfunction. Netilmicin, an aminoglycoside, and methotrexate are nephrotoxic and accumulate in renal failure. Tinzaparin, unlike heparin, depends on renal elimination. Metformin is associated with a greatly increased risk of lactic acidosis in renal impairment.
- 7 C Inhibition of aldosterone secretion by heparin, including LMWHs, can cause hyperkalaemia. Those with diabetes, chronic renal failure,

acidosis and those on potassium-sparing drugs are most at risk. The other drugs listed are associated with hypokalaemia.

- 8 C It takes approximately four times the half-life to reach 93.75 per cent of steady state plasma concentration. A loading dose is rational for a drug with a long half-life if a rapid onset of action is required, the effect is related to plasma concentration and administering the loading dose is safe.
- 9 C Acute illness is precipitated by drugs because of inherited enzyme deficiencies in the pathway of haem synthesis. Drug-induced exacerbations of acute porphyria (neurological, psychiatric, cardiovascular and gastrointestinal disturbances that are occasionally fatal) are accompanied by increased urinary excretion of 5-aminolevulinic acid (ALA) and porphobilinogen.
- 10 C An oral atypical antipsychotic drug (e.g. amisulpride, olanzapine, quetiapine, risperidone, zotepine) is considered by the National Institute for Health and Clinical Excellence (NICE) the treatment option of choice for managing an acute schizophrenic episode when discussion with the individual is not possible. Atypical antipsychotics have the advantage that extrapyramidal adverse effects (associated with increased binding to and receptor occupancy of D<sub>2</sub> receptors) are much less common than with the conventional D<sub>2</sub> antagonists.
- 11 A Amitriptyline is an effective, sedative, tricyclic antidepressant. It is much more dangerous in overdose (coma, convulsions and dysrhythmias) than the selective serotonin reuptake inhibitors (SSRIs) listed here.
- 12 B Concomitant non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, ACE inhibitors, angiotensin receptor blockers (ARBs) and diuretics cause increased lithium concentrations.
- 13 D Diet and drug interactions are a danger with MAO inhibitors. The tyramine reaction is much less of a danger with moclobemide (reversible, selective MAO type A) inhibitor and selegiline (selective MAO type B inhibitor).
- 14 D Vigabatrin, a structural analogue of gamma-aminobutyric acid (GABA), inhibits GABA transaminase, increasing cerebral GABA (an inhibitory neurotransmitter). It is associated with visual field defects in approximately one-third of patients in whom it is used. These defects may persist in spite of drug withdrawal.
- 15 E Ethosuxamide and valproate are regarded as the first-line drugs for absence seizures.
- 16 D Nefopam is chemically and pharmacologically unrelated to other analgesics. It inhibits 5HT uptake and potentiates adrenergic pathways that operate the gate mechanism for pain.

- 17 B Carbidopa, a peripheral dopa decarboxylase inhibitor, inhibits the extracerebral metabolism of levodopa to dopamine.
- 18 D Paroxetine is an SSRI. Indications include major depression, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder and anxiety. Extrapyramidal reactions (including orofacial dystonias) have been reported with paroxetine.
- 19 C Lipid-soluble beta blockers such as propranolol, which penetrate the blood-brain barrier, are useful for prophylaxis. Ergotamine and sumatriptan are used for treatment of an acute migraine attack (ergotamine has now largely been superseded by drugs such as the triptans), and are not useful for regular use to prevent migraine attacks.
- 20 A Antimuscarinic drugs are useful for reducing the symptoms of parkinsonism induced by dopamine antagonist drugs such as the antipsychotics, and given parenterally are the drugs of choice for acute dystonic reactions caused by dopamine antagonists. Parenteral benzodiazepines are also effective in acute drug-induced dystonia. Levodopa and bromocriptine are only available as oral preparations.
- 21 E Intravenous naloxone should immediately reverse the signs of opioid overdose.
- 22 E Diclofenac is effective for the acute inflammation of gout. Paracetamol is less anti-inflammatory and ordinary doses of aspirin can increase plasma uric acid. Probenecid (uricosuric) and allopurinol (blocks uric acid synthesis) are contraindicated during the acute attack.
- 23 D The symptoms described are characteristic of digoxin toxicity.
- 24 B Amiodarone has class III antidysrhythmic activity, and can be used for chemical cardioversion of atrial fibrillation. Digoxin has some effect in slowing resting heart rate in patients with atrial fibrillation, but does not convert patients to sinus rhythm. Beta blockers are good for rate control in atrial fibrillation, but (with the exception of sotalol) do not convert patients to sinus rhythm. Lidocaine is only effective for ventricular tachydysrhythmias. Diltiazem, like verapamil, is of some use in rate control and in prevention of paroxysms of atrial fibrillation.
- 25 C He is unstable and hypotensive so beta blockade is not appropriate. Although unstable he does not have signs of pulmonary oedema and morphine is not indicated. The raised urea with normal creatinine suggests pre-renal impairment which would be worsened by metolazone. Digoxin improves symptoms and reduces readmission rates in patients with severe heart failure.

- 26 B He is drinking excessively and has marked hypertriglyceridaemia. Alcohol increases HDL. He would be at risk of rhabdomyolysis on a fibrate and the first line should be to stop drinking alcohol. Ezetimibe has little effect on HDL and eicosapentaenoic acid has little or no effect on total cholesterol or LDL.
- 27 E Isolated systolic hypertension is common in the elderly, in whom it is an important cardiovascular risk factor. Lowering systolic pressure reduces this excess risk. Renin is seldom elevated in this age group and a calcium antagonist or diuretic is appropriate initial drug treatment.
- 28 E The appropriate antibacterial in this situation is a macrolide, e.g. clarithromycin or erythromycin.
- 29 C In hepatitis C the liver function may remain normal for months to years. The course of the liver damage often fluctuates. Up to 60 per cent of patients with hepatitis C do not clear the virus spontaneously. Chronic liver disease, cirrhosis and hepatocellular carcinoma may develop. NICE has recommended peginterferon alfa and ribavarin for chronic hepatitis C with caveats.
- 30 B Chronic systemic corticosteroid therapy causes iatrogenic Cushing's syndrome. Weight gain is characteristic.
- 31 D She probably has Graves' disease. A beta blocker will improve her symptoms while the results of thyroid function tests are awaited. If confirmed, prolonged specific antithyroid treatment with carbimazole (or a related drug) will be indicated. <sup>131</sup>Iodine-treatment may be useful if this fails provided pregnancy is excluded/avoided.
- 32 A Approximately one-third of people with type 2 diabetes benefit from insulin. Glitazones are contraindicated in heart failure, beta blockers are likely to worsen her diabetic control, she is not obese and metformin is contraindicated in renal impairment and congestive heart failure.
- 33 D The probable diagnosis is mild primary hyperparathyroidism since PTH is inappropriately high for the plasma calcium concentration, and phosphate is at the lower end of the normal range. Alfacalcidol or teriparatide would further increase plasma calcium and sevelamer (phosphate binder) is also contraindicated. Surgery would only be appropriate if  $\text{Ca}^{2+}$  was to rise further and symptoms occur.
- 34 D The probable diagnosis is Addison's disease. This may be confirmed by a stimulation test with tetracosactide. Definitive treatment would be with glucocorticosteroid replacement supplemented by fludrocortisone (mineralocorticoid) only if necessary. Her gynaecological symptoms should be reassessed when Addison's disease has been dealt with.

- 35 B The history suggests Sheehan's syndrome with superimposed acute pyelonephritis. In addition to i.v. antibiotics she should be treated urgently with i.v. hydrocortisone since she may well be hypoadrenal (from lack of pituitary ACTH) in addition to hypogonadal (from lack of FSH/LH) and possibly hypothyroid (from lack of TSH). Unlike glucocorticosteroid replacement, replacement of sex hormones and thyroid hormone is less urgent and should await investigation.
- 36 C Calcium gluconate (i.v.) is effective in urgent treatment of broad complex tachycardia caused by hyperkalaemia. A cation-exchange resin such as calcium resonium (rather than a bile acid-binding resin such as colestyramine) might subsequently be used while arranging urgent dialysis.
- 37 D Cyproterone is an anti-androgen. In women it has been used to treat hyperandrogenic effects (often seen in polycystic ovary disease) including acne, hirsutism and male pattern baldness.
- 38 B If HRT is contraindicated as in breast cancer, clonidine may be used to reduce vasomotor symptoms.
- 39 A Amoxicillin is suitable for treatment for lower urinary tract infections, pending results of urine cultures, and is not harmful to the embryo or fetus. Tetracycline, erythromycin and flucloxacillin are not good choices for urine infections, and tetracycline can affect skeletal development (this has been seen in animal studies) and causes dental discolouration in the fetus. Trimethoprim is potentially teratogenic in the first trimester, because of its action at inhibiting folate biosynthesis (dihydrofolate reductase).
- 40 B Most falciparum malaria is chloroquine resistant these days. Quinine is a suitable treatment, and should be given for 5–7 days followed by a 7-day course of doxycycline or a single dose of Fansidar<sup>®</sup> (pyrimethamine with sulfadoxine). Malarone<sup>®</sup> (proguanil combined with atovaquone) is a good alternative treatment, its advantages being that it need only be given for 3 days and does not need to be followed by any other drugs.
- 41 B Rifabutin is a rifamycin which is active against mycobacteria. In patients with low CD4 count it is indicated as prophylaxis against *Mycobacterium avium* complex infections. Ritonavir, an anti-HIV protease inhibitor, inhibits drug metabolism of CYP3A substrates and some CYP2D6 substrates. It increases the risk of uveitis if prescribed with rifabutin. The combination should be avoided.
- 42 E Intercostal nerve block would promptly alleviate her main symptom. Fentanyl patches could be better than oral morphine because she is vomiting. Colon cancer is not very sensitive to radiotherapy or

chemotherapy although radiotherapy to the presumed vertebral metastasis could be useful symptomatically in the medium term.

- 43 A Cytarabine interferes with pyrimidine synthesis and is used in the induction of remission in acute myeloblastic leukaemia. Its main toxicity is myelosuppression. With high doses approximately 10 per cent of patients have cerebellar toxicity.
- 44 E Vincristine, and other vinca alkaloids, are only weakly emetogenic. Peripheral and autonomic neuropathies are associated with vincristine. All vinca alkaloids are very irritant and can cause severe local tissue damage if extravasation occurs.
- 45 D Intramuscular adrenaline 500  $\mu\text{g}$  (0.5 mL adrenaline injection 1 in 1000) may be life-saving in acute anaphylaxis. The dose is repeated if necessary at 5-minute intervals.
- 46 E Nystatin, ketoconazole, clotrimazole, miconazole, terbinafine and amorolfine may all be used topically for candida infections of the skin, vulvovaginitis or balanitis. Systemic therapy may be required in refractory cases. Consider underlying diabetes mellitus.
- 47 C Acute glaucoma is a medical emergency, and initial treatment should be with i.v. mannitol, usually with the addition of a carbonic anhydrase inhibitor (i.v. acetazolamide or topical dorzolamide). This can then supplemented with either a topical beta blocker (e.g. timolol) or a topical cholinergic agonist (e.g. pilocarpine), or both. Latanoprost is a prostaglandin  $F_{2\alpha}$  analogue, which can be used topically in the more chronic situation, in patients who are intolerant of beta blockers or as add-on therapy when the initial response has been inadequate. Tropicamide is a muscarinic antagonist used to dilate the pupil for fundoscopic examination, and raises intraocular pressure, so is contraindicated in this situation.
- 48 B Intravenous acetylcysteine is potentially life-saving following paracetamol overdose.
- 49 D In salicylate overdose blood gases and arterial pH normally reveal a mixed metabolic acidosis and respiratory alkalosis. Respiratory alkalosis is due to direct stimulation of the respiratory centre. Metabolic acidosis is due to uncoupling of oxidative phosphorylation and lactic acidosis. If acidosis predominates, the prognosis is poor.
- 50 C Patients with a left ventricular aneurysm are at high risk of forming intra-aneurysmal clot and subsequent arterial embolic disease, and in the absence of compelling contraindications should be anticoagulated with warfarin. Antiplatelet treatment is of little or no use in this situation.

## ANSWERS TO PROBLEM SOLVING QUESTIONS

**PROBLEM 1****Question 51, Answers:** T F T T F**Question 52, Answers:** T F T T F**Question 53, Answers:** T T F T T**Comment**

Initial treatment with metformin is problematic in view of congestive heart failure (CHF). Her acute deterioration could have been precipitated by a gastrointestinal bleed (aspirin) or acute ischaemia and appears to be complicated by acidosis – probably lactic acidosis (predisposed by metformin) in view of only 1<sup>+</sup> urine ketones and only moderately elevated blood glucose. This is not the presentation of rhabdomyolysis and CK is only moderately elevated. Hyperbaric O<sub>2</sub> is not evidence based and not available in ITU.

**PROBLEM 2****Question 54, Answers:** F F F F T**Question 55, Answers:** F T T T T**Question 56, Answers:** F F T F T**Comment**

Carpal tunnel syndrome is a common presentation of hypothyroidism (confirmed by measuring serum thyrotropin). This can cause a raised serum cholesterol, macrocytosis and mildly raised CK. There is a family history of autoimmune disease and she may well be developing vitamin B12 deficiency in addition to hypothyroidism. Appropriate medical treatment is oral thyroxine. This may obviate the need for surgery and may correct her dyslipidaemia. Thyroxine has a long half-life so occurrence of angina after four weeks treatment when accumulation will have occurred and serum levels have increased, suggests that she may have underlying ischaemic heart disease which has been masked by bradycardia and hypothyroidism. The dose of thyroxine should be reduced and a beta blocker added. The acute event is strongly suggestive of an acute coronary syndrome. Aspirin 300 mg rapidly blocks platelet cyclo-oxygenase (COX) and is the appropriate starting dose in this acute setting. Carbimazole blocks thyroid hormone synthesis so would not antagonize exogenous thyroxine.

**PROBLEM 3****Question 57, Answers:** F F T T F**Question 58, Answers:** T T T F T**Question 59, Answers:** T F F F T

**Comment**

Possible explanations of loss of BP control and occurrence of renal impairment include onset of renal disease (e.g. renal artery stenosis or obstructive uropathy) and/or inhibition of renal COX by naproxen. Paracetamol, codeine and low-dose aspirin do not share these effects on BP and renal function. Atenolol suppresses renin, making measurement of this uninformative. An ACE inhibitor or ARB can protect against progressive renal dysfunction, but can precipitate acute renal failure if there is haemodynamically significant bilateral renal artery stenosis (possible in view of the irregularities seen). Angioplasty is not indicated unless renal function deteriorates and is not particularly effective in atheromatous disease. Verapamil is less likely to cause oedema than amlodipine but will make constipation worse and may precipitate heart failure with concomitant atenolol.

**PROBLEM 4**

**Question 60, Answers:** F T F F F

**Question 61, Answers:** T F T T F

**Question 62, Answers:** T T F F T

**Comment**

LMWH does not cross the placenta. Warfarin is contraindicated in the last trimester because of the risk of intracranial haemorrhage in the infant and of maternal bleeding. After delivery warfarin can be used and appears safe in breastfeeding. Antiplatelet therapy is inadequate prophylaxis in deep vein thrombosis (DVT). The acute episode following delivery is presumably due to pulmonary embolism which may have precipitated atrial fibrillation but other causes of atrial fibrillation remain possible. Serum thyroxine is difficult to interpret peripartum but serum thyrotropin can be interpreted (a depressed level would signal probable hyperthyroidism). Anticoagulation would not need to be indefinite since DVT occurred in the setting of pregnancy. If there has been a large pulmonary embolus, this may cause pulmonary hypertension.

**PROBLEM 5**

**Question 63, Answers:** F F T T F

**Comment**

If bacterial meningitis is suspected, as in this case, i.v. antibiotic should be started without waiting for microscopy/culture results from the cerebrospinal fluid, due to the often rapid progression of the disease with potentially devastating consequences. Intravenous ceftriaxone is a good initial broad-spectrum treatment, pending bacteriology results. Since fundoscopy was not possible, a lumbar puncture should not be performed until a CT scan has confirmed the absence of raised intracranial pressure, due to the possibility of coning being induced in this situation.



**Question 64, Answers: F T F F T****Comment**

*H. influenzae* meningitis should be treated with a third-generation cephalosporin intravenously for at least 10 days. Chloramphenicol can be substituted where there is a history of anaphylaxis to penicillin or to cephalosporins, or if the organism is resistant to cephalosporins. For *H. influenzae* type b, rifampicin should be given for 4 days before hospital discharge, to prevent carriage. Metronidazole is active against anaerobic organisms.

**Question 65, Answers: F F T T F****Comment**

This patient has developed pseudomembranous colitis, due to *Clostridium difficile* overgrowth in the gut, whose toxin gives rise to this condition. It can occur following treatment with any antibiotic, but appears to be a particular hazard with clindamycin and cephalosporins. Oral metronidazole or oral vancomycin are used as specific treatment.