## Contents

## SECTION 1 General principles

## 1 What is pharmacology? 1

What is a drug? 1

Origins and antecedents 1

Pharmacology in the 20th and 21st centuries 2

Alternative therapeutic principles 3
The emergence of biotechnology 4
Pharmacology today 4

## 2 How drugs act: general principles 6

Introduction 6

Protein targets for drug binding 6

Drug receptors 6

Drug specificity 7
Receptor classification 8

Drug-receptor interactions 8

Competitive antagonism 11

Partial agonists and the concept of efficacy 12

Constitutive receptor activation and inverse

agonists 14

Biased agonism 16

Allosteric modulation 17

Other forms of drug antagonism 17

Desensitisation and tolerance 19

Change in receptors 19

Translocation of receptors 19

Exhaustion of mediators 20

Altered drug metabolism 20

Physiological adaptation 20

Quantitative aspects of drug-receptor

interactions 20

The binding reaction 20

Binding when more than one drug is present 21

The nature of drug effects 22

## 3 How drugs act: molecular aspects 24

#### Protein targets for drug action 24

Receptors 24

Ion channels 24

Enzymes 25

Transporters 25

#### Receptor proteins 26

Types of receptor 26

Molecular structure of receptors 26

Type 1: ligand-gated ion channels 28

Type 2: G protein-coupled receptors 30

Type 3: kinase-linked and related

receptors 42

Type 4: nuclear receptors 44

#### lon channels as drug targets 47

Ion selectivity 49

Gating 49

Malecular architecture of ion channels 49

Pharmacology of ion channels 50

Control of receptor expression 51 Receptors and disease 51

# 4 How drugs act: cellular aspects — excitation, contraction and secretion 54

## Regulation of intracellular calcium 54

Calcium entry mechanisms 54

Calcium extrusion mechanisms 57

Calcium release mechanisms 57

Calmodulin 58

#### Excitation 58

The 'resting' cell 59

Electrical and ionic events underlying the action

potential 59

Channel function 60

Muscle contraction 65 Skeletal muscle 65

Cardiac muscle 65

Smooth muscle 65

#### Release of chemical mediators 67

Exocytosis 68

Non-vesicular release mechanisms 69

Epithelial ion transport 69

# 5 How drugs act: biopharmaceuticals and gene therapy 72

Introduction 72

### Protein and peptide biopharmaceuticals 72

Monoclonal antibodies 74

Pharmacology of protein biopharmaceuticals 75

Oligonucleotides 77

RNA drugs that target proteins 77

RNA drugs that target other nucleotides 79

RNA drugs that are used to encode proteins 79

Miscellaneous other RNA species with pharmacological potential 80

Problems with RNA biopharmaceuticals 80

#### Gene therapy 81

Gene delivery 82

Controlling gene expression 84

Safety and societal issues 84

Therapeutic applications 85

Future directions 85

6 Cell proliferation, apoptosis, repair and regeneration 87

### Cell proliferation 87

The cell cycle 87

Interactions between cells, growth factors and the extracellular matrix 90

Angiogenesis 91

#### Apoptosis and cell removal 91

Morphological changes in apoptosis 92

The major players in apoptosis 92

Pathways to apoptosis 92

Pathophysiological implications 94

Drug interactions caused by altered absorption 137

Repair and healing 94

Hyperplasia 95

10 Drug metabolism and elimination 140 The growth, invasion and metastasis of tumours 95 Stem cells and regeneration 95 Introduction 140 Therapeutic prospects 95 Drug metabolism 140 Apoptotic mechanisms 96 Phase 1 reactions 140 Angiogenesis and metalloproteinases 96 Phase 2 reactions 142 Cell cycle regulation 96 Stereoselectivity 142 Inhibition of P450 143 7 Cellular mechanisms: host defence 98 Induction of microsomal enzymes 143 Introduction 98 Presystemic ('first-pass') metabolism 143 The innate immune response 98 Pharmacologically active drug metabolites 144 Pattern recognition 99 Drug interactions due to enzyme induction or The adaptive immune response 104 inhibition 144 The induction phase 105 Drug and metabolite excretion 146 The effector phase 106 Biliary excretion and enterohepatic Systemic responses in inflammation 109 circulation 146 Renal excretion of drugs and metabolites 146 The role of the nervous system in inflammation 109 Unwanted inflammatory and immune responses and Drug interactions due to altered drug their unintended consequences 109 excretion 148 The outcome of the inflammatory response 110 Pharmacokinetics 150 8 Method and measurement in pharmacology 112 Introduction: definition and uses of Bioassay 112 pharmacokinetics 150 Biological test systems 112 Uses of pharmacokinetics 151 General principles of bioassay 114 Scope of this chapter 151 Animal models of disease 116 Drug elimination expressed as clearance 151 Pharmacological models 116 Single-compartment model 153 Genetically altered animal models 116 Repeated dosing 154 Reducing use of animals in research 117 Effect of variation in rate of absorption 154 Pharmacological studies in humans 118 More complicated kinetic models 155 Clinical trials 118 Two-compartment model 156 Risk of bias in randomised controlled trials 119 Saturation kinetics 157 The size of the sample 120 Population pharmacokinetics 157 Clinical outcome measures 120 Limitations of pharmacokinetics 158 Placebos 120 12 Individual variation, pharmacogenomics and Meta-analysis 121 Clinical consideration of benefit and risk 121 personalised medicine 160 Absorption and distribution of drugs 123 Introduction 160 Epidemiological factors and inter-individual variation of Introduction 123 drug response 161 Physical processes underlying drug disposition 123 Ethnicity 161 The movement of drug molecules across cell Age 161 barriers 123 Pregnancy 162 Binding of drugs to plasma proteins 129 Disease 162 Partition into body fat and other tissues 130 Drug interactions 163 Drug absorption and routes of administration 130 Genetic variation in drug responsiveness 164 Oral administration 131 Single-gene pharmacokinetic disorders 165 Oromucosal (sublingual or buccal) administration 133 Therapeutic drugs and clinically available Rectal administration 133 pharmacogenomic tests 166 Application to epithelial surfaces 133 Incorporating pharmacogenetic data into daily clinical Intravitreal injection 134 workflows 167 Distribution of drugs in the body 135 Conclusions 168 Body fluid compartments 135 Volume of distribution 136

Drug interactions caused by altered distribution 137

Special drug delivery systems 137

## SECTION 2 Chemical mediators

# Chemical mediators and the autonomic nervous system 170

Historical aspects 170

The autonomic nervous system 171

Basic anatomy and physiology 171

Transmitters in the autonomic nervous system 174

## Some general principles of chemical transmission 174

Presynaptic modulation 174

Postsynaptic modulation 176

Transmitters other than acetylcholine and

noradrenaline 177

Co-transmission 177

Termination of transmitter action 177

Denervation supersensitivity 179

Basic steps in neurochemical transmission: sites of drug action 180

## 14 Cholinergic transmission 182

Muscarinic and nicotinic actions of acetylcholine 182

Acetylcholine receptors 182

Nicotinic receptors 182

Muscarinic receptors 183

Physiology of cholinergic transmission 185

Acetylcholine synthesis and release 185

Electrical events in transmission at fast cholinergic synapses 186

## Effects of drugs on cholinergic transmission 188

Drugs affecting muscarinic receptors 189

Drugs affecting autonomic ganglia 192

Drugs that act presynaptically 198

Drugs that enhance cholinergic transmission 198

Other drugs that enhance cholinergic

transmission 203

## 15 Noradrenergic transmission 205

Catecholamines 205

Classification of adrenoceptors 205

Physiology of noradrenergic transmission 208

The noradrenergic neuron 208

Uptake and degradation of catecholamines 210

## Drugs acting on noradrenergic transmission 210

Drugs acting on adrenoceptors 211

Drugs that affect noradrenergic neurons 221

## 16 5-Hydroxytryptamine and the purines 225

5-Hydroxytryptamine 225

Distribution, biosynthesis and degradation 225

Pharmacological effects 228

Drugs acting at 5-HT receptors 229

Clinical conditions in which 5-HT plays a role 231

Serotonin and carcinoid syndrome 231

Pulmonary hypertension 231

Purines 231

Purinergic receptors 232

The purinergic system in health and disease 234

The cardiovascular system 234

Asthma and inflammation 234 Platelets 235

Purines as neurotransmitters 235

Summary 235

# 17 Local hormones: histamine, lipids, peptides and proteins 237

Introduction 237

What is a 'mediator'? 237

Histamine 238

Synthesis and storage of histamine 238

Histamine release 238

Histamine receptors 238

Histamine actions 238

#### Eicosanoids 240

General remarks 240

Structure and biosynthesis 240

Prostanoids 242

Leukotrienes 245

Leukotriene receptors 245

Leukotriene actions 246

## Other important fatty acid derivatives 247

Platelet-activating factor 248

Biosynthesis 248

Actions and role in inflammation 248

#### Sphingosine 1-phosphate 248

Biosynthesis and metabolism 248

Receptors and actions 249

## Protein and peptide mediators 250

General principles 250

Types of protein and peptide mediator 250

#### Biosynthesis and regulation of peptides 250

Peptide precursors 251

Diversity within peptide families 252

Peptide trafficking and secretion 252

Bradykinin 252

Source and formation of bradykinin 252

Metabolism and inactivation of bradykinin 253

Bradykinin receptors 253

Actions and role in inflammation 253

## Neuropeptides 254

Cytokines 254

Interleukins and related compounds 255

Chemokines 255

Interferons 257

The 'cytokine storm' 257

## Proteins and peptides that down-regulate

inflammation 257

Concluding remarks 258

## 18 Cannabinoids 260

## Plant-derived cannabinoids ('phytocannabinoids') and their pharmacological effects 260

Pharmacological effects 260

Pharmacokinetic aspects 261

Adverse effects 261

Tolerance and dependence 261

Cannabinoid receptors 261

Endocannabinoids 263

Biosynthesis of endocannabinoids 263

Termination of the endocannabinoid signal 263
Physiological mechanisms 264
Pathological involvement 264
Synthetic cannabinoids 265
Clinical applications 265

## 19 Nitric oxide and related mediators 267

Introduction 267

Biosynthesis of nitric oxide and its control 267 Degradation and carriage of nitric oxide 269

Effects of nitric oxide 270

Biochemical and cellular aspects 270

Vascular effects 271

Neuronal effects 271

Host defence 271

### Therapeutic aspects 271

Nitric oxide 271

Nitric oxide donors/precursors 271

Inhibition of nitric oxide synthesis 272

Nitric oxide replacement or potentiation 272

Clinical conditions in which nitric oxide may play a part 272

Related mediators 273

# SECTION 3 Drugs affecting major organ systems

## 20 The heart 275

Introduction 275

Physiology of cardiac function 275

Cardiac rate and rhythm 275

Cardiac contraction 279

Myocardial oxygen consumption and coronary blood flow 280

Autonomic control of the heart 281

Sympathetic system 281

Parasympathetic system 282

Cardiac natriuretic peptides 283

Ischaemic heart disease 283

Angina 283

Acute coronary syndrome 283

Drugs that affect cardiac function 284

Antidysrhythmic drugs 284

Drugs that act on myocardial contraction 287

Anti-anginal drugs 289

## 21 The vascular system 294

Introduction 294

Vascular structure and function 294

Control of vascular smooth muscle tone 295

The vascular endothelium 295

The renin-angiotensin system 298

Vasoactive drugs 299

Vasoconstrictor drugs 299

Vasodilator drugs 300

Clinical uses of vasoactive drugs 305

Systemic hypertension 305

Heart failure 307

Wasodillatory shock and hypotensive states 309

Peripheral vascular disease 310 Raynaud's disease 310 Pulmonary hypertension 310

## 22 Atherosclerosis and lipoprotein metabolism 313

Introduction 313

Atherogenesis 313

Lipoprotein transport 314

Dyslipidaemia 315

Prevention of atheromatous disease 316

Lipid-lowering drugs 316

Statins: HMG-CoA reductase inhibitors 317

Bempedoic acid 318

Inhibition of PCSK9 318

Fibrates 319

Drugs that inhibit cholesterol absorption 319

Microsomal triglyceride transport protein (MTP)

inhibitors 320

Antisense oligonucleotides 320

## 23 Haemostasis and thrombosis 322

Introduction 322

Blood coagulation 322

Coagulation cascade 322

Vascular endothelium in haemostasis and

thrombosis 324

Drugs that act on the coagulation cascade 325

Coagulation defects 325

Thrombosis 326

Platelet adhesion and activation 330

Antiplatelet drugs 332

Fibrinolysis (thrombolysis) 334

Fibrinolytic drugs 334

# 24 Haematopoietic system and treatment of anaemia 337

Introduction 337

The haematopoietic system 337

Types of anaemia 339

Haematinic agents 339

Iron 339

Folic acid and vitamin B<sub>12</sub> 342

Haematopoietic growth factors 343

Haemolytic anaemia 347

Drugs used to treat haemolytic anaemias 347

# 25 Anti-inflammatory and immunosuppressant drugs 350

Introduction 350

Cyclo-oxygenase inhibitors 350

Mechanism of action 351

Pharmacological actions 352

Some important NSAIDs and COXIBs 356

Antirheumatoid drugs 359

Disease-modifying antirheumatic drugs 359

Immunosuppressant drugs 361

Biologic disease-modifying antirheumatic drugs, anticytokine drugs and other biopharmaceuticals 364

Drugs used in gout 365

Antagonists of histamine 367

Passible future developments in anti-inflammatory therapy 369

## 26 Skin 371

Introduction 371

Structure of skin 371

Common diseases of the skin 374

Acne 374

Rosacea 374

Baldness and hirsutism 376

Eczema 376

Pruritus 376

Urticaria 376

Psoriasis 377

Warts 377

Other infections 377

Melanoma 377

Drugs acting on skin 377

Formulation 377

Principal drugs used in skin disorders 378

Antimicrobial agents 378

Biopharmaceuticals 378

Glucocorticoids and other anti-inflammatory agents 379

Drugs used to control hair growth 380

Refinoids 380

Witamin D analogues 381

Agents acting by other mechanisms 381

Conduding remarks 382

## 27 The eye 384

Immoduction 384

Special pharmacokinetic considerations in the eye 384

Autonomic control of the lens and pupil, and related therapeutic drugs 385

Treatment of inflammation and infection in the eye 386

alaucoma 387

Postaglandin FP receptor agonists 387

6 adrenoceptor antagonists 387

and adrenoceptor agonists 387

Carbonic anhydrase inhibitors 387

Inhibitors of rho kinase 388

Muscarinic agonists 388

Caular vasculature and vascular endothelial growth

factor inhibitors 388

## Respiratory system 390

The physiology of respiration 390

Control of breathing 390

Regulation of musculature, blood vessels and glands of the airways 390

Fullmonary disease and its treatment 391

Branchial asthma 391

Drugs used to treat and prevent asthma 393

Severe acute asthma (status asthmaticus) 398

Allergic emergencies 398

Chronic obstructive pulmonary disease 398

Branchiectasis 399

Idiopathic pulmonary fibrosis 399 Surfactants 400 Cough 400

## 29 The kidney and urinary system 402

Introduction 402

Outline of renal function 402

The structure and function of the nephron 402

Tubular function 404

Acid-base balance 407

Potassium balance 408

Excretion of organic molecules 408

Natriuretic peptides 408

Prostaglandins and renal function 409

Drugs acting on the kidney 409

Diuretics 409

Drugs that alter the pH of the urine 413

Drugs that alter the excretion of organic

molecules 413

Drugs used in renal failure 414

Hyperphosphataemia 414

Hyperkalaemia 414

Drugs used in urinary tract disorders 414

## 30 The gastrointestinal tract 416

## The innervation and hormones of the gastrointestinal tract 416

Neuronal control 416

Hormonal control 416

Gastric secretion 416

The regulation of acid secretion by parietal cells 416

The coordination of factors regulating acid secretion 418

Drugs used to inhibit or neutralise gastric acid

secretion 418
Transment of Holicobarder pulsari infection 420

Treatment of Helicobacter pylori infection 420 Drugs that protect the mucosa 421

Vomiting 421

The reflex mechanism of vomiting 421

Antiemetic drugs 423

The motility of the GI tract 424

Purgatives 425

Drugs that increase gastrointestinal motility 425

Antidiarrhoeal agents 426

Drugs for chronic bowel disease 427

Drugs affecting the biliary system 428

Future directions 428

## The control of blood glucose and drug treatment of diabetes mellitus 429

Introduction 429

Control of blood glucose 429

Pancreatic islet hormones 430

Insulin 431

Glucagon 433

Somatostatin 434

Amylin (islet amyloid polypeptide) 434

Incretins 434

#### Diabetes mellitus 434

Drugs used in the treatment of diabetes 435 Treatment of diabetes mellitus 440

## Obesity 443

#### Introduction 443

Definition of obesity 443

### Obesity as a health problem 443

## Homeostatic mechanisms controlling energy

balance 444

The role of peripheral signalling in body weight regulation 444

Neurological circuits that control body weight and eating behaviour 445

## The pathophysiology of human obesity 447

Food intake and obesity 448

Physical exercise and obesity 448 Genetic factors and obesity 448

#### Pharmacological approaches to the problem of obesity 449

Centrally acting appetite suppressants 449 Orlistat 450

GLP-1 receptor agonists 450

New approaches to obesity therapy 451

## 33 The pituitary and the adrenal cortex 452

### The pituitary gland 452

The anterior pituitary gland 452 Hypothalamic hormones 453 Anterior pituitary hormones 454 Posterior pituitary gland 457

#### The adrenal cortex 458

Glucocorticoids 459 Mineralocorticoids 466

New directions in glucocorticoid therapy 466

## 34 The thyroid 469

### Synthesis, storage and secretion of thyroid hormones 469

Uptake of plasma iodide by the follicle cells 469 Oxidation of iodide and iodination of tyrosine residues 469

Secretion of thyroid hormone 469

## Regulation of thyroid function 469

#### Actions of the thyroid hormones 471

Effects on metabolism 471

Effects on growth and development 471

Mechanism of action 471

### Transport and metabolism of thyroid hormones 472 Abnormalities of thyroid function 472

Hyperthyroidism (thyrotoxicosis) 472 Simple, non-toxic goitre 473

Hypothyroidism 473

Drugs used in diseases of the thyroid 473

Hyperthyroidism 473

Hypothyroidism 474

## 35 The reproductive system 476

Introduction 476 Endocrine control of reproduction 476 Neurohormonal control of the female reproductive system 476

Neurohormonal control of the male reproductive system 478

Behavioural effects of sex hormones 478

## Drugs affecting reproductive function 478

Oestrogens 478

Progestogens 481

Postmenopausal hormone replacement therapy (HRT) 481

Androgens 482

Anabolic steroids 483

Anti-androgens 483

Gonadotrophin-releasing hormone (GnRH): agonists and antagonists 483

Gonadotrophins and analogues 484

## Drugs used for contraception 485

Oral contraceptives 485

Other drug regimens used for contraception 486

#### The uterus 486

The motility of the uterus 486 Drugs that stimulate the uterus 486

Drugs that inhibit uterine contraction 488

Erectile dysfunction 488

## 36 Bone metabolism 491

#### Introduction 491

#### Bone structure and composition 491 Bone remodelling 491

The action of cells and cytokines 493

The turnover of bone minerals 493

Hormones involved in bone metabolism and remodelling 493

## Disorders of bone 496

## Drugs used in bone disorders 496

Bisphosphonates 496

Oestrogens and related compounds 497

Parathyroid hormone and analogues 498

Vitamin D preparations 498

Biopharmaceuticals 498

Calcitonin 499

Calcium salts 499

Calcimimetic compounds 499

## SECTION 4 Nervous system

## 37 Chemical transmission and drug action in the central nervous system 501

Introduction 501

Chemical signalling in the nervous system 501

Targets for drug action 504

Drug action in the central nervous system 504 Blood-brain barrier 506

The classification of psychotropic drugs 507

## Amino acid transmitters 509

#### Excitatory amino acids 509

Excitatory amino acids as CNS transmitters 509

Metabolism and release of excitatory amino acids 509

#### Glutamate 510

Glutamate receptor subtypes 510

Synaptic plasticity and long-term potentiation 512

Drugs acting on glutamate receptors 515

### γ-aminobutyric acid 518

Synthesis, storage and function 518

GABA receptors: structure and

pharmacology 518

Drugs acting on GABA receptors 519

Glycine 520

Concluding remarks 522

## Other transmitters and modulators 524

#### Introduction 524

#### Noradrenaline 524

Noradrenergic pathways in the CNS 524

Functional aspects 524

#### Dopamine 526

Dopaminergic pathways in the CNS 526

Dopamine receptors 527

Functional aspects 527

#### 5-Hydroxytryptamine 529

5-HT pathways in the CNS 529

5-HT receptors in the CNS 529

Functional aspects 530

Clinically used drugs 531

#### Acetylcholine 531

Cholinergic pathways in the CNS 531

Acetylcholine receptors 531

Functional aspects 532

#### Purines 533

Histomine 534

#### Other CNS mediators 534

Melatonin 534

Nitric oxide 535

Lipid mediators 535

A final message 537

## Neurodegenerative diseases 539

#### Protein misfolding and aggregation in chronic meurodegenerative diseases 539

#### Mechanisms of neuronal death 540

Excitotoxicity 541

Apoptosis 541

Oxidative stress 543

#### Ischaemic brain damage 543

Pathophysiology 544

Therapeutic approaches 544

#### Dementia 544

Pathogenesis of Alzheimer's disease 545

Fathogenesis of dementia with Lewy

bodies 546

Therapeutic approaches to dementia 547

#### Flankinson's disease 548

Features of Parkinson's disease 548

Pathopenesis of Parkinson's disease 549

The treatment of Parkinson's disease 550

Essential tremor 553

Huntington's disease 554 Amyotrophic lateral sclerosis 554 Spinal muscular atrophy 554

Multiple sclerosis 554

## General anaesthetic agents 557

#### Introduction 557

### Mechanism of action of anaesthetic drugs 557

Lipid solubility 557

Effects on ion channels 558

Effects on the nervous system 559

Effects on the cardiovascular and respiratory systems 559

Intravenous anaesthetic agents 560

Propofol 560

Thiopental 560

Etomidate 561

Other intravenous agents 562

#### Inhalation anaesthetics 563

Pharmacokinetic aspects 563

#### Individual inhalation anaesthetics 565

Isoflurane, desflurane, sevoflurane, enflurane and

halothane 566

Nitrous oxide 566

Sedation and balanced anaesthesia 567

## Headache 568

#### Headache 568

#### Types of headaches 568

Migraine 568

Tension-type headaches 570

Trigeminal autonomic cephalalgias 571

Miscellaneous primary headaches 571

## Drug therapy for headache 571

Drugs acting on the 5-HT system 571

Drugs acting on the CGRP system 572

Anti-inflammatory drugs 573

Centrally acting drugs 573

Cardiovascular drugs 573

Miscellaneous group 574

Other non-pharmacological treatments 574

Summary 574

## Analgesic drugs 575

## Introduction 575

## Neural mechanisms of pain 575

Modulation in the nociceptive pathway 576

Chemical signalling in the nociceptive pathway 579

## Analgesic drugs 581

Opioid drugs 581

Paracetamol 590

### Chronic pain 591

Treatment of chronic secondary pain 591

Treatment of chronic primary pain 592

Other drugs used to treat pain 592

## 44 Local anaesthetics and other drugs affecting sodium channels 595

Local anaesthetics 595

# SECTION 5 Drugs used for the treatment of infections and cancer

# Basic principles of antimicrobial chemotherapy 690

Background 690

The molecular basis of chemotherapy 690

Bacteria 690

Biochemical reactions as potential targets 691

The formed structures of the cell as potential targets 696

Resistance to antibacterial drugs 697

The spread of antibiotic resistance 698

Biochemical mechanisms of resistance to antibiotics 700

Current status of antibiotic resistance in bacteria 701

Resistance to other antimicrobials 702

## 52 Antibacterial drugs 704

Introduction 704

Gram staining and its significance for drug action 704

Antibacterial agents that interfere with folate synthesis or action 704

Sulfonamides 704

Trimethoprim 706

β-lactam antibiotics and other agents that interfere with bacterial wall or membrane synthesis 707

Penicillins 707

Cephalosporins and cephamycins 709

Other  $\beta$ -lactam antibiotics 710

Other antibiotics that inhibit bacterial cell wall peptidoglycan synthesis 710

Antimicrobial agents affecting bacterial protein synthesis 711

Tetracyclines 711

Aminoglycosides 713

Macrolides 713

Oxazolidinones 714

Fusidic acid 714

Streptogramins 714

Clindamycin 714

Antimicrobial agents affecting topoisomerase 715

Quinolones 715

Miscellaneous antibacterial agents 716

Antimycobacterial agents 716

Drugs used to treat tuberculosis 716

Drugs used to treat leprosy 718

Prospects for new antibacterial drugs 719

## 53 Antiviral drugs 721

#### Background information about viruses 721

An outline of virus structure 721

The lifecycle of viruses 721

Mechanisms of viral replication 722

The host-virus interaction 723

Host defences against viruses 723

Viral plays to circumvent host defences 724

#### HIV and AIDS 725

Induction of the disease 725

Progress of infection 725

#### COVID-19 728

## Antiviral drugs 729

DNA polymerase inhibitors 729

Reverse transcriptase inhibitors 730

Non-nucleoside reverse transcriptase

inhibitors 731

Protease inhibitors 731

Neuraminidase inhibitors and inhibitors of viral coat

disassembly 732

Drugs acting through other mechanisms 732

Biopharmaceutical antiviral drugs 732

Other agents 733

Combination therapy for HIV 733

COVID-19 pharmacotherapy 734

Prospects for new antiviral drugs 735

## 54 Antifungal drugs 736

Fungi and fungal infections 736

Drugs used to treat fungal infections 737

Antifungal antibiotics 737

Synthetic antifungal drugs 739

Future developments 740

## 55 Antiprotozoal drugs 742

Background 742

Host-parasite interactions 742

Malaria and antimalarial drugs 742

The life cycle of the malaria parasite 744

Antimalarial drugs 745

Potential new antimalarial drugs 751

Amoebiasis and amoebicidal drugs 752

Trypanosomiasis and trypanocidal drugs 753

Other protozoal infections and drugs used to treat

them 754

Leishmaniasis 754

Trichomoniasis 754

Giardiasis 755

Toxoplasmosis 755

Pneumocystis 755

Future developments 755

## 56 Antihelminthic drugs 757

#### Helminth infections 757

Antihelminthic drugs 758

Benzimidazoles 760

Praziquantel 761

Piperazine 761

Diethylcarbamazine 761

Niclosamide 761

Levamisole 762

Ivermectin 762

Resistance to antihelminthic drugs 762

## Vaccines and other novel approaches 763

## 57 Anticancer drugs 764

Introduction 764
The pathogenesis of cancer 764

The genesis of a cancer cell 765

The special characteristics of cancer cells 765

General principles of cytotoxic anticancer drugs 767 Anticancer drugs 768

Alkylating agents and related compounds 771

Antimetabolites 773

Cytotoxic antibiotics 774

Plant derivatives 775

Hormones 776

Hormone antagonists 776

Monoclonal antibodies 777

Protein kinase inhibitors 778

Miscellaneous agents 779

Resistance to anticancer drugs 780

Combination therapies 780

Control of emesis and myelosuppression 781

Future developments 781

## SECTION 6 Special topics

## 58 Harmful effects of drugs 783

Introduction 783

Classification of adverse drug reactions 783

Adverse effects related to the known pharmacological action of the drug 784

Adverse effects unrelated to the known pharmacological action of the drug 784

Drug toxicity 784

Toxicity testing 784

Antiasychotic drugs \_626 '

General mechanisms of toxin-induced cell damage and cell death 785

virulure developments 755

Mutagenesis and assessment of genotoxic potential 787

Pleaver omiententententententen 6827 zizoinomiziel

Vaccines and other novel approaches 763-

And the second of the second o

Immunological reactions to drugs 791

Immunological mechanisms 791 Clinical types of allergic response to drugs 791

## 59 Lifestyle and drugs in sport 794

What are lifestyle drugs? 794

Classification of lifestyle drugs 794

Cognitive enhancers 795

Drugs and sex 796

Drugs in sport 797

Anabolic steroids and related compounds 798

Drugs that increase oxygen delivery to muscles 799

Regulatory, societal and ethical issues 800

Conclusion 801

## 60 Drug discovery and development 802

Drug discovery: background 802

The stages of a project 803

The drug discovery phase 804
Preclinical development 806
Clinical development 807

Clinical development 807

Biopharmaceuticals 808 Commercial aspects 808

Drug repurposing 809 Generic drugs 809

Future prospects 809 A final word 811

Index 812

Self-assessment questions compiled by Dr. Christine Edmead, University of Bath, are available through eBooks. Health. Elsevier.com

Miscellaneous antibactierial agents (T.6

Prospects for new doll-legislate and streets and streets