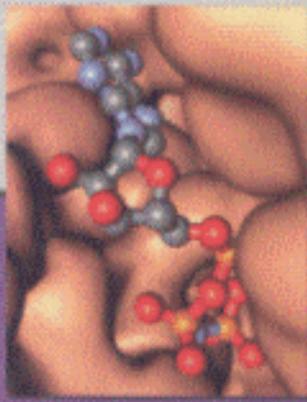
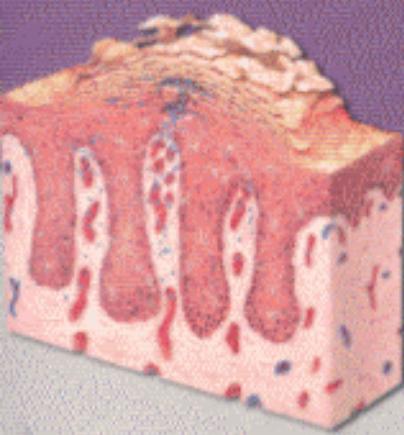


Netter's Illustrated Pharmacology

Robert B. Raffa

Scott M. Rawls

Elena Portyansky Beyzarov



J. Netter
M.D.

CONTENTS

CHAPTER 1. BASIC PRINCIPLES OF PHARMACOLOGY

Overview	1
Major Ways in Which Drugs Work	
Eliminate External and Internal Threats.....	2
Replenish or Neutralize Endogenous Chemicals	4
Modulate Physiologic Processes	5
Chemical Communication	
Chemical Transmission at the Synapse.....	6
Synapse Morphology.....	7
Pharmacodynamics	
Receptors and Signaling	8
Receptor Subtypes	9
Agonists	10
Antagonists.....	11
Stereochemistry and 3-Dimensional Fit	12
Receptor-Effector Coupling	13
Signal Transduction and Cross Talk.....	14
Second-Messenger Pathways.....	15
Ligand-Gated Ion Channels	16
G Protein-Coupled Receptors.....	17
<i>Trk</i> Receptors.....	18
Nuclear Receptors	19
Up-regulation and Down-regulation of Receptors.....	20
Dose-Response Curves	21
Potency.....	22
Efficacy	22
Inverse Agonists	23
Antagonists: Surmountable (Reversible) and Nonsurmountable (Irreversible)	24
Pharmacokinetics	
Routes of Administration	25
First-Pass Effect	26
Membrane Transport.....	27
Distribution	28
Barriers	29
Metabolism (Biotransformation) of Drugs.....	30
Cytochrome P-450 (CYP450) Enzymes	31
Metabolic Enzyme Induction and Inhibition.....	32
Elimination	33

CONTENTS

CHAPTER 2. DRUGS USED TO AFFECT THE AUTONOMIC AND SOMATIC NERVOUS SYSTEMS

Overview	35
Organization of the Nervous System	
Organization of the Nervous System	36
Action of Drugs on Nerve Excitability	37
Somatic Nervous System	
Interface of the Central and Peripheral Nervous Systems and Organization of the Somatic Division	38
Neuromuscular Transmission.....	39
Nicotinic Acetylcholine Receptor	40
Physiology of the Neuromuscular Junction.....	41
Pharmacology of the Neuromuscular Junction	42
Mechanism of Action of Acetylcholinesterase Inhibitors.....	43
Neuromuscular Blocking Agents: Nondepolarizing and Depolarizing	44
Autonomic Nervous System	
Autonomic Nervous System: Schema	45
Sympathetic Fight or Flight Response.....	46
Cholinergic and Adrenergic Synapses	47
Example of Cholinergic and Adrenergic Drug Treatment: Glaucoma	48
Cholinergic Receptors.....	49
Cholinergic Drugs.....	50
Example of Cholinergic Drug Treatment: Myasthenia Gravis	52
Adrenergic Receptors	53
Adrenergic Drugs	54
Drugs That Act on the Autonomic Nervous System	55
Drug Side Effects.....	56

CHAPTER 3. DRUGS USED IN DISORDERS OF THE CENTRAL NERVOUS SYSTEM AND TREATMENT OF PAIN

Overview	57
Introduction to the CNS and Drug Action	
Development of the Nervous System	58
Anatomy of the Nervous System.....	59
Functional Correlations and Visualization of Brain Structures.....	60
Resting Membrane and Action Potentials.....	61
Excitatory and Inhibitory Postsynaptic Potentials.....	62
Central Nervous System Neurotransmitters, Receptors, and Drug Targets	63
Sedative-Hypnotic Drugs	
GABA _A Receptor Complex and Sedative-Hypnotic Drugs	64
Anxiolytic Agents	
Clinical Anxiety	65
Anxiolytic Agents	66

Antiepileptic Agents	
Causes of Seizures and Their Treatment	67
Epilepsy: Generalized Seizures and Status Epilepticus	68
Epilepsy: Partial and Absence Seizures	69
Antidepressants	
Clinical Depression.....	71
Antidepressants: Mechanisms of Action	72
Drugs Affecting Bipolar Disorder and OCD	
Bipolar Disorder and Compulsive Behavior	73
Antipsychotic Agents	
Psychosis and Dopamine Pathways	74
Drugs Affecting Movement Disorders and Other Neurodegenerative Disorders	
Motor Tracts, Basal Ganglia, and Dopamine Pathways	75
Parkinsonism: Symptoms and Defect.....	77
Parkinsonism: Levodopa, Carbidopa, and Other Drugs.....	78
Huntington Disease and Tourette Syndrome	79
Alzheimer Disease: Symptoms, Course, and Pathology.....	80
Alzheimer Disease: Cholinergic Involvement and Drugs.....	81
Stroke: Symptoms and Drug Treatment.....	83
CNS Skeletal Muscle Relaxants	
Motor Neurons and Drugs.....	84
Analgesics and Anesthetics	
Pain Pathways	85
Local Anesthetics: Spinal Afferents and Local Anesthetic Mechanisms of Action	86
General Anesthetics: Properties	87
Opioids: Endogenous Opioid Pathway	88
Opioids: Receptor-Transduction Mechanisms	89
Nonopioids: NSAIDs, Selective Cyclooxygenase-2 Inhibitors, and Acetaminophen	90
Sumatriptans and Reuptake Inhibitors	91
CHAPTER 4. DRUGS USED IN DISORDERS OF THE CARDIOVASCULAR SYSTEM	
Overview	93
Cardiovascular System: Anatomy, Function, and Regulation of the Heart	
Cardiovascular Function: Anatomy.....	94
Cardiovascular Function: Definition of Terms and Regulation	95
Role of Catecholamines in Heart Function	96
Sympathetic and Parasympathetic Regulation of Heart Function	97
Synthesis and Storage of Catecholamines.....	98
Regulation of Norepinephrine Release	99
Inactivation of Norepinephrine	100
Hypercholesterolemia and Atherosclerosis	
Hypercholesterolemia: Causes	101

CONTENTS

Hypercholesterolemia: Pharmacologic Therapy	102
Angina	
Angina Overview	103
Nitrates for Angina Treatment: Classes, Administration Routes, Pharmacology, and Adverse Effects	104
Nitroglycerin in Angina Treatment	105
Nitroglycerin: Mechanism of Action	106
Calcium Channel Antagonists	107
Drug Summary for Angina	108
Heart Failure	
Heart Failure Overview	109
Heart Failure: Treatment	110
Heart Failure Treatment: β -Adrenergic Stimulators and Blockers	111
Heart Failure Treatment: Cardiac Glycosides	112
Arrhythmias	
Cardiac Arrhythmias: General	113
Cardiac Arrhythmias: Treatment	115
Cardiac Arrhythmias: Drug Classification	117
Hypertension	
Hypertension Overview	118
Hypertension: Causes	119
Hypertension Treatment: Diuretics	120
Hypertension Treatment: Angiotensin-Converting Enzyme Inhibitors	121
Hypertension Treatment: β and α Blockers	122
Hypertension Treatment: Minoxidil	123
Hypertension Treatment: Clonidine	124
Hypertension in Elderly Patients	125
Pheochromocytoma-Induced Hypertension	126
Hypertension in Cushing Syndrome	127
Peripheral Vascular Disease	
Peripheral Vascular Disease	128
CHAPTER 5. DRUGS USED IN DISORDERS OF THE ENDOCRINE SYSTEM	
Overview	129
Hypothalamic and Pituitary Disorders	
Regulation of Hypothalamic and Pituitary Hormones	130
Hypopituitarism	132
Growth Hormone Deficiency and Treatment	133
Growth Hormone Excess (Acromegaly) and Treatment	134
Thyroid Disorders	
Thyroid Hormones	135
Thyroid Hormones: Synthesis, Release, and Regulation	136

Hypothyroidism	137
Hypothyroidism: Treatment of Choice.....	138
Liothyronine and T ₄ /T ₃ Combinations	139
Hyperthyroidism.....	140
Hyperthyroidism: Treatment.....	141
Thioamides	142
Thioamides: Adverse Effects.....	143
Radioactive Iodine	144
Iodide	145
Adrenergic Antagonists.....	146
Corticosteroids and Adrenocortical Dysfunction	
Regulation of Adrenal Hormones.....	147
Mineralocorticoids and Glucocorticoids.....	148
Corticosteroids	149
Cushing Syndrome.....	150
Ketoconazole	151
Metyrapone.....	152
Aminoglutethimide.....	153
Addison Disease, or Primary Adrenal Insufficiency.....	154
Diabetes Mellitus	
The Pancreas and Insulin Production	155
Insulin Secretion.....	156
Lack of Insulin	157
Type 1 Diabetes Mellitus	158
Type 2 Diabetes Mellitus	159
Insulin Therapy	160
Reactions to Insulin: Hypoglycemia and Adipose Tissue Changes	161
Sulfonylureas	162
Biguanides	163
Meglitinides	164
α-Glucosidase Inhibitors	165
Thiazolidinediones	166
Thiazolidinediones: Clinical Rationale and Adverse Effects.....	167
CHAPTER 6. DRUGS USED IN DISORDERS OF THE GASTROINTESTINAL SYSTEM	
Overview	169
Function and Regulation of the GI System	
Enteric Nervous System	170
Integration of the Autonomic and Enteric Nervous Systems.....	171
Gastrointestinal Motility	172
Control of Peristalsis.....	174
Hormones of the Gastrointestinal Tract.....	175
Parietal Cell Function Regulation	176

CONTENTS

Pancreatic Secretion	177
Defecation.....	178
Protein Digestion	179
Fat Digestion	180
Disorders of Colonic Motility	
Colonic Motility and Treatment of Diarrhea.....	181
Antidiarrheal Drugs and Their Adverse Effects.....	182
Causes of Constipation.....	183
Treatment of Constipation	184
Functional Disorder of the Large Intestine	
Treatment of Irritable Bowel Syndrome.....	185
Protozoal GI Infection	
Giardiasis	187
Peptic Ulcer	
<i>Helicobacter pylori</i> Infection Overview.....	188
Treatment of <i>Helicobacter pylori</i> Infection	189
Peptic Ulcer Treatment	190
Gastroesophageal Reflux Disease	
Gastroesophageal Reflux Disease Overview	191
Gastroesophageal Reflux Disease Treatment.....	192
Pancreatitis	
Treatment of Pancreatitis	193
Cholelithiasis	
Pathologic Features of Gallstones.....	195
Gallstone Pathogenesis and Treatment	196
Liver Physiology and Pathology	
Liver Function	197
Bilirubin Production and Excretion	198
Cirrhosis	199
Ascites	200
Nausea and Vomiting	
Physiology of Emesis	202
Antiemetics	204
CHAPTER 7. DRUGS USED IN DISORDERS OF THE RESPIRATORY SYSTEM	
Overview.....	205
Respiration: Introduction to Physiology and Pathology	
Respiration Overview	206
Respiratory Diseases	207

Allergy

Allergy	208
Leukocyte Function	209
Allergic Rhinitis	210

Asthma

Introduction to Asthma	211
Extrinsic and Intrinsic Asthma	212
Asthma Pharmacotherapy	214
Anti-IgE Antibodies	215
Mast Cell Degranulation Blockers	216
Bronchodilators	217
Methylxanthines	218
Methylxanthine: Adverse Effects	219
β -Adrenergic Agonists	220
Nonselective β -Adrenergic Agonists	221
Selective β_2 -Adrenergic Agonists	222
Antimuscarinic Antagonists	223

Antiinflammatory Agents: Corticosteroids

Corticosteroids	224
Corticosteroids: Clinical Uses	225
Corticosteroids: Adverse Effects	226

Antiinflammatory Agents: Leukotriene Antagonists

Leukotrienes	227
Leukotriene Antagonists	228

Cough

Cough	229
Cough Suppressants (Antitussive Agents)	230

Chronic Obstructive Pulmonary Disease

Chronic Obstructive Pulmonary Disease	231
Emphysema	232
Emphysema: Causes	233
Inherited Emphysema	234
Chronic Bronchitis	235
COPD: General Treatment Measures	236
COPD: Specific Drug Treatments	237

Restrictive Pulmonary Disease

Restrictive Pulmonary Disease	238
-------------------------------------	-----

Pneumonia

Pneumonia	239
Viral Pneumonia	241
Bacterial Pneumonia	243

CONTENTS

CHAPTER 8. DRUGS USED IN DISORDERS OF THE REPRODUCTIVE SYSTEM

Overview	245
Organization and Function of the Reproductive System	
Organization of the Reproductive System	246
Regulation of Estrogen and Testosterone	247
Events of the Normal Menstrual Cycle	248
Contraception	
Combination Oral Contraceptives	249
Major Adverse Effects of Combination Oral Contraceptives	250
Estrogen and Coagulation	251
Progestin-Only Contraceptives	252
The Morning-After Pill	253
The Abortion Pill	254
Endometriosis and Treatment	
Endometriosis	255
Danazol	256
Gonadotropin-Releasing Hormone Agonists, Combination Oral Contraceptives, and Progestin	257
Postmenopausal Hormone Changes and Therapy	
Estrogen Decline	258
Vasomotor Symptoms	259
Genitourinary Atrophy	260
Osteoporosis and Estrogen	261
Role of Progestins in Hormone Replacement Therapy	262
Route of Hormone Administration	263
General Adverse Effects	264
Cardiovascular and Neurologic Risks	265
Cancer Risks	266
Selective Estrogen Receptor Modulators and Antiestrogens	
Selective Estrogen Receptor Modulators	267
Antiestrogens	268
Hypogonadism	
Hypogonadism	269
Hypogonadism Treatment and Adverse Effects	270

CHAPTER 9. DRUGS USED TO AFFECT RENAL FUNCTION

Overview	271
Organization and Functions of the Renal System	
Macroscopic Anatomy	272
The Nephron	273
Blood Vessels Surrounding Nephrons	274
The Glomerulus	275

Practical Application: Measuring the Glomerular Filtration Rate	276
Tubular Segments.....	277
Ion and Water Reabsorption	278
Bicarbonate Reabsorption	279
Potassium Excretion.....	280
Volume Regulation	
Antidiuretic Hormone	281
Renin-Angiotensin-Aldosterone System.....	282
Diuretics	
General Considerations: Volume Homeostasis	283
Mercurial Diuretics	285
Carbonic Anhydrase Inhibitors	286
Thiazide Diuretics	287
Potassium-Sparing Agents.....	288
Loop (High-Ceiling) Diuretics	289
Osmotic Agents	290
Summary of Therapeutics.....	291
Urinary Incontinence	
Urinary Incontinence.....	293
Urinary Tract Calculi	
Urinary Tract Calculi (Kidney Stones).	294
Renal Insufficiency and Dialysis	
Effect of Renal Insufficiency on Drug Action	295
Effect of Hemodialysis on Drug Action	296
CHAPTER 10. DRUGS USED IN INFECTIOUS DISEASE	
Overview.....	297
Bacterial Infections: Antibiotics	
Classification of Antibiotics	298
Definitions: Bacteriostatic Versus Bactericidal	299
Spectrum of Activity	300
Mechanisms of Resistance	301
Examples of Resistance.....	302
Natural Penicillins: Penicillin G and Penicillin V	303
Aminopenicillins: Amoxicillin and Ampicillin	304
Antipseudomonal Penicillins: Carbenicillin, Piperacillin, and Ticarcillin	305
β -Lactamase Inhibitors.....	306
β Lactamase-Resistant Penicillins: Cloxacillin, Dicloxacillin, Oxacillin, and Nafcillin.....	307
Adverse Effects of Penicillins	308
Cephalosporins.....	309
Carbapenems: Imipenem-Cilastatin, Ertapenem, and Meropenem	310
Monobactams: Aztreonam.....	311

CONTENTS

Vancomycin.....	312
Vancomycin Treatment Difficulties: Resistance and Adverse Effects.....	313
Tetracyclines	314
Aminoglycosides.....	315
Macrolides: Erythromycin, Azithromycin, and Clarithromycin	316
Clindamycin.....	317
Quinolones	318
New-Generation Quinolones.....	319
Quinupristin/Dalfopristin	321
Linezolid.....	322
Sulfonamides.....	323
Fungal Infections: Antifungal Drugs	
Nature of Fungal Infections and Therapy	324
Amphotericin B.....	325
Azole Antifungal Agents and Other Antifungal Agents	326
Viral Infections and Antiviral Agents	
Nature of Viral Infections	327
Herpesviruses	328
Acyclovir and Famciclovir.....	329
Ganciclovir	330
Influenza and Its Treatment	331
HIV Infection: Antiretroviral Agents	
HIV Infection.....	332
Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and Non-NRTIs.....	333
Protease Inhibitors.....	334
Other Antiretroviral Agents for AIDS: Tenofovir and Enfuvirtide	335
CHAPTER 11. DRUGS USED IN NEOPLASTIC DISORDERS	
Overview.....	337
Introduction to Chemotherapy	
Cell Cycle.....	338
Combination Chemotherapy.....	339
Adverse Effects of Chemotherapy	340
Antimetabolites	
Folate Analogs: Methotrexate	341
Purine Analogs: Mercaptopurine and Thioguanine.....	342
Pyrimidine Analogs: 5-Fluorouracil	343
Pyrimidine Analogs: Capecitabine	344
Pyrimidine Analogs: Cytarabine and Fludarabine	345
Pyrimidine Analogs: Gemcitabine.....	346
Substituted Ureas: Hydroxyurea	347

Alkylating Agents	
Nitrogen Mustards: Mechlorethamine and Melphalan	348
Cyclophosphamide and Ifosfamide	349
Nitrosoureas: Carmustine and Lomustine.....	350
Platinum Compounds: Cisplatin, Carboplatin, and Oxaliplatin.....	351
Microtubule Inhibitors	
Vinca Alkaloids: Vincristine, Vinblastine, and Vinorelbine.....	352
Taxanes.....	353
Antibiotics	
Anthracyclines: Doxorubicin and Daunorubicin	354
Hormonal Therapies	
Estrogen Antagonists: Tamoxifen and Toremifene.....	355
Aromatase Inhibitors: Anastrozole, Letrozole, and Exemestane	356
Gonadotropin-Releasing Hormone Analogs: Leuprorelin and Goserelin	357
Antiandrogens: Flutamide, Bicalutamide, and Nilutamide.....	358
Monoclonal Antibodies	
Unconjugated Antibodies: Trastuzumab, Alemtuzumab, and Rituximab.....	359
Conjugated Antibodies: Ibritumomab Tiuxetan and Tositumomab and Iodine I 131 Tositumomab	360
Newer Miscellaneous Agents	
Imatinib Mesylate	361
Gefinitib	362
Bortezomib	363
CHAPTER 12. DRUGS USED FOR SKIN DISORDERS	
Overview	365
Organization of the Skin	
Anatomy of the Skin	366
Hair Loss	
Alopecia.....	367
Blister Diseases	
Bullous (Blister) Skin Diseases	368
Eczema	
Common Dermatoses Including Eczema	369
Psoriasis	
Psoriasis	370
Mite and Louse Infestations	
Scabies and Pediculosis.....	371
Hives	
Urticaria	372

CONTENTS

CHAPTER 13. VITAMINS: DEFICIENCIES AND DRUG INTERACTIONS

Overview	373
Fat-Soluble Vitamins	
Deficiency of Vitamin A (Retinol) and Other Fat-Soluble Vitamins	374
Water-Soluble Vitamins	
Deficiency of Thiamine (B ₁) and Other B Vitamins.....	375
Niacin or Nicotinic Acid Deficiency (Pellagra).....	376
Vitamin C Deficiency (Scurvy).	377
Vitamin-Drug Interactions	
Fat-Soluble Vitamin-Drug Interactions	378
Water-Soluble Vitamin-Drug Interactions	379

CHAPTER 14. DRUG ALLERGY, ABUSE, AND POISONING OR OVERDOSE

Overview	381
Drug Allergy	
Allergic Reactions to Drugs	382
Type I (Acute, Anaphylactic) Reactions	383
Type II (Cytotoxic, Autoimmune) Reactions.....	384
Type III (Immune Complex, Serum Sickness, Arthus) Reactions.....	385
Type IV (Cell-Mediated, Delayed-Hypersensitivity, Contact Dermatitis) Reactions	386
Drug Abuse	
Brain Reward Circuit	387
Ethanol: Deleterious Effects	388
Ethanol Abuse: Treatment.....	389
Withdrawal: Opioids, Benzodiazepines, and Barbiturates.....	390
Poisoning or Overdose	
Sympathomimetic Drugs	392
Cholinergic Drugs	393
Anticholinergic Drugs	394
Serotonergics	395
Opioids.....	396
Over-the-Counter Products	397
Management of Poisoning and Overdose	398
Index	399