Essentials of Medical Pharmacology

Essentials of

Medical Pharmacology

Sixth Edition

KD TRIPATHI MD

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Essentials of Medical Pharmacology, 6th edition

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Preface

The unprecedented pace of developments over the recent years in the field of drugs (medicines) has further emphasized the relevance of Pharmacology to health professionals. Molecular targets of drug action are being defined at greater resolution, refining new drugs design. Practice of medicine is transforming from 'experience (impression) based' to 'evidence based', since more and more credible evidence from well designed clinical studies is now available on the impact of different treatments on mortality, morbidity and other therapeutic outcomes. The present edition is oriented to reflect the contemporary advancements.

Adopting the 'prototype drug' approach and a structured, systematic and user-friendly format, the actions, mechanisms, kinetics and toxicological aspects of drugs are described along with the pharmacological basis of their use and role/status in the therapy of various diseases/conditions. By a unique synthesis of pharmacology with clinical medicine, the book is designed to be useful both to the uninitiated medical student, as well as to prescribing physicians.

All chapters have been updated to include recently introduced drugs and published information. Latest therapeutic guidelines from leading professional bodies, WHO and National Health Programmes have been incorporated, especially in areas like hypertension, hyperlipidaemias, stroke prevention, surgical prophylaxis, tuberculosis, leprosy, malaria, and HIV-AIDS. Recent developments have been highlighted, notably in hormone replacement therapy, aromatase inhibitors, bisphosphonates, selective COX-2 inhibitors, atypical antipsychotics, therapy of diabetes mellitus, heart failure, acute coronary syndromes, Alzheimer's disease, parkinsonism, glaucoma, kala azar, etc. A chapter is devoted to the principles of 'rational use of medicines', elements of 'evidence based medicine' and the process of 'new drug development' to reflect current importance of these topics. Another new chapter compiles the clinically important drug interactions. Some other topics added are drug transporters, pharmacogenomics, pharmacovigilance, expiry date of pharmaceuticals, single enantiomer drugs, biological response modifiers, prescribing in pregnancy, etc.

New drugs marketed in India till mid 2007 are included, while obsolete ones are deleted. Infrequently used drugs and those not available in India are described briefly in extract type. Important points are summarized in boxes. Leading trade names with dosage forms are given. Emphasis is placed on the profile of diseases and drug use in India and other tropical countries, so as to be particularly useful to students and doctors in these regions; a need not well addressed by many texts.

Thanks are due to my colleagues and students for their valuable feedback and suggestions. As previously, the major impetus for this edition has come from Shri J.P. Vij, the ever agile Chairman of Jaypee Brothers. Commendable type setting, proof reading and improvement in illustrations has been done respectively by Ms Sunita Katla, Ms Geeta Srivastava and Mr Manoj. The editorial management and moral support of my wife has been a boon.

New Delhi 5th Nov. 2007

Extract from Preface to the First Edition

Pharmacology is both a basic and an applied science. It forms the backbone of rational therapeutics. Whereas the medical student and the prescribing physician are primarily concerned with the applied aspects, correct and skilful application of drugs is impossible without a proper understanding of their basic pharmacology. Medical pharmacology, therefore, must include both fundamental background and clinical pharmacological information. Objective and quantitative data on the use of drugs in man, i.e., relationship between plasma concentration and intensity of therapeutic/toxic actions, plasma half lives, relative efficacy of different medications and incidence of adverse effects etc., are being obtained with the aim of optimising drug therapy. The concepts regarding mechanism of action of drugs are changing. In addition, new drugs are being introduced in different countries at an explosive pace. A plethora of information thus appears to be important. However, trying to impart all this to a medical student would be counter-productive.

One of the important aims of this book is to delineate the essential information about drugs. The opening sentence in each chapter defines the class of drugs considered. A 'prototype' approach has been followed by describing the representative drug of a class followed by features by which individual members differ from it. Leading trade names have been included. Clinically relevant drug interactions have been mentioned. Clear-cut guidelines on selection of drugs and their clinical status have been outlined on the basis of current information. Original, simple and self-explanatory illustrations, tables and flow charts have been used with impunity. Selected chemical structures are depicted. Recent developments have been incorporated. However, discretion has been used in including only few of the multitude of new drugs not yet available in India. This is based on their likelihood of being marketed soon. The information and views have been arranged in an orderly sequence of distinct statements.

I hope this manageable volume book would serve to dispel awe towards pharmacology from the minds of medical students and provide a concise and uptodate information source for prescribers who wish to remain informed of the current concepts and developments concerning drugs.

My sincere thanks are due to my colleagues for their valuable comments and suggestions.

New Delhi 1st Jan., 1985 KD Tripathi

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List of Abbreviations

/ /			
	Angiotensin I/II/III		Ascending limb of Loop of Henle
	Amino acid		Antithrombin III
	ATP-binding cassette (transporter)	ATG	Antithymocyte globulin
	Amphotericin B lipid complex		Adenosine triphosphate
	Antibody	ATPase	Adenosine triphosphatase
AC	Adenylyl cyclase		Adult treatment panel III
	Angiotensin II converting enzyme		Antitetanic serum
	Acetylcholine	A-V	Atrioventricular
	Acetylcholinesterase	AVP	Arginine vasopressin
	Artemisinin-based combination therapy	AZT	Zidovudine
	Adrenocorticotropic hormone		
	Alzheimer's disease		British anti lewisite
	Adverse drug event	BAN	British approved name
	Antidiuretic hormone	BB	Borderline leprosy
ADP	Adenosine diphosphate		Bacillus Calmette Guérin
Adr	Adrenaline	BCNU	Bischloroethyl nitrosourea (Carmustine)
ADR	Adverse drug reaction		Twice daily
ADS	Anti diphtheritic serum	β-ARK	β adrenergic receptor kinase
AES	Atrial extrasystole		Benzene hexachloride
AF	Atrial fibrillation	BHP	Benign hypertrophy of prostate
	Atrial flutter	BI	Bacillary index
AG	Antigen		Borderline lepromatous leprosy
AGS	Antigasgangrene serum		Bone mineral density
	Antihaemophilic globulin		Basal metabolic rate
ΑI	Aromatase inhibitor	BNP	Brain nartriuretic peptide
AIDS	Acquired immunodeficiency syndrome	BOL	1 1
AIP	Aldosterone induced protein	BP	
ALA	Alanine		Bisphosphonate
Am	Amikacin		Biologic response modifiers
AMA	Antimicrobial agent		Body surface area
AMB	Amphotericin B		Borderline tuberculoid leprosy
amp	Ampoule	BuChE	Butyryl cholinesterase
AMP	Adenosine mono phosphate	BW	
AMPA	α-Aminohydroxy methylisoxazole	BZD	Benzodiazepine
	propionic acid		1
ANC	Acid neutralizing capacity	C-10	Decamethonium
ANP			Catecholamine
ANS	Autonomic nervous system	CaBP	Calcium binding protein
AP		CAD	Coronary artery disease
APC			Calmodulin
APD		cAMP	
aPTT	Activated partial thromboplastin time		Capsule
ARB	Angiotensin receptor blocker		Conditioned avoidance response
ARC	AIDS related complex		Carbonic anhydrase
ARS	Anti rabies serum		Computerized axial tomography
	Antiretrovirus		Cerebral blood flow
5-ASA		CBG	
	J		

xii Abbreviations

	Colloidal bismuth subcitrate		Diabetes insipidus
	Calcium channel blocker	DIT	Diiodotyrosine
CCNU	Chloroethyl cyclohexyl nitrosourea	dl	Decilitre
	(lomustine)	DLE	Disseminated lupus erythematosus
CD	Collecting duct	DMA	Dimethoxy amphetamine
CFTR	Cystic fibrosis transport regulator	DMARD	Disease modifying antirheumatic drug
	3', 5' Cyclic guanosine monophosphate	DMPA	Depot medroxyprogesterone acetate
CGRP	Calcitonin gene related peptide	DMPP	Dimethyl phenyl piperazinium
CH	Cholesterol	DMT	Dimethyl tryptamine/Divalent metal
ChE	Cholinesterase		transporter
CHE	Cholesterol ester	DNA	Deoxyribose nucleic acid
Chy	Chylomicron	DOC	Deoxycholate
Chy. rem.	Chylomicron remnants	DOCA	Desoxy corticosterone acetate
CHF	Congestive heart failure		Dimethoxymethyl amphetamine
CI	Cardiac index	dopa	Dihydroxyphenyl alanine
CL	Clearance	DOPAC	3, 4, Dihydroxyphenyl acetic acid
CLcr	Creatinine clearance		Dioctyl sulfosuccinate
CMI	Cell mediated immunity		Directly observed treatment short course
	Cytomegalovirus	DPD	Dihydropyrimidine dehydrogenase
CNS	Central nervous system	DPT	Diphtheria-pertussis-tetanus triple antigen
	Cardiac output	DRC	Dose-response curve
	Coenzyme-A	DT	Distal tubule
	Catechol-O-methyl transferase	DT-DA	Diphtheria-tetanus double antigen
	Cyclooxygenase		d-Tubocurarine
	Cycles per second	DTIC	Dacarbazine
	Complex partial seizures	DTPA	Diethylene triamine pentaacetic acid
	Chlorpromazine	DYN	Dynorphin
	Cellular retinoic acid binding protein		
	Cellular retinol binding protein	E	Ethambutol
CRF	Corticotropin releasing factor	EACA	Epsilon amino caproic acid
CSF	Cerebrospinal fluid		Early after-depolarization
CTZ	Chemoreceptor trigger zone	e.c.f.	Extracellular fluid
	Cardiovascular	ECG	Electrocardiogram
CVP	Central venous pressure		Electroconvulsive therapy
CVS	Cardiovascular system	ED	Erectile dysfunction
CWD	Cell wall deficient	EDTA	Ethylene diamine tetraacetic acid
CYP450	Cytochrome P450	EEG	Electroencephalogram
Cys	Cycloserine	ELAM-1	Endothelial leukocyte adhesion molecule-1
			β-Endorphin
DA	Dopamine	ENS	Enteric nervous system
$DA-B_{12}$	Deoxyadenosyl cobalamin		Extraneuronal amine transporter
	Delayed after-depolarization	EPEC	Enteropathogenic E. coli
	Diacyl glycerol	EPO	Erythropoietin
	Diacetyl monoxime	EPP	End plate potential
DAMP	Diphenyl acetoxy-N-methyl piperidine	ERP	
	methiodide	EPSP	Excitatory postsynaptic potential
DAT	Dopamine transporter	ER	Estrogen receptor
dDAVP	Desmopressin	ES	Extrasystole
DDS	Diamino diphenyl sulfone (Dapsone)	ESR	Erythrocyte sedimentation rate
DDT	Dichloro diphenyl trichloroethane	ETEC	Enterotoxigenic E. coli
DEC	Diethyl carbamazine citrate	Etm	Ethionamide
DHA	Dihydroartemisinin		T 1:
DHE	Dihydroergotamine		Folic acid
DHFA	Dihydro folic acid		Flavin adenine dinucleotide
DHFRase	Dihydrofolate reductase	5-FC	,
DHP	Dihydropyridine	FDT	Fixed duration therapy (of leprosy)
DHT	Dihydrotachysterol	FEV_1	Forced expiratory volume in 1 second

FFA	Free fatty acid	5-HTP	5-Hydroxytryptophan
	Favin mononucleotide	HVA	Homovanillic acid
	Ferroportin		
	Fluoroquinolone		Indeterminate leprosy
	Folate reductase		Inflammatory bowel disease
FSH	Follicle stimulating hormone		Irritable bowel syndrome
5-FU	5-Fluorouracil		Intracellular adhesion molecule-1
		ICSH	Interstitial cell stimulating hormone
	Genetic	i.d.	Intradermal (injection)
GABA	Gamma amino butyric acid	IDL	Intermediate density lipoprotein
	GABA-transporter	IG	Immuneglobulin
	Guanylyl cyclase	IGF	Insulin-like growth factor
	Good clinical practice	IL	
	Granulocyte colony stimulating factor	ILEU	Isoleucine
GDP	Guanosine diphosphate	i.m.	Intramuscular
GERD	Gastroesophageal reflux disease	INH	Isonicotinic acid hydrazide
	Glomerular filtration	INR	
g.f.r.	Glomerular filtration rate	i.o.t.	
GH	Growth hormone		Inositol trisphosphate
GHRH	Growth hormone releasing hormone		Inositol tetrakisphosphate
	Growth hormone release inhibitory hormone	IPSP	Inhibitory postsynaptic potential
GIP		IPV	Inactivated poliomyelitis vaccine
	dependent insulinotropic polypeptide	IRS	Insulin response substrate
g.i.t.	Gastrointestinal tract	ISA	Intrinsic sympathomimetic activity
ĞITS	Gastrointestinal therapeutic system	ISH	
	Glucagon-like peptide	IU	International unit
	Glucose transporter	IUCD	Intrauterine contraceptive device
	Granulocyte macrophage colony stimulating	i.v.	Intravenous
	factor	1. v .	Intraverious
GnRH	Gonadotropin releasing hormone	JAK	Janus-kinase
	G-protein coupled receptor	JAK	Janus-Kinasc
G-6-PD	Glucose-6-phosphate dehydrogenase	Vma	Vanamyain
	Globus pallidus interna	KTZ	Kanamycin Ketoconazole
	Generalised tonic-clonic seizures	KIZ	Retoconazoie
	Glyceryl trinitrate	TΛ	Local anaesthetic
	Guanosine triphosphate		
011	Cauriconic dipriosprace		Lecithin cholesterol acyl transferase
Н	Isoniazid (Isonicotinic acid hydrazide)	LDL	Low density lipoprotein
	Highly active antiretroviral therapy		Lower esophageal sphincter
	Haemoglobin		Leucine enkephalin
			Luteinizing hormone
TIDV	Hepatitis B virus		
	Human chorionic gonadotropin	LL	Lepromatous leprosy
	Human diploid cell vaccine		Low molecular weight
HDL	High density lipoprotein		Lipoxygenase
5-HIAA	5-Hydroxyindole acetic acid	LSD	
	Hydroxyethyl starch		Leukotriene
HETE	Hydroxyeicosa tetraenoic acid	LVF	Left ventricular failure
HIV	Human immunodeficiency virus	MAC	Minimal alveolar concentration
HMG-CoA	Hydroxymethyl glutaryl coenzyme A	MAC	Mycobacterium avium complex
	High molecular weight	MAO	Monoamine oxidase
	Hypothalamo-pituitary-adrenal axis	MAP	Muscle action potential
HPETE		MAPKinase	Mitogen activated protein kinase
hr	, , ,	max	Maximum
	Heart rate	MBC	Minimum bactericidal concentration
HRIG		MBL	Multibacillary leprosy
HRT	O		
111/1			
5-HT	1 17	MDI MDMA	Manic depressive illness Methylene dioxy methamphetamine

xiv Abbreviations

MDR	Multidrug resistant	NTS	Nucleus tractus solitarius
MDT	Multidrug therapy (of leprosy)	NVBDCP	National vector borne diseases control
	Methionine enkephalin		programme
mEq	milliequivalent	NYHA	New York Heart Association
methyl B ₁₂	Methyl cobalamin		
Mf	Microfilariae		Organic anion transporter
MF	Multifactorial		Organic anion transporting polypeptide
MHC	Major histocompatibility complex		Oral contraceptive
MHT	Methylene dioxy methamphetamine		Obsessive-compulsive disorder
MI	Myocardial infarction	OCT	Organic cation transporter
MIC	Minimal inhibitory concentration	OD	Once daily
MID	Multi infarct dementia	OPG	Osteoprotegerin
MIF	Migration inhibitory factor		Oral poliomyelitis vaccine
min	Minimum		Oral rehydration salt (solution)
MIT	Monoiodo tyrosine	OKI	Oral rehydration therapy
	Myosin light chain kinase	рлвл	Paraamino benzoic acid
MMF	, .		Post antibiotic effect
6-MP	6-Mercaptopurine		Platelet activating factor
MPPT	Methylprednisolone pulse therapy		Pralidoxime
MPTP	, ,		Primary afferent neurone
MRP2	Multidrug resistance associated protein-2		Paraamino salicylic acid
MRSA			Protein bound iodine
MSH			Penicillin binding proteins
Mtx	Methotrexate		Paucibacillary leprosy
mV		PCA	Patient controlled anaesthesia
MW			Purified chick embryo cell vaccine (rabies)
1,1,,	Wolcettar Weight	PCI	Percutaneous coronary intervention
NΙΔ	Noradrenaline	PCPA	Parachloro phenylalanine
	N-acetyl-p-benzoquinoneimine		Parkinsons's disease
NADP	,		Phosphodiesterase
NADI			Phenylethyl malonamide
NADDU	phosphate Reduced nicotinamide adenine dinucleotide	PEP	Postexposure prophylaxis
NADIH		PF	Purkinje fibre
NIAC	phosphate		Pyruvate: ferredoxin oxidoreductase
	N-acetyl glucosamine	PG	Prostaglandin
	N-acetyl muramic acid		Prostacyclin
	Nonadrenergic noncholinergic		P-glycoprotein
	N-acetyl procainamide		Protease inhibitor
NaSSA	0 1	PIG	Phosphatidyl inositol glycan
	antidepressant		Phosphatidyl inositol-4,5-bisphosphate
	N-acetyl transferase		Protein kinase: cAMP dependent
	National cholesterol education programme		Protein kinase C
	Norethindrone enanthate	PL_A	Phospholipase A
NET	1 1		Phospholipase C
	Nuclear factor of activated T-cell	Pl. ph.	Platelet phospholipid
NLEP	National leprosy eradication programme	PnG	Penicillin G
NMDA	N-methyl-D-aspartate	POMC	Pro-opio melanocortin
nNOS	Neural nitric oxide synthase	PP	Partial pressure
NNRTI	Nonnucleoside reverse transcriptase inhibitor	PPA	Phenyl propanolamine
NPY	Neuropeptide-Y	PPARγ	Paroxysome proliferator-activated receptor γ
NR	Nicotinic receptor	PPH	Post partum haemorrhage
N-REM	Non rapid eye movement (sleep)	PPI	Proton pump inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor	ppm	Part per million
NSAID	Nonsteroidal antiinflammatory drug	PPNG	Penicillinase producing N. gonorrhoeae
NSTEMI	Non ST-segment elevation myocardial	PRA	Plasma renin activity
	infarction	PRF	Prolactin releasing factor

	Prolactin release inhibitory hormone		Single nucleotide polymorphism
	Paroxysmal supra-ventricular tachycardia	SN-PC	Substantia nigra-pars compacta
PT	Proximal tubule	SN-PR	Substantia nigra-pars reticularis
PTCA	Percutaneous transluminal coronary	SNRI	
	angioplasty		inhibitor
PTH	Parathyroid hormone	s.o.s.	
PTMA	Phenyl trimethyl ammonium	S/P	Sulfonamide + pyrimethamine
	Post-tetanic potentiation	SPF	
PTZ	Pentylenetetrazol		Simple partial seizures
PUV A	Psoralen-Ultraviolet A		Sustained release
PVP	Poly vinyl pyrrolidone		Slow reacting substance of anaphylaxis
PVRV	Purified verocell rabies vaccine	SSG	Sodium stibogluconate
		CCDI ₂	Surgical site infection
QID	Four times a day	STAT	Selective serotonin reuptake inhibitors Signal transducer and activator of transcription
	·		ST-segment elevation myocardial infarction
R	Rifampin (Rifampicin)	StK	Streptokinase
RANK	Receptor for activation of nuclear factor KB	SULT	
	RANK ligand		Sulfonyl urea receptor
	Renin-angiotensin system		Suspension
	Red blood cells	SWS	
RBP	Retinol binding protein	syr	Syrup
	Respiratory centre	- 7 -	-)F
	Reticuloendothelial	t½	Half life
	Rapid eye movement (sleep)	T_3	Triiodothyronine
	Rabies immuneglobulin		Thyroxine
	Reversible inhibitor of MAO-A		Tablet
rINN	Recommended international nonproprietary	TAB	Typhoid, paratyphoid A and B vaccine
	name	TB	Tubercle bacilli
RMP		TBG	Thyroxine binding globulin
RNA	Ribonucleic acid		Transcobalamin II
	Revised National Tuberculosis Control	TCAs	Tricyclic antidepressants
	Programme	$TCID_{50}$	Tissue culture infectious dose 50%
RP	Refractory period	TDM	Therapeutic drug monitoring
RTF			Three times a day
RXR	Retinoid X receptor		Transferrin
	Ryanodine receptor	TG	Triglyceride
Tty It	ryunounc receptor	6-TG	6-Thioguanine
S	Streptomycin		Tetrahydrocannabinol
	Sinoauricular (node)		Tetrahydro folic acid
	Slow acting antirheumatic drug		Triethylene thiophosphoramide
	Subacute bacterial endocarditis		Threonine
S.C.			Transient ischaemic attacks
SCC			Tumour necrosis factor α
SCh	Succinylcholine		Target organ damage
SCID	Severe combined immunodeficiency disease		Train of four
SERDs	•	t-PA	Tissue plasminogen activator
SERDS	Selective estrogen receptor down regulators Selective estrogen receptor modulator	TPMT	Thiopurine methyl transferase
SERT	· .	t.p.r. TR	Total peripheral resistance Thyroid hormone receptor
	Serotonin transporter	TRE	
SGA	Second generation antihistaminic	TRH	Thyroid hormone response element
SGLT SHBG	Sodium-glucose transporter Sex hormone binding globulin	TSH	Thyrotropin releasing hormone Thyroid stimulating hormone
		TT	Tuberculoid leprosy
s.l. SLC	Sublingual Solute carrier	TTS	Transdermal therapeutic system
SLE	Systemic lupus erythematosus	TX	Thromboxane
SMON	Subacute myelo-optic neuropathy	Tzn	Thiacetazone
DIVIOIN	Subacute myero-optic neuropatity	1 2 1 1	THREEMZOIC

xvi Abbreviations

U	Unit	VMA	Vanillyl mandelic acid
UDP	Uridine diphosphate	VMAT	Vesicular monoamine transporter
UFH	Unfractionated heparin	VRE	Vancomycin resistant enterococci
UGDP	University group diabetic programme	VRSA	Vancomycin resistant Staphylococcus aureus
UGT	UDP-glucuronosyl transferase		Vasopressin regulated urea transporter
USAN	United States adopted name	VT	Ventricular tachycardia
UTI	Urinary tract infection	vWF	von Willebrand factor
	•		
V	Volt	WBC	White blood cells
V	Volume of distribution	WCVs	Water channel containing vesicles
VAL	Valine	WHO	World Health Organization
VDR	Vit D receptor	WPW	Wolff-Parkinson-White syndrome
VES	Ventricular extrasystole		•
VF	Ventricular fibrillation	XDR-TB	Extensively drug resistant-TB
VIP	Vasoactive intestinal peptide		, ,
Vit	Vitamin	Z	Pyrazinamide
VLDL	Very low density lipoprotein	ZE (syndrome)	Zollinger-Ellison (syndrome)