

EIGHTH EDITION

# CLINICAL BIOCHEMISTRY & METABOLIC MEDICINE



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# Preface

Were it not for the textbook *Clinical Chemistry in Diagnosis and Treatment* by Joan Zilva and Peter Pannall, I would not be a chemical pathologist. As a medical student, I was so struck by its clarity, depth and clinical relevance that I decided that theirs was the medical field I wished to work in.

Over the years, the field of clinical biochemistry has changed radically. Confusingly, there is no consensus on the name for this field of medicine, which is known variously as clinical chemistry, chemical pathology or clinical biochemistry, to name but a few. Additionally, the field now overlaps with that of metabolic medicine, a clinical specialty involved with the management and treatment of patients with disorders of metabolism. Clinical biochemistry laboratories have become further automated, molecular biology technologies have entered the diagnostic arena, and chemical pathologists have become more clinically orientated towards running out-patient clinics for a variety of biochemical disturbances. This book aims to address these new changes. Indeed, it is difficult to imagine a branch of medicine that does not at some time require clinical biochemistry tests, which may not be too surprising, given the fact that every body cell is composed of chemicals!

Unfortunately, there have been some difficulties in recent times, with a relative shortage of graduates entering the specialty, which has not been helped by some people's attitude that clinical biochemistry is merely a laboratory factory churning out results that anyone can interpret. There are also concerns that medical student clinical biochemistry teaching may become 'diluted' as part of an expanding curriculum. It is hoped that this book will excite a new generation to enter this fascinating and essential field, as well as benefit patients as their doctors learn more about their biochemical and metabolic problems.

I am most grateful to Dr Sethsiri Wijeratne, Dr Alam Garrib (particularly for molecular biology expertise) and Dr Paul Eldridge for constructive criticism of the text. I am also grateful to Professor Philip Mayne for his earlier contributions and the anonymous medical student reviewer(s) who commented on the text. The book has also greatly benefited from the wise, helpful and experienced input of Dr Andrew Day – many thanks. Although every effort has been made to avoid inaccuracies and errors, it is almost inevitable that some may still be present, and feedback from readers is therefore welcome.

Martin Crook  
London, 2012

*Disclaimer* The publishers and author accept no responsibility for errors in the text or misuse of the material presented. Drugs and their doses should be checked with a pharmacy, and the investigation protocols with an appropriate clinical laboratory. Dynamic test protocols should be checked with an accredited clinical investigation unit and may require different instructions in the elderly, children and the obese.

# List of abbreviations

<b>ABC1</b>	adenosine triphosphate-binding cassette protein 1	<b>CA</b>	carbohydrate antigen
<b>ACE</b>	angiotensin-converting enzyme	<b>CaE</b>	calcium excreted per litre of glomerular filtrate
<b>ACP</b>	acid phosphatase	<b>CAH</b>	congenital adrenal hyperplasia
<b>ACR</b>	albumin to creatinine ratio	<b>cAMP</b>	cyclic adenosine monophosphate
<b>ACTH</b>	adrenocorticotrophic hormone (corticotrophin)	<b>CaSR</b>	calcium-sensing receptor
<b>ADH</b>	antidiuretic hormone (arginine vasopressin)	<b>CAT</b>	computerized axial tomography
<b>A&amp;E</b>	accident and emergency (department)	<b>CBG</b>	cortisol-binding globulin (transcortin)
<b>AFP</b>	$\alpha$ -fetoprotein	<b>CD</b>	carbonate dehydratase (carbonic anhydrase)
<b>AIDS</b>	acquired immunodeficiency syndrome	<b>CEA</b>	carcinoembryonic antigen
<b>AIS</b>	autoimmune insulin syndrome	<b>CETP</b>	cholesterol ester transfer protein
<b>AKI</b>	acute kidney injury	<b>CK</b>	creatinine kinase
<b>ALA</b>	5-aminolaevulinic acid	<b>CKD</b>	chronic kidney disease
<b>ALP</b>	alkaline phosphatase	<b>CNP</b>	C-type natriuretic peptide
<b>ALT</b>	alanine aminotransferase (also known as glutamate pyruvate aminotransferase, GPT)	<b>CNS</b>	central nervous system
<b>AMC</b>	arm muscle circumference	<b>CoA</b>	coenzyme A
<b>ANA</b>	antinuclear antibody	<b>COPD</b>	chronic obstructive pulmonary disease
<b>ANCA</b>	antineutrophil cytoplasmic antibody	<b>CRH</b>	corticotrophin-releasing hormone
<b>ANP</b>	atrial natriuretic peptide	<b>CRP</b>	C-reactive protein
<b>APA</b>	aldosterone-producing adenoma	<b>CSF</b>	cerebrospinal fluid
<b>apo</b>	apolipoprotein	<b>CT</b>	computerized tomography
<b>APRT</b>	adenine phosphoribosyl transferase	<b>CV</b>	coefficient of variation
<b>APUD</b>	amine precursor uptake and decarboxylation	<b>Cys C</b>	cystatin C
<b>ARA</b>	angiotensin II receptor antagonist	<b>2,3-DPG</b>	2,3-diphosphoglycerate
<b>ARB</b>	angiotensin II receptor blocker	<b>DDAVP</b>	1-desamino-8-D-arginine vasopressin (desmopressin acetate)
<b>ARMS</b>	amplification refractory mutation system	<b>DHEA</b>	dehydroepiandrosterone
<b>AST</b>	aspartate aminotransferase (also known as glutamate oxaloacetate aminotransferase, GOT)	<b>DHEAS</b>	dehydroepiandrosterone sulphate
<b>ATPase</b>	adenosine triphosphatase	<b>DIT</b>	di-iodotyrosine
<b>ATP</b>	adenosine triphosphate	<b>DNA</b>	deoxyribonucleic acid
<b>BJP</b>	Bence Jones protein	<b>DPP-4</b>	dipeptidyl peptidase-4
<b>BMD</b>	bone mineral density	<b>DVT</b>	deep vein thrombosis
<b>BMI</b>	body mass index	<b>ECF</b>	extracellular fluid
<b>BMR</b>	basal metabolic rate	<b>ECG</b>	electrocardiogram
<b>BNP</b>	brain natriuretic peptide	<b>EDTA</b>	ethylenediamine tetra-acetic acid
<b>BPH</b>	benign prostatic hyperplasia	<b>eGFR</b>	estimated glomerular filtration rate
		<b>ENA</b>	extractable nuclear antigen
		<b>ENT</b>	ear, nose and throat (department)
		<b>ERCP</b>	endoscopic retrograde cholangiopancreatography
		<b>ESR</b>	erythrocyte sedimentation rate



EUS	endoscopic ultrasonography	5-HT	hydroxytryptamine (serotonin)
FAD	flavine adenine dinucleotide	5-HTP	hydroxytryptophan
FCH	familial combined hyperlipidaemia	HVA	homovanillic acid
FDH	familial dysalbuminaemic hyperthyroxinaemia	IAH	idiopathic adrenal hyperplasia
FENa%	fractional excretion of sodium	IDL	intermediate-density lipoprotein
FEPi%	fractional excretion of phosphate	IDMS	isotope dilution mass spectrometry
FH	familial hypercholesterolaemia	IEM	inborn errors of metabolism
FMN	flavine mononucleotide	IFG	impaired fasting glucose
FSH	follicle-stimulating hormone	IFN	interferon
fT <sub>4</sub>	free T <sub>4</sub>	Ig	immunoglobulin
fT <sub>3</sub>	free T <sub>3</sub>	IGF	insulin-like growth factor
GAD	glutamic decarboxylase	IGT	impaired glucose tolerance
GDM	gestational diabetes mellitus	IL	interleukin
GFR	glomerular filtration rate	INR	international normalized ratio
GGT	γ-glutamyl transferase	LADA	latent autoimmune diabetes of adults
GH	growth hormone	LCAT	lecithin-cholesterol acyltransferase
GHRH	growth hormone-releasing hormone	LDH	lactate dehydrogenase
GIP	gastric inhibitory peptide	LDL	low-density lipoprotein
GLP-1	glucagon-like peptide 1	LH	luteinizing hormone
GnRH	gonadotrophin-releasing hormone	LR	likelihood ratio
G6P	glucose-6-phosphate	MCADD	medium-chain acyl coenzyme A dehydrogenase deficiency
G6PD	glucose-6-phosphate dehydrogenase	MCH	mean corpuscular haemoglobin
GRA	glucocorticoid remediable aldosteronism	MCV	mean corpuscular volume
HAV	hepatitis A virus	MDRD	modification of diet in renal disease (formula)
Hb	haemoglobin	MEGX	monoethylglycinexylidide
HbA <sub>1c</sub>	glycated haemoglobin	MEN	multiple endocrine neoplasia
HB <sub>s</sub> Ag	viral surface antigen	MGUS	monoclonal gammopathy of undetermined significance
HBD	hydroxybutyrate dehydrogenase	MIBG	metaiodobenzylguanidine
HBV	hepatitis B virus	MIT	mono-iodotyrosine
hCG	human chorionic gonadotrophin	MODY	maturity-onset diabetes of the young
HCV	hepatitis C virus	MPS	mucopolysaccharidosis
HDL	high-density lipoprotein	MRCP	magnetic resonance cholangiopancreatography
HELP	heparin extracorporeal low-density lipoprotein precipitation	MRI	magnetic resonance imaging
HFE	human haemochromatosis protein	mRNA	messenger ribonucleic acid
HGPRT	hypoxanthine-guanine phosphoribosyl transferase	MSH	melanocyte-stimulating hormone
5-HIAA	5-hydroxyindole acetic acid	mtDNA	mitochondrial DNA
HIV	human immunodeficiency virus	MTHFR	methylenetetrahydrofolate reductase
HLA	human leucocyte antigen	NAD	nicotinamide adenine dinucleotide
HMG-CoA	3-hydroxy-3-methyl glutaryl coenzyme A	NADP	nicotinamide adenine dinucleotide phosphate
HMMA	4-hydroxy-3-methoxymandelic acid	NAFLD	non-alcoholic fatty liver disease
HNF	hepatocyte nuclear factor	NAG	N-acetyl-β-D-glucosaminidase
HONK	hyperosmolar non-ketotic (coma)		
HRT	hormone replacement therapy		
hs-CRP	high-sensitivity C-reactive protein		

NASH	non-alcoholic steatotic hepatitis	SCID	severe combined immunodeficiency
NEFA	non-esterified fatty acid	SD	standard deviation
NGAL	neutrophil gelatinase-associated lipocalin	SHBG	sex-hormone-binding globulin
NHS	National Health Service	SIADH	syndrome of inappropriate antidiuretic hormone secretion
NICTH	non-islet cell tumour hypoglycaemia	SLE	systemic lupus erythematosus
NP	natriuretic peptide	STEMI	ST-segment elevation myocardial infarction
NSAID	non-steroidal anti-inflammatory drug		
NSTEMI	non-ST segment elevation myocardial infarction		
		T <sub>3</sub>	tri-iodothyronine
OGTT	oral glucose tolerance test	T <sub>4</sub>	thyroxine
OTC	ornithine transcarbamylase	TBG	thyroxine-binding globulin
		TBW	total body water
PABA	para-amino benzoic acid	TCA	tricarboxylic acid
PBG	porphobilinogen	TfR	transferrin receptor
PCR	polymerase chain reaction	TIBC	total iron-binding capacity
PEG	polyethylene glycol	TNF	tumour necrosis factor
PH	primary hyperaldosteronism	TPO	thyroid peroxidase
PI	protease inhibitor	TPMT	thiopurine methyltransferase
PIVKA	proteins induced by vitamin K absence	TRH	thyrotrophin-releasing hormone
PKU	phenylketonuria	TSH	thyroid-stimulating hormone
PNI	prognostic nutritional index	TSI	thyroid-stimulating immunoglobulin
POCT	point-of-care testing	TTKG	transtubular potassium gradient
PPAR	peroxisome proliferator-activated receptor		
PRPP	phosphoribosyl pyrophosphate	UGT	uridine glucuronyl transferase
PSA	prostate-specific antigen	UIBC	unsaturated iron-binding capacity
PTH	parathyroid hormone	URL	upper reference limit
PTHRP	parathyroid hormone-related protein		
		VIP	vasoactive intestinal polypeptide
RBP	retinol-binding protein	VLCFA	very long-chain fatty acid
RDS	respiratory distress syndrome	VLDL	very low-density lipoprotein
RFLP	restriction fragment length polymorphism	VDBP	vitamin D-binding protein
		VDR	vitamin D receptor
RNA	ribonucleic acid		
ROC	receiver operating characteristic (curve)	WHO	World Health Organization
RRT	renal replacement therapy		