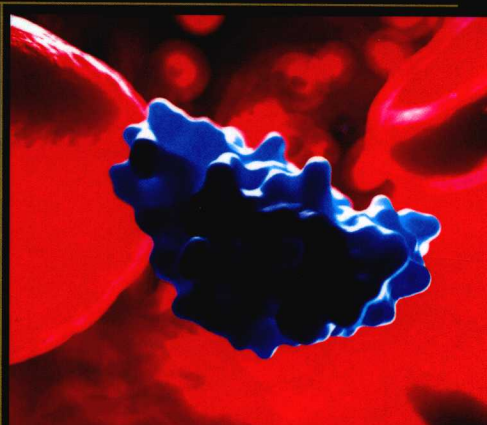
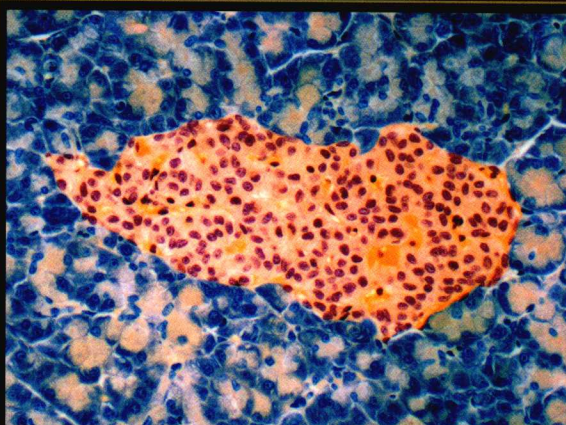
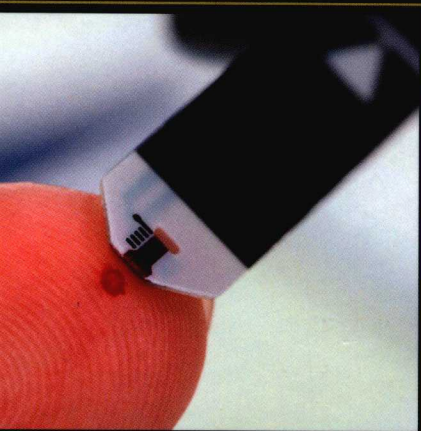


TEXTBOOK OF DIABETES



FIFTH EDITION

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WILEY Blackwell

Textbook of Diabetes

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Textbook of Diabetes

We dedicate this book to all people living with diabetes and the healthcare professionals who look after them. We would also like to dedicate this book to our families without whose support and encouragement the book would never have been finished.

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Preface to the Fifth Edition

It is seven years since the last edition of the *Textbook of Diabetes* was published and despite many advances in the understanding of diabetes and its treatment over that time, the management of diabetes still remains a major global burden for people with diabetes, their families, and the wider society in which they live. Whereas the global prevalence of diabetes according to the International Diabetes Federation affected 246 million people in 2010, the current estimate is 415 million and is projected to rise further. One in 10 of the world's population has diabetes and one person dies because of diabetes every 6 seconds. Twelve percent of global health expenditure is spent on diabetes. The challenge to people with diabetes and their healthcare professionals has never been greater.

Despite the ever-increasing numbers, better management is starting to pay dividends. The outlook for those with diabetes appears to be improving, at least in high income countries where an individual's risk of developing complications and losing years to diabetes is falling. If the variation between the best and worst care could be obliterated, much morbidity and mortality would be prevented.

Ironically, as the volume of information and the vast numbers of resources available in this digital age have increased, many are finding it overwhelming to keep abreast of the new advances. It is particularly challenging to determine the validity of many source materials. In this textbook, we aim to bring together a series of *up-to-date* chapters from an international group of leading diabetes specialists who provide accurate and clinically relevant information to both academic and practicing diabetes healthcare professionals. Having the key information in one volume still has its merits, and this is further enhanced by *online* access and searchability.

The editors have retained the structure from the previous edition, with a similar length and number of chapters. We begin with a history of diabetes that provides many valuable insights from the past. The book then takes us through the epidemiology of diabetes, the physiology and pathogenesis of diabetes before moving onto management. We have taken a broad view in these

sections recognizing that diabetes management encompasses so much more than drug therapy alone. A discussion of the microvascular and macrovascular complications then follows before a new section on the psychosocial aspects of diabetes. Different models of care as well as the management of diabetes in special groups are included before the final section looks into the future. There are new chapters on the biology of glucagon, the microbiome and diabetes, cancer, non-alcoholic fatty liver disease, and end-of-life care. These additions reflect the advances in our understanding of diabetes, its management, and have implications for a variety of related disorders.

As editors, we are only too aware of the hard work that goes into the production of a comprehensive and up-to-date book such as this. Our thanks go to each and every chapter author, who, despite busy academic and professional lives, were prepared to devote the time, energy, and expertise to provide their essential contributions to the text. Thank you for your forbearance of our nagging e-mails!

We are also grateful for the immense help we have received from our publisher, Wiley-Blackwell. Our commissioning editor, Priyanka Gibbons, who took over from Oliver Walter, during the book's development, has provided guidance, encouragement, and support. Our thanks also go to Gill Whitley who kept the momentum going when Rob Blundell left, and to the rest of the production team. The book looks even better than the last edition!

We hope you enjoy reading the book, whether it be dipping in or reading from cover to cover, as much as we did editing it. We have all taken away useful novel information that will aid our daily professional lives and we hope that this book will help you to support those with diabetes in the widest sense of this meaning.

Richard Holt
Clive Cockram
Allan Flyvbjerg
Barry Goldstein
February 2016

List of Abbreviations

AACE	American Association of Clinical Endocrinologists	CDC	cardiosphere-derived stem cell
AAV	adeno-associated vectors	CDC	Centers for Disease Control and Prevention
ABP	ankle blood pressure	CDE	Certified Diabetes Educator
ACCORD	Action to Control Cardiovascular Risk in Diabetes	CEMACH	Confidential Enquiry into Maternal and Child Health
ACE	angiotensin-converting enzyme	CETP	cholesteryl ester transfer protein
ACHOIS	Australian Carbohydrate Intolerance Study in Pregnant Women	CGM	continuous glucose monitoring
ACR	albumin : creatinine ratio	CI	confidence interval
ADA	American Diabetes Association	CKD	chronic kidney disease
ADP	adenosine diphosphate	CML	carboxymethyllysine
AICAR	5-aminoimidazole-4-carboxamide-1 β -D-ribofuranoside	CNS	central nervous system
AMDCC	Animal Models for Diabetes Complications Consortium	COC	combination oral contraceptive
AMP	adenosine monophosphate	COX	cyclooxygenase
Apo	apolipoprotein	CPC	cardiac progenitor cell
Δ PWV	aortic pulse wave velocity	CRP	C-reactive protein
Arx	aristaless-related homeobox	CSII	continuous subcutaneous insulin infusion
ATP	adenosine triphosphate	CT	computed tomography
AUC	area under the curve	CV	coefficient of variation
BCAA	branched-chain amino acid	CVD	cardiovascular disease
BMD	bone mineral density	DAWN	Diabetes Attitudes, Wishes, and Needs study
BMI	body mass index	DCCT	Diabetes Control and Complications Trial
BM-MNC	mononuclear bone marrow-derived stem cell	DKA	diabetic ketoacidosis
BPH	benign prostatic hyperplasia	DPP	dipeptidyl peptidase
bpm	beats per minute	DSN	diabetes specialist nurse
BTX-A	botulinum toxin type A	DVLA	Driver and Vehicle Licensing Agency
CABG	coronary artery bypass grafting	EASD	European Association for the Study of Diabetes
CA-MRSA	community-associated methicillin-resistant <i>Staphylococcus aureus</i>	ECG	electrocardiography/electrocardiogram
CAPD	continuous ambulatory peritoneal dialysis	eGFR	estimated glomerular filtration rate
CBG	capillary blood glucose	EMA	European Medicines Agency
CBT	cognitive-behavioral therapy	ER	endoplasmic reticulum
CCM	corneal confocal microscopy	ERCP	endoscopic retrograde cholangiopancreatography
CDA	Canadian Diabetes Association	ERK	extracellular signal-regulated kinase
		ERM	ezrin-radixin-moesin
		ESC	embryonic stem cell
		ESRD	end-stage renal disease
		ESRF	end-stage renal failure

List of Abbreviations

FDA	Food and Drug Administration (USA)	IDRS	Indian Diabetes Risk Score
FDC	fixed-dose combination	IgG	immunoglobulin G
FDKP	fumaryl diketopiperazine	IGR	impaired glucose regulation
FFA	free fatty acid	IGT	impaired glucose tolerance
FGF	fibroblast growth factor	IKK β	inhibitor κ B kinase- β
FHWA	Federal Highways Administration	IL	interleukin
FMD	flow-mediated endothelium-dependent arterial dilation	IMT	intima-media thickness
FOXO	forkhead box O	InsR	insulin receptor
FXR	farnesoid-X receptor	IRMA	intraretinal microvascular abnormality
G6P	glucose-6-phosphatase	ISPAD	International Society for Pediatric and Adolescent Diabetes
G-6-P	glucose-6-phosphate	IT	information technology
G6PD	glucose-6-phosphate dehydrogenase	IVUS	intravascular ultrasound
GAD	glutamine acid decarboxylase	IWGDF	International Working Group on the Diabetic Foot
GCGR	glucagon receptor	JBDS	Joint British Diabetes Societies
GCK	glucokinase	KDIGO	Kidney Disease: Improving Global Outcomes
G-CSF	granulocyte colony-stimulating factor	K_m	Michaelis constant
GDF	growth differentiation factor	LADA	latent autoimmune diabetes in adults
GDM	gestational diabetes mellitus	LDL	low-density lipoprotein
CF	cystic fibrosis	LDL-C	low-density lipoprotein cholesterol
GI	gastrointestinal	LDLR	low-density lipoprotein receptor
GLO	glyoxalase	LGA	large-for-gestational age
GLP-1RA	GLP-1 receptor agonist	LIRKO	liver-specific InsR knockout
GLUT	glucose transporter	LPS	lipopolysaccharide
GPR	G-protein-coupled receptor	Lst	limostatin
GRPP	glicentin-related pancreatic polypeptide	LV	left ventricular
GWA	genome-wide association	LVEF	left ventricular ejection fraction
GWAS	genome-wide association studies	MAOI	monoamine oxidase inhibitor
HAPO	Hyperglycemia and Adverse Pregnancy Outcomes	MDI	multiple daily injection
HbA _{1c}	hemoglobin A _{1c}	MDRD	Modification of Diet in Renal Disease
HBV	hepatitis B virus	MG53	mitsugumin 53
HCV	hepatitis C virus	mGDP	mitochondrial glycerolphosphate dehydrogenase
HDL	high-density lipoprotein	MGO	methylglyoxal
HGF	hepatocyte growth factor	MI	myocardial infarction
hGH	human recombinant growth hormone	MIBG	<i>m</i> -iodobenzylguanidine
HHS	hyperosmolar non-ketotic hyperglycemic state	MIRKO	muscle-specific InsR knockout
HR	hazard ratio	MODY	maturity-onset diabetes of the young
HRT	hormone replacement therapy	MPGF	major proglucagon fragment
HRV	heart rate variability	MPO	myeloperoxidase
HSC	hematopoietic stem cell	MRI	magnetic resonance imaging
hsCRP	high-sensitivity C-reactive protein	MSC	mesenchymal stem cell
IADPSG	International Association of Diabetes Pregnancy Study Groups	MS	mass spectrometry
IAsp	insulin aspart	mTOR	mammalian or mechanistic target of rapamycin
IAUC	incremental area under the blood glucose curve	mTORC1	mechanistic target of rapamycin complex 1
ICA	islet cell antibody	MTPI	microsomal transfer protein inhibitor
ICU	intensive care unit	NAD	nicotinamide adenine dinucleotide
i.d.	intradermal	NaDIA	National Diabetes Inpatient Audit
IDDM	insulin-dependent diabetes mellitus	NAFLD	non-alcoholic fatty liver disease
IDeg	insulin degludec	NANC	non-adrenergic, non-cholinergic
IDF	International Diabetes Federation	NCV	nerve conduction velocity
IDL	intermediate-density lipoprotein	NEFA	non-esterified fatty acid

MFMU	Maternal–Fetal Medicine Units Network	RDN	renal denervation
NEP	neutral endopeptidase	RECORD	Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes
NFκB	nuclear factor κB	REMS	Risk Evaluation and Mitigation Strategy
Ngn3	neurogenin 3	rHuPH20	recombinant human hyaluronidase
NHANES	National Health and Nutrition Examination Survey	RMR	resting metabolic rate
NHS	National Health Service	ROS	reactive oxygen species
NICE	National Institute for Health and Care Excellence	RR	relative risk
		RR	risk ratio
NIDDM	non-insulin-dependent diabetes mellitus	RT-PCR	reverse transcriptase polymerase chain reaction
NIH	National Institutes of Health	SCFA	short-chain fatty acid
NMU	neuromedin U	s.c.	subcutaneous
Nox	NAD(P)H oxidase	sdHDL	small, dense high-density lipoprotein
NOD	non-obese diabetic	sdLDL	small, dense low-density lipoprotein
NPH	neutral protamine Hagedorn	SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
NRTI	nucleoside reverse-transcriptase inhibitor	SGA	second-generation antipsychotics
NSAID	non-steroidal anti-inflammatory drug	SHP	short heterodimer protein
NT-3	neurotrophin-3	SMBG	self-monitoring of blood glucose
NT-proBNP	N-terminal pro-brain-type natriuretic peptide	SMI	severe mental illness
OCP	oral contraceptive pill	SNP	sub-basal nerve plexus
OGIS	oral glucose insulin sensitivity	SSRI	selective serotonin reuptake inhibitor
OGTT	oral glucose tolerance test(ing)	T1DM	type 1 diabetes mellitus
OR	odds ratio	T2DM	type 2 diabetes mellitus
oxLDL	oxidation of low-density lipoprotein	TAG	triacylglyceride
PAS	periodic acid–Schiff	TB	tuberculosis
PBA	phenylboronic acid	TCF7L2	transcription factor 7 like 2
PC	prohormone convertase	TE	transient elastography
PCB	polychlorinated biphenyl	TIND	treatment-induced neuropathy in diabetes
PCI	percutaneous coronary intervention	TLR	toll-like receptor
PCR	polymerase chain reaction	TNDM	transient neonatal diabetes mellitus
PCSK-9	proprotein convertase subtilisin kexin type 9	TNFα	tumor necrosis factor alpha
PDH	pyruvate dehydrogenase	TREG	regulatory T cell
Pdx1	pancreatic duodenal homeobox 1	TSH	thyroid-stimulating hormone
PGF	placental growth factor	TZD	thiazolidinedione
PI	protease inhibitor	UKPDS	UK Prospective Diabetes Study
PI3K	phosphatidylinositol 3-kinase	US	ultrasound
PID	proportional integral derivative	UT	University of Texas
P/KX	combined pancreas/kidney transplantation	VEGF	vascular endothelial growth factor
PNDM	permanent neonatal diabetes mellitus	VLCD	very low calorie diet
PPAR	peroxisome proliferator-activated receptor	VLDL	very low-density lipoprotein
PROactive	Prospective Pioglitazone Clinical Trial in Macrovascular Events	VRIII	variable-rate intravenous insulin infusion
PTDM	post-transplantation diabetes mellitus	WGS	whole-genome sequencing
PTP1B	protein tyrosine phosphatase 1B	WHO	World Health Organization
PYY	polypeptide YY	XO	xanthine oxidase
QoL	quality of life	YY1	Yin Yang 1
RA	receptor agonist		
RAMP	receptor activity-modifying protein		
RCT	randomized controlled trial		

About the Companion Website and Companion Digital Edition

COMPANION WEBSITE

This book is accompanied by a companion website:

www.wiley.com/go/textbookofdiabetes

The website includes:

- Interactive Multiple-Choice Questions for each chapter
- Reference lists with external links
- Figures from the book for downloading

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