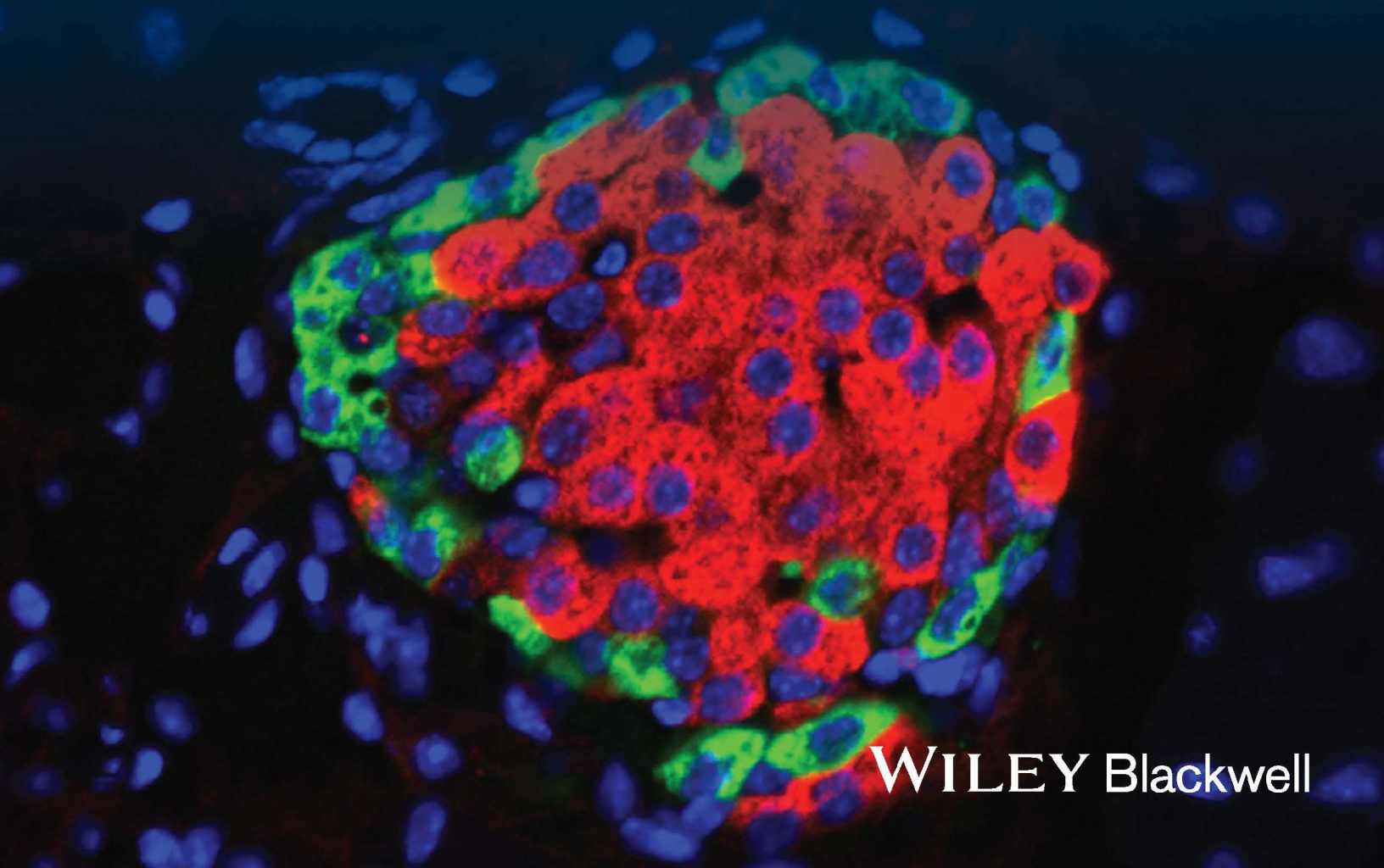


Sixth Edition

Textbook of Diabetes

Edited by **Richard I.G. Holt** • **Allan Flyvbjerg**



WILEY Blackwell

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.

Textbook of Diabetes

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Preface

It is nearly seven years since the last edition of the *Textbook of Diabetes* was published, during which time there have been many exciting developments in our understanding of diabetes and novel treatments that have improved the lives of those living with diabetes. Despite our ability to alleviate the risk of its long-term complications, the global burden of diabetes continues to rise as the prevalence inexorably increases. According to the International Diabetes Federation, diabetes now affects 537 million adults, compared with 415 million when the last edition was published. Over three-quarters of people with diabetes live in low- and middle-income countries and diabetes causes 6.7 million deaths a year, approximately one every five seconds. The cost of treating diabetes has reached almost US\$1 trillion per annum, a threefold increase over the last 15 years. The need for accurate and up-to-date information to help healthcare professionals support people with diabetes has never been greater.

Ironically, as the volume of information and diversity of digital resources 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 chapters from internationally leading diabetes experts who provide accurate and clinically relevant information to both academic and practising diabetes healthcare professionals.

We have retained the structure from the previous edition, with a similar length and number of chapters. The centenary of the discovery of insulin has just passed and the book begins with a history of diabetes that provides many valuable insights from the past. We then move through the epidemiology of diabetes, the physiology of glucose metabolism, and the pathogenesis of diabetes, before sections on clinical management. A discussion of the microvascular and macrovascular complications then follows, after which there are sections on the psychosocial aspects of diabetes, the management of diabetes in special groups, and models of care, before a final section to glimpse into the future. New chapters include an overview of glucose homeostasis and the central control of glucose metabolism, as well as chapters on the genetics and management of obesity to recognize the close relationship between obesity and type 2 diabetes. There is a new chapter on the emerging topic of biomarkers and precision medicine, while the rapid advance in

diabetes technology has necessitated a split into separate chapters on glucose monitoring and insulin delivery. Transplantation has moved from future treatments to current management to acknowledge its current place in clinical care. In the macrovascular section, we have added a new chapter on heart failure, which has come to the fore as a result of the sodium–glucose cotransporter 2 (SGLT-2) inhibitor cardiovascular outcome trials. Oral health and sleep are added to the list of other areas of diabetes complications, while the importance of social determinants of health and ethnicity, culture, and religion is now included in the psychosocial aspects of diabetes section. The final new chapter describes managing diabetes in low- to middle-income countries, where the majority of people with diabetes live.

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. For this edition the pressures of the Covid-19 pandemic added to the challenges of bringing the book to fruition. Our thanks go to each and every chapter author who, despite busy academic, clinical, and professional lives, was 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 support we have received from our publisher, Wiley-Blackwell. Our commissioning editor Jennifer Seward, who took over from Priyanka Gibbons during the book's development, has provided guidance and encouragement. Our thanks also go to Rajalaxmi Rajendrasingh, Sally Osborn, and the rest of the Wiley-Blackwell team. The book looks even better than the last edition! We would like to pay tribute to Clive Cockram and Barry Goldstein, our editing colleagues for the fourth and fifth editions. You were missed this time round.

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 taken away useful, novel information that will aid in our daily professional lives and hope that this book will help you to support the people with diabetes you know in the widest sense of this meaning.

Richard I.G. Holt
Allan Flyvbjerg
February 2023

List of Abbreviations

AACE	American Association of Clinical Endocrinologists	CML	carboxymethyllysine
AAV	adeno-associated vectors	CNS	central nervous system
ABP	ankle blood pressure	COC	combination oral contraceptive
ACCORD	Action to Control Cardiovascular Risk in Diabetes	COX	cyclooxygenase
ACE	angiotensin-converting enzyme	CPC	cardiac progenitor cell
ACHOIS	Australian Carbohydrate Intolerance Study in Pregnant Women	CRP	C-reactive protein
ACR	albumin : creatinine ratio	CSII	continuous subcutaneous insulin infusion
ADA	American Diabetes Association	CT	computed tomography
ADP	adenosine diphosphate	CV	coefficient of variation
AICAR	5-aminoimidazole-4-carboxamide-1 β -D-ribofuranoside	CVD	cardiovascular disease
AMDCC	Animal Models for Diabetes Complications Consortium	DAWN	Diabetes Attitudes, Wishes, and Needs study
AMP	adenosine monophosphate	DCCT	Diabetes Control and Complications Trial
Apo	apolipoprotein	DKA	diabetic ketoacidosis
aPWV	aortic pulse wave velocity	DPP	dipeptidyl peptidase
Arx	aristaless-related homeobox	DSN	diabetes specialist nurse
ATP	adenosine triphosphate	DVLA	Driver and Vehicle Licensing Agency
AUC	area under the curve	EASD	European Association for the Study of Diabetes
BCAA	branched-chain amino acid	ECG	electrocardiography/electrocardiogram
BMD	bone mineral density	eGFR	estimated glomerular filtration rate
BMI	body mass index	EMA	European Medicines Agency
BM-MNC	mononuclear bone marrow-derived stem cell	ER	endoplasmic reticulum
BPH	benign prostatic hyperplasia	ERCP	endoscopic retrograde cholangiopancreatography
bpm	beats per minute	ERK	extracellular signal-regulated kinase
BTX-A	botulinum toxin type A	ERM	ezrin-radixin-moesin
CABG	coronary artery bypass grafting	ESC	embryonic stem cell
CA-MRSA	community-associated methicillin-resistant <i>Staphylococcus aureus</i>	ESRD	end-stage renal disease
CAPD	continuous ambulatory peritoneal dialysis	ESRF	end-stage renal failure
CBG	capillary blood glucose	FDA	Food and Drug Administration (USA)
CBT	cognitive-behavioral therapy	FDC	fixed-dose combination
CCM	corneal confocal microscopy	FDKP	fumaryl diketopiperazine
CDA	Canadian Diabetes Association	FFA	free fatty acid
CDC	cardiosphere-derived stem cell	FGF	fibroblast growth factor
CDC	Centers for Disease Control and Prevention	FHWA	Federal Highways Administration
CDE	Certified Diabetes Educator	FMD	flow-mediated endothelium-dependent arterial dilation
CEMACH	Confidential Enquiry into Maternal and Child Health	FOXO	forkhead box O
CETP	cholesteryl ester transfer protein	FXR	farnesoid-X receptor
CGM	continuous glucose monitoring	G6P	glucose-6-phosphatase
CI	confidence interval	G-6-P	glucose-6-phosphate
CKD	chronic kidney disease	G6PD	glucose-6-phosphate dehydrogenase
		GAD	glutamine acid decarboxylase
		GCGR	glucagon receptor
		GCK	glucokinase
		G-CSF	granulocyte colony-stimulating factor

GDF	growth differentiation factor	LV	left ventricular
GDM	gestational diabetes mellitus	LVEF	left ventricular ejection fraction
CF	cystic fibrosis	MAOI	monoamine oxidase inhibitor
GI	gastrointestinal	MDI	multiple daily injection
GLO	glyoxalase	MDRD	Modification of Diet in Renal Disease
GLP-1RA	GLP-1 receptor agonist	MG53	mitsugumin 53
GLUT	glucose transporter	mGDP	mitochondrial glycerolphosphate dehydrogenase
GPR	G-protein-coupled receptor	MGO	methylglyoxal
GRPP	glicentin-related pancreatic polypeptide	MI	myocardial infarction
GWA	genome-wide association	MIBG	<i>m</i> -iodobenzylguanidine
GWAS	genome-wide association studies	MIRKO	muscle-specific InsR knockout
HAPO	Hyperglycemia and Adverse Pregnancy Outcomes	MODY	maturity-onset diabetes of the young
HbA _{1c}	hemoglobin A _{1c}	MPGF	major proglucagon fragment
HBV	hepatitis B virus	MPO	myeloperoxidase
HCV	hepatitis C virus	MRI	magnetic resonance imaging
HDL	high-density lipoprotein	MSC	mesenchymal stem cell
HGF	hepatocyte growth factor	MS	mass spectrometry
hGH	human recombinant growth hormone	mTOR	mammalian or mechanistic target of rapamycin
HHS	hyperosmolar non-ketotic hyperglycemic state	mTORC1	mechanistic target of rapamycin complex 1
HR	hazard ratio	MTPI	microsomal transfer protein inhibitor
HRT	hormone replacement therapy	NAD	nicotinamide adenine dinucleotide
HRV	heart rate variability	NaDIA	National Diabetes Inpatient Audit
HSC	hematopoietic stem cell	NAFLD	non-alcoholic fatty liver disease
hsCRP	high-sensitivity C-reactive protein	NANC	non-adrenergic, non-cholinergic
IADPSG	International Association of Diabetes Pregnancy Study Groups	NCV	nerve conduction velocity
IAsp	insulin aspart	NEFA	non-esterified fatty acid
IAUC	incremental area under the blood glucose curve	MFMU	Maternal–Fetal Medicine Units Network
ICA	islet cell antibody	NEP	neutral endopeptidase
ICU	intensive care unit	NFκB	nuclear factor κB
i.d.	intradermal	Ngn3	neurogenin 3
IDDM	insulin-dependent diabetes mellitus	NHANES	National Health and Nutrition Examination Survey
IDeg	insulin degludec	NHS	National Health Service
IDF	International Diabetes Federation	NICE	National Institute for Health and Care Excellence
IDL	intermediate-density lipoprotein	NIDDM	non-insulin-dependent diabetes mellitus
IDRS	Indian Diabetes Risk Score	NIH	National Institutes of Health
IgG	immunoglobulin G	NMU	neuromedin U
IGR	impaired glucose regulation	Nox	NAD(P)H oxidase
IGT	impaired glucose tolerance	NOD	non-obese diabetic
IKKβ	inhibitor κB kinase-β	NPH	neutral protamine Hagedorn
IL	interleukin	NRTI	nucleoside reverse-transcriptase inhibitor
IMT	intima-media thickness	NSAID	non-steroidal anti-inflammatory drug
InsR	insulin receptor	NT-3	neurotrophin-3
IRMA	intraretinal microvascular abnormality	NT-proBNP	N-terminal pro-brain-type natriuretic peptide
ISPAD	International Society for Pediatric and Adolescent Diabetes	OCP	oral contraceptive pill
IT	information technology	OGIS	oral glucose insulin sensitivity
IVUS	intravascular ultrasound	OGTT	oral glucose tolerance test(ing)
IWGDF	International Working Group on the Diabetic Foot	OR	odds ratio
JBDS	Joint British Diabetes Societies	oxLDL	oxidation of low-density lipoprotein
KDIGO	Kidney Disease: Improving Global Outcomes	PAS	periodic acid–Schiff
K _m	Michaelis constant	PBA	phenylboronic acid
LADA	latent autoimmune diabetes in adults	PC	prohormone convertase
LDL	low-density lipoprotein	PCB	polychlorinated biphenyl
LDL-C	low-density lipoprotein cholesterol	PCI	percutaneous coronary intervention
LDLR	low-density lipoprotein receptor	PCR	polymerase chain reaction
LGA	large-for-gestational age	PCSK-9	proprotein convertase subtilisin kexin type 9
LIRKO	liver-specific InsR knockout	PDH	pyruvate dehydrogenase
LPS	lipopolysaccharide	Pdx1	pancreatic duodenal homeobox 1
Lst	limostatin	PGF	placental growth factor
		PI	protease inhibitor

List of Abbreviations

PI3K	phosphatidylinositol 3-kinase	SGA	second-generation antipsychotics
PID	proportional integral derivative	SHP	short heterodimer protein
P/KX	combined pancreas/kidney transplantation	SMBG	self-monitoring of blood glucose
PNDM	permanent neonatal diabetes mellitus	SMI	severe mental illness
PPAR	peroxisome proliferator-activated receptor	SNP	sub-basal nerve plexus
PROactive	Prospective Pioglitazone Clinical Trial in Macrovascular Events	SSRI	selective serotonin reuptake inhibitor
PTDM	post-transplantation diabetes mellitus	T1DM	type 1 diabetes mellitus
PTP1B	protein tyrosine phosphatase 1B	T2DM	type 2 diabetes mellitus
PYY	polypeptide YY	TAG	triacylglyceride
QoL	quality of life	TB	tuberculosis
RA	receptor agonist	TCF7L2	transcription factor 7 like 2
RAMP	receptor activity-modifying protein	TE	transient elastography
RCT	randomized controlled trial	TIND	treatment-induced neuropathy in diabetes
RDN	renal denervation	TLR	toll-like receptor
RECORD	Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes	TNDM	transient neonatal diabetes mellitus
REMS	Risk Evaluation and Mitigation Strategy	TNF α	tumor necrosis factor alpha
rHuPH20	recombinant human hyaluronidase	Treg	regulatory T cell
RMR	resting metabolic rate	TSH	thyroid-stimulating hormone
ROS	reactive oxygen species	TZD	thiazolidinedione
RR	relative risk	UKPDS	UK Prospective Diabetes Study
RR	risk ratio	US	ultrasound
RT-PCR	reverse transcriptase polymerase chain reaction	UT	University of Texas
SCFA	short-chain fatty acid	VEGF	vascular endothelial growth factor
s.c.	subcutaneous	VLCD	very low calorie diet
sdHDL	small, dense high-density lipoprotein	VLDL	very low-density lipoprotein
sdLDL	small, dense low-density lipoprotein	VRIII	variable-rate intravenous insulin infusion
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis	WGS	whole-genome sequencing
		WHO	World Health Organization
		XO	xanthine oxidase
		YY1	Yin Yang 1