Textbook of Diabetes

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

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

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

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