CHURCHILL'S POCKETBOOKS

Diabetes

SUJOY GHOSH
ANDREW COLLIER

FOREWORD BY
JOHN PICKUP

SECOND EDITION

CHURCHILL LIVINGSTONE
ELSEVIER

Diabetes

For Elsevier
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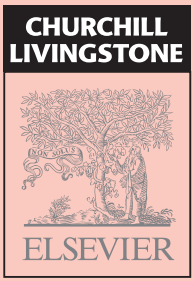

EDINBURGH LONDON NEW YORK OXFORD
PHILADELPHIA ST LOUIS SYDNEY TORONTO 2012

CHURCHILL
LIVINGSTONE
ELSEVIER

First edition 2000
Second edition 2012

ISBN 978-0-443-10081-9

British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

Library of Congress Cataloging in Publication Data
A catalog record for this book is available from the Library of Congress

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Printed in China

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FOREWORD

The practice and the science of diabetes, and the patients who suffer from this disease, have never remained the same. When I was beginning to learn about diabetes at medical school, about 40 years ago, insulin was of course extracted from animal pancreases (though highly purified, 'monocomponent' insulin was being introduced at that time). Glass syringes and needles had to boiled to sterilize them and monitoring of diabetes control was by urine testing. Beds on the medical ward were frequently occupied by diabetic patients, many with gangrenous feet. Within just a decade, when I was well into my career as a diabetologist, injected insulin was of human sequence and made by semi-synthesis or recombinant DNA technology, disposable plastic syringes and needles had been introduced (after a long fight), insulin 'pens' were appearing and even insulin pumps had been in use for five years. Patients monitored their own metabolic control using capillary blood samples and portable meters and not by urine testing. Type 2 diabetes was no longer called 'mild diabetes', though we thought it was a disease of the middle aged and elderly.

Change in diabetes has shown no signs of diminishing in the last decade, and in fact it is accelerating. Scientific advances in the understanding of diabetes and its complications are being translated into improved clinical practice at ever faster rates. But the increasing prevalence, costs and human suffering associated with diabetes have produced a global health nightmare which challenges us to do better – in public health, scientific and clinical research, clinical care and social policy.

What has changed recently? The relentless increase in obesity and inactivity amongst all age groups has caused the emergence of this type of diabetes in children and adolescents, as well as adults. Type 2 diabetes is now increasingly recognised as a disorder of the immune system, though it seems to be a disease of activated innate immunity. Rapid- and long-acting insulin analogues are now the insulins of choice for many people with diabetes, and newer insulins are just around the corner – analogues with even longer duration for better basal replacement, and rapid-acting formulations with even faster absorption for meal-time use. New technologies such as smart insulin pumps and continuous glucose monitoring are playing an increasing part in the management of selected patients with type 1 diabetes and sub-optimal glycaemic control. In type 2 diabetes, new blood glucose-lowering drugs such as gliptins and GLP-1 agonists are proving effective, and in the grossly obese patient with diabetes, bariatric surgery is becoming a recognised treatment option. In the everyday diabetes clinic, management of hypertension and lipids are

now seen as being as integral to diabetes care as blood glucose control. And many more advances could be mentioned.

Diabetes is common, costly, complex and constantly changing. There is much to learn. The management of people with diabetes is not the same today as it was even a few years ago. Sujoy Ghosh and Andrew Collier have produced in this book a clear, up-to-date guide to modern diabetes and its management that will help all practitioners. I am sure it will make a substantial contribution both to our understanding of diabetes and to improving the care of the patients who suffer from it.

London 2012 John Pickup

PREFACE

The incidence of diabetes is increasing at epidemic proportions worldwide. The first *Pocketbook of Diabetes* was published in 2000 and the structure of this edition follows similar lines. However, diabetes expertise has moved on considerably, with greater understanding of aetiopathogenesis of the different types of diabetes, the emerging roles of novel pharmacological agents, and the importance of multidisciplinary team working and multi-risk-factor treatment.

Re-writing this book was easy and difficult at the same time. Our predecessor, Professor Andrew Krentz, who wrote the previous edition, had done a wonderful job and hence it was incredibly difficult to improve upon his work. At the same time his work provided us with a platform to update the book, keeping in view the advances in knowledge.

The emphasis of this book is on clinical management and the aim has been to provide a balanced view of current clinical practice. This book is not meant to be an alternative to time tested exhaustive text-books on diabetes. This pocketbook is meant to be a be a concise companion for all health professionals involved in diabetes management, providing easily accessible information and guidance.

Finally no words of praise are enough for the constant help and support that we received from our publishers, especially Sheila Black, for bearing with the unbearable!

Calcutta and Ayr, 2012

Sujoy Ghosh
Andrew Collier

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ABBREVIATIONS

4 S Scandinavian Simvastatin Study

AAP atypical antipsychotic

ABPI ankle : brachial pressure index

AC abdominal circumference

ACCORD Action to Control Cardiovascular Risk in Diabetes

ACE angiotensin converting enzyme

ACR albumin/creatinine ratio

ACT acceptance and commitment therapy

ADA American Diabetes Association

ADOPT A Diabetes Outcome Progression Trial

ADVANCE Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation

AED antiepileptic drug

AER albumin excretion rate

ALLHAT Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial

ARB angiotensin receptor blocker

ARI aldose reduction inhibitor

ASCOT Anglo-Scandinavian Cardiac Outcomes Trial

ASH alcoholic steatohepatitis

ASSIGN Assessing cardiovascular risk using SIGN guidelines to assign preventive treatment

ATP adenosine triphosphate

BDI Beck Depression Inventory

BERTIE Bournemouth Type 1 Intensive Education

BGAT Blood Glucose Awareness Training

BHS British Hypertension Society

BITES Brief Intervention in Type 1 Diabetes – Education for Self-efficacy

BMD bone mineral density

BMI body mass index

BMS bare metal stents

BNF British National Formulary

BP blood pressure

BSA body surface area

BUN blood urea nitrogen

CABG coronary artery bypass grafting

CAPD continuous ambulatory peritoneal dialysis

CARDS Collaborative Atorvastatin Diabetes Study

CARE Cholesterol and Recurrent Events

CBT cognitive behavioural therapy

CCB calcium channel blocker

CES-D Centre for Epidemiological Studies – Depression Scale

cGMP cyclic guanosine monophosphate

CHD coronary heart disease

CHF congestive heart failure

CI confidence interval

CKD chronic kidney disease

CMG continuous monitoring of interstitial glucose

CoA coenzyme A

COC combined oral contraceptive

COPD chronic obstructive pulmonary disease

CRP C-reactive protein

CSI continuous subcutaneous insulin infusion

CSMO clinically significant macular oedema

CT computed tomography

CTG cardiotocography

CVD cardiovascular disease

DAFNE Dose Adjustment for Normal Eating

DCCT Diabetes Control and Complications Trial

DES drug-eluting stents

DESMOND Diabetes Education and Self-Management for Ongoing and Newly Diagnosed

DHAP dihydroxy acetonephosphate

DIGAMI Diabetes mellitus, Insulin-Glucose infusion in Acute Myocardial Infarction

DISH diffuse idiopathic skeletal hyperostosis

DISN diabetes inpatient specialist nurse

DKA diabetic ketoacidosis

DPP dipeptidyl peptidase

DR diabetic retinopathy

DRS Diabetic Retinopathy Study

DSME diabetes self-management education

DVLA Driver and Vehicle Licensing Agency

ED erectile dysfunction

EDHF endothelium-derived hyperpolarizing factor

ER endoplasmic reticulum

ESRD end-stage renal disease

FDA Food and Drug Administration

FFA fundus fluorescein angiography

FIELD Fenofibrate Intervention and Event Lowering in Diabetes

FLD fatty liver disease

FPG fasting plasma glucose

FSH follicle-stimulating hormone

GA3P glyceraldehyde 3-phosphate

GAD glutamic acid dehydrogenase

GDM gestational diabetes mellitus

GFR glomerular filtration rate

GHbSD standard deviations of glycosylated haemoglobin

GI glycaemic index

GIP glucose-dependent insulinotropic peptide

GLP-1 glucagon-like peptide-1

GLUT glucose transporter

GnRH gonadotropin-releasing hormone

GP general practitioner

HAATT Hypoglycaemia Anticipation, Awareness and Treatment Training

HADS Hospital Anxiety and Depression Scale

HAPO Hyperglycaemia and Adverse Pregnancy Outcome

HbA1c glycated haemoglobin

HDL high density lipoprotein

HF heart failure

HHS hyperosmolar hyperglycaemic state

HIV human immunodeficiency virus

HLA human leukocyte antigen

HNF hepatocyte nuclear factor

HOMA homeostasis model assessment

HONK hyperosmolar non-ketotic (coma)

HOPE Heart Outcomes Prevention Evaluation

HOT Hypertension Optimal Treatment

HPS Heart Protection Study

HR hazard ratio

HTA Health Technology Assessment

IDF International Diabetes Federation

IFCC International Federation of Clinical Chemistry and Laboratory Medicine

IFG impaired fasting glucose

IGT impaired glucose tolerance

IPF insulin promoter factor

IPPV intermittent postive-pressure ventilation

IRMA intraretinal microvascular anomaly

IRS insulin receptor substrate

IUD intrauterine device

IUGR intrauterine growth restriction

IUS intrauterine systems

IV intravenous

JBS 2 Joint British Societies' guideline

LADA latent autoimmune diabetes in adults

LCD low calorie diet

LDL low density lipoprotein

LED low energy diets

LH luteinizing hormone

LVSD left ventricular systolic dysfunction

MDI multiple daily injections

MDRD Modification of Diet in Renal Disease

MELAS mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like

MI myocardial infarction

MNT medical nutrition therapy

MODY maturity-onset diabetes of the young

MR modified release

MRI magnetic resonance imaging

NAD nicotinamide adenine dinucleotide

NASH non-alcoholic steatohepatitis

NCEP National Cholesterol Education Program

NDH non-diabetic hyperglycaemia

NGSP National Glycohemoglobin Standardization Program

NHS QIS NHS Quality Improvement Scotland

NICE National Institute for Health and Clinical Excellence

NPDR non-proliferative diabetic retinopathy

NPH neutral protamine Hagedorm

NPWT negative pressure wound therapy

NYHA New York Heart Association (classification)

OCT optical coherence tomography

OGTT oral glucose tolerance test

OR odds ratio

PAD peripheral arterial disease

PAID Problem Areas in Diabetes

PCI percutaneous coronary intervention

PCOS polycystic ovary syndrome

PCR protein/creatinine ratio

PCT porphyria cutanea tarda

PDR poliferative diabetic retinopathy

PHQ Patient Health Questionnaire

PPR peroxisome proliferator-activated receptor

PROactive PROspective pioglitAzone Clinical Trial In macroVascular Events

PUFA omega-3 polyunsaturated fatty acids

PVD peripheral vascular disease

QALY quality-adjusted life year

QOF quality outcomes framework

QoL quality of life

QUICKI quantitative insulin sensitivity check index

RAAS renin–angiotensin–aldosterone system

RARS refractory anaemia with ringed sideroblasts

RCT randomized controlled trial

RR relative risk

RRT renal replacement therapy

SBP systolic blood pressure

SCID Structured Clinical Interview for DSM-IV-TR

SD standard deviation

SE standard error

SGA small for gestational age

SGLT sodium–glucose co-transporter inhibitor

SHBG sex hormone-binding globulin

SIGN Scottish Intercollegiate Guidelines Network

SMBG self-monitoring of blood glucose

SMD standardized mean difference

SMUG self-monitoring of urine glucose

SREBP sterol regulatory element-binding protein

SSRI selective serotonin reuptake inhibitor

SU sulphonylurea

TCA tricyclic antidepressant

TG triglycerides

TSH thyroid-stimulating hormone

TZD thiazolidinedione

UGDP University Group Diabetes Program

UKPDS UK Prospective Diabetes Study

VADT Veterans Affairs Diabetes Trial

VEGF vascular endothelial growth factor

VLCD very low calorie diet

VLED very low energy diet

WHO World Health Organization

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SECTION 1

DIAGNOSIS, CLASSIFICATION, EPIDEMIOLOGY AND BIOCHEMISTRY

THE SYNDROME OF DIABETES MELLITUS

Diabetes mellitus is defined as a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action, or both. The clinical diagnosis of diabetes is often indicated by the presence of symptoms such as polyuria, polydipsia and unexplained weight loss, and is confirmed by documented hyperglycaemia.

The clinical presentation ranges from asymptomatic type 2 diabetes to the dramatic life-threatening conditions of diabetic ketoacidosis (DKA) or hyperosmolar non-ketotic coma (HONK)/ hyperosmolar hyperglycaemic state (HHS). The principal determinants of the presentation are the degrees of insulin deficiency and insulin resistance, although additional factors may also be important. In addition, pathological hyperglycaemia sustained over several years may produce functional and structural changes within certain tissues. Patients may present with macrovascular complications that include ischaemic heart disease, stroke and peripheral vascular disease, whereas the specific microvascular complications of diabetes include retinopathy, nephropathy, neuropathy.

DIAGNOSTIC CRITERIA FOR DIABETES MELLITUS

Assigning a type of diabetes to an individual often depends on the circumstances present at the time of diagnosis, and many diabetic individuals do not easily fit into a single specific type. An example is a person who has acquired diabetes because of large doses of exogenous steroids and who becomes normoglycaemic once the glucocorticoids are discontinued. In addition, some patients may present with major metabolic decompensation yet can subsequently be treated successfully with oral agents. Thus, for the clinician and patient, it is less important to label the particular type of diabetes than it is to understand the pathogenesis of the hyperglycaemia and to treat it effectively.

The American Diabetes Association (ADA, 2011) gives the following **criteria for the diagnosis of diabetes:**

- A1C $\geq$ 6.5%. The test should be performed in a laboratory using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized to the Diabetes Control and Complications Trial (DCCT) assay, or

- fasting plasma glucose (FPG) $\geq$126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h, or
- 2-h plasma glucose $\geq$200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test (OGTT). The test should be performed as described by the World Health Organization (WHO), using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water
- in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose $\geq$200 mg/dL (11.1 mmol/L)
- in the absence of unequivocal hyperglycaemia, the result should be confirmed by repeat testing.

The symptoms of thirst, polyuria, polyphagia and weight loss, coupled with a raised plasma glucose level, are diagnostic. In the absence of symptoms two abnormal results (i.e. two raised fasting levels) or an abnormal OGTT result is diagnostic. However, the OGTT is influenced by many factors other than diabetes, including age, diet, state of health, gastrointestinal disorders, medications and emotional stress.

Tip box

Chronic hyperglycaemia is the sine qua non of diabetes mellitus.

CATEGORIES OF INCREASED RISK FOR DIABETES (PRE-DIABETES): IMPAIRED FASTING GLUCOSE (IFG)/IMPAIRED GLUCOSE TOLERANCE (IGT)

The ADA criteria introduced the category of impaired fasting glucose, defined as fasting venous plasma level of 5.6–6.9 mmol/L. The diagnosis of impaired glucose tolerance can be made only using a 75-g oral glucose tolerance test; a 2-h glucose measurement points to the diagnosis of impaired glucose tolerance when the plasma glucose is found to be greater than 7.7 mmol/L but less than 11.1 mmol/L. Recently another category, impaired glycated haemoglobin, HbA1c (A1C 5.7–6.4%), has been added.

Categories of increased risk for diabetes (pre-diabetes) (ADA, 2011)

FPG 100–125 mg/dL (5.6–6.9 mmol/L): IFG
or