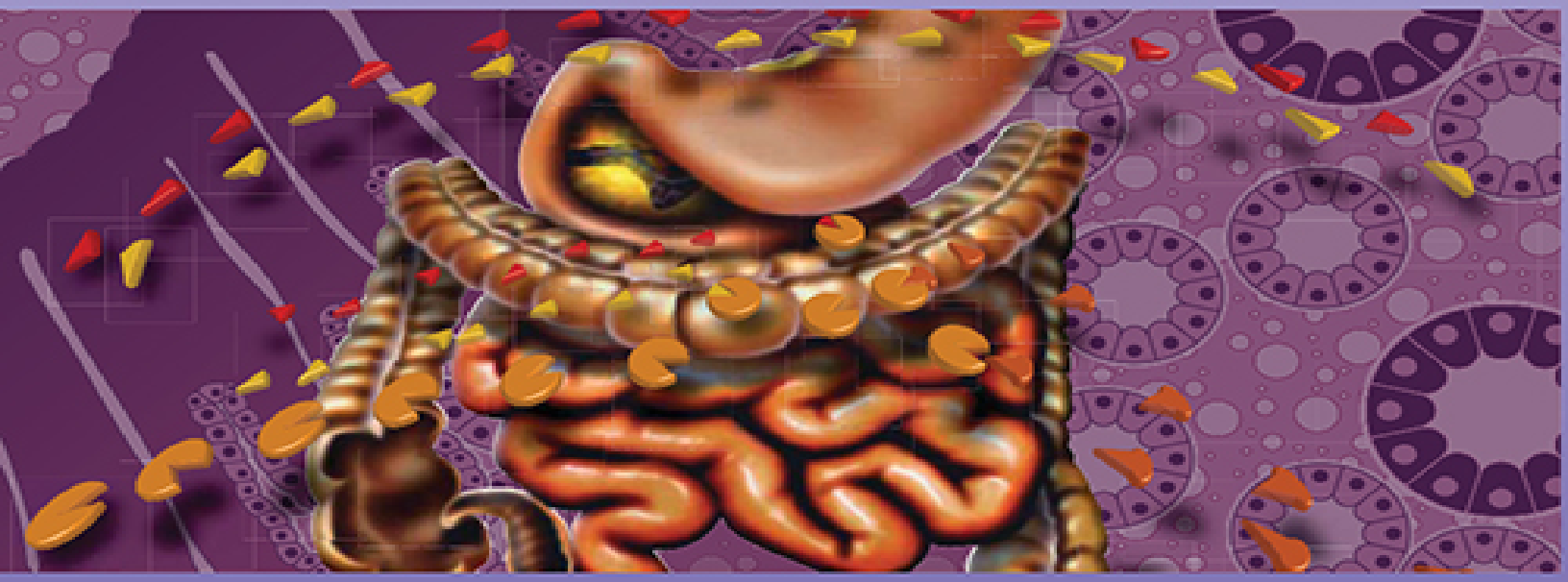
NEW MECHANISMS IN GLUCOSE CONTROL



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Contents

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Preface

Whilst insulin was first isolated in 1921 and produced commercially by 1923, it was not until the mid 1950s that oral agents for type 2 diabetes came to the market, first sulphonylureas and then the first biguanide. We then waited another 30 years for the first alpha-glucosidase inhibitor, but since then there has been a veritable explosion in interest for new drugs in the diabetes market with a number now commercially available.

It is clear that the traditional agents remain important therapies, but they have their downside from the point of view of tolerability/side-effect problems. Moreover, they appear not to influence the natural history of the disease. The latter is an important issue given the progressive nature of type 2 diabetes and the need to achieve good glycaemic control to reduce the risk of devastating long-term vascular complications.

In the past few decades a revolution in our approach to treating type 2 diabetes has occurred following the recognition that the disease is caused by multiple defects. A range of new treatments are now available with differing mechanisms of action, and many more are in the pipeline, which will allow us to target this multifactorial disease more effectively than ever before.

The increasing requirement in the UK to move much of diabetes practice into the community requires a much more detailed knowledge of the condition by GPs and practice nurses. In this bespoke book, the authors aim to show how new mechanisms of glucose control and advances in treatments arising from this can be translated into primary care. The book will cover the epidemiology and pathogenesis of type 2 diabetes as well as provide an overview of current diabetes management including the

pros and cons of traditional therapies. This will be followed by an in-depth discussion of the incretin system and the new drugs based on this approach – the incretin mimetics (glucagon-like peptide-1 (GLP-1) agonists) and dipeptidyl peptidase-4 (DPP-4) inhibitors. The authors will also review other drug classes in development as well as discussing the often observed resolution of type 2 diabetes that occurs after weight-loss surgery. Finally, they will consider effective approaches for diabetes care within that arena.

This book is particularly timely given the recent guidelines from the National Institute for Health and Clinical Excellence (NICE) on *Newer Agents for Blood Glucose Control in Type 2 Diabetes*, and is intended primarily for the multi-professional diabetes care team. It should, however, also be of interest to hospital specialists in training and other relevant staff. It is hoped that by increasing awareness of the expanding therapeutic options for type 2 diabetes and their mechanisms, we can better target the multitude of physiological defects that characterize the disease and customize treatment regimens to fit the individual needs of each patient.

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CHAPTER 1

Epidemiology and Pathogenesis of Type 2 Diabetes

Throughout the world the increasing prevalence of diabetes is posing significant strains on already overburdened healthcare systems. Type 2 diabetes accounts for most of the projected increase, which reflects not only population growth and the demographics of an aging population, but also the increasing numbers of overweight and obese people who are at increased risk of diabetes.

The current prevalence of diabetes

Latest estimates from the International Diabetes Federation indicate that in 2010 the global prevalence of diabetes will be 285 million, representing 6.4% of the world's adult population, with a prediction that by 2030 the number of people with diabetes will have risen to 438 million (IDF, 2009).

In Europe, there is a wide variation in prevalence by country, but the total number of adults with diabetes in the region is expected to reach 55.2 million in 2010, accounting for 8.5% of the adult population (IDF, 2009). Estimates indicate that at least € 78 billion will be spent on healthcare