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156

The Role of Viruses and the Immune System in Diabetes Mellitus

Experimental Models

Edited by T. Dyrberg

With 15 Figures

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Foreword

Research in diabetes has accelerated in two areas, both of which are being reviewed in CTMI. The first is the use of a variety of animal models; the second is basic research in human investigation, islet cell antigens, and mapping of genes associated with susceptibility to disease. Dr. Thomas Dyrberg accepted editorial responsibility for this volume, which covers the first area. A second book, to be published later in the year, is edited by Drs. Bækkeskov and Hansen (CTMI 164, see page VI for contents). Although the contributors to both volumes represent the international scientific community, the editors are from the Hagedorn Research Laboratory in Denmark. Work at this institute and the Steno Memorial Hospital has been dedicated to research in diabetes for decades, and the institutions were appointed WHO Collaborating Centres for Research and Training on the Pathogenesis of Diabetes Mellitus in 1983. It is worth noting that while addressing the hypothesis of the role of class II major histocompatibility glycoproteins in autoimmune diabetes (insulin-dependent diabetes, IDDM) a number of investigators established animal models in which class II molecules were expressed under the control of the rat insulin promoter. While generating interesting information on IDDM, the finding of immunologic tolerance in such transgenic mice has attracted the attention of several basic immunologic laboratories for quite different reasons. Thus, we are reminded again of the Pasteur dictum that "chance favors the prepared mind."

Michael B. A. Oldstone, M.D.
La Jolla, California, November 1989

This collection of studies was conceived as part of a two-volume review of the immunology of diabetes. The contents of Volume 164, which forms part 2, are listed below.

Current Topics in Microbiology and Immunology, Volume 164

Human Diabetes

(Edited by S. BÆKKESKOV and B. HANSEN)

Preface

Insulin-dependent (type 1) diabetes mellitus (IDDM) is a chronic disease caused by specific destruction of the pancreatic β cells. Replacement therapy with insulin nearly normalizes glucose metabolism; however, IDDM is still associated with excessive mortality due to severe secondary complications. An important aspect of diabetes research is to clarify the etiology and pathogenesis of IDDM. This knowledge may enable us to identify individuals who are beginning to develop diabetes and to intervene in the pathogenic processes, thereby preventing clinical onset of disease. Although the exact mechanisms responsible for β cell destruction have not yet been determined, it is known that:

—Autoimmunity is of major significance in the pathogenesis, but the initial events leading to the break in self-tolerance to β cell autoantigens remain obscure.

—Susceptibility to IDDM is closely associated with certain MHC class II genes, but other genes may also play a role.

—Environmental factors can cause IDDM and are probably important in inducing the initial lesions.

Animal research has had a place in the study of diabetes since Minkowski reported on the pivotal role of the pancreas in the development of diabetes 100 years ago. The three animal models which have been of particular importance for the study of IDDM are reviewed in this volume—low-dose streptozotocin diabetes in mice, the BB rat, and the NOD mouse. The diabetic syndrome of the latter two shares many similarities with IDDM in humans; most prominently they develop diabetes subsequent to autoimmune destruction of their β cells. Studies on the pathogenic mechanisms in these animals may help to uncover mechanisms which are difficult to study in humans such as tolerance and prediabetes pathogenesis.

Although diabetes research has focused on autoimmune phenomena, the association between IDDM and virus needs

to be explored further. Viruses have been implicated by various indirect observations, but direct evidence that virus can cause IDDM is limited. Infection with Coxsackie B virus has precipitated an acute onset of IDDM in a few cases. Individuals with congenital rubella infection are particularly prone to develop IDDM, but it remains to be established whether rubella virus is the etiologic agent. Viruses can, however, cause autoimmune disease by multiple mechanisms, either directly, by interacting with the target cells or indirectly, by interfering with the function of the immune system.

Recent developments in molecular genetics have illuminated the role of major histocompatibility complex molecules in IDDM and the genetics of IDDM in the BB rat. These subjects are also reviewed in this volume.

Taken together, it is obvious from the contributions in this book that major advances have been made in understanding the pathogenesis of IDDM, but that a host of questions are still unanswered. In the long run, it will be necessary to improve and enhance the interdisciplinary approach for not until then will it be possible to design effective preventive IDDM therapy.

January 1990 T. Dyrberg

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