The Respiratory Burst and Diabetes Mellitus

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1. INTRODUCTION

Diabetes mellitus is known as a general disturbance of glucose utilization at the cellular level. However, the precise pathomechanism is unclear, according to the 1985 classification of the WHO study Group. Two (clinical) types of the disease—insulin-dependent diabetes mellitus (IDDM) and noninsulin-dependent diabetes mellitus (NIDDM)—have been used. The discovery and accessibility of the hormone insulin have fundamentally changed the outcome of the patients, but complications of the disease have become conspicuous; such as increased sensitivity of the organism against different infectious illnesses.

Insulin depletion at the intracellular level leads to serious metabolic abnormalities and a consequent disturbance of many cellular functions, including immunological activity. This is one possible explanation why the relative immunodeficiency, which is considered to be of metabolic origin, was not widely studied by immunologists. Recently, with the advance in the therapy of diabetes mellitus (e.g., continuous insulin pumping), an adequate control of the carbohydrate metabolism is possible. Episodes of excessive hyperglycemia or ketosis are not frequent in diabetics. Therefore, the direct effect of metabolic abnormalities on the immunological status is negligible. Moreover, during the past two to three decades, IDDM has come to seem to be a more complicated disease than was thought with a possibility of autoimmune origin suggested by identification in the sera of patients of different autoantibodies against pancreatic islet cells, as well as against the hormone insulin, and in special cases against the insulin receptor. The genetics of diabetes was also studied, and a higher incidence of HLA-DR3 and -DR4 haplotypes was

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observed.\textsuperscript{10,11} By contrast, the phenomenon of decreased resistance against infectious diseases also exists in NIDDM patients in whom evidence of an autoimmune origin or any connection with genetic factors are undemonstrable.\textsuperscript{12,13}

According to our present knowledge, diabetes mellitus appears to be a disorder of carbohydrate metabolism, with different abnormalities of the specific and nonspecific immune response present to some degree independent of the metabolic disturbances.

The role of the reactive oxygen species (ROS)-generating system in the host defense has also been intensively studied during the past 20 years,\textsuperscript{14,15} but it seems that the advances in the study of the diabetes, and of the respiratory burst, were not synthesized by the different teams. However, it is evident that superoxide, hydrogen peroxide, and other short-lived oxygen derivatives have significant importance in the bactericidal killing of phagocytic cells,\textsuperscript{16} and disturbed resistance of the diabetics against infectious disease is also well known\textsuperscript{17,18}; the number of reports in which the ROS of diabetics was studied is relatively small. A possible explanation is that the interest of immunologists turned first to the immunological processes involved in the pathomechanism of the disease and the biochemists studied especially the so-called pure forms of ROS disturbances (e.g., chronic granulomatous disease).

We believe that a special connection between the so-called immunological recognition and the effector function of phagocytic cells exists in diabetes mellitus. The aim of this short review is to give a possible view of this connection, including the special role of the ROS in it.

2. ALTERATION OF THE IMMUNE SYSTEM IN DIABETES MELLITUS

The confusion in the classification of diabetes makes evaluation of the different immunological findings difficult. Inaccuracies of correct and routine methods appear to have a common origin; i.e., the recent classification based on the insulin requirement of the patients has nothing to do with the pathomechanism of the disease. Although is abundant enough in everyday clinical practice, it is insufficient for immunological and biochemical measurements, in general.

A review of theories on the pathophysiology of diabetes mellitus is far beyond the dimensions of this chapter, but several facts must be taken into account:

1. There is an existing form of diabetes mellitus of juvenile onset, characterized by absolute insulin need, but the so-called immunological findings are very different. Autoantibodies against pancreatic islet cells are present only in about 50\% of the sera.\textsuperscript{19,20} Another small proportion of patients has antibodies against insulin\textsuperscript{21} and, very rarely, antibodies against insulin receptors\textsuperscript{22,23} are detectable as well. It is significant that a great number of cases show no laboratory signs of autoimmune diseases. All these patients appear in the literature as IDDM or as type 1 DM.