Modern Problems in Paediatrics

Diabetes in Juveniles

Medical and Rehabilitation Aspects

12

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Zvi Laron, Petah Tiqwa
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Editor:
ZVI LARON, Professor of Pediatric Endocrinology

Assistant:
MOSHE KARP

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Opening Address

ZVI LARON

Last year we celebrated the jubilee anniversary of the discovery of insulin. During these 50 years, in which many millions of lives have been saved, the therapeutic approach to diabetes has undergone continuous change. It is paradoxical that while diabetes is by definition an endocrine disease, it has long been rejected as such by endocrinologists and even more so by pediatric endocrinologists. Diabetics are treated, in most cases, not within the framework of the endocrinology clinics but in separate clinics by "diabetologists." Furthermore, since most diabetics are adults, little actual attention has been paid to the problem of diabetes in patients below the age of 20, and there is only a very scant amount of published material on this subject, as you all know.

One of the first attempts to bring together the people involved in the care of diabetics was the foundation in 1950 of the *International Diabetes Federation*, which, in contradistinction to other professional organisations in the medical field, includes among its members both *laymen and diabetics*; it does not, however, have a special committee for the problems of diabetic children.

In March 1970 we took a significant step forward in the treatment of juvenile diabetics when we inaugurated in this same auditorium the *Israel Counselling Center for Juvenile Diabetics*. We have developed and successfully applied an *ambulatory, comprehensive, multidisciplinary scheme for the treatment of juvenile diabetes*. We found that it is not as well known as it should be that diabetes in children, once established, is a psychosomatic disease, mostly of familial dimensions, and that the psychic factor plays a major role in the metabolic control of diabetes. It was our aim to treat and possibly prevent the aggravation of the *psycho-social component* in the

management of the young diabetic. For this purpose, we developed a comprehensive, multidisciplinary, approach applied on an ambulatory basis involving not only the young diabetic but his family as well.

Our work at the Center has shown us that many problems remain to be solved. We would like to develop easy methods for the early detection of diabetes and to establish the priorities for mass detection as well as to find ways of preventing the complications of the disease. We would also like to do more toward educating the general public and the various institutions, which often discriminate against the diabetic, and to do all we can toward bringing our team concept into the patient's home.

Needless to say, we shall not be able to solve all these problems at this symposium. However, the fact that the attendance at this second meeting is so much larger than at the first indicates the magnitude of the interest in this subject, and the presence of the leading scientists in the field of diabetes ensures that by the time it is ended our knowledge will have been much enriched. Hopefully, our juvenile patients will feel the benefit of this exchange of information and collaboration, and will be able to look forward to a brighter, healthier future.

I would like to thank the Ministry of Health, Kupat Holim (General Sick Fund), the Tel Aviv University Medical School, and the Israel Academy of Sciences for sponsoring this meeting.

Introduction

Although many of the problems related to diabetes have not yet been clarified, it is generally agreed that diabetes is a progressive disease, often of slow onset. We know that there is a stage of prediabetes, which may develop into latent diabetes, later into chemical diabetes and ultimately into clinical or overt diabetes (1). It is also possible that some of these stages may be reversible. In general, pre- or chemical diabetes is characterized by a certain degree of abnormality in glucose tolerance and in the insulin response to glucose.

If the latter is true, many of the conditions and diseases of childhood which present abnormalities in carbohydrate tolerance and insulin secretion may be considered to be associated with prediabetes or chemical diabetes. Is this really so? It is important to clarify this point, since the early recognition and treatment of these abnormalities may make it possible to prevent or delay the onset of overt diabetes (2). How strong are the genetic factors of diabetes in determining the progress from pre- to overt diabetes? What is the meaning of vascular changes? These are also known to be progressive. The thickness of the basement membrane has been found to be increased in subjects with mild glucose intolerance as well as in those with prediabetes (3), but it is not yet clear whether this hypertrophy is directly related to hyperglycemic states since these findings have been contested by other workers (4). To add to the confusion, yet another group of investigators has found that one third of a series of 35 patients with glucose intolerance and myopathies showed a thickening of the basement membrane, while 10 patients with normal glucose tolerance also showed similar findings (5). Are these changes absolutely related to diabetes and the known vascular

changes in the eyes, kidneys and heart due to this disease? Very little data on this subject have been obtained in children.

What are all the facts of diabetes in children? We shall not be able to answer all these questions at this meeting but I know that we shall be adding to our collective knowledge.

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Criteria for Diagnosis of Glucose Intolerance

R. Jackson, D. Y. N. Murthy and R. A. Guthrie
Department of Pediatrics, University of Missouri School of Medicine, Columbia, Missouri, U. S. A.

Public detection drives using current screening methods involving urine examinations or single blood sugar determinations will identify very few children with diabetes. There is a growing body of evidence that the glucose tolerance test results of children may be abnormal for many years before the onset of clinical or overt diabetes (1). The early identification of children with chemical diabetes years before they have symptoms of the disease provides us with an opportunity to observe the natural pattern of development of the disease, and to extend our knowledge of the pathophysiology of the disorder. The pattern of development of diabetes mellitus and the terms used are delineated in Figure 1.

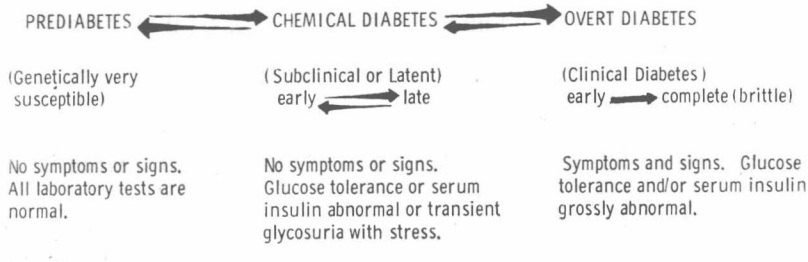

Fig. 1. The pattern of development of diabetes mellitus.

There are many factors which influence the OGTT (2). The utilization of a more standardized technique in all clinics would help minimize the variability of the tests. The effect of diet, particularly the level of carbohydrate intake, on the OGTT has been well documented (3). While we always prescribe a diet with at least 60 percent of the calories derived from carbohydrate for three days preceding the test, we have found that the diet of most American children has about 50% of its calories from carbohydrates. For pre-diabetic or chemical diabetic subjects who may be somewhat restricting their carbohydrate intake, carbohydrate supplementation for a few days preceding the test is important. Studies involving continuous monitoring of blood sugar levels of exercising patients have been reported (4). Exercising patients have somewhat lower blood sugar values while beb restricted patients have higher ones. To control variation in physical activity and emotional stress, we do our testing in a special room provided with books and toys, so that the children can play and move about in quiet activity (5). Blood glucose determinations are performed by the neocuproine method on a Somogyi filtrate in an autoanalyzer (6). The blood sugar determinations are verified by the Glucose Standardization Laboratory, USPHS, Atlanta, Georgia; their variability is less than 3 mg/100 ml. Serum insulin values are determined by the Morgan and Lazarow double antibody method (7). Both blood sugar and serum insulin determinations are done on capillary blood samples.

We have published normal ranges for blood sugar and serum insulin values during OGTT's in normal children without a family history of diabetes (8) Figure 2. We use percentile rather than standard deviation values in our graphs because of skewing of data toward higher values.

We have evolved the following criteria for the diagnosis of chemical diabetes in children. To establish a diagnosis, the results must be confirmed by another set of abnormal findings after a time interval of 2 months.

A. *Chemical Diabetes*

1. Three blood sugar values at or above the 97th percentile at the first, second and third hours;

2. Two blood sugar values at or above the 97th percentile at the first and second hours and a value below the 50th percentile at the third hour;

3. One value at or above the 97th percentile at the first or at the second hour and another value at the first or second hour above the 90th percentile; and/or a value below the 10th percentile at the third hour.

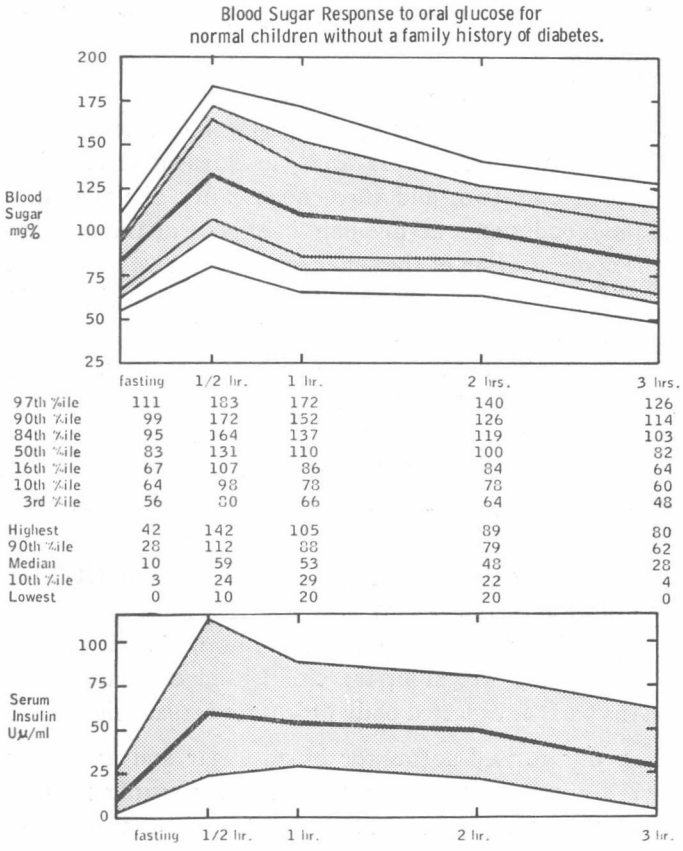

Fig. 2. Blood sugar and serum insulin during the standard oral glucose tolerance test in children.

B. *Probable Chemical Diabetes (highly suspect)*

1. Two blood sugar values at or above the 90th percentile at the first and second hours and a value at the third hour above the 90th percentile or below the 10th percentile;

2. A blood sugar value at the third hour below the 3rd percentile (other values within normal range).

C. *Possible Chemical Diabetes(suspect)*

1. Two or three blood sugar values at or above the 84th percentile at the first, second and third hours;

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