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Inheritance of childhood diabetes

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In the parents of 250 diabetic children the occurrence of juvenile and maturity onset diabetes was found to be more frequent than in the parents of 230 medical students. Assuming a multifactorial poligeneic heredity, the role of common genes predisposing to diabetes cannot be neglected in the manifestation of the two types of the disease. In the families where juvenile diabetes had occurred, the probability of occurrence of juvenile diabetes is considerably higher than that of maturity onset diabetes. This might be in connection with the fact that the provocative factors are different in juvenile and maturity onset diabetes.

Inheritance is of less importance in juvenile than in maturity onset diabetes [14, 18]. On the other hand, convincing data confirm the higher rate of hereditability of juvenile diabetes [7, 17]. The aim of the present study was to elucidate the correctness of a sharp differentiation between insulin dependent juvenile, and maturity onset insulin non-dependent, diabetes on the basis of familial hereditability.

MATERIAL

A total of 250 diabetic children were involved in the study. Their disease had manifested itself before the age of 15 years. Table I shows the length of the observation period of their diabetes. The frequency of juvenile and maturity onset diabetes in the parents was estimated on the basis of the history. Diabetics among the parents of 230 medical students 21 to 26 years of age served as controls. Since the parents of diabetic children are well aware of the symptoms of the disease, their data were assumed to be fairly reliable, just as well as the information obtained from the medical students.

RESULTS

Table II shows the frequency of diabetes among parents of diabetic children as compared to the control group. In the insulin dependent par-

TABLE I

Period of observation

	< 5 years	6–10 years	11–15 years	15–20 years	> 21 years
Diabetic children n = 250	40%	26%	16%	16%	16%

TABLE II

Occurrence of diabetes in the parents of the diabetic children and of the controls

Type of diabetes	Parents of diabetic children n = 500	Control group n = 460
Insulin-dependent diabetes	2.2% (11)	0.43 (2)
Insulin non-dependent diabetes	3.0% (15)	3.48% (16)

ents of diabetic children the disease had manifested itself under the age of 30 years in 9 out of 11 cases. They were given insulin immediately because of acidosis and a quick progression of the symptoms. Among the controls, only two juvenile type diabetics were found. At the time of manifestation one parent was 19, the other 26 years old. Thus, the frequency of juvenile diabetes in parents of diabetic children was more than 5 times higher than in the control group. In the whole material, insulin non-dependent maturity onset diabetes occurred in 3% of the parents of diabetic children, in contrast with the 3.5% of the control group. Besides, 7 sibs were found among the 250 diabetic children and none in the control group.

At the time of the survey the parents of the medical students were older than the parents over 40 of the diabetic children, whose age ranged from 10 to 26 years. This correlation agrees well with the data in Table III.

In Table IV the manifestation of insulin non-dependent diabetes is plotted against the age of the parents. The diabetic parents of the control group were all over 40 years of age, therefore the percentual rate of those under 40 years could not change any more, while among the parents of diabetic children the rate may still undergo changes. Owing to the great number of young parents of whom 25% were less that 30 years of age.

In the parents of diabetic children who were older that 40 years the occurrence of maturity onset diabetes was 2.2 times higher than in the control group, in spite of their having been younger that the parents of the medical students ($P < 0.01$).

TABLE III

Distribution of the manifestation of insulin-non-dependent diabetes in parents of diabetic children and of controls according to age

	< 40 years	41–50 years	51–60 years
Parents of diabetic children	3.0	10.0	2.0
Control group	2.0	6.0	8.0

TABLE IV

Manifestation of the insulin-non-dependent diabetes and the parents' age

	< 40 years n = 358	> 40 years n = 142
Insulin-non-dependent parents of diabetic children	0.83%	7.7%
	n = 460+	
Controls	0.43%	3.48%

+ At the time of the study the parents were over 40 years of age.

DISCUSSION

The frequency of diabetes increased significantly in the last decades, the rate is around 10% in the 5th decade [13]. Of the diabetics 7 to 36% are diagnosed by screening [9], and even when the diabetic status is estimated under strict conditions, many chemical diabetics are classified as manifest diabetes. These high values are considered irrealistic by several authors [12, 16], as in the majority of cases diagnosed by screening, manifest diabetes could not be proved after 5 years [10]. The number of new cases diagnosed under strict experimental conditions by oral glucose loading is 0.28% and of those by insulin level determination, 0.02% of the population [12]. The 3.5% occurrence in our control group is in close agreement with data in the literature. The manifestation rate of diabetes is estimated at 3% between 45 and 65 years of age, while the population rate of diabetes is 1.5% [11].

Our results revealed a fivefold frequency of juvenile diabetes among the parents of diabetic children as compared to the control group. If there would be no relationship between juvenile and maturity onset diabetes, the rate of appearance in the age group over 40 would be higher among the older parents of the medical students. In spite of this the occurrence of insulin non-dependent diabetes was more than twofold among the parents over 40 years of age of diabetic children.

Oral glucose tolerance tests carried out earlier in parents of diabetic children, showed that 18% of the cases were chemical diabetes [1], and in their first grade relatives chemical diabetes is more frequent than the accepted frequency in the population. This is in agreement with the findings of other authors [3, 6] and confirms the observation of an increased frequency of disturbances of carbohydrate regulation in the family of diabetic children. This means that the danger of manifestation of juvenile diabetes is greater than that of insulin non-dependent diabetes in the family of juvenile type diabetics.

The frequency of manifestation of insulin non-dependent diabetes in the parents of diabetic children was found

to be higher than in the control group. If the distribution according to age is not taken into consideration, the control values appear misleadingly higher than the values found in the parents of the diabetics.

Childhood diabetes is a comparatively rare, while maturity onset diabetes is a frequent, disease. In the Birmingham study [13] the occurrence of diabetes amounted to 2% in the 0—29 year age group, so it was 24fold of the population rate among the first grade relatives of diabetics. In the age group between 70—80 years the rate is 2.1%, but among first grade relatives of diabetics it is only 1.5 times higher than the population rate. Our results are in accordance with these results, if we consider that diabetes was relatively frequent among the sibs of diabetic children.

Diabetes is regarded as a multifactorial disease, but the manifestation of the two types depends on different factors, and juvenile and maturity onset diabetes can be distinguished by the clinical picture and the genetic factors. Obesity is an important risk factor in maturity onset cases, while the juvenile type occurs mainly in lean subjects. The maturity onset type occurs more frequently in families of childhood diabetics, which assuming a polygeneic heredity refers to the fact that there are common diabetoid genes in both types of the disease. This is not a negligible heredity factor. In manifestation of juvenile diabetes B8, Bw15, Dw3 and Dw4 antigens out of the B and D locus of the HLA system have an important role [2, 5]. These factors are without any influence on the manifestation of maturity onset diabetes. The role of autoimmune processes and viral infections as provocative factors of juvenile diabetes are in connection with the above-mentioned factors [8]. Considering the constitutional and genetical factors, diabetes might manifest itself in infancy or early childhood in individuals who incline to juvenile diabetes, and an accumulation of diabetic cases can be expected in their families.

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