

## Glycosylated Haemoglobin and Red Blood Cells in Diabetes

Glycosylated haemoglobin has an increased affinity for oxygen [1], and in diabetics the number of red blood cells has been found to correlate with glycohaemoglobin (GHb) level [2]. If confirmed, this could indicate compensatory polycythaemia resulting from chronic hypoxaemia. We have reviewed in this respect our data relating to 79 adult diabetic males and 48 postmenopausal women, all of them living in the coastal area, non-smokers and suffering from no known heart, lung or blood diseases. No differences were found between patients treated by diet alone, oral drugs or insulin. Blood count was done in the Coulter counter, and GHb was determined by the Biorex 70 column method [3]. Results are presented in the table and show statistically significant but very weak correlation for GHb positively with of red blood cells ( $p = 0.04$ ), and negatively with mean corpuscular volume ( $p = 0.034$ ) in males only.

**Table.** Red blood cells (RBC), haematocrit, mean corpuscular volume (MCV), and glycohaemoglobin (GHb) in diabetics ( $M \pm SD$ )

	Males	Females
RBC, $10^6/\text{mm}^3$	$5.00 \pm 0.488$	$4.58 \pm 0.462$
Haematocrit, %	$44.4 \pm 3.85$	$40.9 \pm 3.77$
MCV $\text{mcm}^3$	$89.4 \pm 4.95$	$89.4 \pm 5.89$

In 21 male patients the tests were repeated after a change in the diabetic control and stabilization of GHb at another level. No significant correlation was found between the changes in GHb on

the one hand and red blood cell number ( $r = -0.274$ ; NS) or MCV ( $r = -0.012$ ; NS) on the other.

Our data do not confirm in this indirect way the chronic hypoxic effect of GHb. The changes in the diabetic control as reflected by GHb were not accompanied by the changes in the opposite direction of MCV or the changes in the same direction of red blood cell number. The unlikelihood of a significant hypoxic effect of increased GHb in human diabetes has been pointed out already by Bunn et al. [2].

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## Prevalence of Permanent Congenital Diabetes Mellitus

The Editor, *Diabetologia*

A recent publication by Crossley in *Diabetologia* furthers our understanding of the epidemiology of juvenile diabetes [1]. Although the increased incidence of juvenile diabetes early in adolescence is well documented in Crossley's and other such reports [2, 3], few if any comment on what appears to be a decreased prevalence seen during the first year of life – especially the number of neonates with a permanent congenital insulin-dependent state.

We have cared for a child who had documented hyperglycaemia within his first twenty-four hours, and who continues to require insulin at the age of three years.

Perinatal history revealed the infant was delivered without complication to a 24-year-old gravida 2, para 2 mother after a 38-week pregnancy marked by glycosuria during the week prior to delivery. Birth weight was 1.950 g, length was 43.5 cm, and Apgar

scores were 6 and 9. The placenta was unremarkable and weighed 510 g.

At 24 h of age, the infant was noted to have 2% glycosuria. Blood glucose was 570 mg/dl and serum electrolytes were normal. An insulin level was  $6 \mu\text{U}/\text{ml}$  and TORCH titres were negative.

Initial treatment consisted of intravenous Ringer lactate and  $1/16$  unit of crystalline insulin administered subcutaneously approximately every 8 h. Daily insulin requirements gradually increased, and the infant was discharged at ten weeks of age on  $3/8$  unit of NPH every 12 h and feedings at 4 h intervals. His weight upon discharge was 2.400 g, length 45.5 cm, and head circumference 36 cm.

The infant's mother was reported to have a normal glucose tolerance test one week after delivery. The remainder of the family history was negative for diabetes or other endocrinopathies.

Developmental milestones were somewhat delayed: the infant sat alone at 10 months, walked at 18 months, and had a limited vocabulary at 18 months. At one year of age, his islet cell antibodies were negative. At three years, the child's diabetes was controlled on 1.5 units of crystalline insulin and 3 units of NPH in the morning, and 1.0 unit of crystalline insulin and 1.5 units of NPH in the evening. His height was 90.0 cm, weight 13.0 kg and head circumference 49.5 cm.

Transient congenital diabetes mellitus seems unlikely since that condition usually resolves within two to three months, with the most prolonged reported case being 18 months [4].

Prior to our case, the youngest known case of juvenile diabetes mellitus was a 60 h infant reported by Greenwood [5]. It is interesting to note that our patient, as well as Greenwood's, was small for gestational age. These two cases and their catch-up growth subsequent to beginning insulin, support the concept of insulin's playing a role in regulating fetal growth [6].

The sparsity of case reports of permanent congenital diabetes mellitus [7, 8, 9], as well as incidence and prevalence studies of juvenile diabetes from various parts of the world, appears to confirm that the lowest prevalence of this condition occurs within the first month of life. In view of the recognized heterogeneity in diabetes mellitus, such observations – although rare – have definite importance in elucidating the aetiology and natural history.

Yours sincerely,

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## Interpretation of the Glucose Tolerance Test

Dear Sir,

The need for meaningful criteria by which to interpret the glucose tolerance test (GTT) has been described by many experts [1–4]. It is the purpose of this letter to describe a flaw in criteria recently recommended by an international workgroup sponsored by the National Diabetes Data Group (NDDG) of the National Institutes of Health [4]. The plasma glucose concentration recommended as diagnostic of overt diabetes is a 2 h value and at least one point between the fasting and 2 h value exceeding 200 mg/100 ml on more than one occasion. The problem is the requirement that the abnormal GTT apply on more than one occasion. The GTT is expensive, inconvenient, and stressful, and many physicians are reluctant to require a repeat performance. Diagnostic decisions are often made on the basis of a single GTT. But the NDDG has no classification for subjects who fulfill the criteria for a diabetic GTT on only one occasion. The NDDG defines impaired glucose tolerance as a single GTT with a 2 h value between 140 and 200 mg/100 ml and one point between the fasting and 2 h value exceeding 200 mg/100 ml. By leaving a gap between criteria for overt diabetes and impaired glucose tolerance, the NDDG has clearly established a borderline area, although ostensibly rejecting attempts to define borderline diabetes. Subjects exhibiting an overt diabetic GTT on only one occasion exist in this borderline area. They cannot be classified as overt diabetics because the GTT was performed only once, and they cannot be classified as having impaired glucose tolerance because the 2 h value exceeds 200 mg per 100 ml. The tendency among many community physicians will be to interpret the single diabetic GTT as diagnostic of overt diabetes. This tendency is indeed fostered by the NDDG which states the criteria for a diabetic GTT in the summary of their report but omits the phrase “on more than one occasion” [4].

The criteria for interpreting the GTT should be clear. If borderline diabetes is to be ignored, the gap between criteria for overt diabetes and impaired glucose tolerance should be removed. Im-

paired glucose tolerance could be defined as anything less than the criteria for an overt diabetic GTT.

Alternatively, the gap between criteria for an overt diabetic GTT and impaired glucose tolerance might be preserved and defined as the criteria for borderline diabetes. Certainly the majority of patients with noninsulin-dependent diabetes pass through a precursor stage of overt disease. Although the GTT is unreliable in detecting this precursor stage, it might be wise to allow for the possibility that the GTT in combination with other tests, such as glycosylated haemoglobin, could detect borderline diabetes with adequate accuracy [5].

Yours sincerely,

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