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GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY IN IRAN AND ITS RELATION TO PHYSIO-PATHOLOGICAL PROCESSES (۞)

I. A Preliminary Report

BY

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The present survey was started in order to map the incidence of glucose – 6 – phosphate dehydrogenase (G – 6 – PD) deficiency in different regions of Iran, to study the disease patterns of the deficient subjects, and to investigate possible therapeutic measures when necessary. This project is the outcome of three separate and independent scientific endeavours .

The first of these is a comparative statistical analysis which suggests that G – 6 -P-D deficient individuals appear to have a lesser probability of developing malignant disease. We have pointed out, however, that no definite conclusion can be drawn from this statistical analysis until a large longitudinal survey has been initiated and followed through for half a generation (1). Biochemical studies carried out concurrently with

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the epidemiological survey show that physiologically and pharmacologi - cally induced changes in glucose metabolism via the pentose phosphate pathway entrain parallel alterations in pentose sugar formation, nucleic acid and protein synthesis, thereby affecting many aspects of cell func - tion including defence, replication and the maintenance of the milieu interieur (2 and 3).

The availability of G - 6 - P-D and the coenzyme TPN will deter - mine to a large extent the response to the body's demand for glucose katabolism through the pentose shunt. In laboratory animals, the decrease of this metabolic route decreases D - ribose production and in turn slows down tumour growth (4). Conversely, local increase in TPNH formation is associated with atherosclerotic changes (5).

The second scientific endeavor was formulated at the First Seminar on Favism held in Teheran in July 1965 under the auspices of the Iranian Ministry of Health. A number of papers were read pointing out the incidence of favism in certain areas of Iran and a continuous increase in the number of hospitalised cases (6). The third was consequent to the initiation of the nation - wide malaria eradication programme, because during the course of this a number of patients taking primaquine de - veloped haemolytic symptoms. In an attempt to ascertain the incidence of the enzyme deficiency in the local population, a judgement sample survey was undertaken in Teheran by S. Hedayat et al (7) of the Institute of Public Health Research where the highest incidence was found among the Jews, 15.23%, followed by the Armenians, 13,39%, and the lowest among the Iranian Muslims, 9.94%.

As a result of the foregoing, it was decided to initiate a combined study which is expected to cover the following points :

1. A full survey of the G - 6 - PD deficiency in different popula - tion groups throughout Iran together with a complete blood picture of those found to be deficient .

For this purpose, Iran has been divided arbitrarily into four areas: (a) Teheran, (b) areas south of the capital, (c) areas west of the capital, and (d) the Caspian littoral. Plans for similar studies in eastern regions will be formulated in the near future.

2. To evaluate the various methods currently in use to test for G - 6 - PD deficiency, and to decide which is most suitable for field work in Iran .

3. To start a registry of the deficients and their families so that these can be followed throughout life for their disease patterns, together with a concurrent control group.

4. To consider therapeutic measures for those conditions which are aggravated by the G - 6 - PD deficiency.

The present report covers only the areas designated as (a) and (b) above. A random sample of the healthy male adult population was taken in each locality. These individuals were tested for G - 6 - PD defi - ciency, their ABO and Rhesus blood groupings done, and their past history of illness recorded. None of them were related by blood or by marriage .

In area (a), Teheran, the deficiency was found to be 6.8 per cent; in area (b), the deficiency in Kazeroun was 8.4 per cent, in Shiraz 9.1 per cent, Esfahan 7.1 per cent, and in the Omman sea area 7 per cent. The survey in Yazd was divided into two groups: Iranian Muslims, who showed a deficiency of 3.5 per cent, and Iranian Zorastrians whose defi - ciency was 3.6 per cent. The distribution of the ABO groupings of the deficient subjects did not differ from the rest of the population; the incidence of group B being between 20 and 30 per cent. This is much higher than the findings in Western Europe where the incidence of group B is about 6 per cent, but where the level of G - 6 - PD deficiency is under one per cent. There were only twenty - two Rhesus negative subjects among the three hundred individuals tested.

The method employed for testing the enzyme deficiency was the methaemglobin reduction test, although in many subjects the Motulsky and Berstein tests were performed for comparison. In all the deficient subjects and a few of the normals a quantitative determination of the enzyme was carried out (see table). For interest, we have also included in the table two post - operative patients, one recovering from gastrectomy for carcinoma and the other from relief of strangulation of umbilical hernia (cases No. 38 and 99).

Twelve deficient subjects had plasma electrolytes, serum bilirubin , alkaline phosphatase, and fasting blood glucose levels estimated. All of these were in the normal range, and investigations on a further series of subjects is in progress. While none of the dificient subjects gave either

a history or symptoms of diabetes and their fasting bloodsugars were normal, eight out of the twelve mentioned above showed a diabetic type of curve in response to glucose tolerance test. Plasma proteins and the albumen globulin ratio were normal in all the deficients, and electro-phoresis of the proteins showed variations within limits. The result of the immunological electrophoresis, the electrophoresis of the isoenzyme, and the detailed study of the haemoglobins as well as other investigations, will be reported later.

In addition to the biochemical tests mentioned above, each patient found to be G-6-PD deficient was recalled and again interviewed in order to obtain a detailed family history. As many members of his family as was practically possible were tested for the enzyme deficiency. In particular we endeavored to test his parents and grandparents, his mother's and his own siblings, his sister's children, his wife and his own children. From these, a geneological tree was drawn which will be published elsewhere.

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It is not proposed at this stage to embark on a discussion of the statistical data and laboratory findings but rather wait until the survey is completed. However, certain clinical observations are worthy of note.

There was only one certain case of death resulting from carcinoma among the families of the deficient subjects. The incidence of cataract, on the other hand, was relatively high, close to 3 per cent.

In areas where malaria is endemic, G-6-PD deficiency was relatively high, about 10 per cent, while in non-malarious regions the deficiency was only between 2 and 3 per cent.

Different ethnic groups in the same locality showed practically no difference in the incidence of deficiency. These populations have been indigenous to the areas for anywhere up to 600 years. Teheran is an exception because the city has quadrupled in the past twenty years by migration into the capital.

The symptoms of favism were confined almost exclusively to children. The youngest case recorded was a breast-fed infant whose mother had ingested fava beans about eight hours previously, but was herself symptom free. Almost all patients were under ten years of age, and several had

had two or three attacks at annual seasonal intervals. In all cases the first attack was the most severe. No adult demonstrated favism; those with haemolytic symptoms had them consequent to the administration of chloramphenicol or primaquine.

In the course of the survey a record card was made for each subject tested; and for each one found to be deficient, a family record card was also started. It is planned to review the deficient subjects annually and record their illnesses on these cards. In due course, when the size and scope of the survey will have enlarged sufficiently, proper statistical analysis of the findings will be possible.

QUANTITATIVE COMPARATIVE ESTIMATIONS OF G-6-P. D. LEVELS IN A SELECTED GROUP OF SUBJECTS

Case No.	G - 6 - PD int. unit	Blood Group	Rh	Hb Gm.%
5+	17.5 D	A	+	—
11+	6.9 D	A	+	—
29+	6.8 D	B	+	—
30	93.9 N	B	+	15.5
35	111.4 N	B	+	14.2
36	114.8 N	B	+	—
37+	13.0 D	A	+	—
38	140.4 P	A	−	13.9
41'	120.0 N	O	+	15.8
42	90.5 N	B	−	13.9
47	112.0 D	B	+	14.7
49+	24.8 D	A	+	14.5
50	111.3 N	O	+	14.9
63	130.5 N	A	+	13.5
64	115.7 N	A	+	15.6
71	109.0 N	AB	+	14.8
91+	16.4 D	A	+	14.0
92	140.3 N	A	+	13.6
93	93.6 N	B	+	15.1
94	119,1 N	A	+	15.3
99	125.7 P	A	+	14.7
100	113.0 N	B	+	13.6

+ = G - 6 - PD deficiency revealed by methaemoglobin reduction test.
D - Deficient
N - Within normal limits
P - Postoperative

SUMMARY

A survey was set up to study the problem of G-6-PD deficiency in Iran. The deficient subjects underwent a detailed haematological investigation, and their geneological tree was drawn and studied. A registry has been started to enable a follow-up of the deficients revealed by the survey. It is proposed to increase the size and scope of the survey by gradual stages so that a statistical analysis of the disease patterns of the deficient subjects can be made. A control group of subjects with normal G-6-PD levels will be studied in parallel.

Sommaire

Une enquete a été organisée pour etudier le probleme de deficience de G-6- P. D en Iran. Des investigations hematologiques detailleés sont faites chez tous les sujets deficients, ainsi que la determination et etude de l'arbre geneologique. En plus un systeme de registration des cas est etabli pour suivre les cas deficients deconverts durant l'enquete. Nous nous proposons d'augmeuter l'etendu de l'enquéte graduellement pour pouvoir faire des analyses statistiques sur les cas deficients ainsi que sur un grope temoin avec des taux normaux de G. 6. P. D.

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