DIABETES IN EAST PAKISTAN

BY

Md. IBRAHIM, M.B., M.R.C.P.

*Professor of Clinical Medicine, Dacca Medical College ;
Officer-in-Charge, Medical Research Centre, East Pakistan
(Under the auspices of Pakistan Medical Research Council)*

Since the advent of oral hypoglycaemic agents in diabetic therapy newer vistas have been opened up in research on diabetes mellitus in regard not only to its management but also to its aetiology and pathogenesis. Peculiarities in the character of diabetes in tropical regions were noted in the early part of this century, and various authors discussed their observations in a symposium in the Section of Tropical Medicine of the British Medical Association's Annual Meeting in 1907 (*British Medical Journal*, 1907). The most significant of these peculiarities were rarity of juvenile diabetes, infrequency of ketosis, and diabetic coma.

During the last decade clinical studies by DeZoysa (1951), Hugh-Jones (1955), and Cosnett (1959) clearly showed that diabetes in the tropics differs widely from that in temperate climates. Different authorities have described various types of diabetes, such as type 1 and type 2 (Lawrence, 1951) and type J (Hugh-Jones, 1955). In a stimulating leading article in the *British Medical Journal* (1959) the types of diabetes were discussed and the need for further studies in the tropics was stressed, concluding with the remark of Sir Harold Himsworth that "a primary deficiency of insulin is only one, and then not the commonest, cause of the diabetic syndrome."

The present paper records the result of a study of 894 cases of diabetes in East Pakistan. As there was no special clinic in the country to deal with these cases, and as illiteracy, poverty, and superstition often made dietary control and insulin treatment difficult or uncertain, a Diabetic Association was organized in the early part of 1956 and arrangements were made to contact as many diabetics as possible by newspapers, seminars, and conferences. A research section was started under the auspices of the Pakistan Medical Research Council in the Medical Research Centre at Dacca, where all the examinations, including repeated glucose-tolerance tests and other relevant biochemical procedures, were done free of cost.

Method and Materials.—The period covers the 28 months from August, 1957, to December, 1959. All the 894 patients were studied in the Medical Research Centre and arrangements were made to call them at regular intervals, fortnightly or monthly, for assessment and glucose-tolerance tests. The procedure of examinations has been fully described (Ibrahim, 1959).

Results

Age-and-Sex Incidence.—Of the 894 patients, 779 (86%) were male and 115 (14%) female. The age at onset of diabetes is shown in the Chart.

Heredity.—A history of diabetes among one or other members of the family was noted in 264 cases (29%). The pattern of hereditary and familial influence as observed in this series is given in Table I.

Body Weight.—This is in agreement with the American Medico-Actuarial Investigation as quoted by Davidson (1957). Table II shows the weight distribution

in various age-groups. Out of 894 cases of the present series, 90 (10%) were overweight, 443 (49.6%) underweight, and 361 (40.4%) of normal weight. This distribution is in conformity with the observations made by Tulloch, Gay, and Irvine (1956) among Jamaican diabetics. As in the present series, many of their patients over the age of 40 were underweight, though in other respects they could be classified under type 2.

Occupation and Social Status.—Diabetes mellitus is more frequent among persons who are of higher social status and are under mental stress and strain, and also among skilled workers with sedentary habits. The occupations of our patients are given in Table III.

Ketosis.—It is really providential, as remarked by Cosnett, that ketosis is rare among East Pakistan diabetics. Diabetic coma is most infrequent among this series in spite of irregularity in treatment. Only 15 out of the 894 cases showed marked ketonuria and signs of precoma on withdrawal of insulin; 30 cases showed temporary ketosis.

TABLE I.—History of Diabetes Mellitus

Father	..	..	..	..	117 cases
Mother	..	..	..	..	36 "
Parents	..	..	..	..	9 "
.. and all siblings	..	..	..	..	44 "
Brothers and sisters	..	..	..	..	17 "
Paternal uncle	..	..	..	..	3 "
Cousins	..	..	..	..	7 "
Paternal grandfather	..	..	..	..	9 "
Maternal	..	..	..	..	13 "
Husband and wife	..	..	..	..	630 "
The patient only	..	..	..	..	

TABLE II.—Distribution of 894 Patients in Relation to Age and Weight

Age:	0-	10-	20-	30-	40-	50-	60-	70-	80-	Total
Overweight		1	5	15	35	27	5	1	1	90
Underweight		10	31	78	113	144	56	11		443
Normal	1	1	8	69	120	108	45	7	2	361

TABLE III.—Distribution of 894 Cases in Relation to Occupation

Business men	..	..	..	..	..	199 cases
Government employees	..	..	..	..	..	357 "
Educationists	..	..	..	..	..	51 "
Medical men	..	..	..	..	..	32 "
Other professional men	..	..	..	..	..	52 "
Skilled workers with sedentary habits	..	..	..	..	..	149 "
Unskilled or semi-skilled workers. Mainly physical	..	..	..	..	..	54 "

Complications.—Other complications, however, are significantly prevalent in all age-groups (Table IV).

Therapeutic Response.—Out of 894 cases, 577 (64.6%) could be controlled with oral hypoglycaemic drugs. A number of cases were controlled by diet for 7 to 10 days. Underweight cases were usually given

TABLE IV.—*Complications of Diabetes Mellitus Encountered Among 894 Patients*

Complications	Type and Criteria	Patients	
		No.	%
Vascular	Hypertension	146	16.3
	Peripheral vascular diseases	13	1.5
	Coronary diseases	14	1.6
	Cerebral vascular diseases	6	0.7
	Retinopathy (specific)	9	1.0
Renal	Without urinary infection, albuminuria	64	7.2
	Kimmelstiel-Wilson syndrome	26	2.9
Infections	Cutaneous and subcutaneous	30	3.4
	Lung abscess	2	0.2
	Pulmonary tuberculosis	34	3.8
	Others	3	0.3
Ketosis	Severe, with no infection	3	0.3
	Mild, with no infection	42	4.7
Neural	Peripheral neuritis	74	8.3
	Cranial nerve affection	1	0.1
Cataracts		28	3.1

diet proportionate to their age and height. Most were put on hypoglycaemic oral therapy after a positive "response test" (with tolbutamide or chlorpropamide).

Clinical Varieties of Diabetes Mellitus

In presenting their analyses Hugh-Jones and Cosnett used scattergrams to classify the different types of diabetes mellitus in Jamaica and Durban respectively. Both made their classification according to the following criteria.

Type 1.—"Severe" diabetes needing insulin to prevent ketosis. Patients are insulin-sensitive and usually underweight. This type of diabetes usually develops before the age of 40, but sometimes in old age (65 or over).

Type 2.—"Mild" diabetes; no ketosis without insulin unless complicated by infection. These patients are often obese, insulin-insensitive, and relatively resistant, but usually do not require insulin when on a suitable diet. They are sometimes cured by weight reduction. Onset occurs in middle or old age; when complicated by infection these cases require insulin and behave temporarily as a clinically different type (2b).

Type J.—Like type 1; these patients, however, are insulin-resistant, require persistently over 80 units a day, and have much less tendency to ketosis; onset in young, usually thin subjects.

Temporary.—Diabetes in young subjects with ketosis, showing apparent spontaneous cure.

Residue.—Anomalous cases often associated with specific endocrine upset.

When attempting to allot the patients in this series it has been found that the majority do not conform to these types. They do not conform to type 1 because they are non-ketotic and not insulin-sensitive, nor to type 2 as most of them are not obese, are not suitable for dietetic treatment, and are not resistant to insulin. In contradiction to the age incidence of type 2 these cases are distributed over a wide age-group (30 to 65). The majority have been controlled by oral hypoglycaemic drugs. These cases might be grouped as type "tropical." Apparently the change in clinico-biochemical pattern is due to a different pathogenesis. The 894 patients in the present series are classified as follows: type tropical, 577; type 1, 15; type 2 (2b and undifferentiated), 298; type J, 4. Table V shows the

distribution of these cases in relation to age, body weight, and therapeutic response (tolbutamide, "diabinese," insulin, and diet).

Discussion

"The more we know about diabetes the less we seem to understand," remarked William Boyd (1958) when discussing the influence of heredity on diabetes. "It would appear that diabetes is present from birth in the form of an inherently defective carbohydrate mechanism which can be triggered off in a variety of ways. The defect may remain in a latent form for many years, but it may be brought to light by various factors, dietetic, hormonal or stress."

I have shown that diabetes in tropical climates varies widely from that of temperate regions. The most important differences lie in the therapeutic response to hypoglycaemic drugs and in the infrequency of ketonuria and coma. Although biological assay could not be done, clinical, biochemical, and therapeutic evidence suggests that these cases do not belong to the group entirely deficient in insulin; in other words, extrapancreatic factors seem to be operative in the pathogenesis of "tropical diabetes."

Kalk (1960), on the basis of histopathological studies of liver biopsies on cases of diabetes mellitus, showed that specific changes occurred in liver-cell nuclei—"vacuolization attributed to the deposition of excessive glycogen": several patients, especially obese ones, although not diabetic, showed changes similar to diabetic fatty liver. Kalk followed these cases for several years and observed that some developed clinical diabetes within one or two years after liver biopsy. A few cases were treated with controlled diet, and none of these developed diabetes. Subsequent liver biopsy showed regression of changes in nuclei and liver cells. Kalk concluded that patients with these characteristic histological features are in a "pre-diabetic phase" of metabolism in which prophylaxis against diabetes can be carried out.

In East Pakistan, owing to dietetic and hygienic factors, helminthiasis (ascariasis, ankylostomiasis), amoebiasis, and peptic ulcer often have a deleterious effect on the liver. Cirrhosis of the liver is a common ailment in this part of the world. The incidence of infectious hepatitis is too high for it to be regarded as an endemic condition. Liver diseases causing changes in the nuclei of liver cells may be the primary factor in this type of diabetes. The resultant metabolic changes may also be related to the disturbance of uric acid metabolism, with destruction or inhibition of beta cells. Prolonged overaction of the beta cells due to predominance of rice in the diet in this area may lead to work-exhaustion and diminished secretion of insulin.

TABLE V.—*Distribution of 894 Patients in Relation to Age, Weight, and Treatment*

Age	Tolbutamide (560)			Diabinese (17)			Insulin (168)			Diet (149)		
	O	U	N	O	U	N	O	U	N	O	U	N
0-10							1	9	1		1	
10-20								18	5	2	4	3
20-30	3	9						16	10	4	9	13
30-40	11	53	45		1			25	8	6	15	23
40-50	21	71	83	2	6	8		30	16	3	25	17
50-60	19	88	73	1	2	5		7	5		10	9
60-70	5	36	29	3	2			2	1		3	2
70-80+	1	6	4									
	1		2									
	61	263	236		6	11	14	107	47	15	67	67

O = Overweight. U = Underweight. N = Normal.

Broadly speaking, diabetics may belong to the entirely insulin-deficient group, in which the onset is usually before maturity, or to a group in which insulin might be sufficient but becomes ineffective owing to the excess of any of a number of hyperglycaemic factors (pituitary, adrenal, glucagon) or to defective storage or release of liver glycogen.

Tropical diabetes appears to be related to liver conditions that disturb the storage and release mechanism of glycogen.

Summary

The pattern of diabetes mellitus in East Pakistan is shown, based on the study of 894 cases in the Medical Research Centre under the auspices of the Pakistan Medical Research Council and the Diabetic Association of Pakistan. They are classified into "tropical diabetes," type 1 and type 2 of Lawrence, and type J of Hugh-Jones. The characteristic features of tropical diabetes, such as infrequency of ketonuria, acidosis, rarity of diabetic coma, and effective therapeutic response with oral hypoglycaemic tablets, are stressed. Relevant literature on diabetes is reviewed and the present conceptions regarding its aetiology and pathogenesis are considered. Diabetes is due either to insulin deficiency or insulin ineffectiveness as a result of overactivity of hyperglycaemic factors such as pituitary, adrenal, and glucagon. It may also be due to obesity and defective storage and release mechanism of liver glycogen. Although biological assay of insulin has not been done, clinical and therapeutic evidence suggests that "tropical diabetes" does not belong to the group entirely deficient in insulin, and that insulin ineffectiveness seems to be related to liver disease due to dietetic, hygienic, or ecological factors. Tropical diabetes may thus be caused by a defect in the storage or release of liver glycogen rather than deficient secretion of insulin. The need for properly controlled and well-organized research on these diabetics is stressed.

REFERENCES

- Boyd, W. (1958). *Pathology for the Physician*, 6th ed., p. 445. Lea and Febiger, Philadelphia.
- Brit. med. J., 1907, 2, 1051.
- 1959, 1, 219.
- Cosnett, J. E. (1959). *Brit. med. J.*, 1, 187.
- Davidson, S. (1957). *The Principles and Practice of Medicine*, 3rd ed., p. 1050. Livingstone, Edinburgh and London.
- DeZoysa, V. P. (1951). *Arch. intern. Med.*, 88, 812.
- Hugh-Jones, P. (1955). *Lancet*, 2, 891.
- Ibrahim, M. (1959). *Pak. J. med. Res.*, 1, 43.
- Kalk, H. (1960). *Germ. med. Monthly*, 5, 81.
- Lawrence, R. D. (1951). *Brit. med. J.*, 1, 373.
- Pyke, D. A. (1956). *Lancet*, 1, 818.
- Tulloch, J. A., Gay, K., and Irvine, R. A. (1956). *W. Indian med. J.*, 5, 256. Quoted by Cosnett (1959).

To help instructors in teaching the "mouth-to-mouth" and "mouth-to-nose" methods of artificial respiration a new film strip has been prepared by the National Dock Labour Board in conjunction with the St. John Ambulance Association. The strip, which has 16 frames and is entitled "Respiratory Resuscitation," has been accepted by the St. Andrew's Ambulance Association and the British Red Cross Society, and lecture notes are supplied. Both strip and lecture notes are based on the new supplement to the *First Aid Manual* dealing with "mouth-to-mouth" resuscitation. The frames, which are numbered serially to correspond with the numbered paragraphs of the lecture notes, may be cut from the strip and mounted in 2 in. by 2 in. slides for use in projectors as separate transparencies. (From Secretary (Visual Aids Section), The St. John Ambulance Association, 10 Grosvenor Crescent, London S.W.1. Price 5s., post free.)

CASE OF FOETAL ANAEMIA DUE TO TRANSPLACENTAL BLEEDING SEEN IN GENERAL PRACTICE

BY

N. L. PAROS, M.B., B.S., D.Obst.R.C.O.G.

General Practitioner, Colchester, Essex

An unexpected complication of an otherwise apparently routine domiciliary obstetric booking which occurred in practice prompts this article. I wonder how often lesser degrees of foetal anaemia, other than cases due to rhesus or other blood-group incompatibility, go unnoticed.

Of all cases of anaemia in the newborn 95% are due to haemolytic anaemia of incompatibility of one sort or another (Rh, ABO, Kell, Duffy, etc.). In the other 5% the anaemias are non-haemolytic; very rarely, they may be due to syphilis or other infections, leukaemia, or neoplasm. The majority are due to neonatal or prenatal haemorrhage (Colebatch *et al.*, 1956). Possible causes as listed by Colebatch are: (1) Haemorrhage due to trauma or from the cord soon after birth. (2) Haemorrhagic disease of the newborn. (3) Placenta praevia, vasa praevia, and other anatomical abnormalities of the placenta, and placental incision during caesarean section. (4) Premature separation of the placenta (abruptio placentae); accidental haemorrhage. (5) Rupture of the cord. (6) Occult bleeding from foetal part of placenta. (I would add here damage to the placenta from high rupture of the membranes during Drew Smythe catheterization, as described in one case by Apley *et al.* (1961).)

Wiener (1948) theorized that some cases of foetal non-haemolytic anaemia might be due to "unapparent haemorrhage from the foetal surface of the placenta into the mother's circulation" and described three cases but without definite serological proof of his hypothesis. Chown (1954) was the first to describe a technique using differential agglutination proving Wiener's theory, though others had described cases which must have had the same cause. Since then Zipursky *et al.* (1959) have described a different technique using acid buffer that does not affect foetal cells but, after staining, leaves adult erythrocytes which appear as "ghosts." This was an adaptation of an observation by Kleihauer *et al.* (1957).

Many cases have been described, but none that can be traced occurred in domiciliary practice, nor did any of the neonates seem to have the degree of anaemia shown in the case described below.

Case Report

The patient was a para-3, gravida-4 aged 25. In her first pregnancy labour had been normal, and the second was complicated only by a very mild toxemia terminating in a spontaneous normal delivery. The third pregnancy, terminating 16 months previously, had been complicated by painful colicky contractions of the uterus in the last month, and to relieve her of these the membranes were ruptured by Drew Smythe catheterization two days after term, the cervix being ripe. Labour ensued in 36 hours and was normal, though the infant had atelectasis of an upper lobe which resolved with antibiotic cover. The expected date