THE DETECTION OF LATENT DIABETES

By JOAN B. WALKER, M.D.

In charge Diabetic Dept., Leicester Royal Infirmary

How far the detection of latent diabetes will reduce the ultimate morbidity and disability caused by the established disease has yet to be proven, but that latent diabetes occurs at all ages has been evident in isolated cases for many years, though the magnitude of the problem has not been fully appreciated. We do not know how far the latent condition gives rise to loss of energy in earlier years. Fatigue or lassitude is the most constant feature of poorly controlled diabetes which, in itself, is a factor no society can afford to ignore, but if these cases can be diagnosed at the earliest possible date, are there any practical methods of preventing the florid diabetic state with its degenerative complications?

It is generally accepted that certain individuals inherit a diabetic factor which may give rise to apparently spontaneous acute diabetes in youth which requires the administration of insulin, but other members of the same family may develop a milder form insidiously in later life with obesity and insulin resistance. In whatever form the disease occurs, in a proportion of cases there seems to be a trigger mechanism needed, such as rapid growth in childhood, endocrine excess at puberty, pregnancy or the menopause, obesity, infection or by some other form of severe or sustained emotional stress. These latter risks are common to us all but only those with the latent condition develop diabetes, so that it would seem rational to find and study the basic make-up of the individuals who may be latent diabetics in a community.

Types of History

It is not uncommon for an elderly patient on his first attendance at the diabetic clinic to say that sugar was found 20 years before but that after a short term of dieting he was 'cured.' However, by the time he is referred there is no doubt about the clinical diagnosis often associated with complicating retinopathy, neuropathy or angopathy.

The recent case of a man, aged sixty, adds to the variety of the tale. Glycosuria was found at life-insurance examination eight years previously when buying a house. A glucose-tolerance test was per-

formed and his curve was reported normal. Now, there has been rapid loss in weight of 2 st. in three months, fatigue, thirst, polyuria and hyperglycaemia. One must ask, was that original curve completely normal and the renal threshold low, or was the patient already partially or intermittently diabetic only shown by a limited rise in blood sugar value?

A third example is that of the woman in late middle age who complains of irritation of the vulva. One is often told that the urine has been tested for sugar with negative results on several occasions before abundant and persistent glycosuria confirms the diagnosis. It is this ill-defined or intermittent onset of diabetes which makes the planning of any research into its detection so complex. How are we to pick up intermittent glycosuria and to correlate it with the blood sugar level?

Diabetes Detection

Diabetes detection has been undertaken more seriously in the United States than anywhere else. 'Diabetes Week' and 'Detection Drives' in certain localities have been undertaken independently with voluntary helpers, sometimes sponsored by the State and sometimes by the American Diabetes Association (MacBryde;¹ Sharkey;² McLoughlin *et al.*;³ Blotner and Marble;⁴ Blotner;⁵ Blotner, Harwood and Marble;⁶ Harwood;⁷ Olmstead *et al.*;⁸ Loube and Alpert⁹). Investigation of this type has a greater appeal in a country where medical examination has to be paid for privately. Very little has so far been done in Britain to obtain a precise picture of the diabetic problem. Burn,¹⁰ in Salford, Andrews,¹¹ in Cornwall, and Cochrane and Miall,¹² in Cardiff, have made studies, but no actual census has even been made of the known diabetics. The figures obtained through the Registrar General's Office^{13, 14} are low, as they are based on limited material.

Methods of Detection

There are six main avenues of approach directed at various groups of people with possibly differing risks through:—1, General Practitioners; 2,

Diabetic Clinics; 3, Local Authority Public Health Departments; 4, Ante-natal Clinics; 5, School, Industrial and Insurance Medical Officers; 6, Planned Survey of an Area.

1. *General Practitioner*

This would seem the natural method of detecting diabetes in all its forms; at present it rests on the initiative of the patient to report early symptoms and to bring urine for examination. If the latter were done regularly twice a year by the 2,000 to 3,000 patients on the doctor's list, as would be necessary to avoid missing early evidence, the doctor's waiting room would be overflowing and bottles of urine would accumulate, get mixed, and not be tested unless special technical help were available.

A pilot survey concerned only with method and not for obtaining statistics on incidence of latent diabetes has already been completed by the College of General Practitioners. Several practices were involved and a sampling method was used. Enzyme test papers in containers ('Clinistix') were distributed to every member of certain families and then returned to be read by the doctor. The work and expense of the organization entailed is considerable and success depends upon the interest of many general practitioners, but this is undoubtedly the right approach to the patient.

The positive glycosurics have to be interviewed and arrangements have to be made for glucose-tolerance tests to be performed, preferably these would be done at a hospital laboratory, but it must be realized that the increase in work would be considerable and might need the appointment of additional technicians or more modern equipment. All the arrangements are most time-consuming to the general practitioner because the individual concerned is not ill and may resent the inconvenience of missing work, and he may fear being found to be diabetic and risk losing his job.

2. *Diabetic Clinic*

It might prove a reasonable proposition to offer the facilities for regular six-monthly urine testing to all first-degree relatives of the diabetics attending a clinic, in the same way as contacts of pulmonary tuberculosis are sought out. Keen¹⁶ reported at the Banting Meeting of the British Diabetic Association, Oxford, 1957, that in 1,201 first-degree relatives of diabetics, glycosuria was found in 24.6 per cent., significantly higher than the incidence of 14.9 per cent. in 531 control relatives without a family history of diabetes, and the distribution of blood sugar values in the two groups showed a predominance of diabetic relatives at the higher levels.

Conn^{16, 17} uses a standard cortisone glucose-

tolerance test to separate the non-diabetic relatives of diabetics into groups which are different from those found when the test is applied to people with no known family history of diabetes.

It seems obvious that in searching for the latent case we should start through the families of the known diabetics. Diabetic clinics throughout the country are working to capacity and this investigation could not be undertaken without increase in staff and technical facilities. It might be reasonable to do this work in conjunction with the general practitioner service limiting it at first to relatives of known diabetics.

3. *Public Health Departments*

Burn,¹⁰ in 1951, 1952 and 1955, made surveys in Salford by inviting the public over the age of fifteen to bring specimens of urine to a centre for testing at the time they attended for mass radiography. The response was 47.3 per cent. It seems possible that greater publicity and education and the setting up of centres to which people might take a post-prandial specimen of urine regularly twice a year, and where standard glucose-tolerance tests could be performed on any positive case, would give a simple and effective method of detection. It should be no more difficult than mass chest radiography, which has paid such excellent dividends, but it requires a special organization.

Much has been done by the Federal Security Agency in the U.S.A., together with the American Diabetes Association and the American Dietetic Association, to inform the public about diabetes during the National Diabetes Week each November, and at public health centres at other times.

4. *Ante- and Post-natal Clinics*

The care of the expectant mother has improved to such an extent that urine testing for albumen and sugar is almost universal, but the significance of glycosuria is not easy to interpret, and it is not always appreciated that a glucose-tolerance test is merited. The curves obtained will be found to fall into three groups, normal, where the renal threshold is lowered, diabetic, and intermediate. If a pure glucose method of blood sugar estimation is used, one may take the arbitrary values above 160 mg. per cent. at one hour, 140 mg. per cent. at one and a half hours, and 120 mg. per cent. at two hours to be indicative of possible diabetes and the case requires close scrutiny, the family history, history of previous pregnancies and size of the babies, and the mother's own weight increase must be assessed. Jackson,^{18, 19} Jackson and Woolf,²⁰ and Hoet and Lukens²¹ first drew attention to the increasing size of the babies in successive pregnancies associated with latent diabetes, and to a

great extent this appears to be so, but what determines the onset of frank diabetes is obscure; it may occur during the pregnancy, soon after, or years later, and is usually associated with increasing obesity of the woman.

To keep careful clinic records of birth weights, glycosuria of pregnancy, and any variation from the standard glucose-tolerance curve during the pregnancy and after the puerperium, or after lactation is justified, and the data in each case should be carefully assessed and its significance be made known to the patient and to her doctor for continued observation.

5. *Industrial and School Medical Officers*

Industrial and school medical officers and those of life insurance companies have opportunities for detecting latent diabetes, but their findings would be of greater significance if the follow-up of the cases found could be recorded. After referral to their own doctor the case is often closed, so that no further information which could be used statistically is available, nor is the case always followed clinically, but with liaison between the medical officers and the general practitioners much valuable material could be obtained and better preventive work accomplished. Up to the present only the undoubted diabetics have been followed.

6. *Survey of an Area*

It was in the original survey of Oxford, Massachusetts, made by Wilkerson and Krall²² in 1947, that, when searching for diabetes, they found as many previously undiagnosed cases as those already known. These findings were confirmed by Kenny, Chute and Best^{23, 24} in their surveys of three Canadian communities in 1951 and 1953. Cochrane and Miall¹¹ found a rather higher proportion of undiagnosed diabetes in their studies in South Wales, 1956.

A comparable survey, to be reported in full elsewhere, has now been made in a Midland village with a static population of 5,405 (1951 census) where fewer than 50 persons come into or leave the village annually, due to its multiple occupations, coal mines, brickworks, agriculture, light industry, home industry, clerical and domestic work.

The general practitioners in the area were already interested in epidemiology, and most of the diabetics living in the village were under the supervision of the diabetic clinic 15 miles away. It thus appeared a suitable locality to study.

AIMS OF THE SURVEY

1. To establish exactly the number of diabetics in a natural area where the population is static.

2. To discover the undiagnosed cases of diabetes.

3. To correlate the families and to investigate the possible hereditary factors.

4. To investigate the possible aetiological factors of (a) stress, (b) diet, (c) occupation.

5. To begin a follow-up survey of any case of diabetes discovered by the research and, if possible, plan to keep these records for 20 years.

6. To repeat the whole survey (a) in the same area, (b) in another area for comparison or control.

THE TEAM AND THE FIELDWORK

The team was composed of three field workers and a technician, with an ex-almoner as observer and honorary photographer. The first was a health visitor, who had previously held a 12 months' appointment attached to the diabetic clinic. She worked for 10 months. The two senior dietitians, who joined the team later, worked for 5½ and 4½ months respectively. The village was surveyed in 20 man-power months between May 1, 1957, and July 1958.

Preliminary contacts were made in the village, and leaflets explaining the project were taken home by the school children, handed out by the doctors in their surgeries, and also distributed through the district nurses and local health visitor, through the Miners' Welfare Association and Townswomen's Guild.

The field workers inevitably called twice at every house, using the complete electoral roll as their target. A pro-forma was partly filled in at the first visit, which acted as a pivot for conversation. Everyone was asked to pass urine before the tea meal and discard it, to add two extra teaspoonfuls of sugar to the meal and save the specimen passed an hour later in the labelled bottle supplied. When the field worker returned next day, she tested all the specimens in view of the family by an enzyme method (Clinistix). The final details were entered on the form and, if sugar was present, the individual was asked to attend at a centre in the village for a standard glucose-tolerance test. Arranging the glucose-tolerance curve sessions in the village was very time-consuming and often disappointing, but, to differentiate the significance of the glycosuria, it is an essential part of the investigation. The true blood glucose method of Asatoor and King²⁵ was used. Capillary blood was taken by the technician into isotonic sodium sulphate-copper sulphate solution and the protein precipitated by sodium tungstate. At this stage the tubes were transported to the laboratory 15 miles away and the estimation was completed in the afternoon. That the glucose-tolerance curves showed a continuous gradation from diabetic to normal made it difficult to decide on the spot how

to report them to the awaiting villagers. However, they and their doctors were informed without delay and appropriate dietetic care was instituted.

FIRST FINDINGS

Eighty-one per cent. of the inhabitants over the age of five years allowed themselves to be investigated; 2,071 males, 2,034 females. There were eight male and 24 female diabetics already diagnosed, plus a boy under five years old (0.8 per cent.). In addition, 105 males and 62 females showed post-prandial glycosuria (4 per cent.). All but 25 submitted to blood sugar examination, and it is probable that the total diabetics in the village amount to 1.5 per cent. of the population examined.

The glucose-tolerance curves obtained show a gradual change from normal to undoubted diabetic. We have arbitrarily divided them into three groups: 1, high or newly diagnosed diabetics; 2, intermediate or pre- or partial diabetics; 3, normal. A comparison of certain factors in the affected and in the unaffected population shows trends that seem to follow the grading of the glucose-tolerance curves to some extent. Which

also appears to follow the rise in age. The sex distribution ratio changed; in the newly-found glycosurics of the younger age group there were twice as many males as females; in the newly-diagnosed diabetics, about equal, 11 m. : 14 f., but the known diabetics were in the proportion of three females to one male.

One is tempted to relate the high incidence of diabetic women to their parity. All the 38 women diabetics were married. Only one was nulliparous. Of the 12 women showing intermediate types of glucose-tolerance curves, 10 were married and all had borne children. The other two were under 16 years of age.

A family history of diabetes was obtained in 13.2 per cent. of the non-affected population; in 19 per cent. of all the newly-found glycosurics; in 24 per cent. of the new diabetics; in 48 per cent. of the established diabetics.

In studying the physique of the population, the incidence of obesity is higher in the affected population, but it was not possible to get accurate diet histories and no correlation is shown between physique and diet habits.

IBSTOCK SURVEY, 1957-58
(Population : 5,405 (1951 Census))

SEX AND AGE DISTRIBUTION OF GLYCOSURIA AND DIABETES OF POPULATION TESTED FOR GLYCOSURIA

Age Sex	5-14		15-24		25-34		35-44		45-54		55-64		65-74		75-79		80+		Totals		Both	%
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.		
Total examined ..	435	397	288	284	278	270	330	330	333	313	221	218	121	146	37	50	28	26	2,071	2,034	4,105	81%
	832		572		548		660		646		439		267		87		54					
A. Unaffected ..	431	391	274	273	266	264	307	318	311	301	200	198	110	133	34	47	25	23	1,958	1,948	3,906	
B. Known diabetes ..	1*	—	3	—	1	—	—	1	—	4	2	10	2	7	—	1	—	1	8	24	32	} Total affected, 199 4.84%
C. Discovered glycosurics	4	6	11	11	11	6	23	11	22	8	19	10	9	6	3	2	3	2	105	62	167	
	1%		3.7%		3.3%		5.1%		4.6%		6.4%		5.6%		7.0%							
C. (a) New diabetes ..	—	—	—	—	—	—	1	2	3	2	3	5	1	3	3	1	—	1	11	14	25	0.6%
(b) Intermediate ..	1	1	2	1	3	1	8	4	5	3	6	1	4	—	—	1	—	—	30	12	42	1.0%
(c) Normal G.T.T. ...	3	5	6	8	6	5	14	4	11	2	6	2	1	1	—	1	1	1	48	27	75	1.8%
(d) No G.T.T. ..	—	—	3	2	2	—	—	1	3	1	4	2	3	2	—	—	1	1	16	9	25	
Possible diabetes in C (d)	—	—	—	—	—	—	—	—	1	—	—	2	1	1	—	—	—	—	2	3	5	
Total confirmed diabetes	1*	—	3	—	1	—	1	3	3	6	5	15	3	10	3	2	—	2	19	38	57	
																			91%	1.86%	1.39%	of population tested

Total diabetes in Ibstock estimated at 1.5%.

* Under 5 years.

History of stress, such as personal or family illness, domestic or financial anxiety or trouble at work was obtained in 23 per cent. of unaffected males, 40 per cent. unaffected females; 50 and 73 per cent. respectively in the newly diagnosed diabetics. I do not, at this stage, present these figures as statistical evidence, but as an impression made from information gathered by experienced field workers.

Conclusion

From the first somewhat superficial examination of the material obtained by the survey of an English village sponsored and aided by the British Diabetic Association, there is confirmation of the findings of workers using other methods. From the practical aspect of detection there seems to be need for integration between the family doctor, the diabetic clinic, the ante-natal clinic, the public health department, and research teams to share the burden and responsibility.

It appears important to find out more about the genetic pattern of inheritance, to observe whether time alone turns latent diabetes into the irreversible condition. It is necessary to know more about the actual health of the latent diabetic, whether or not there is significant loss of efficiency at the time he or she is latent and whether it is proper to continue to ignore this phase until symptoms are prominent. It would be of value to ascertain whether dietetic control of obesity during this phase would alter absolutely or delay the onset of symptomatic diabetes. There seems particular reason to observe the parous woman, her own weight and the size of her infant.

Until we have more evidence such as might be obtainable over a period of 10, 20, or 30 years by continuous observation of two or three static natural communities, the answers will possibly evade us.

Acknowledgement

The field work of the British survey was undertaken by Muriel Blacklock, S.R.N., health visitor, Helen Donald, B.Sc.Lond., M.A.Toron., dietitian, Emily Hope-Johnston, S.R.N., dietitian. Ann Richards, A.I.M.C.T., undertook the biochemical estimations and we are indebted to Messrs. Ames & Co. who kindly supplied the testing material and gave financial support.

REFERENCES

1. MACBRYDE, C. M. (1949), *J. Mo. med. Ass.*, **41**, 776.
2. SHARKEY, T. P., et al. (1950), *J. Amer. med. Ass.*, **144**, 914.
3. MCLOUGHLIN, C. J., PETRIE, L. M., and FETZ, R. H. (1951), *J. med. Ass. Georgia*, **40**, 285.
4. BLOTNER, H., and MARBLE, A. (1951), *New Engl. J. Med.*, **245**, 567.
5. BLOTNER, H. (1953), *Diabetes*, **2**, 1.
6. BLOTNER, H., HARWOOD, R., and MARBLE, A. (1951), *New Engl. J. Med.*, **245**, 147; (1952), **246**, 520.
7. HARWOOD, R. (1953), *Diabetes*, **2**, 43, 46.
8. OLMSTEAD, W. H., DREY, N. W., AGRESS, H., and ROBERTS, H. K. (1953), *Ibid.*, **2**, 37, 42.
9. LOUBE, S. D., and ALPERT, L. K. (1954), *Ibid.*, **3**, 274.
10. BURN, J. L. (1956), *Med. Offr*, **96**, July 5.
11. ANDREWS, C. T. (1957), *Brit. med. J.*, **1**, 427.
12. COCHRANE, A. L., and MIAL, W. E. (1956), *Proc. roy. Soc. Med.*, **49**, 5, 261.
13. 'Registrar-General's Statistical Review of England and Wales for the year 1954,' H.M.S.O., London.
14. GENERAL REGISTER OFFICE (1956), 'Studies on Medical and Population Subjects,' No. 9, H.M.S.O., London.
15. KEEN, H. (1957), Lecture, Banting Memorial Meeting, Oxford.
16. CONN, J. W. (1948), *Proc. Amer. Diabetes Ass.*, **8**, 213.
17. CONN, J. W. (1958), *Diabetes*, **7**, 446.
18. JACKSON, W. P. U. (1955), *Lancet*, **ii**, 625.
19. JACKSON, W. P. U. (1958), *Diabetes*, **7**, 446.
20. JACKSON, W. P. U., and WOOLF (1957), *Lancet*, **i**, 614.
21. HOET, J. P., and LUKENS, F. D. W. (1954), *Diabetes*, **3**, 1.
22. WILKERSON, H. L. C., and KRALL, L. P. (1947), *J. Amer. med. Ass.*, **135**, 209.
23. KENNY, A. J., CHUTE, A. L., and BEST, C. H. (1951), *Canad. med. Ass. J.*, **65**, 233.
24. KENNY, A. J., and CHUTE, A. L. (1953), *Diabetes*, **2**, 187.
25. ASATOOR, A., and KING, E. J. (1956), 'Micro-Analysis in Medical Biochemistry,' J. & A. Churchill Ltd., London, 3rd edition, p. 25.

NOTICE OF SPECIAL INTEREST TO SUBSCRIBERS:

'WHY NOT HAVE YOUR COPIES OF THIS JOURNAL BOUND INTO YEARLY VOLUMES?'

You can have your twelve monthly issues fully bound in dark green pin head cloth, lettered in gilt on spine with name of Journal, Volume Number and year, complete with index at front, for 22s. 6d. post free. A limited number of out of print journals are available to bind into volumes and make your library complete. Price on application giving details of issues required to complete back volumes.

THE FELLOWSHIP OF POSTGRADUATE MEDICINE

60 PORTLAND PLACE, LONDON, W.1

**WHY NOT
HAVE YOUR
JOURNALS
BOUND ?**