Diabetes Screening during Pregnancy

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Summary. A study was undertaken to determine the most suitable method of screening for diabetes during pregnancy. Glycosuria was compared with blood sugar estimations measured by the Autoanalyser Technique, and a rapid enzyme-strip paper-Dextrostix. Based on the results of approximately 2000 tests, it could be concluded that glycosuria is unsuitable for diabetes screening since it is subject to a high degree of error. Blood sugar estimations on blood taken 2 h following a 100 g glucose load were much more reliable, and could be accurately assessed by the Dextrostix test reagent. The need for diabetes screening programmes during pregnancy is discussed.

Dépistage du diabète au cours de la grossesse

Résumé. Une étude a été entreprise pour déterminer la méthode la plus appropriée pour le dépistage du diabète au cours de la grossesse. La glycosurie a été comparée avec les valeurs de la glycémie mesurée par la technique de l'autoanalyseur et par une bande de papier Dextrostix imprégné d'enzyme. En se basant sur les résultats de 2000 tests environ, on a pu conclure que la glycosurie n'est pas appropriée pour le dépistage du diabète, car elle est sujette à une forte proportion d'erreur. Les valeurs de la glycémie, mesurées sur du sang prélevé 2 h après une charge en glucose de 100 g, étaient bien

plus sûres, et pouvaient être déterminées de façon précise par le test au Dextrostix. La nécessité de programmes de dépistage du diabète pendant la grossesse est discutée.

Reihenuntersuchungen auf Diabetes während der Schwangerschaft

Zusammenfassung. Mit dieser Studie sollte das geeignetste Verfahren für Diabetes-Reihenuntersuchungen während der Schwangerschaft ermittelt werden. Die Harnzuckerausscheidung wurde mit Blutzuckerspiegeln verglichen, wie sie sich mit Hilfe des Autoanalyzers und des enzymatischen Blutzucker-Teststreifens Dextrostix ergaben. Die Ergebnisse von etwa 2000 Untersuchungen weisen darauf hin, daß sich die Harnzuckerausscheidung als Suchmethode für Diabetes nicht eignet, da sie eine erhebliche Fehlerbreite aufweist. Messungen der Blutzuckerwerte 2 Std nach Zufuhr von 100 g Glucose waren wesentlich verlässlicher und konnten mit dem Dextrostix Streifen ausreichend genau abgeschätzt werden. Es wird diskutiert, wie weit Diabetes-Suchaktionen während der Schwangerschaft erforderlich sind.

Key-words: Pregnant diabetic, diabetes detection, glycosuria, blood sugar analysis.

Recent population surveys [2, 12, 6], have indicated that the traditional approach to the detection of asymptomatic or latent diabetes — urinalysis — is subject to a high degree of error. This was confirmed in a recent study in our own unit [20] when it was noted that no fewer than 35% of established diabetics presented with aglycosuria, whereas only 18.4 per cent of pregnant subjects with glycosuria were found to have abnormal glucose tolerance tests.

It was therefore decided to determine the most suitable method of screening for diabetes during pregnancy, and to evaluate whether "Dextrostix" (Ames) — a rapid enzyme-strip for estimating blood sugar — would fulfil the requirements of such a programme.

Method and Materials

"Dextrostix" is a paper strip impregnated with a buffered mixture of glucose oxidase, peroxidase and a chromogen system, and coated with a semi-permeable membrane. The technique simply involves the application of a drop of blood to the active end of the paper strip for exactly 60 sec, after which it is washed off in a jet cold water. The colour change is then compared with a graded colour chart which has shades and values

varying from a pale grey (equivalent to 40 mg of glucose/100 ml) to a dark blue (equivalent to 200 mg of glucose/100 ml). The samples of blood were obtained either by a stab-wound in the fingertip, or by venepuncture. Control, "true" blood sugar values were measured by the Technicon Autoanalyser method [8], and the urine samples were tested for glucose with glucose oxidase test papers.

To minimize the element of observer-error, the results of the Dextrostix determinations were assessed by two persons only — a trained technician, and a recently matriculated but inexperienced laboratory assistant. The Auto-analyser values were obtained from the central laboratory of the King Edward VIII Hospital, and the results were therefore not known to the observers until the strip estimate had been recorded.

Based on previous experience [20, 25] it was decided to assess normality according to the following criteria:

a) *True blood sugar* — 2 h post prandial or post glucose values of 140 mg/100 ml or more, were classified as "diabetic": values between 120—140 mg/100 ml as "suspect" and values below 120 mg/100 ml as "normal".

b) *Dextrostix* — 2 h post prandial or post glucose values 150 mg/100 ml or more were regarded as "diabetic"; between 130—150 mg/100 ml as "suspect" and below 130 mg/100 ml as "normal".

A total of 2000 tests were performed on approximately 1500 African and Indian women, all of whom had attended the University of Natal's Antenatal Unit, at the King Edward VIII Hospital, Durban.

Results

Screening Procedures during Pregnancy

1. Random Sample Survey: As a preliminary screening survey a hundred pregnant women chosen at random, had urine and capillary blood samples tested for glucose. The results are reflected in Table 1, and

Table 1. Random urinalysis compared with dextrostix determinations of blood glucose in 100 unselected pregnant Natal Indians

	Negative 130	Suspect 130–150	Positive 150
Blood Sugar mg/100 ml			
Glycosuria 'Dextrostix'	NIL 76	1 21	NIL 3

show that whereas 21 patients had Dextrostix blood sugar levels between 130–150 mg/100 ml (i.e. in the "suspect range" of abnormality) only one had evidence of glycosuria. The same was true of the three diabetics that were detected, all of whom were aglycosuric.

These results thus confirmed our previous studies [20] regarding the discrepancy between urinalysis and blood sugar estimation in diabetes screening surveys during pregnancy, and served to emphasize the need for a more reliable screening programme.

2. Carbohydrate Load: Patients (including a number of diabetics) from the lying-in-wards were tested on 2 consecutive days in the fasting state, two hours after the ingestion of 100 g of glucose, and 2 h after the main meal of the day (lunch). The caloric value of the meal closely approximated to that of the glucose load. Based on "true" blood sugar values, it can be seen from Table 2

Table 2. Diabetic 'screening' and carbohydrate load, a comparison in 154 pregnant subjects

Load	"True" Blood sugar >140 mg/100 ml	"True" Blood sugar <140 mg/100 ml
Fasting	6	148
2 h Post Prandial	9 ^a	145
2 h Post Glucose	31	123

^a one false positive.

that only 6 of the fasting specimens would have been classified as diabetic, compared with 8 following the meal, and 31 after the glucose load — a difference of definite statistical significance ($p = < 0.01$).

3. Carbohydrate Load and Method of Screening:

A comparison of the carbohydrate load with the various methods used in the screening survey (Table 3), revealed that of the 450 tests performed, urinalysis gave erroneous results in 43 instances, Dextrostix in 11, and the autoanalyser values proved to be wrong in 8 patients. Although most of the discrepancies occurred in the post-glucose group, it was decided that the rest of the survey should be based on glucose-primed patients, since the objective of this study was to define a technique for the detection of the greatest and not the least number of women with suspect or latent diabetes (cf. Table 2).

4. 50 versus 100 g Loading Dose: It has been suggested that the stress of 100 g of glucose during pregnancy is excessive and produces a large number of false positive results [10]. To ascertain whether this was of any significance during screening-surveys, patients who had been given 50 g and 100 g glucose loads were compared (Table 4). The pattern of abnormality among the African women was highly similar, with only a slight (but not significant) increase in the percentage of patients in the suspect and diabetic groups following the 100 g glucose load. However, among the Indian subjects, a greater number of diabetics were detected following the smaller 50 g dose — 9.8% compared with 1.4% — indicating that the type of patient screened is probably more significant than the stimulating glucose load.

5. 2-h versus 3-h Post Glucose Values: The 2 h post glucose interval was chosen for this study as values of normality had been previously determined on this basis [20]. However, to establish whether a 3 h period would improve the sensitivity and specificity of Dextrostix as a screening medium, a number of patients were tested at 2 and 3 h intervals following the usual 100 g glucose load.

The results were assessed according to two criteria, namely a) the difference in mg/100 ml between the 2 and 3 h blood sugar levels, and b) the difference, if any, in the classification of patients into normal, suspect and diabetic categories. As anticipated, the 3 h blood sugar values were usually (although not invariably) lower. Nevertheless, no fewer than 61.0% of the determinations were within 10 mg/100 ml, and 82.5% within 20 mg/100 ml of each other, with the result that the sensitivity and specificity at the two time intervals were almost identical (Table 5). A more noticeable feature of this aspect of the study, was the increased tendency of patients to default before completion of the longer 3 h test.

6. A Racial Comparison. Tables 6 and 7 provide a summary of the results obtained after screening two

groups of unselected pregnant African and Indian subjects. All had received 100 g of glucose prior to the assessment of capillary blood and freshly voided specimens of urine. The two racial groups responded in a similar fashion, 12.2% of the Africans and 11.2%

detected had glycosuria subsequent to the glucose load but *not* in the fasting state.

Based on the results of the preceding investigations, it was concluded that the most efficient method of screening for diabetes during pregnancy is by

Table 3. *A comparison of the 'method' and 'load' in diabetic screening surveys*

	Fasting State		Post Prandial		Post Glucose	
	False +	False -	False +	False -	False +	False -
Urinalysis	4	5	5	2	13	14
Dextrostix	0	1	2	0	8	0
Autoanalyser	0	0	1	4	1	2
Total Number of Tests Performed:	450					
False Results:	Urinalysis 43;		Dextrostix 11;		Autoanalyser 8	

Table 4. *A comparison of 100 g and 50 g loading doses for diabetic screening purposes*

	Dose	Blood Sugar mg/100 ml	<130	130—150	150+
African No.					
300	100 g		71.9%	27.0%	1.9%
305	50 g		73.7%	25.6%	0.7%
Indian No.					
200	100 g		61.1%	37.5%	1.4%
231	50 g		50.0%	40.2%	9.8%

Table 5. *Diabetic screening survey 2 h vs 3 h postglucose values*

Difference in Blood Sugar Levels	<10 mg/100 ml	10—20 mg/100 ml	20—30 mg/100 ml	30+ mg/100 ml
%	61.0	21.5	10.0	7.5
Classification	Normal	Suspect	Diabetic	
2 h	179	19	2	
3 h	183	15	2	

Table 6. *Diabetic screening survey following 100 g glucose load in 285 pregnant African subjects*

Blood Sugar mg/100 ml	Negative <130	Suspect 130—150	Positive 150+
Glycosuria	25	14	3
Dextrostix	205	77	3
False Positives:	12.2%	on urinalysis	
False Negative:	81.8%		

Table 7. *Diabetic screening survey following 100 g glucose load in 208 pregnant Indians*

Blood Sugar mg/100 ml	Negative <130	Suspect 130—150	Positive 150
Glycosuria	14	38	3
Dextrostix	127	78	3
False Positives:	11.2%	on urinalysis	
False Negatives:	51.3%		

of the Indians exhibiting glycosuria in the presence of normoglycaemia. Of possibly even greater significance, however, was the absence of glycosuria in the "suspect" groups — 81.8% and 51.3% for the African and Indian groups respectively. The six diabetics that were

measuring blood sugar levels 2 h following a 100 g glucose load. To assess further the accuracy and reliability of Dextrostix for this purpose, three more comparative tests were performed.

Dextrostix as a screening Device

1. *Comparison with Autoanalyser Determinations:* Single Dextrostix and Autoanalyser determinations were performed on the same specimens of blood, and the specificity and sensitivity of the techniques compared. Based on previously mentioned criteria (see before: Table 8) the Dextrostix estimates yielded erroneous results in 2.4% of the 450 tests performed,

range was 27.7 and 23.7%, and where the difference exceeded 20 mg/100 ml, 7.5 and 9.3%.

3. *Experience and Training:* It was the author's clinical impression that inaccuracies in the interpretation of Dextrostix values were more frequently related to a lack of the observer's experience, than with the test medium itself. This hypothesis proved to be correct when the values obtained by a trained and those by an

Table 8. *Reliability of dextrostix as a screening device compared with single autoanalyser determinations*

Classification			
Dextrostix	<130 Normal	130–150 Suspect	>150 Diabetic
Autoanalyser	<120 Normal	120–140 Suspect	>140 Diabetic
		Dextrostix	Autanalyser
False Positive:		10	2
False Negative:		1	6
Failure Rate in 450 Tests:		2.4%	1.7%

compared with a 1.7% incidence of Autoanalyser results — a difference of no statistical significance ($p = > 0.01$).

When the differences between the two methods were measured in mg/100 ml (Fig. 1), 64.8% of the values were found to be within 10 mg/100 ml of each other, 27.7% were between 10–20 mg/100 ml, and the difference exceeded 20 mg/100 ml in only 7.5% of the estimates.

Fig. 1. Reliability of dextrostix as a screening device compared with single autoanalyser determinations

2. *Venous and Capillary Blood:* A further group of patients was tested to determine whether the Dextrostix assessment of capillary blood was associated with a lesser or greater degree of accuracy when compared with Dextrostix estimates made on venous blood samples. To serve as a control, "true" venous blood sugar values were determined on the Autoanalyser. Reference to Table 9 shows that the values obtained were almost identical. Thus a difference of 10 mg/100 ml or less between the Dextrostix and control values was observed in 64.8% of the venous blood samples compared with 67.0% of the capillary blood samples. The respective percentages in the 10–20 mg/100 ml

untrained observer were compared (Table 10). Thus only 37.9% of the untrained observer's initial 150 results were within the 10 mg/100 ml difference range (when compared with control autoanalyser tested specimens), the degree of accuracy improving to 51.4% with his second 150 determinations. The equivalent result achieved by the trained technician was 64.8%.

A consistent feature of this comparison was the number of assessments which occurred in 10–20 mg/100 ml difference-range — approximately 30% — irrespective of the observer's experience or training. On further analysis it was found that the majority of these errors occurred at the two extremes of the Dextrostix range — values above 180 mg/100 ml being invariably underestimated, whereas values in the lower range were overestimated. It is pertinent to note, that despite these differences, the classification of patients into normal, suspect and diabetic groups was not affected to any significant degree.

Discussion

Are Diabetes Surveys justified?

The detection of diabetes is only of value if it will lead to an improvement in the health of the persons concerned.

In the non-pregnant subject, there is much evidence to suggest that even minor elevations of blood sugar are associated with an increased tendency to arterial disease [3], and furthermore, diabetes (even when asymptomatic) is rapidly becoming the commonest single cause for the registration of defective vision [29]; is responsible for chronic renal disease and peripheral neuritis [13]; and contributes significantly to the pathogenesis and morbidity resulting from increased cardiovascular disease [22].

A recent follow-up of subjects screened in the original Birmingham survey has shown that even minor abnormalities in glucose tolerance are of importance, since no fewer than 20% of such patients, when retested

that screening for diabetes by enzyme-tested urinalyses is a wasteful procedure. This is particularly true of the pregnant subject, and is due to a decreased tubular reabsorption of glucose combined with an increased

Table 9. *Reliability of dextrostix as a diabetic screening device*

Difference in mg%	Venous vs Capillary Blood (295 Determinations)	
	Dextrostix/Autoanalyser Venous/Venous %	Dextrostix/Autoanalyser Capillary/Venous %
0-10	64.8	67.0
10-20	27.7	23.7
20+	7.5	9.3

Table 10. *Reliability of Dextrostix as a diabetic screening device*

Difference in mg%	Training and Experience		
	Untrained (300 Determinations)		Trained (224 Determinations)
	1st 150 %	2nd 150 %	%
0-10	37.9	51.4	64.8
10-20	27.2	30.0	27.7
20+	34.9	17.6	7.5

5 years later, had "florid" diabetes [17]. This observation is of importance because the early use of sulphonyl-urea therapy may result in a long-term improvement of the diabetic state [4, 26] and it has even been suggested that careful treatment by present day methods, will delay if not prevent, diabetic angiopathy [7].

Although some authorities have failed to find an increase in the foetal loss during the prediabetic period [18, 5], a recent survey of the literature has produced convincing evidence that a high perinatal mortality rate — approaching 50% of all births in some series — commonly occurs at this time [14]. This finding has been confirmed recently by both Jackson and his associates [11] and ourselves [21]. In our own series (Table 11), the previous perinatal loss in patients with "recently" diagnosed and "established" diabetes was significantly greater than in a non-diabetic control group.

There is therefore abundant reason to detect even the mildest form of maternal diabetes, for not only will treatment of such a state result in an improvement in foetal survival [1], but pregnancy, by virtue of its diabetogenic influence will bring evidence of latent diabetes (and its associated complications) to the fore, and so allow for possible prophylactic or preventative therapy.

Methods of diabetic Screening

Glycosuria of Pregnancy: The results of recent population [2, 12] and other surveys [6, 20] have indicated

Table 11. *A comparison of the previous obstetrical histories in normal controls, "recently diagnosed", "established" diabetics, and positive screenings in the present series*

	Abortions	Neonatal Deaths	Stillbirths
Normal Controls	8.3%	1.6%	3.3%
"Recently" Diagnosed Diabetics	23.6%	7.8%	25.8%
"Established" Diabetics	22.8%	17.7%	34.3%
Dextrostix Survey Positive Screenings	9.0%	9.0%	13.6%

glomerular filtration rate. Thus, depending upon the method of analysis and the glucose load, it has been established [6] that between 16.2 to 90% of pregnant women will demonstrate evidence of sugar in the urine. These findings were confirmed in a personal series [21] when no fewer than 21.5% of pregnant patients had glycosuria compared with 2% in a non-pregnant control group.

The high percentage of false positives obtained on urinalysis in the present series (see Table 3) is probably accounted for by a similar mechanism.

Blood Sugar Analysis: The method of choice for screening of diabetes (particularly during pregnancy) is the measurement of the blood sugar after a glucose load [2, 12, 6, 20].

However there is no uniformity of opinion as to the type or amount of the stimulating dose, the time of assessment or the method of blood sugar analysis.

Type of Carbohydrate

West *et al.* [27] recently compared glucose tolerance following breakfast, and following a glucose load, both of which contained the equivalent of 75 g of carbohydrate, and found that the blood sugar levels were

significantly higher following glucose administration. This was confirmed in our present study, and it is therefore recommended that either glucose or a suitable substitute (e.g. Glucola [15]) be used as a stimulating test dose. However, it must be emphasized that this method may not always be convenient (e.g. in Private Practice) in which case, a carbohydrate-rich test meal should still be employed.

Dosage: Jackson [10] believes that many false positives are obtained during pregnancy because too large a loading dose (100 g) is used. He compared 50 g tolerance tests in normal pregnant women, with tests based on 1.75 g/kg body-weight, and found that the difference between the mean 2 h level of the 50 g test and that of the IBW test was highly significant statistically. It is therefore surprising to note that similar dosage schedules did not significantly alter the classification of the African and Indian patient screened in the present series; although it must be conceded that individual determinations yielded higher values, with the larger glucose load. The increased number of diabetics among the Indian patients primed with the 50 g dose can only be explained on the assumption that there were more asymptomatic diabetics in the group screened. We therefore feel that the 100 g glucose dosage should be used, since it is surely wiser to err on the side of having to deal with a few extra false positives than to investigate the cause of an unexplained stillbirth.

Time Interval: The standard 3 h glucose tolerance test is the most reliable method when assessed in terms of reproducibility, sensitivity and specificity; and it is known [9] that the 'lag-type' response which occurs during pregnancy, frequently results in "abnormal" 2 h values "becoming normal", an hour later. When Dextrostix is used as a screening method however, it appears that the accuracy of the 3 h level is not substantially greater than the 2 h value (Table 5). In our experience, the shorter interval is associated with a much higher patient-acceptance rate and still allows ample time for a full obstetrical assessment. Therefore when large numbers of patients have to be screened, the convenience of 2 h tests outweighs the possible improvement in specificity of the 3 h alternative.

Screening 1 h after the loading dose was not considered since it precludes adequate opportunity for ante-natal supervision, and the higher blood sugar levels that occur at this time interval render the Dextrostix method less reliable.

Methods of Blood Sugar Analysis: West *et al.* [28] in a review of the literature noted that most authors confirm a definite correlation between blood glucose as estimated by Dextrostix, with values determined by more precise laboratory methods, but that a considerable variation of opinion exists as to its degree of accuracy.

Thus Rennie *et al.* [24] concluded from their study that Dextrostix is satisfactory as an initial screening procedure, but that the results obtained in the 130–200 mg/100 ml range were frequently misleading. Marks and Dawson [19] reported that the results obtained with Dextrostix (within the physiological range of 40–200 mg/100 ml) differed by less than 20 mg/100 ml from the true value in 73% of their cases, and West *et al.* found that 82% of their one-hour Dextrostix estimates were within 30% of the actual blood glucose values.

The results obtained in the present study were highly comparable, for 64.8% of all the Dextrostix estimates were within 10 mg/100 ml, and 92.5% were within 20 mg/100 ml of the control Autoanalyser values. These figures do not take into account the variability of blood sugar levels that can occur with automated methods [28] and which may account for as much as 10% of the apparent Dextrostix error [28]. As with West *et al.* [28] and others [24, 19], we found that the greatest degree of variance occurred at glucose concentrations below 120 mg/100 ml and above 200 mg/100 ml.

However, the main purpose of this investigation was to assess the value of Dextrostix as a screening procedure, and in this regard, it has proved as reliable as the more precise Autoanalyser technique, for only 2.4% of strip estimates were wrongly classified compared with 1.7% of laboratory tested samples. Other authors [28, 16] have found the specificity of this procedure to be 90%, thus ensuring a high degree of accuracy in separating normal from abnormal.

The value of Dextrostix as a screening device was even further enhanced when estimates on capillary blood samples were found to be as accurate as venous tested blood samples (see Table 9). Therefore accurate rapid estimations can be determined without the need for syringes, or trained personnel to perform the venepunctures.

It has been said that the role of the observer does not introduce significant error in the assessment of Dextrostix estimations [24]. The results of our study however, have shown the reverse, for the degree of accuracy was directly related to the experience of the observer: only 37.9% of the untrained laboratory assistant's initial estimates were within 10 mg/100 ml of the true value, his assessment (after a period of two months) improving to 51.4%. The trained or more experienced technician placed 64.8% of her estimates within the 10 mg/100 ml range, probably because of less hesitation in reading off the value at the end of the 60 sec period.

Conclusion

We have found that Dextrostix meets most of the requirements of an ideal screening device and is certainly the most reliable method available today. The technique is easily mastered and therefore highly

skilled personnel are not required; the results may be rapidly and accurately assessed; it obviates the need for venepuncture; and it is inexpensive and convenient to use. A major advantage of this medium is that a reliable estimate is available before the patient leaves the clinic or doctor's consulting room, thus obviating the unnecessary and often costly repeat visits.

It is therefore recommended that all pregnant patients, both in private and hospital practice, be screened with Dextrostix (as indicated previously) in each of the three trimesters of pregnancy; that values below 130 mg/100 ml be regarded as normal; between 130—150 mg/100 ml as suspect, and above 150 mg/100 ml as diabetic and in need of further investigation.

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References

1. Carrington, E.R.: The effect of maternal pre-diabetes. *Clin. Obstet. Gynec.* **3**, 911 (1960).
2. College of General Practitioners. The Family History of Diabetes. *Brit. med. J.* **1965 I**, 960.
3. Early diagnosis of Diabetes (Leading article). *Brit. med. J.* **1966 I**, 497.
4. Fajans, S.S., Conn, J.W.: Tolbutamide-induced improvement in carbohydrate tolerance of young people with mild diabetes mellitus. *Diabetes* **9**, 83 (1960).
5. Farquhar, J.W.: The child of the diabetic woman. *Arch. Dis. Childh.* **34**, 76 (1959).
6. Fine, J.: Glycosuria of Pregnancy. *Brit. med. J.* **1967 I**, 205.
7. Grant, D.R., Moorhouse, J.A.: Pilot study for a diabetes detection program based upon rapid glucose microanalysis of postprandial capillary blood. *Canad. med. Ass. J.* **94**, 1213 (1966).
8. Hoffman, W.S.: Rapid Photoelectric Method for determination of Glucose in Blood and Urine. *J. biol. Chem.* **120**, 51—55 (1937).
9. Hurwitz, D., Jensen, D.: Carbohydrate Metabolism in Normal Pregnancy. *New Engl. J. Med.* **234**, 327 (1946).
10. Jackson, W.P.U.: Studies in Pre-Diabetes. Part. 1. *Brit. med. J.* **1952 I**, 690.
11. — Diabetes and Pregnancy. Section IV. Pre-diabetes and Pregnancy. *Acta Diabetol. Lat.* **4**, 507—528 (1968).
12. Keen, H.: The Bedford Survey; a critique of methods & findings. *Proc. roy. Soc. Med.* **57**, 200 (1964).
13. — The presymptomatic diagnosis of diabetes. *Proc. roy. Soc. Med.* **59**, 1169 (1966).
14. Kyle, G.C.: Diabetes and Pregnancy. *Ann. intern. Med.* **59**, Suppl. 3, 1—82 (1963).
15. Leonards, J.R., McCulloch, E.P., Christopher, T.C.: A new carbohydrate solution for testing glucose tolerance. *Diabetes* **14**, 96 (1965).
16. Macy, Dorothy, Jr.: Diabetes screening with dextrostix in an industrial plant. *J. Amer. med. Wom. Ass.* **21**, 33 (1966).
17. Malins, J.M.: The presymptomatic diagnosis of diabetes. *Proc. roy. Soc. Med.* **59**, 1175 (1966).
18. — Fitzgerald, M.G.: Childbearing prior to recognition of diabetes; recollected birth weights and still-birth rate in babies born to parents who developed diabetes. *Diabetes* **14**, 175 (1965).
19. Marks, V., Dawson, A.: Rapid stick method for determining blood-glucose concentration. *Brit. med. J.* **1965 I**, 293.
20. Notelovitz, M.: The Pregnant Natal Indian Diabetic.—Facts & Fancies: *S. Afr. med. J.* **42**, 895 (1968).
21. — The Pregnant Natal Indian Diabetic; with Chapters on Carbohydrate Metabolism. Thesis: University of Witwatersrand 1968.
22. Ostrander, L.D., Jr., Francis, J., Jr., Hayner, N.S., Kjelsberg, O., Epstein, F.H.: The relationship of cardiovascular disease to hyperglycaemia. *Ann. intern. Med.* **62**, 1188 (1965).
23. O'Sullivan, J.B., Kantor, N.: Variability of blood sugar levels with an automated method. *Publ. Hlth Rep.* **78**, 1023 (1963).
24. Rennie, I.D.B., Keen, H., Southon, A.: A rapid enzyme-strip method for estimating blood-sugar. *Lancet* **1964 II**, 884.
25. Semple, B.: Personal communication.
26. Stowers, J.M.: Treatment of sub-clinical diabetes. *Proc. roy. Soc. Med.* **59**, 1177 (1966).
27. West, K.M., Wulff, J.A., Reigel, D.G., Fitzgerald, D.T.: Oral Carbohydrate Tolerance Tests. *Arch. intern. Med.* **113**, 64 (1964).
28. — Stein, J.H., Sanders, T.J.: Dextrostix estimates of blood glucose in mass screening for diabetes. *Amer. J. publ. Hlth.* **56**, 2059 (1966).
29. U.S. Public Health Service. Division of Chronic Diseases. Diabetes Source Book. Washington, Diabetes and Arthritis Program, Division of Chronic Diseases, 1964, U.S. Public Health Service Publication no. 1168.

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