THE ORAL GLUCOSE TOLERANCE TEST

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Blood contains reducing substances other than glucose. These non-sugar reducing substances, mainly glutathione and thionine, are present in the corpuscles and therefore "sugar" values do not actually represent the level of glucose. Thus the generally accepted fasting blood sugar level in normal subjects, 80 — 120mg. per 100ml. of blood (Lovatt Evans, 1947; Conybeare, 1949; Bayliss, 1950; Price, 1950; Harrison, 1957), is not the 'true glucose' value. 'True glucose' values may be obtained by deducting 20mg. (Harrison, 1957; Baron, 1957) from this total 'apparent glucose' value when the Shaffer-Hartman method is employed. It is now possible however, to estimate directly the 'true glucose' value by a modification of the Shaffer-Hartman technique as proposed by Asatoor and King (King and Wootton, 1956). The fasting 'true glucose' values in capillary blood of healthy individuals at rest obtained by this method range from 68mg. to 96mg per 100 ml of blood. Other workers give slightly lower values, 53 — 93 mg. per 100ml. (Lovatt Evans, 1947), or even slightly higher values, 70-100mg. (Harper, 1957) and 70-110mg. (Baron, 1957), but the technique used is not stated. The normal 'renal threshold' value for glucose is generally accepted to be 175-180mg. per 100 ml. of capillary blood. In normal persons the blood sugar does not usually rise above 160 mg. per 100ml after the ingestion of carbohydrate (King and Wootton, 1956; Baron, 1957; Harper, 1957).

The object of this investigation is to find out whether the accepted normal 'renal threshold' value, 175-180mg. per 100ml. is altered when the technique for estimating 'true glucose' (King and Wootton, 1956) is used. Furthermore, blood glucose estimations were extended over a period of 3 hours after the ingestion of glucose in order to see whether any additional information on glucose tolerance would be forthcoming.

Material and Methods

An oral glucose tolerance test was carried out on 56 patients referred for investigation from various departments of the hospital; in the majority of these cases reducing substances had been detected in the urine at one time or another. No attempt was made to select the material; all cases of pregnant women were, however, not included in the series. A clinical history of the patient was taken on the day of the test. The age-groups, sex-distribution and the incidence of diabetes mellitus in these cases is shown in the accompanying histogram (Fig. 1).

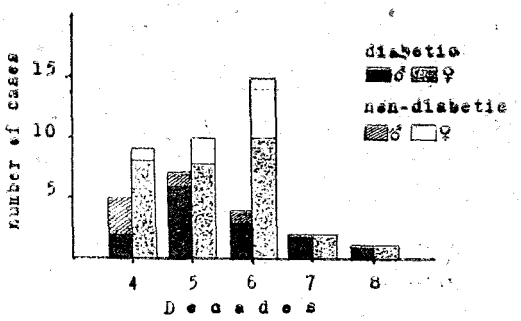

Fig. 1. — Age-groups, sex-distribution and incidence of cases of diabetes mellitus in the series.

All tests were carried out in the morning after an overnight fast, only a cup of tea or coffee with no added sugar or milk being allowed on rising. A fasting capillary blood specimen was taken and glucose was administered. Fifty grams

of glucose was given in 170 ml. of weak coffee in each case. Capillary blood was taken and urine specimens were collected at half-hourly intervals for three hours after administering the glucose.

Blood sugar estimations were carried out on the same day of the test by the Shaffer — Hartman method as modified by Asatoor and King (King and Wootton, 1956). The amount of glucose present in the urine specimens giving a positive reaction to Benedict's qualitative reagent, was estimated by Meyer's modification of Benedict's quantitative technique (King and Wootton, 1956).

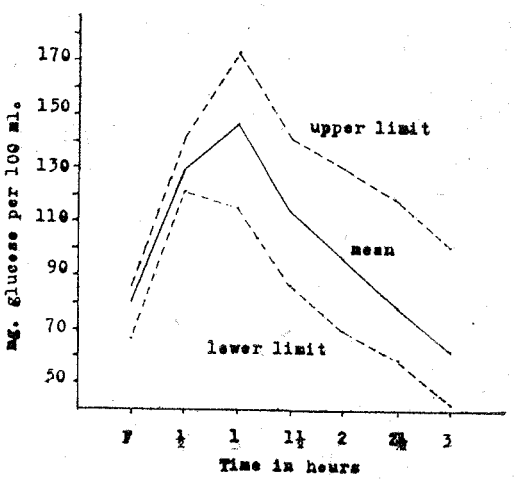

Fig. 2 — Showing the upper and lower limits of normality and the mean curve resulting from the values in Table I.

Results

In six cases no reducing substances were present in the urine specimens collected during the test, and in no instance does the peak of the curve exceed the value of 173 mg. per 100ml . Table I shows the values obtained in each case as well as their mean. Fig 2. represents the upper and lower limits of normality and a mean curve derived from the values in these six cases.

The blood glucose fasting level in these cases ranges from 66 mg. to 86 mg. per 100 ml.; and the highest value is reached within one hour in all cases. Return to the normal fasting level occurs within 2½ hours except in case No. 20. The mean of these values yields a curve with a fasting level of 80 mg. per 100 ml., a peak value at one hour and a return to normal fasting level within two hours.

In the remaining 50 cases, glucose was present in the urine in measureable quantities at some time during the test. These cases have been subdivided according to whether the resulting curve is of the diabetic or non-diabetic type. In four cases the curve is not of a diabetic type: the blood and urine glucose values (Table II) in these cases support the diagnosis of a 'renal' or an 'alimentary' type of glycosuria.

Table I. — Normal Glucose Tolerance Tests in Six Subjects and their Mean Values.

Case No.	Blood Glucose (mg./100ml.). F.	½hr.	1hr.	1½hr.	2hr.	2½hr.	3hr.
2	66	121	144	141	123	83	49
3	77	126	141	86	69	63	55
20	86	127	158	141	130	118	101
44	86	130	144	115	86	72	57
45	78	141	173	101	81	58	52
54	86	130	115	101	86	72	58
Mean	80	129	146	114	96	78	62

Table II. — Results of Glucose Tolerance Tests in Four Cases of Non-diabetic Glycosuria.

Case No.		Time in Hours F.	½	1	1½	2	2½	3	Type of Curve *
22	Blood (mg./100 ml.)	84	127	141	121	107	84	72	R
	Urine (G.)	—	—	0.06	0.08	—	—	—	
28	Blood (mg./100 ml.)	80	144	172	109	89	74	66	R
	Urine (G.)	—	1.06	2.04	0.42	0.04	—	—	
37	Blood (mg./100 ml.)	109	150	193	147	86	78	58	A
	Urine (G.)	—	0.19	1.20	1.15	0.10	—	—	
56	Blood (mg./100 ml.)	86	115	130	115	86	75	72	R
	Urine (G.)	—	—	0.65	1.21	—	—	—	

*R = 'renal'; A = 'alimentary'

Cases 22, 28 and 56 are typical examples of a 'renal' or 'low threshold' type of curve: glycosuria is present, but there is no hyperglycaemia. Case 37 is an example of an 'alimentary' or 'lag' type of curve. Hyperglycaemia and glycosuria are present but the blood glucose falls to normal limits within 2 hours. Moreover, the symptoms complained of by the patient were not typical of diabetes, and no family history of this condition was forthcoming.

In the remaining 46 cases the findings of the glucose tolerance test establish the presence of diabetes mellitus. In these cases there were no complications directly attributable to the diabetic state. One of these patients gave a history of repeated episodes of diabetic coma: ketone bodies were however absent in the urine at the time of the test.

The fasting blood glucose level falls within the range 58-98 mg. per 100 ml in only 6 of these cases (13 per cent); the values obtained after glucose ingestion show the presence of a mild or moderate degree of diabetes. Cases of severe diabetes show a fasting glucose level either above or just below 200 mg. per 100 ml. In 31 cases (67.4 per cent) the peak of the curve is reached 1 hour after glucose administration; the values recorded fall within the range 179-400 mg. per 100 ml. with a mean value of 287 mg. per 100 ml. The blood glucose reaches its highest level 1½ hours after glucose ingestion in 14 of these cases (30.4 per cent). In this group of cases the values recorded range between 201 and 414 mg. per 100 ml. with a mean value of 270 mg. per 100 ml. In only 1 case is the peak reached at the first ½ hour of the test with a blood glucose level of 244 mg. per 100 ml.

In these cases of diabetes mellitus the 3 hour glucose level in the blood is found to be significantly lower than the 2½ hour level. In 30 of these cases (65.2 per cent) there is a fall ranging between 10 mg. and 30 mg. per 100 ml.; in 13 cases (28.3 per cent) the difference is greater, and the values obtained range from 30 mg. to 64 mg. per 100 ml. Only in one instance does the 3 hour level exceed the 2½ hour one, and that by only 7 mg. This variation cannot be correlated either with the height of the

curve or with the urinary glucose output during the period of the test. Moreover, 3 hour blood glucose values exceed the level of 145 mg. per 100 ml. in 34 of these patients (74 per cent); in 8 other cases (17 per cent) the levels recorded fall within the range 65-110mg. It has also been observed that in 7 cases (15.2 per cent) a return to the original fasting level occurs within 2½ hours, and in yet another 7 cases (15.2 per cent) within 3 hours.

Discussion

Though the number of tests yielding a normal response is undoubtedly limited, yet the resulting mean curve is considered to be representative of the normal. A fasting glucose value above 96 mg. per 100 ml. is strong evidence in favour of diabetes mellitus, and little additional information of signficance may be derived from an oral glucose tolerance test. It is only when the fasting glucose level in the blood is normal and reducing substances have been repeatedly detected in the urine, possibly in variable amounts, that a glucose tolerance test is necessary for diagnosis.

Analysis of the findings recorded shows that there is no scope in prolonging the test to 3 hours. It may even be suggested that for the purpose of establishing a diagnosis of diabetes mellitus, the customary 2½ hour oral glucose tolerance test may very well be simplified. Instead of taking the usual six half-hourly samples of blood, only three are really essential to complete the test: a fasting specimen, a second specimen 1 hour after administering the dose of glucose and a third after 2½ hours. Baron (1957) maintains that a blood glucose level above 145 mg. 3 hours after the ingestion of 50 G. of glucose indicates impaired tolerance; while a value between 65 mg. and 110 mg. points to normal tolerance. Analysis of the 46 curves classified as diabetic shows that the 3 hour level exceeds 145 mg. per 100 ml. in 73.9 per cent of cases. However, in 17 per cent of these diabetic patients the 3 hour glucose values fall within the normal fasting range of 68-96 mg. per 100 ml. (King and Wootton, 1956). This latter finding indicates that the 2½ hour level of blood glucose is a more reliable indication of diabetes mellitus than the 3 hour level suggested by Baron (1957).

The simplified oral glucose tolerance test proposed above has some practical advantages. It reduces considerably the number of technical procedures, and in those cases where venous blood is collected it limits the number of venepunctures to three. This simplified test makes possible more frequent studies of glucose tolerance in diabetic patients under treatment. This is an important consideration now more than ever for in addition to Insulin, BZ 55 and D 860, aspirin is also known to lower the blood glucose in diabetics (Reid, Macdougall and Andrews, 1957; Reid and Lightbody, 1959). The modified glucose tolerance test is not recommended in those cases where 'renal' glycosuria is suspected, and in endocrine disorders other than diabetes mellitus.

No convincing evidence can be adduced from the findings presented in this paper that the normal 'renal threshold' for glucose is set at a lower level than 175-180 mg. per 100 ml. of blood In the normal cases a level of 173 mg. per 100 ml. is recorded in 1 case.

Summary

Fifty-six oral glucose tolerance tests were carried out on different subjects; of these 46 showed a diabetic type of response.

Fasting glucose values ranging from 66 mg. to 86 mg. per 100 ml. of blood have been obtained in normal individuals, in diabetics and in cases of non-diabetic glycosuria.

In the great majority of cases, whether diabetic (69.6 per cent of diabetic cases) or non-diabetic (90 per cent of

non-diabetic cases) the peak of the curve is reached at 1 hour. It is observed that in cases of diabetes mellitus the 3 hour glucose level in the blood is significantly lower than the 2½ hour one.

No information of value is derived by prolonging the test to 3 hours instead of the usual 2½ hours.

It is proposed that the test be carried out employing only three blood specimens: a fasting, a 1 hour and a 2½ hour blood specimen. This modification satisfies all requirements for the diagnosis of diabetes mellitus.

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