

TEAR GLUCOSE IN DIABETICS*

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THE purpose of this investigation was to evaluate a method of screening suspected diabetics, suitable for those without hospital facilities. This has been made possible by the recent use of a specific enzyme, glucose-oxidase, which is so sensitive as to detect glucose in solution in concentrations as low as 5 mg./100 ml. A commercial preparation, Clinistix (Ames Co.), has been used to detect glycosuria, to estimate blood sugar levels and tear glucose in diabetics (Hunt, Gray, and Thorogood, 1956; Kohn, 1957; Lewis, 1957). In diabetes associated with hyperglycaemia there is an increase in tear glucose concentration and because it was possible that there might be a quantitative as well as qualitative relationship between tear glucose levels and blood glucose levels, two series of tests were done.

Method

Qualitative Tests.—In 200 diabetics the tear reaction was performed and compared with the blood sugar levels. The tip of a Clinistix was applied to the everted lower conjunctiva and moistened with tears, and the result was read after a minute. The patient was told to look up, so as to prevent the stick touching the cornea. Where the stick was not adequately moistened, it was wetted with water and reapplied. The blue colour change is due to an incorporated indicator and is dependent on glucose concentration and the time taken to read the result, so that some standard timing is desirable. The colour changes were arbitrarily divided into no change (white), green-blue, light blue, blue, and deep blue. Similar blue shades to these are found on the Clinistix bottle.

Quantitative Tests.—These were carried out on diabetic and non-diabetic subjects. 0.1 ml. of tears was taken and the total reducing substances found by the method of King (1951). The tears were also tested with Clinistix, and a guide to the amount of glucose present was obtained by comparing the results with the colour changes seen in aqueous solutions of known strengths of glucose.

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Results

Qualitative Tests.—No strict correlation was found but a general trend was apparent (Figure). Deep blue colours suggested a blood sugar over 250 mg./100 ml., and lighter shades of blue suggested levels between 150 and 250 mg./100 ml. In some cases positive tear tests were obtained with blood sugars at 100 to 150 mg./100 ml. It is possible that these results represent a lag from previous hyperglycaemia. A negative result often indicated normoglycaemia, but inefficient application, lack of co-operation, and faulty Clinistix which turned brown through light exposure accounted for some failures in testing hyperglycaemia. Of 119 cases in which hyperglycaemia was present, a positive colour change was seen in 101 (85 per cent.). Taking the group as a whole, a positive tear test was obtained, irrespective of the blood sugar levels, in 131 out of 200 diabetics. In a control series of fifty readings on normal subjects, the low glucose concentration and sensitivity of Clinistix was such that no reaction occurred within 1 to 2 minutes.

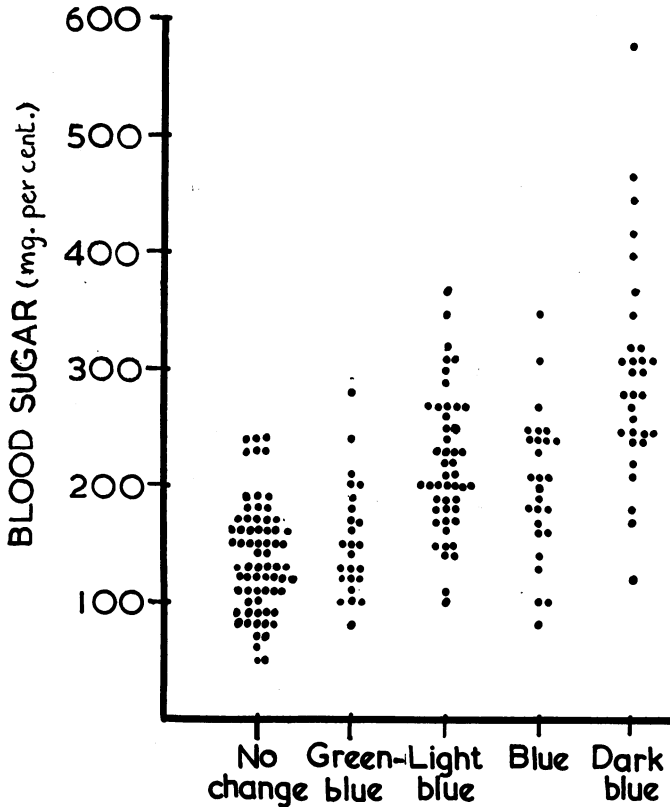


FIGURE.—Colour changes related to percentage blood sugar.

Quantitative Tests.—The Table shows the blood sugar levels, total tear reducing substances, and Clinistix reaction in thirty subjects (fifteen diabetic and fifteen non-diabetic). In the control series of non-diabetics the range of total reducing substances was 0 to 40 mg./100 ml. (average 14 mg./100 ml.). Feeding with large amounts (*i.e.* 100 g. glucose) produced tear concentrations capable of giving faint colour changes, but only after a delay of 3 to 5 minutes. In the diabetics there was the expected increase in levels but these bore no definite relationship to the blood sugar. When the total reducing substances were above the normal range with a minimal Clinistix reaction, it is probable that non-glucose substances were responsible.

Discussion

It has been stated that subjects with normal carbohydrate metabolism have a low glucose concentration in their tears. Values given have varied

TABLE
RESULTS IN FIFTEEN NORMAL SUBJECTS AND FIFTEEN DIABETICS

Series	Subject	Blood Sugar (mg. per cent.)	Clinistix Reading	Total Reducing Substances in Tears (mg. per cent.)
Normal Subjects	A	77 83 126	No change No change No change	20 26 40
	B	—	No change	20
	C	83	No change	—
	D	90	No change	16
	E	87	No change	22
	F	97	No change	—
	G	82	—	17
	H	82	—	10
	I	71	—	12
	J	75	—	10
	K	70	—	11
	L	75	—	15
	M	— —	No change No change	0 4
	N	— —	No change No change	6 10
	O	— —	No change No change	16 12

continued—

TABLE—(continued)

Series	Subject	Blood Sugar (mg. per cent.)	Clinistix Reading	Total Reducing Substances in Tears (mg. per cent.)
Diabetics	a	300	Dark blue	41
	b	160 206 267 243 203	Blue Light blue Light blue Light blue Green-blue	67 50 53 57 43
	c	110 94 100	No change No change No change	21 19 10
	d	106 120 100	Light blue Light blue Light blue	67 73 60
	e	167 120 143	Light blue Blue Blue	67 120 150
	f	220 173 186	Light blue Light blue Green-blue	116 83 33
	g	167 100 160	Green-blue Green-blue No change	26 33 26
	h	310	Green-blue	20
	i	133	No change	15
	j	280	Green-blue	20
	k	250	Dark blue	105
	l	—	Green-blue	36
	m	—	Blue	62
	n	—	Light blue	32
	o	— —	Light blue Blue	23 55

widely from zero to 65 mg./100 ml. of total reducing substances. Giardini and Roberts (1950) found that the total reducing substances in tears averaged 6.06 mg./100 ml., of which 41 per cent. (2.5 mg./100 ml.) was glucose. Our results have not differed greatly from theirs. The highest reading of 40 mg./100 ml. was only obtained after ingestion of 100 g. glucose. The method of King and Garner (King, 1951) does not give the true glucose level but a higher figure depending on the additional non-glucose reducing substances present. Glutathione, a reducing substance normally present in

tears, is not included, as it is precipitated with the proteins. Chromatography for sugars was done on several occasions and showed that glucose was the only sugar present.

The test has the disadvantage of being temporarily uncomfortable in a minority of patients but no after-effects were found. Filter or absorbent paper, as used in Tes-Tape (Eli-Lilly), would be preferable, but its sensitivity is too low for use with tears. An enzyme strip combining a non-irritant absorbent tape with the sensitivity of Clinistix might be of more practical value. The commonest cause of failure of the test was inadequate wetting of the Clinistix with tears.

On the basis of these tests it is apparent that the tear sugar level is often raised in diabetics, and this can be used as a simple test to confirm the diagnosis. In our experience a blue coloration developing at 1 to 2 minutes indicated diabetes, and the deeper the colour the greater the certainty of the diagnosis.

Summary

In 200 diabetics blood sugar levels above 160 mg./100 ml. were present in 119, and in 85 per cent. the level of tear glucose was such to produce a positive reaction. 15 per cent. showed no colour change, so that a negative test cannot be used as evidence against the presence of diabetes. Under the same conditions normal subjects showed no reaction.

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