Papers and Originals

Glucose Content of Normal Urine

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The present investigation was undertaken as a preliminary to an inquiry into the incidence and significance of pregnancy glycosuria, since it became clear at an early stage of this inquiry that the interpretation of the findings necessitated a similar study in a non-pregnant population.

The earlier studies on urine glucose by Benedict *et al.* (1918), Folin and Berglund (1922), and others are largely invalidated by the non-specific methods used—chiefly copper reduction—and it is comparatively recently that more specific methods have been introduced, resulting in a truer picture of glycosuria incidence.

Most recent work, particularly in pregnancy studies, is based on the use of Clinistix, but it is now recognized that there is some uncertainty about the level of glucose detected in the urine by this method. Anti-enzyme substances—chiefly uric acid—interfere with the action of glucose oxidase to a variable extent, so that, whereas glucose in pure solution can be detected at a concentration of 5 mg./100 ml., detection in urine is uncertain and inconstant until a concentration of 40 mg./100 ml. is reached.

Another cause of variability in the results obtained is the lack of uniformity in the concentration of enzymes present in the paper, partly due to deterioration as a result of age. A further serious source of inaccuracy in glycosuria studies is the absence of a clear-cut distinction between a positive and a negative Clinistix result. Thus in a population study by a working party of the College of General Practitioners (1963) 21% of the men had glucosuria detectable by Clinistix after a glucose drink, but only 9.3% of the specimens were positive to Benedict. This discrepancy is much more marked than in the study to be described later, in which Clinistix-positive specimens formed 8.6% of the total, against a figure of 6.6% positive Benedict results.

The high percentage of the positive Clinistix results in the former study may be explained by the fact that in many tests a duskiness develops in the paper, short of actual green, which may be differently interpreted by investigators, especially if the reading is delayed for more than a minute.

It is possible to remove the enzyme-inhibiting substances in the urine by treating with charcoal and filtering, but when this is done most of the specimens become frankly though weakly positive to Clinistix; this is not surprising, since the average glucose content of urine (6 mg./100 ml.) is above the lower limit detectable by Clinistix.

In view of the objections to Clinistix described it was felt that the actual determination of the glucose content of urine would produce more consistent results and would further yield valuable information in a study of glycosuria incidence.

Several methods are available for the quantitative determination of the low glucose levels found in urine. Conway (1950) describes a gaseous diffusion technique based on yeast fermentation, and Apthorp (1957) investigated the urine glucose in a small series of normal adults and children, using a chromatographic procedure.

The method of choice suitable for determinations on a large scale, such as is necessary for a serious population study, is in my view the glucose oxidase one, and the following technique, similar to that used by Marks (1959) and based on Huggett and Nixon's (1957) oxidase method of blood-sugar estimation, was employed throughout the investigation.

Estimation of Glucose in Urine by Glucose Oxidase

1. The urine is first tested by Clinistix, and if positive is diluted until only a weak reaction is given.

2. 10 ml. of the urine, suitably diluted as above when necessary, is then pipetted in two test-tubes labelled U and UG: to the latter, 0.1 ml. of a 1% glucose solution is added and the mixture shaken.

3. 0.5 g. of activated charcoal (B.D.H.) is weighed into each of two boiling tubes, to which the urines are transferred; the tubes are shaken for one minute, and allowed to stand for 15 minutes.

4. The contents of the tubes are then filtered through 44 Whatman paper, and 0.2 ml. of filtrate from each is transferred to a small tube of centrifuge size.

5. Finally, 2.5 ml. of an enzyme mixture is added containing buffered glucose oxidase-peroxidase and *o*-dianisidine; this was prepared from reagents supplied by Boeringer.

6. After incubation at room temperature for 45 minutes or at 37° C. for 15 minutes the optical densities (O.D.) were read at a wavelength of 450 mμ.

7. A standard glucose solution of 10 mg./100 ml. was treated in the same way as the filtered urine, 2.5 ml. of enzyme mixture being added to 0.2 ml. standard: a water blank of 0.2 of distilled water plus 2.5 ml. of enzyme was similarly put up.

8. Calculation:

If x=O.D of U minus O.D. of blank
and y=O.D. of UG minus O.D. of blank

$$\text{Then glucose content of urine} = \frac{(x)}{y-x} \times 10$$

If the anti-enzyme action of the urine was entirely removed by the charcoal the value $y-x$ should theoretically equal the O.D. of standard minus O.D. of blank. In practice this rarely occurred, but since an average of 80% of the added glucose (and presumably of the glucose originally present in the urine) was recovered, the loss in sensitivity was not significant.

Preliminary filtration of the urine was not found necessary except where charcoal had no effect on the unfiltered specimen: this was of rare occurrence.

The use of chlorhexidine (Hibitane) (1 in 1,000) as a urine preservative was of great advantage when analysis had to be deferred for one or two days.

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Glucose Content of Urine in 700 Adults

Most of the specimens were from volunteers from a large industrial firm: 537 specimens were obtained from this source; a further 50 were obtained from a second firm and the remaining volunteers were members of the hospital staff. The ages ranged from 16 to 65, and 537 of the total were males. Specimens were obtained one to two hours after a meal.

The results of the analyses are summarized in Table I. The lowest value found was 0.2 mg./100 ml. and the highest 9,328 mg., but 91% were contained within the range of 1–15 mg.

Fig. 1 shows the results in histogram form, and confirms the division of the population into two groups according to glucose content. The larger group, comprising 91% of the population studied, and containing urines within a range of 1–15 mg. of glucose per 100 ml., has a typically normal percentage distribution curve, with a mean of 6 mg., a mean deviation of 2.3, and a standard deviation of 3.2: within this group three-quarters of the values lie within the range of 3–10 mg./100 ml. and 90% within 1–12 mg. The remaining 9% of the series comprises urines with values ranging from 16 mg. upwards: it has no characteristic pattern, and there is no very sharp demarcation between the two groups.

TABLE I.—*Glucose Content of Urine in 700 Adults*

Range mg./100 ml.) Glucose	No. of Persons	Range (mg./100 ml.) Glucose	No. of Persons	Range (mg./100 ml.) Glucose	No. of Persons
0–1	2	–18	1	–300	1
–2	24	–19	0	–400	1
–3	40	–20	5	–500	4
–4	68	–25	6	–600	1
–5	78	–30	6	–700	2
–6	71	–35	2	–800	0
–7	84	–40	3	–900	0
–8	68	–45	2	–1,000	0
–9	70	–50	3	–2,000	0
–10	36	–55	0	–3,000	1
–11	24	–60	1	–4,000	0
–12	24	–65	0	–5,000	1
–13	12	–70	5	–6,000	1
–14	16	–80	3	–7,000	0
–15	17	–90	1	–8,000	0
–16	5	–100	2	–9,000	0
–17	5	–200	3	–10,000	1

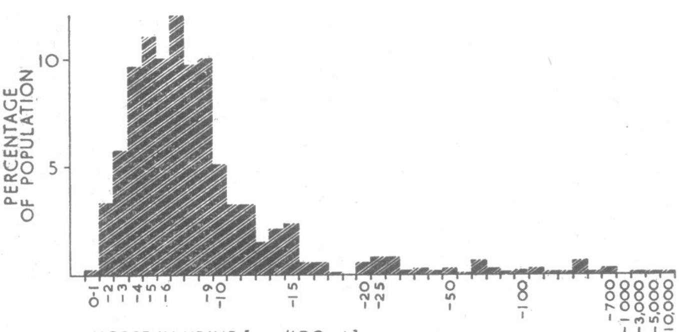

FIG. 1.—Glucose content of urine in 700 adults.

Correlation of Clinistix Tests with Glucose Content of Urine

Although this subdivision into a larger group of 91% and a smaller of 9% corresponds roughly to the Clinistix-negative and Clinistix-positive groups in the population studied, analysis showed considerable overlap, the Clinistix being positive in some urines with low glucose content and vice versa; in the total the discrepancies almost wholly cancelled out, producing an appearance of agreement. This is brought out in Table II, in which the correlation of glucose content with the results of Clinistix test is studied in 500 urines.

TABLE II.—*Correlation of Glucose Content With Results of Clinistix Tests in 500 Urines*

Glucose Content (mg./100 ml.)	No. of Specimens Examined	Clinistix Negative	Clinistix Positive
0–5	147	147	0
–10	238	237	1
–15	64	62	2
–20	11	8	3
–40	13	3	10
–50	5	0	5
> 50	22	0	22
Total	500	457	43

In this series 51 urines had a content of over 15 mg./100 ml.: only 40 of these were positive to Clinistix, whereas three positive Clinistix results were obtained in the urines with less than 15 mg/100 ml. Table II also shows that only when the glucose content reaches a level of 40 mg./100 ml. does Clinistix constantly give a positive result: in the range of 15 to 40 mg. only 13 out of 24 urines were Clinistix positive.

Significance of Raised Glucose Values

All cases with a urine glucose content of over 15 mg./100 ml. —usually, but not always, Clinistix-positive—were investigated

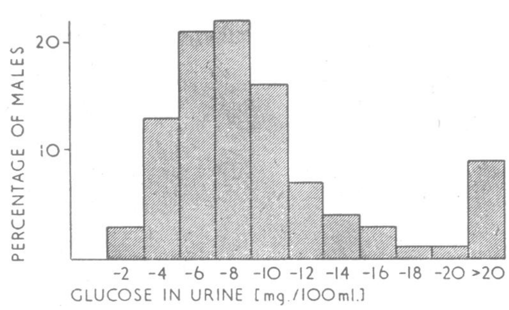

FIG. 2

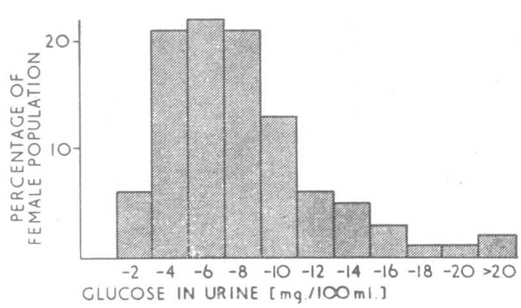

FIG. 3

FIG. 2.—Glucose content of urine in 537 males. FIG. 3.—Glucose content of urine in 163 females.

TABLE III.—*Glucose Content of Urine in 700 Adults According to Age and Sex*

	Age group:	–20	–30	–40	–50	–60	–70	Total –40	Total 40+	Grand Total
Both sexes	No. of persons	113	158	135	139	118	37	406	294	700
	Over 15 mg./100 ml. No.	6	8	10	19	14	9	24	42	66
	Over 15 mg./100 ml. %	5·6	5	7·5	13·6	12	24·3	5·9	14·3	9·4
Males	No. of persons	73	112	111	106	101	34	296	241	537
	Over 15 mg./100 ml. No.	6	6	9	17	14	8	21	39	60
	Over 15 mg./100 ml. %	8·2	5·4	8·1	16	14	23·5	7·1	16·2	11·2
Females	No. of persons	40	46	24	33	17	3	110	53	163
	Over 15 mg./100 ml. No.	0	2	1	2	0	1	3	3	6
	Over 15 mg./100 ml. %	0	4·3	4·1	6	0	33	2·7	5·7	3·6

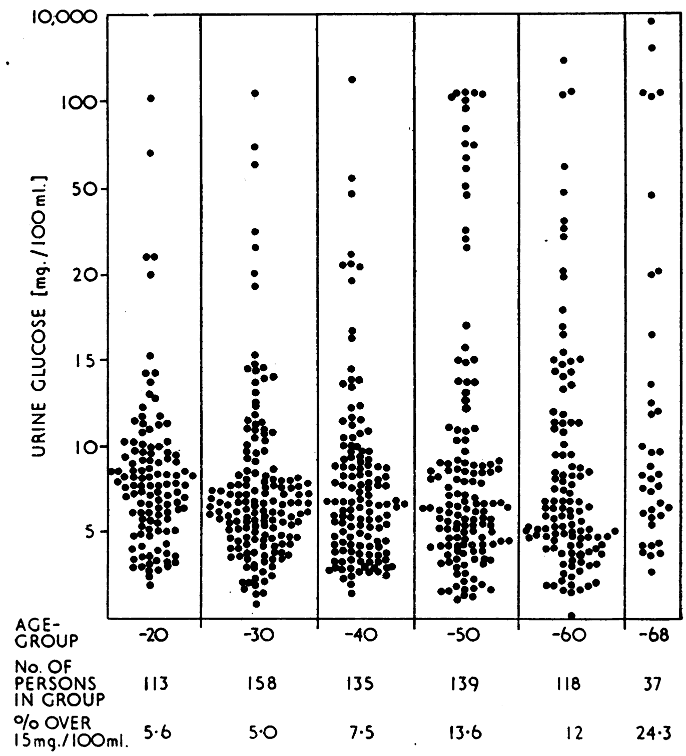

FIG. 4.—Urine glucose in 700 adults, according to age groups.

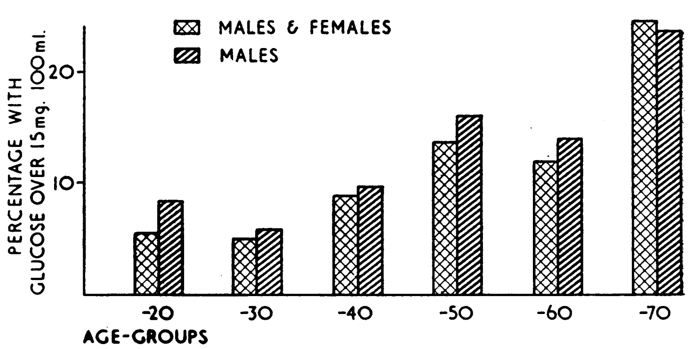

FIG. 5.—Percentage of raised urine glucose in 700 adults, according to age and sex.

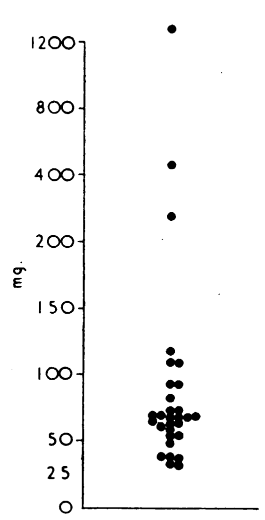

FIG. 6

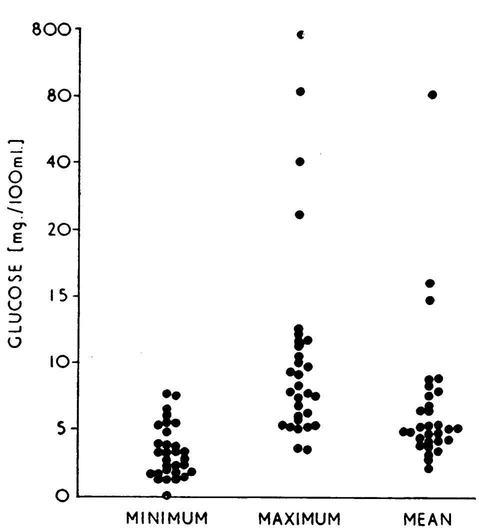

FIG. 7

FIG. 6.—Excretion of glucose in 24 hours, in 30 adults. FIG. 7.—Minimum and maximum concentration of urine glucose in 24 hours, in 30 adults.

wherever possible for diabetes by blood-sugar estimations. This was carried out systematically with the largest section of the volunteers—537 employees of the firm of Stewarts and Lloyds—with the following results.

Total employees examined	537		
Diabetics { Previously known	4	} 1·6%	} 8·4%
Diabetics { Discovered as a result of the tests	5		
Non-diabetic glycosurias			
Renal glycosurias	15	} 6·8%	
Lag glycosurias	7		
Glycosurias not fully investigated, but with blood-sugar values within normal limits and probably not diabetic	15		

Glucose Content According to Sex and Age

Of the 700 subjects, 537 were males and 163 females. Figs. 2 and 3 show the percentage distribution of glucose content in the two groups. The main difference is in the percentage of urines containing over 15 mg. of glucose per 100 ml.: of a total of 65 cases with these values 59 (11%) were male, while only 6 (3.7%) were female.

With regard to the range 1–15 mg./100 ml. there was no significant difference in the distribution curves: the mean value for the males was 6 mg., for the females 6.2 mg.

In Table III the glucose content is classified according to age in each sex, and the results are shown in Fig. 4 (all cases).

Expression of these data in histogram form in Fig. 5 reveals a definite relation between glucose content and age, the percentage of high glucose values (over 15%) rising from under 9% in the lowest age group (15–20) to over 23% in the highest age group (60–70). The increase in higher glucose incidence with age is shown to be significantly greater in the male than in the mixed group: female data are not shown here as the numbers were too small for breaking down into six age groups.

TABLE IV.—*Excretion of Glucose in 24 Hours in 30 Adults*

No.	Age	Sex	mg. in 24 hr.	No.	Age	Sex	mg. in 24 hr.
1	62	M	68·2	16	62	F	117·0
2	35	F	33·8	17	22	F	36·0
3	24	F	38·2	18	28	F	66·7
4	18	F	63·8	19	32	F	449·5
5	19	F	38·6	20	32	F	279·0
6	52	M	1,280·6	21	35	M	109·8
7	16	M	60·8	22	28	M	71·3
8	19	F	57·1	23	27	F	66·1
9	21	M	74·1	24	20	F	54·0
10	19	M	82·8	25	24	F	69·3
11	35	M	69·4	26	17	F	90·4
12	30	F	93·0	27	52	F	65·5
13	30	F	61·3	28	20	F	70·2
14	48	F	31·7	29	42	F	109·9
15	43	F	54·8	30	18	F	48·7

Excretion of Glucose in 24 Hours

The glucose content of urine in the 700 subjects studied was biased in that specimens were collected one to two hours after a meal: there is evidence that ingestion of carbohydrate is followed by a rise in urine glucose, and evidence of this is submitted later in this paper.

A study of the total output and the mean concentration of urine glucose over 24 hours was carried out in 30 volunteers, the results of which are shown in Table IV and plotted in Fig. 6.

Four of the volunteers, however, were found to be cases of renal glycosuria, with outputs of 110 to 1,280 mg. in 24 hours; in the remaining 26 cases the range of total excretion was 31.7 to 93 mg., with a mean of 65 mg. The concentration of glucose in the latter specimens, plotted in Fig. 7, ranges from 2.1 to 8.9 mg./100 ml., with a mean value of 5.1 mg.

In a similar study of 30 normal subjects by Froesch and Renold (1956) the findings were: range of glucose excretion 16–132 mg./100 ml., mean 72 mg.

Fluctuation of Glucose Concentration

The collection of urine in the previous investigation was carried out by preserving the separate specimens passed in 0.1% chlorhexidine, and by estimating the glucose in each individual sample it was possible to study the variation in concentration throughout the 24-hour period.

The number of specimens passed per subject varied from 3 to 13, with a mean of 7: a total of 207 samples were analysed.

The results are shown in Table V, which gives the minimum and maximum glucose concentrations in each subject, as well as the mean value calculated by dividing the 24-hour glucose output by the 24-hour urine volume. Considerable fluctuation in glucose concentration throughout the 24 hours was found. Excluding the cases of renal glycosuria, the minimum concentrations reached ranged from 0.2 to 7.5 mg./100 ml., with an average of 2.8 mg.; the maximum values reached ranged from 3.5 to 12.5 mg./100 ml., with an average of 7.5 mg.; and the concentration of the pooled 24-hour specimens, ranged from 2.1 to 8.9 mg., with an average of 5.1 mg. Graphical representation of the results (Fig. 7) shows that only when the maximum values are compared can all the cases of renal glycosuria be recognized; when the mean values for each subject are considered only three of the cases can be distinguished from the remainder by their raised glucose content, while minimum values are close-clustered and distinction between the renal glycosuric and the other cases vanishes.

TABLE V.—*Fluctuation of Urine Glucose Concentration in 24 Hours in 30 Adults*

No.	Minimum (mg./100 ml.)	Maximum (mg./100 ml.)	Mean (mg./100 ml.)	No.	Minimum (mg./100 ml.)	Maximum (mg./100 ml.)	Mean (mg./100 ml.)
1	3·6	11·4	6·9	17	1·5	5·2	2·7
2	3·5	3·7	3·6	18	1·6	9·7	4·9
3	2·2	5·0	4·0	19*	6·1	100	1·6
4	1·9	6·9	4·7	20*	5·4	41	14·7
5	2·7	6·1	4·0	21	2·7	5·1	3·8
6*	7·6	734	80·3	22	5·4	12·2	8·2
7	2·4	5·7	4·2	23	4·6	9·3	6·5
8	3·2	10·5	6·5	24	3·2	7·6	4·8
9	6·5	9·2	7·5	25	2·3	8·2	5·0
10	1·2	11·7	5·3	26	7·5	11·7	8·9
11	3·3	5·0	3·8	27	1·4	7·5	4·6
12	3·4	7·6	5·1	28	5·2	12·5	7·9
13	1·1	10	5·1	29*	1·7	24·8	8·7
14	1·6	5·1	3·1	30	1·2	6·2	4·1
15	0·2	3·5	2·1	Range	0·2–7·5	3·5–12·5	2·1–8·9
16	3·7	7·4	5·0	Mean†	(2·8)	(7·1)	(5·1)

* Renal glycosuria. † Excluding renal glycosurias.

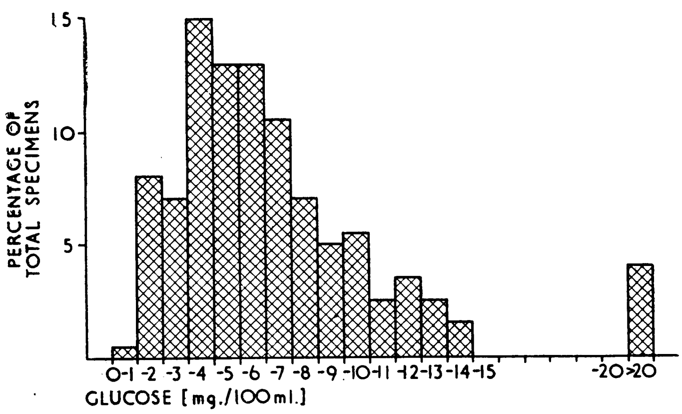

FIG. 8.—Urine glucose in 207 specimens from 30 persons over 24-hour period.

The range of concentration in the 207 specimens from the 30 subjects is also shown in Fig. 8. There the values resolve into two groups similar to those seen in the 700 adults in Fig. 1: the larger group with glucose values of 1–14 mg./100 ml. and with a normal though skewish distribution curve, and a small group of higher values, all derived from the cases of renal glycosuria.

Rate of Glucose Excretion

The rate of glucose excretion is not often determined in glycosuria investigations, being less readily obtainable than simple glucose concentrations. It does nevertheless provide very useful information in such studies as it is normally more constant in level and is less influenced by factors—such as diuresis and food intake—which cause fluctuations in glucose concentration.

The contrast between glucose concentration and rate of excretion is illustrated in Figs. 9 and 10, which show the results of analyses of a series of urine samples obtained over a period of 24 hours in two volunteers. Case 12 (Fig. 9) shows a continuous, almost uninterrupted fall in the rate of glucose excretion; the concentration, however, rose in the earlier part of the day, owing to reduction in volume output from 3 to 1 ml./min.—that is, owing to urine concentration. In Case 13 (Fig. 10) the urine concentrations fluctuated markedly in correlation with dilution and concentration of urine, but these changes had no influence on the rate of glucose excretion throughout the 24-hour period.

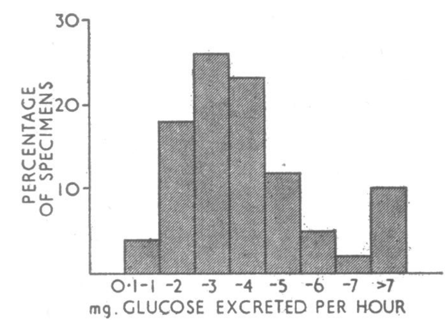

FIG. 11.—Rate of excretion of glucose in 207 samples of urine from 30 subjects.

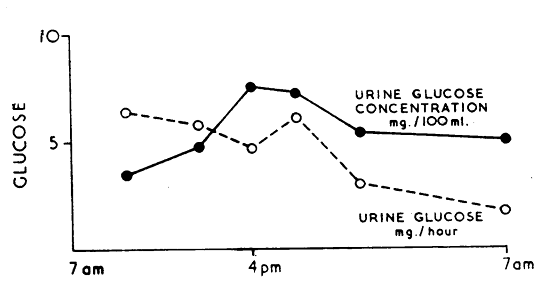

FIG. 9

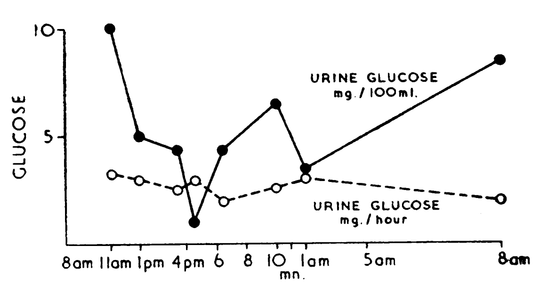

FIG. 10

FIG. 9.—Case 12. Comparison between glucose concentration and rate of excretion. FIG. 10.—Case 13. Comparison between glucose concentration and rate of excretion.

Normal Range of Excretion Rate of Glucose.—The excretion rate was determined in 207 samples of urine collected over a period of 24 hours from the 30 volunteers previously mentioned. The results are shown in Fig. 11. In 180 (87%) of the specimens the rate ranged from 0.3 to 6.8 mg./hour and formed a normal percentage distribution curve with a mean of 3 mg./hour: the remaining 27 specimens, with secretion rates up to 364 mg./hour, were from the four cases of renal glycosuria and from two others with a high output of glucose in 24 hours.

Nocturnal Excretion of Glucose.—Examination of the overnight specimens of the 30 volunteers showed that in 10 cases these specimens had the highest glucose concentration of all the 24-hour samples ; in another 10 cases the glucose concentration was greater than the mean value of the samples. A very different picture was obtained if the rate of glucose secretion was examined: this value was found to be the lowest of all the 24-hour samples in half the cases, and in 90% of the cases it was below the mean 24-hour secretion rate. Thus a nocturnal drop in glucose excretion demonstrable by excretion rate studies was masked by the figures for glucose concentration.

Relation of Carbohydrate Intake to Glucose Excretion

Apthorp (1957) found no increase in glucose concentration following a meal, and Froesch and Renold (1956) also think that this value is relatively independent of dietary influence.

Although random samples taken before and after meals may show no constant relation in glucose content, an increase can invariably be demonstrated if the procedure of a glucose-tolerance test be followed: moreover, if the rate of excretion in mg./hour be calculated for each specimen a curve is obtained which more closely parallels the blood-sugar values than it does the glucose concentration levels.

TABLE VI.—*Concentration and Rate of Excretion of Glucose After Ingestion of 50 g. Glucose in 8 Normal Adults*

Subject	Sex and Age	No. of Specimen	Vol. (ml.)	Hours since Previous Specimen	Urine Glucose mg./100 ml.	Urine Glucose mg./hr.	Blood Glucose mg./100 ml.
A	F 18	1 (fasting)	53	1¼	5·3	2·2	
		2	132	½	1·2	3·2	
		3	128	½	1·3	3·2	
		4	23	½	5·8	2·6	
		5	55	½	2·7	3·0	
		6	27	½	2·8	1·5	
B	F 35	1 (fasting)	54	1⅓	4·3	1·7	
		2	15	½	11·4	3·4	
		3	11	½	9·0	2·0	
		4	15	½	7·5	2·3	
		5	11	½	6·3	1·4	
		6	14	½	5·4	1·6	
C	F 20	1 (fasting)	93	2¼	2·4	1·0	83
		2	90	½	4·6	8·3	142
		3	192	½	1·9	7·3	123
		4	231	½	1·5	6·9	97
		5	132	½	1·9	4·9	65
		6	32	½	2·8	1·8	52
D	F 24	1 (fasting)	126	2½	4·2	2·1	
		2	26	½	8·5	4·4	
		3	158	½	1·4	4·4	
		4	74	½	1·4	2·0	
		5	35	½	3·3	2·3	
		6	27	½	3·5	1·9	
E	F 19	1 (fasting)	231	1 7/12	1·3	1·6	
		2	119	½	1·5	3·6	
		3	48	½	2·7	2·6	
		4	15	½	7·6	2·3	
		5	17	½	5·3	1·8	
		6	27	½	4·2	2·3	
F	M 18	1 (fasting)	38	1⅔	5·7	1·3	
		2	19	½	9·2	3·5	
		3	35	½	5·8	4·1	
		4	216	½	0·7	2·8	
		5	148	½	0·6	1·9	
		6	33	½	2·9	1·9	
G	F 17	1 (fasting)	340	1 11/12	1·2	2·1	77
		2	36	¾	5·3	2·5	110
		3	214	½	1·0	4·3	97
		4	42	7/12	4·4	3·2	84
		5	9	½	8·3	1·5	84
		6	14	½	8·8	2·5	71
H	M 58	1 (fasting)	11·5	1¼	7·2	0·7	80
		2	26	¾	8·6	3·0	120
		3	21	½	11·7	4·9	100
		4	16	½	20·6	6·6	90
		5	10	½	10·2	2·0	90
		6	19	½	12·2	4·6	100

In Table VI a number of examples are shown of the effect of 50 g. of glucose orally administered on the glucose content of subsequent urine specimens. Only in Case A is the fasting urine glucose higher than in the subsequent specimen, but a rise is demonstrated later. However, in all cases the glucose secretion rate in the fasting specimen is lower than in the following one.

Fig. 12 is an example of a better correlation of the blood-sugar curve with the urine glucose excretion rate than with urine glucose concentration. Joplin *et al.* (1961) has also reported an increased rate of glucose excretion during glucose-tolerance tests.

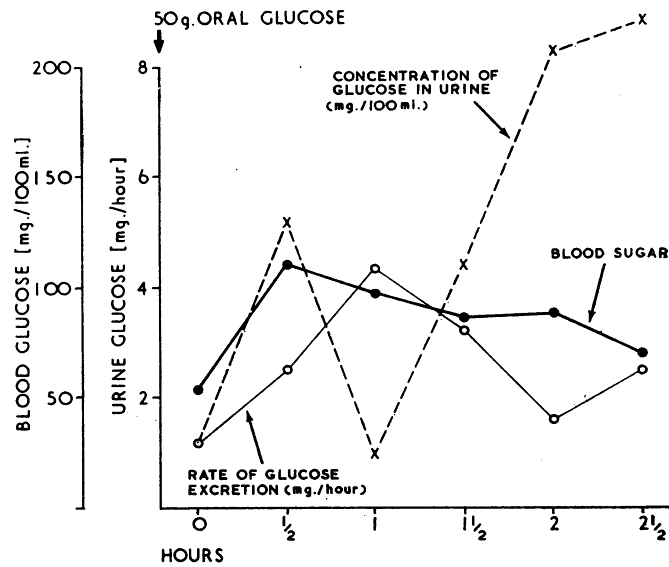

FIG. 12.—Comparison between blood-sugar curve, curve of urine glucose concentration, and curve of urine glucose rate of excretion in normal adult.

Discussion

Although the presence of glucose in normal urine has been recognized in theory for many years, in practice the fact has been ignored largely on account of the difficulty of demonstrating its presence, and the term glycosuria has therefore been confined to cases in which positive results were obtained by the use of particular reagents.

Now that methods are available for the detection of glucose normally present in urine the use of the term glycosuria would seem untenable, unless linked with the reagent used—for example, Benedict-glycosuria or Clinistix-glycosuria.

Since the normal glucose content of urine is in the range of 1–15 mg./100 ml., and since Clinistix cannot detect with certainty a concentration level below 40 mg., there is a considerable zone above the normal range (15 to 40 mg.) which can be effectively explored only by the use of quantitative methods. This is important in at least two ways—the diagnosis of renal tubular defect, and in diabetes detection. In tubular disease such as Fanconi syndrome—where reabsorption of glucose as well as amino-acids is defective—a negative Clinistix may fail to indicate the presence of an abnormal level of urine glucose, and in the same way potential diabetics might be missed because of the insensitiveness of Clinistix. In one instance in the present series of 700 a diabetic was detected after the finding of 20 mg. of glucose per 100 ml. of urine—a level to which Clinistix is normally insensitive.

The term glycosuria could well be replaced by the terms " normoglucuria " and " hyperglucuria," the former indicating the presence of normal amounts of glucose—that is, 1–15 mg./100 ml.—the latter indicating levels in excess of this (see Fig. 13). The use of such terms would serve to indicate that a negative Clinistix might well conceal an abnormal amount of glucose, while a weakly positive result may arise merely on account of a low uric acid content in the presence of a normal amount of glucose.

Another term requiring re-examination is renal glycosuria, which is regarded as a manifestation of glucose intolerance. Since it has been demonstrated that carbohydrate intake in the normal subject is followed by an increase in the excretion of glucose, it follows that glucose intolerance is a normal phenomenon differing, it might be argued, only in degree from

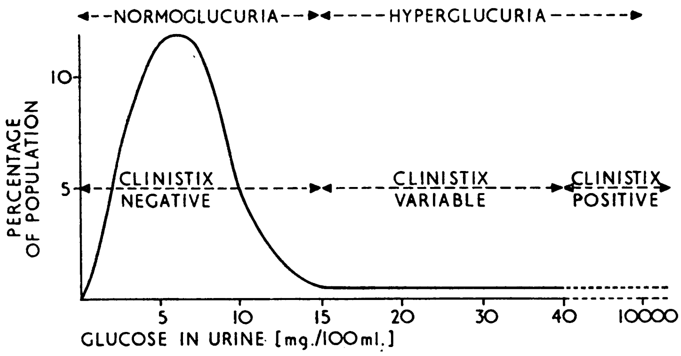

FIG. 13.—Normoglucuric and hyperglucuric zones.

renal glycosuria as ordinarily understood. There is, however, one difference. The normal increase in glucose excretion following carbohydrate intake is relatively slight, and is comparable to the rise in blood sugar: the glucose clearance is therefore little affected by food.

In the case of renal glycosuria the increase in glucose excretion greatly outstrips the rise in blood sugar, with a consequent increase in glucose clearance from the normal figure of about 0.06 ml. (5 mg./100 ml. normal urine glucose and 80 mg./ 100 ml. blood glucose) to a value approaching the glomerular filtration rate.

The study of glucose clearance may in fact assist in distinguishing between normal and abnormal glucose intolerance, and in assessing the severity of the latter when present; such studies would, of course, be of value in all cases of hyperglucuria, including the reabsorption defect of tubular renal disease.

There has hitherto been a preoccupation with tests of glucose concentration in glycosuria investigations, and little use has been made of excretion rate studies. Such studies can be of considerable value, since the excretion rate is little influenced by dilution of concentration owing to variation in intake and other causes. The normal range of glucose excretion per hour is 2–7 mg., with a mean of 4 mg.: values higher than this are found in diabetes, renal glycosuria, and lag glycosuria.

Recently Joplin has applied the method of excretion rate study to the diagnosis of prediabetes in his prednisone glycosuria test.

Summary

The glucose content of urine from 700 adults was determined quantitatively: 91% contained 1–15 mg./100 ml., with a mean of 6 mg., the remaining 9% had a higher glucose content, up to over 9,000 mg.

Investigation of the second group showed 20% to consist of diabetics, the remaining 80% were renal glycosurias and lag glycosurias in the ratio of 2 : 1.

The results of Clinistix tests were not wholly correlated to the quantitative findings: thus a few positive results were obtained in the normal group (1–15 mg./100 ml.), while a number of negative results were obtained in the group with higher glucose content.

Males had a higher percentage of urines with raised glucose content (12.1%) than females (3.7%).

The influence of age was studied, and the higher age groups were found to contain a larger percentage of glucose-rich urines, in both sexes.

Excretion of glucose in 24 hours was studied in 30 volunteers: excluding renal glycosurics, the range was 31.7–93 mg., with a mean of 65 mg.

The rate of glucose excretion was studied, and was found to be less subject to fluctuation than the glucose concentration of the specimens. The rate of nocturnal excretion was found to be less than diurnal: this fact was obscured by raised glucose content resulting from concentration of the overnight specimens.

Both concentration and rate of excretion of glucose are increased after carbohydrate intake, indicating that glucose intolerance is a normal phenomenon.

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REFERENCES

Apthorp, G. H. (1957). *J. clin. Path.*, **10**, 84.
Benedict, S. R., Osterberg, E., and Neuwirth, I. (1918). *J. biol. Chem.*, **34**, 217.
College of General Practitioners (1963). *Brit. med. J.*, **2**, 655.
Conway, E. J. (1950). *Microdiffusion Analysis and Volumetric Error*, 3rd revised ed., p. 225. Crosby Lockwood, London.
Folin, O., and Berglund, H. (1922). *J. biol. Chem.*, **51**, 209.
Froesch, E. R., and Renold, A. E. (1956). *Diabetes*, **5**, 1.
Huggett, A. St. G., and Nixon, D. A. (1957). *Lancet*, **2**, 368.
Joplin, G. F., Fraser, R., and Keeley, K. J. (1961). Ibid., **2**, 67.
Marks, V. (1959). *Clin. chim. Acta*, **4**, 395.