CXIV. AFTERNOON GLYCOSURIA¹.

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IN a previous paper [Harding and Selby, 1931] a phenomenon termed "afternoon glycosuria" was described. This meant that individuals who showed no, or little, fermentable urinary sugar after ingestion of 50 g. of glucose under the usual fasting morning conditions, showed some, or more, after a similar test at 4 p.m. "Afternoon glycosuria" was connected with the height of the blood-sugar curve, for, though at both times the blood returned to its original level in 2 hours, the peak of the curve in the afternoon was usually higher than in the morning.

The amounts of urinary fermentable sugar (and under the conditions this was presumed to be glucose) were small, being often only a few mg. in 2 hours. The morning blood-sugar curves were mainly of the "ideal" type because the subjects were selected as examples of those who had never shown urinary sugar under ordinary clinical tests.

Will "afternoon glycosuria" be observed in those subjects who, though non-diabetic, show clinical urinary sugar, either because they are types of renal glycosuria or cyclic hyperglycaemia? We have subsequently carried out morning and afternoon glucose tolerance tests on subjects who have shown a positive Benedict test for urinary sugar, when examined at the University Health Examination Clinic, and who present no other sign of disability.

Analytical methods.

Blood-sugar. 0.3 cc. cutaneous blood was precipitated in a centrifuge-tube by the method of Herbert and Bourne [1930]. The clear supernatant liquid after centrifuging yields true sugar with about 3 mg. per 100 cc. of non-fermentable reducing material. At the beginning we were troubled by laking and non-precipitation of plasma-protein. This, we found, was due to insufficient stirring of the blood and reagents.

Urinary sugar. Fermentable sugar was determined by the method previously described [Harding and Selby, 1931].

Modified Shaffer-Hartmann solution for sugar determinations. Part of the results was obtained by the use of the modified Shaffer-Hartmann reagent previously described, part by a further modification.

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The new reagent is very similar to that described by Spannuth and Power [1931]. A short description has been given by Harding and Downs [1932]. The new solution has the advantage of being more sensitive to glucose and less sensitive to the non-fermentable reducing substances present both in blood and urine.

"Afternoon glycosuria."

The fermentable urinary sugar is shown in Tables I and II. The frequent occurrence of small amounts of fermentable sugar in the fasting urine is to be contrasted with its non-occurrence in the subjects of the previous paper. This

Table I. *Excretion of "fermentable sugar" per 2 hours in subjects showing "afternoon glycosuria."*

Subject	Fermentable sugar, mg. per 2 hours.			
	7-9 a.m.	*9-11 a.m.	2-4 p.m.	*4-6 p.m.
22 (Nov.)	8	1479	321	3788
22 (Feb.)	20	792	241	2012
13	7	12	393	1213
27	5	0	31	612
31	23	113	105	562
11	0	21	22	309
29	3	18	5	124
6	22	13	10	55
10	2	10	10	53
33	7	3	3	36
26	5	5	11	32
24	0	7	14	21
19	0	6	3	18
20	0	2	0	10
28	0	0	5	5

* 50 g. glucose at 9 a.m.; at 4 p.m.

Table II. *Excretion of "fermentable sugar" per 2 hours in subjects failing to show "afternoon glycosuria."*

Subject	Fermentable sugar, mg. per 2 hours.			
	7-9 a.m.	*9-11 a.m.	2-4 p.m.	*4-6 p.m.
9	0	17	9	14
16	0	0	9	0
18	0	5	15	4
21	7	—	19	36
23	19	28	16	10
25	5	6	4	7
30	12	0	1	0
1	—	0	13	14
2	0	0	10	5
4	8	—	8	15
12	0	8	4	6
17	0	7	5	0
32	5	6	4	0

* 50 g. glucose at 9 a.m.; at 4 p.m.

probably represents in part a real difference corresponding to the difference in their behaviour to glucose and to the finding of excess urinary reducing substance in the routine examination. Part of it, however, may be due to

improper emptying of the bladder and collection of specimens. We have discussed this previously: these subjects were unused to strict metabolism observations; they corresponded much more closely than our previous group to the ordinary patient in private or hospital practice.

Because of these irregularly occurring amounts of fermentable sugar, we have scrutinised more carefully than formerly the figures on which we have based the conclusion that "afternoon glycosuria" is of common occurrence. Table I shows "afternoon glycosuria" in 14 subjects, representing, in this series, an incidence of 50 %. The phenomenon can evidently be repeated in the same individual, for subject 22 showed it on two occasions, although our previous experience had made us distrustful. Three months, however, had elapsed between the two sets of tests on subject 22. If the corresponding blood-sugar curves of this subject and some of the others be studied, it will be seen that renal glycosurians exhibit the phenomenon. Table II contains the results which cannot be interpreted as representing "afternoon glycosuria."

We have found, since writing the previous paper, that "afternoon glycosuria" is known to many of the medical officers of Life Assurance Companies. It is their practice to ask for a urine specimen after the evening meal in doubtful cases.

Morning and afternoon glucose tolerance curves.

In Figs. 1 and 2 are shown the blood-sugar curves of the subjects whose urinary sugar is represented in the tables. All subjects showing "afternoon glycosuria" also show a higher peak blood-sugar curve in the afternoon. In addition there are some who fail to show "afternoon glycosuria," yet who show high peak blood-sugar curves. This is understandable in some of the subjects who show no fermentable urinary sugar either morning or afternoon. In others, although there is fermentable sugar present in the 4-6 p.m. urine, yet it is not certain if this has arisen from the glucose ingested at 4 p.m., or is a continued excretion from the noon meal. Actually 26 out of the 28 experiments show a higher peak blood-sugar curve in the afternoon compared with the morning. In some the difference between the morning and afternoon blood-sugar peaks is very small. In 21, however, the difference is 10 mg. or over.

"Lag" type glucose tolerance curves.

In the previous paper attention was drawn to several blood-sugar curves fulfilling MacLean's [1922] definition of "lag" type. These showed small amounts of fermentable urinary sugar, but not sufficient to be detected by any of the usual clinical tests. It was suggested that the difference between our results and the clinical results was due to the latter being obtained on individuals possessing thresholds for sugar lower than normal.

Our contention is illustrated by subject 22. In November his morning tolerance curve reaches the peak of 187 mg. true glucose, or 212 mg. sugar

as determined by the older methods, and the urine shows clinical sugar. He would thus be classified as a "lag" type, since there is no other disability and he is a healthy vigorous young man. In February a repetition of the

Fig. 1.

Fig. 1. Showing morning and afternoon tolerance curves after 50 g. glucose in subjects showing "afternoon glycosuria."

Fig. 2.

Fig. 2. Showing morning and afternoon tolerance curves after 50 g. glucose in subjects failing to show "afternoon glycosuria."

Morning curves - - - -

Afternoon curves ———

morning curve gives a result of the "ideal" type, and the urine again shows clinical sugar. He now appears as a renal glycosuric, of the type recognised by Graham [1923]. We have determined the 2-hourly excretion of urinary

fermentable sugar in this subject for 3 days continuously. At no time is he actually free from urinary sugar, though the amounts before breakfast are too small to be detected by any usual clinical test. His fasting blood-sugar is within normal limits, and he thus appears to possess a threshold slightly below or at this level. On a single glucose tolerance test the accident of a determination in November or in February would classify him either as a "lag" type normal or a renal glycosuric. Contrast these results with the morning curve of subject 27 who shows a peak of 219 (old standards) and shows no urinary fermentable sugar. Here the sugar threshold is evidently high. Subject 7 (Fig. 3) shows a peak of 237 (old standards) on the morning curve and gives

Fig. 3. Showing morning and afternoon tolerance curves after 50 g. glucose in subject 7.

Morning curve - - - -
Morning glycosuria = 34 mg.

Afternoon curve ———
Afternoon glycosuria = 384 mg.

a urinary fermentable sugar excretion of 34 mg., an amount insufficient to give an ordinary clinical test. It is thus evident that to obtain clinical sugar in the urine of non-diabetics the sugar threshold in the blood must probably be lower than normal to allow of the escape of sufficient quantity. Further point is lent to our contention when we notice that all the subjects quoted by MacLean as of the "lag" type possessed small amounts of clinically demonstrable sugar the hour previous to the glucose tolerance test.

An unusual result.

In the previous paper and in this it has been assumed that "afternoon glycosuria" is related to the difference between the peaks of the morning and afternoon blood-sugar curves. The renal threshold has been assumed to remain constant for the individual. There has been a considerable discussion on this point. Faber [1927] upholds strongly the view of the constancy of the threshold. Many others, as summarised by Peters and Van Slyke [1930], have concluded that at least two thresholds for sugar exist, the first during the ascent of a blood-sugar curve, and a second during the descent.

The data on subject 7 point to the possible variation of the threshold for glucose. Fig. 3 shows the morning and afternoon blood-sugar curves and the urinary excretion. This subject apparently excretes small amounts of fermentable sugar continuously. The amount definitely increases after the morning test. The 2-4 p.m. urine again shows a little fermentable material. The afternoon blood-sugar curve is so similar to the morning curve that it is difficult to imagine two curves on the same individual showing greater agreement. Yet the afternoon urinary sugar excretion is over 10 times the morning excretion. In our present state of knowledge we can only state that the threshold appears to have altered. Hamburger [1919] has demonstrated variation to sugar permeability in the kidney of the frog under experimental changes in the ionic concentration of the perfusate, but so far such results have not been observed in the human organ. The possibility of a diurnal change of this character complicates enormously the explanation of the physiological glycosurias.

SUMMARY.

1. "Afternoon glycosuria" has been found in 14 out of 28 subjects, who showed "sugar" on routine urine examination. Renal glycosurians can show "afternoon glycosuria."
2. Over 60 % of the total subjects show a blood-sugar peak after 50 g. glucose higher at 4 p.m. than at 9 a.m.
3. One subject showing almost identical a.m. and p.m. glucose tolerance curves, gave marked "afternoon glycosuria." It is assumed that alterations in the renal threshold for glucose occur during the day in some subjects.

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