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Research Article

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GLUCOSE EXCRETION IN BRIGHT'S DISEASE¹

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The occurrence of hyperglycemia and glycosuria in nephritis has been observed and studied by Neubauer in 1910 and a number of subsequent investigators. A review of this subject has been included in the article on carbohydrate metabolism in nephritis by Linder, Hiller and Van Slyke (1925). They found that hyperglycemia and glycosuria were most frequent in cases with marked deficit of renal function; that nephritics with fasting hyperglycemia when fed glucose showed abnormally high and prolonged blood sugar curves, similar to those in mild diabetes; that nevertheless the respiratory quotients after glucose feeding rose as in normal subjects, indicating a normal combustion of glucose. The abnormality appeared to lie in a retarded transfer of glucose from blood to tissues, rather than in a retarded combustion. The renal threshold of sugar excretion appeared to be low in some cases, as evidenced by the appearance of a positive qualitative Benedict test for reducing substances in the urine.

However, as shown by Eagle (1926-27) and by Van Slyke and Hawkins (1929), normal urine may contain substances equivalent in reducing power to 0.1 per cent or more of glucose; but only about one-tenth of the reduction is actually due to sugar capable of fermentation, like glucose. To obtain interpretable data concerning the permeability of nephritic kidneys to glucose it is therefore necessary to base conclusions upon determinations of the fermentable sugar in the urine. The present studies are based on such determinations.

¹ A preliminary report of results was presented by the authors at the 1928 meeting of the American Society of Biological Chemists (Hawkins, MacKay, and Van Slyke, 1928).

METHODS

The blood sugar determinations were made by the microgasometric ferricyanide method of Van Slyke and Hawkins (1928) on cutaneous blood obtained by a clean deep prick with a sharp needle. The blood obtained in this way is practically arterial (Lundsgaard and Möller, 1922). We did not determine the fermentable blood sugar, but used "total blood sugar" values, because the non-fermentable material determined in blood by the ferricyanide method has been shown to be a relatively small and constant value (Van Slyke and Hawkins, 1929).

The reducing substances of the urine, fermentable and non-fermentable, were determined quantitatively by the Van Slyke-Hawkins gasometric methods (1928, 1929). In considering urinary excretions our conclusions have been based entirely on fermentable sugar values, since the unidentified non-fermentable reducing material in urine is relatively so much that in normal subjects it constitutes nearly all of the total reducing material.

Glucose ingestion tests. The subjects of these studies were given no food or fluids for a 12-hour period preceding the determinations. Each subject was given 200 cc. of water at 7:00 a.m. Blood was taken at 7:00 and 8:00 a.m., and urine collected for the period from 7:00 to 8:00 a.m. Glucose was given in 200 cc. of water at room temperature at 8:00 a.m. All intervals indicated on the charts are measured from this point. Blood specimens were taken at 0.25, 0.5, 0.75, 1.0, 1.25, 1.75, 2.15, 2.75, 3.15 and 3.75 hours. The urine specimens were collected at 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, and 4.0 hours. The subject remained in bed throughout the test and received no other fluid, food, or medication during this period. The amount of glucose given was 1 gram for each kilo of ideal weight estimated for the subject's height, age and sex, by figure 1 of McIntosh, Möller, and Van Slyke (1928). The glucose used was Merck's "C.P."

RESULTS

Blood sugar curves, and curves indicating the amounts of fermentable and non-fermentable reducing substances in the urine were obtained on 3 normal persons and on 19 patients with nephritis.

The blood and urine curves of the normal subjects are given in figure 1. Figures 2 to 11 show the curves obtained in the different forms and stages of nephritis.

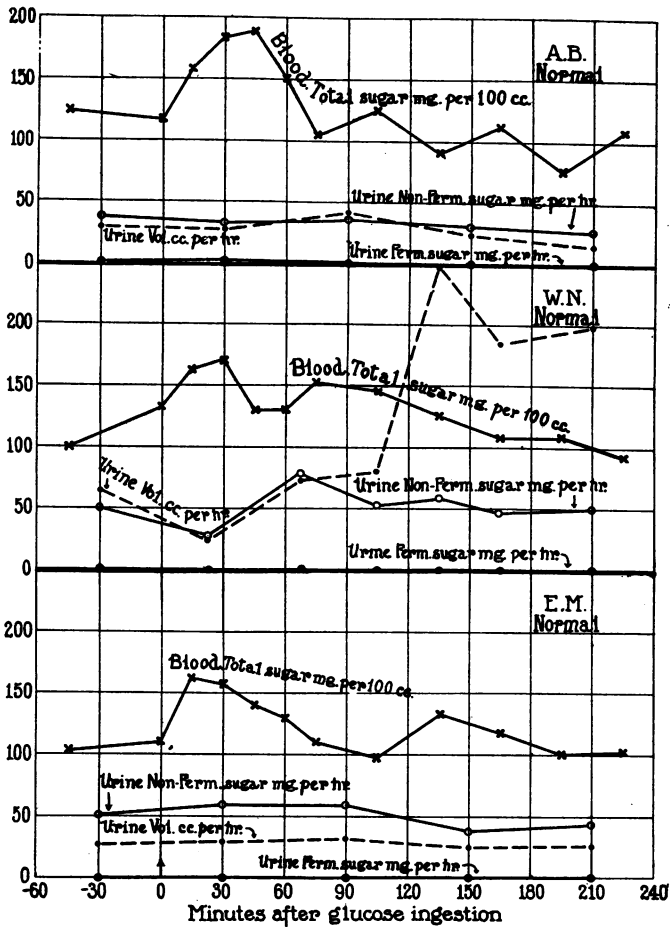


FIG 1. DATA ON NORMAL SUBJECTS

In table 1 is given a summary of the tests made on patients with Bright's disease. The Addis classification (1925) for Bright's disease is used, and the patients are grouped according to the divisions and subdivisions of this classification. The age, sex, blood pressure and

relative extent of edema at the time of the test are reported in Table 1 in order to give some aid in judging the patient's clinical status. The 2-hour phtalein excretion and the urea excreting ability in terms of the blood urea clearance (cc. of blood cleared of urea by 1 minute's excretion determined as described by Möller, McIntosh, and Van Slyke, 1928) are noted to indicate the state of renal function at the time of the tests. The clearance values are given in per cent of average

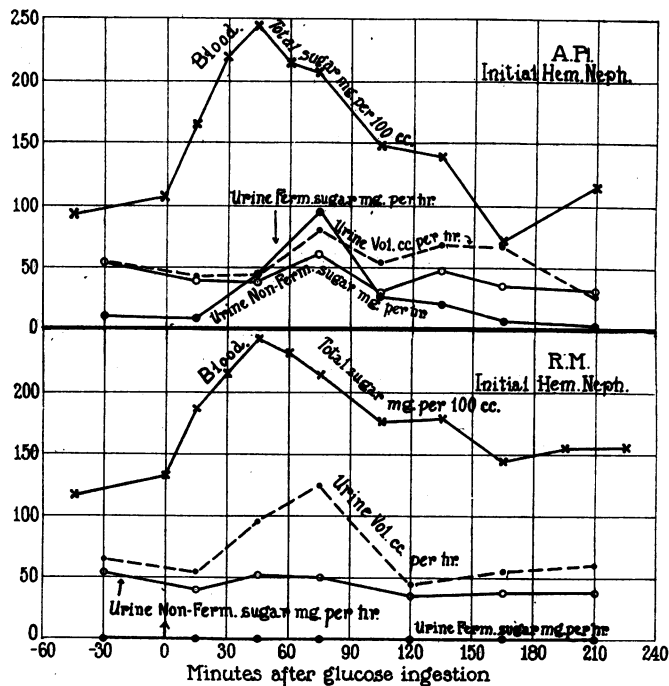


FIG. 2. DATA ON SUBJECTS WITH INITIAL HEMORRHAGIC NEPHRITIS

normal, viz., 54 cc. of blood per minute for the "standard clearance," estimated for urine output of 1 cc. per minute; 75 cc. per minute for "maximum clearance" with urine volumes exceeding 2 cc. per minute.

DISCUSSION

In normal subjects our data, taken with those of Eagle (1926-27) indicate that excretion of fermentable sugar is usually less than 5 mgm.

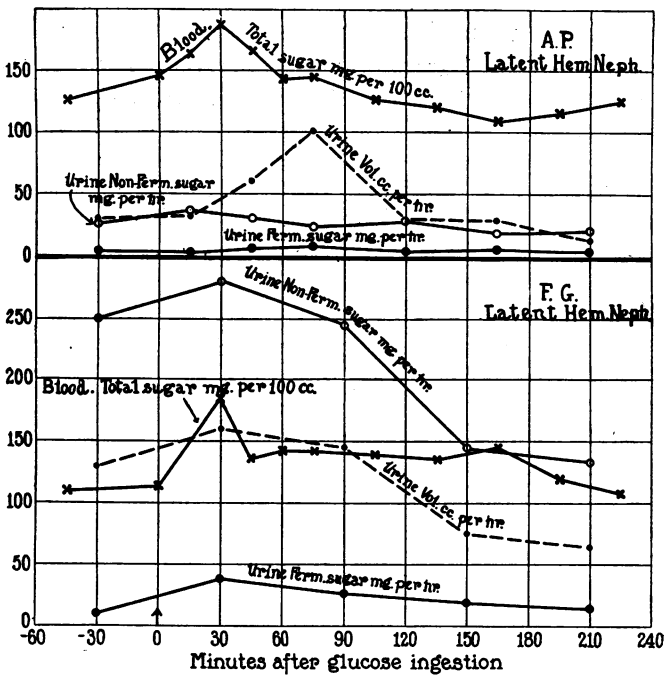


FIG. 3. DATA ON SUBJECTS WITH LATENT HEMORRHAGIC NEPHRITIS

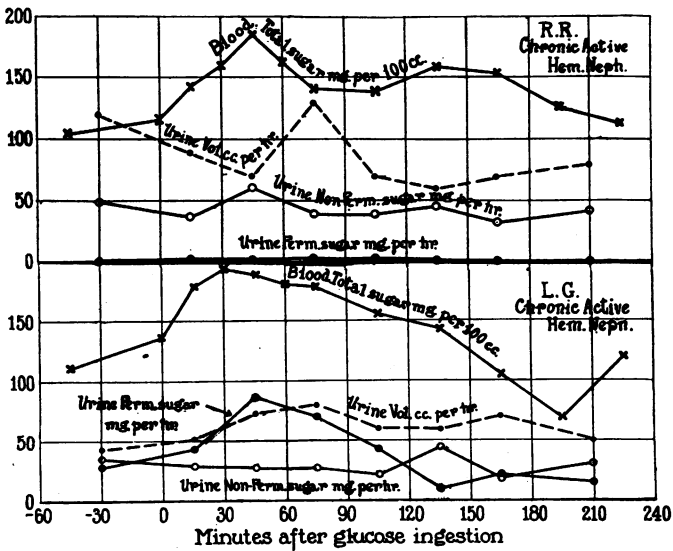


FIG. 4. DATA ON SUBJECTS WITH CHRONIC ACTIVE HEMORRHAGIC NEPHRITIS

per hour during fast, and is not increased above this level after consumption by mouth of 1 gram of glucose per kilo body weight. It is known, of course, that there are otherwise normal subjects who have

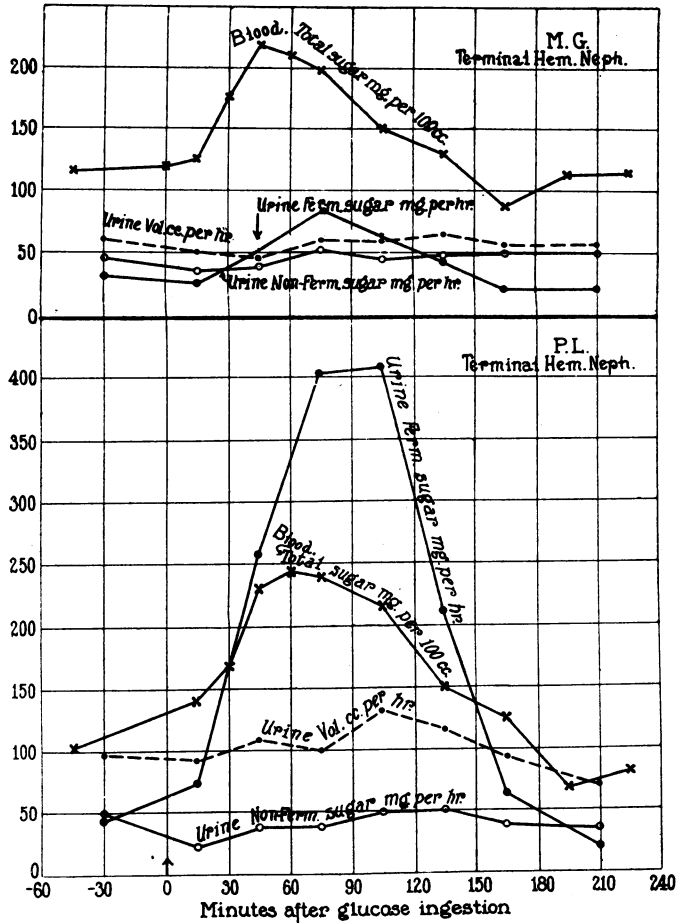


FIG. 5. DATA ON SUBJECTS WITH TERMINAL HEMORRHAGIC NEPHRITIS

continual or intermittent glycosuria, which appears attributable to a low renal threshold for glucose, since the glycosuria occurs in the presence of normal blood sugar values. Such cases appear, however, to be relatively rare. Our controls and those of Eagle may be taken

to represent the usual normal behavior, marked departure from which, if frequent in any given condition, may be considered as evidence of deviation from the probable normal behavior of the subjects examined.

Abnormal glycosurias (compared with the above controls) were shown by all our cases with degenerative Bright's disease (nephrosis)

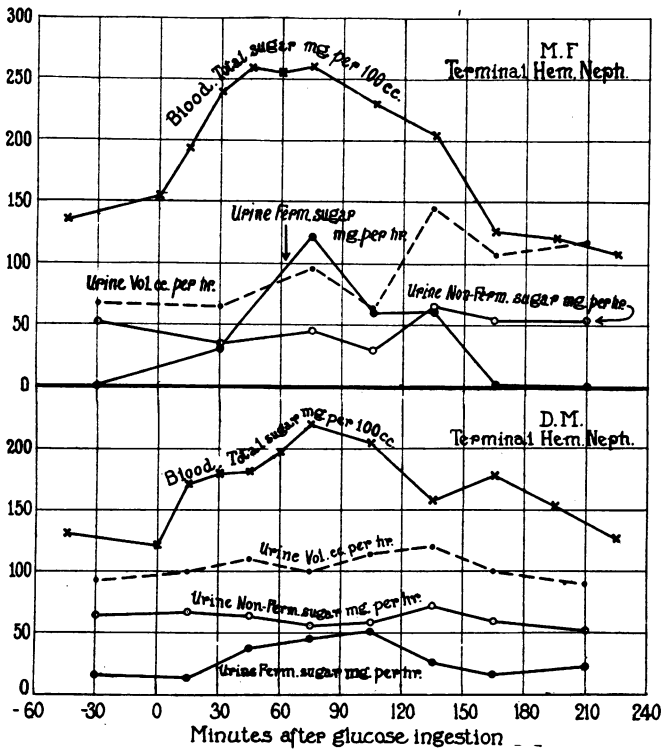


FIG. 6. DATA ON SUBJECTS WITH TERMINAL HEMORRHAGIC NEPHRITIS

and by all in the terminal stage of hemorrhagic nephritis. In excretion of fermentable sugar after glucose feeding all these patients exceeded the normal controls, and in excretion during fasting all except one, a terminal hemorrhagic, exceeded the controls.

The most marked glycosurias occurred in the degenerative group: 3 out of 6 cases showed over 0.3 per cent of fermentable sugar in the urine during fast, and over 1 per cent after glucose feeding.

In cases of initial and moderately advanced hemorrhagic nephritis, about half showed relative glycosuria, both fasting and after glucose ingestion.

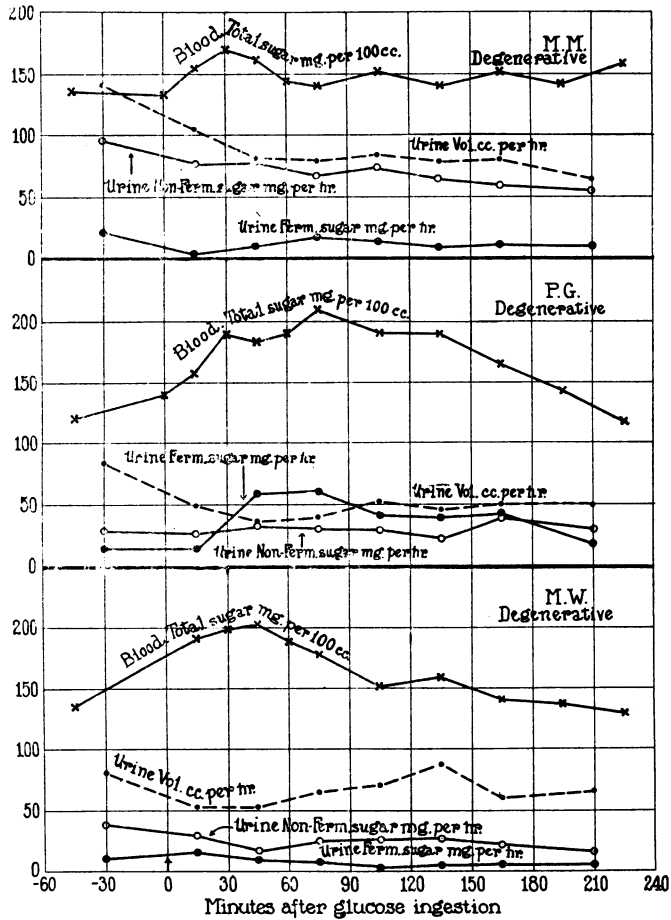


FIG. 7. DATA ON SUBJECTS WITH DEGENERATIVE HEMORRHAGIC NEPHRITIS

Of the 3 arteriosclerotic cases one showed a definite glycosuria (50 mgm. per hour) after glucose feeding, none while fasting.

Comparison of blood sugar curves with fermentable sugar excretion indicates that the glycosurias in all types of the disease appear attribut-

able to low excretion thresholds rather than to high blood sugar values. In some cases, it is true, particularly in the terminal hemorrhagic group, the blood sugar peak after glucose ingestion is so high (210–266 mgm. per cent) that glycosuria would be expected over a normal threshold. However, nearly all such cases showed glycosuria also in the fasting state, with relatively low blood sugar values. The work of Linder, Hiller, and Van Slyke (1925) has shown that somewhat high

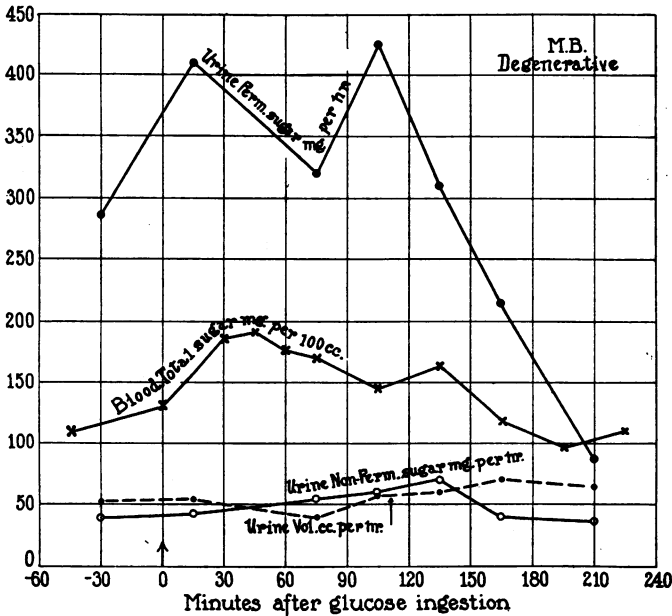


FIG. 8. DATA ON A SUBJECT WITH DEGENERATIVE HEMORRHAGIC NEPHRITIS

and prolonged blood sugar curves after glucose feeding are common in nephritis, and are unconnected with any retardation in the rate at which glucose can be burned, or with any other evidence of diabetes.

In the degenerative cases showing gross glycosuria, both fasting and after glucose feeding, the blood sugar curves were within normal limits.

It appears probable that many cases heretofore reported as combined nephritis and diabetes have been nephritis with renal glycosuria.

It is possible that the glycosuria is due to failure of the renal tubules to reabsorb glucose from the glomerular filtrate. Such an hypothesis

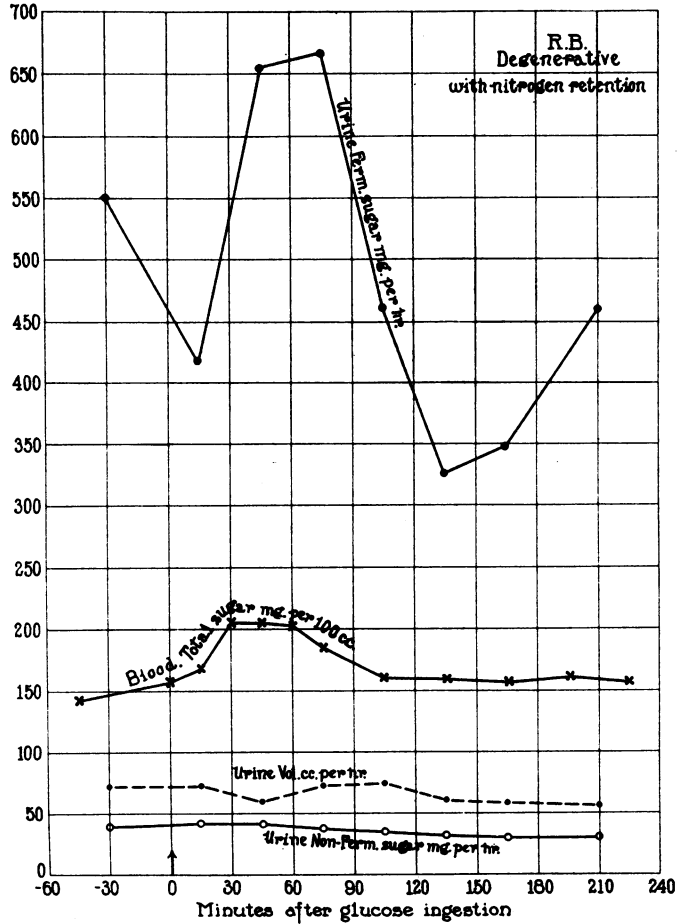


FIG. 9. DATA ON A SUBJECT, R. B., WITH DEGENERATIVE HEMORRHAGIC NEPHRITIS WITH NITROGEN RETENTION

appears somewhat plausible because of the especially marked glycosuria observed in certain of the degenerative cases, in which the tubules are known to be especially involved.

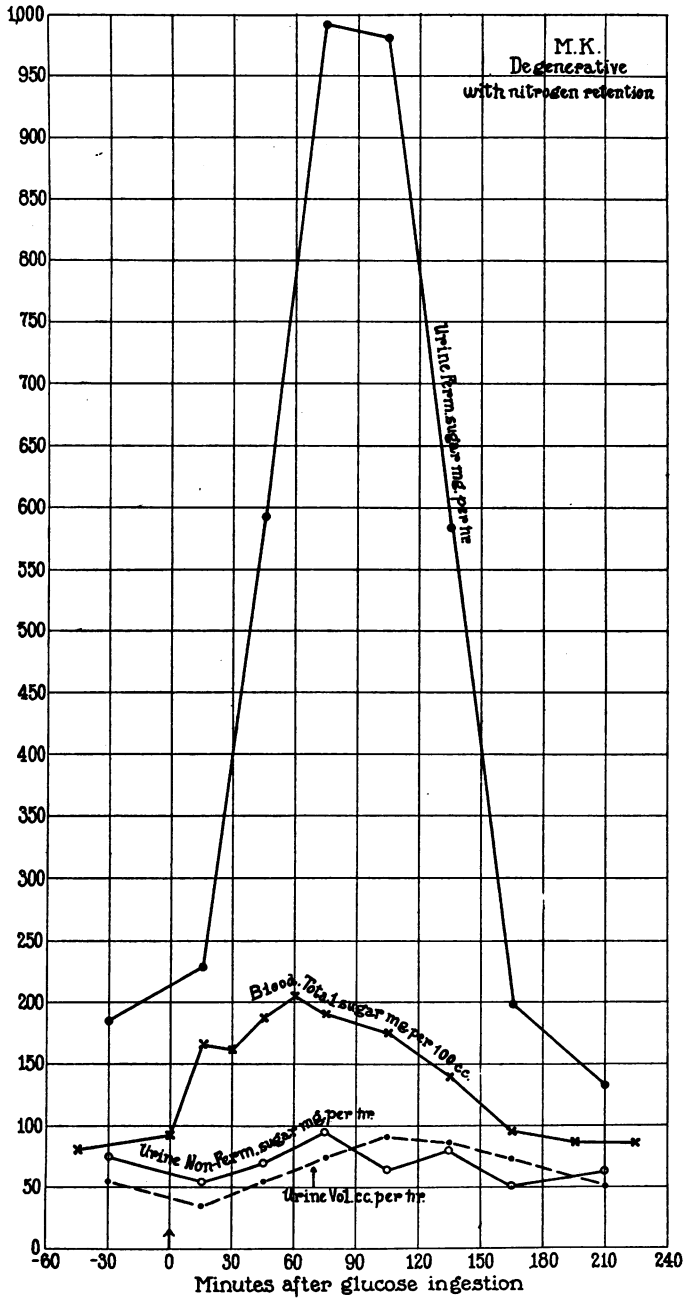


FIG. 10. DATA ON A SUBJECT, M. K., WITH DEGENERATIVE HEMORRHAGIC NEPHRITIS WITH NITROGEN RETENTION

Case number	Hospital number	Diagnosis		Complications	Age	Sex	Heart size	Blood pressure	Eye grounds	Edema	Plasma			
		Bright's disease									Urea nitrogen	N.P.N.	Creatinine	Cholesterol
		Type	Stage											
R. M.	6353	Hemorrhagic	Initial		38	F.	Normal	138/90	Normal	0	mg. per cent	mg. per cent	mg. per cent	mi. per cent
A. Pl.	6139	Hemorrhagic	Initial		19	M.	Normal	150/95	Normal	0	23.8	35.0	48.0	1.97
A. P.	6251	Hemorrhagic	Latent		13	M.	Increased	110/60	Normal	+	8.2	31.0	1.30	
F. G.	6162	Hemorrhagic	Latent		20	F.	Slightly increased	200/115	Normal	0	12.5	28.0	1.58	45
L. G.	6123	Hemorrhagic	Active		19	F.	Normal	150/105	Hemorrhages	+	30.6	51.0	2.26	81
R. R.	6475	Hemorrhagic	Active		25	F.	Normal	165/114	Normal	++	8.8	27.0	1.36	
M. G.	5074	Hemorrhagic	Terminal	Chronic middle ear	15	M.	Normal	150/90		0	45.0	59.0	4.10	
P. L.	5210	Hemorrhagic	Terminal		30	M.	Slightly increased	150/90		0	78.2	118.0	4.50	28
D. M.	6238	Hemorrhagic	Terminal		16	M.	Increased	135/85	Normal	0	46.1	64.0	4.39	27
M. F.	6183	Hemorrhagic	Terminal		30	F.	Increased	220/150	Hemorrhages, retinitis	0	68.4	102.0	9.00	
P. G.	6482	Degenerative	Active	Pulmonary tuberculosis	25	M.	Normal	105/75	Normal	+++	8.8	22.0	1.36	58
M. M.	6184	Degenerative	Active		18	M.	Normal	105/75	Normal	+++	6.6	20.0	1.33	53
M. B.	6172	Degenerative	Active		29	M.	Normal	110/70	Normal	+	12.7	33.0	1.67	83
M. W.	6473	Degenerative	Active	Empyema	12	M.	Normal	115/70	Normal	+++	18.8	28.0	1.36	60
R. B.	5505	Degenerative	Terminal		11	M.	Normal	115/60	Normal	++	22.3	49.0	3.16	
M. K.	5949	Degenerative	Terminal		20	M.	Normal	130/80	Normal	+++	37.3	50.0	3.10	68
K. C.	6102	Arterio-sclerotic			51	F.	Slightly increased	150/85	Normal	0	15.7	36.0	1.67	
M. Fe.	6446	Arterio-sclerotic			49	F.	Normal	235/155	Normal	0	11.4	14.0	1.36	31:
M. Go.	6466	Arterio-sclerotic		Cardiac failure	49	F.	Greatly increased	240/145	Retinitis	+	31.1	57.0	1.76	

TABLE 1
Laboratory data on patients

Patient	Blood					Urine (excretion per 12 hours)											Renal function		Sugar in blood and urine								
	Plasma proteins					Protein	Formed elements											Phthalein excretion (2 hours)	Standard blood urea clearance	Fasting blood sugar	Fasting fermentable urine sugar	Maximum blood sugar after glucose ingestion	Maximum fermentable sugar in urine after glucose ingestion				
	Hemoglobin	Albumin	Globulin	Total	A/G ratio		Erythrocytes	Leucocytes and epithelial cells	Casts							Phthalein excretion (2 hours)	Standard blood urea clearance							Fasting blood sugar	Fasting fermentable urine sugar	Maximum blood sugar after glucose ingestion	Maximum fermentable sugar in urine after glucose ingestion
									Total	Hyaline	Blood	Fatty	Epithelial	Granular	Waxy												
0	15.7	4.46	3.15	7.61	1.41	0.9	106.00	50.88	0.58	100	0	0	0	0	0	0	0	60.9	48.3	117	0.0	243	2.0				
1	16.1	4.32	2.54	6.86	1.70	1.6	13.49	11.48	1.08	83	3	0	0	14	0	0	37.0	33.5	94	12.0	245	97.0					
1	20.1	1.52	4.26	5.78	0.36	3.1	7.27	4.10	0.26	100	0	0	0	0	0	0	83.2	74.7	125	5.0	187	8.0					
1	17.0	3.06	2.08	5.14	1.47	2.5	11.02	3.39	1.75	100	0	0	0	0	0	0	54.8	35.2	109	22.0	184	50.0					
0	16.5	2.29	2.60	4.89	0.88	5.4	9.20	27.00	13.95	16	0	0	28	64	0	0	19.8	19.8	109	31.0	192	86.0					
8	15.0	1.23	2.68	3.91	0.46	2.9	25.46	26.80	12.46	90	0	8	0	2	0	0	56.4	46.3	104	0.0	186	8.0					
8	14.2	3.68	2.26	5.94	1.63	3.3	39.44	23.20	4.06	0	0	0	0	0	0	100	15.6	15.9	115	32.0	218	89.0					
8	7.7	3.31	2.03	5.34	1.63	3.6	36.48	5.93	0.52	0	0	0	0	0	0	100	4.9	13.5	102	46.0	243	410.0					
9	11.5	3.07	2.54	5.61	1.21	4.6	190.68	77.20	4.48	67	13	0	0	12	0	8	14.1	18.7	131	18.0	221	52.0					
9	11.5	3.69	2.44	6.13	1.50	1.9	++	+	+	0	0	0	0	0	0	100	8.0	6.3	135	4.7	261	122.0					
1	16.5	0.71	3.35	4.06	0.21	5.4	0.24	12.40	4.96	33	0	25	0	34	8	0	56.7	58.3	121	14.0	210	62.0					
9	10.1	1.34	3.47	4.81	0.39	6.5	0.31	6.82	1.86	70	0	20	10	0	0	0	67.8	144.0	134	25.0	169	20.0					
9	17.1	1.92	2.72	4.64	0.70	7.5	0.33	24.48	5.30	80	0	16	4	0	0	0	54.6	55.9	111	287.0	188	410.0					
0	13.0	1.65	2.32	3.97	0.71	3.8	0.06	14.11	0.88	65	0	35	0	0	0	0	50.1	45.8	135	12.0	202	16.0					
2	19.9	1.29	3.12	4.41	0.41	3.9	0.40	4.29	1.48	30	0	0	0	43	0	27	10.2	22.2	143	550.0	205	628.0					
2	10.5	1.96	2.90	4.86	0.68	3.7	0.39	38.53	7.57	10	0	10	10	25	5	40	7.0	18.6	80	189.0	204	1,095.0					
3	19.0	4.32	3.05	7.37	1.42	0.1	0.58	0.43	0.14	100	0	0	0	0	0	0	50.0	78.2	117	1.0	157	1.0					
3	20.0	4.46	2.81	7.27	1.59	0.3	0.58	0.32	0.32	100	0	0	0	0	0	0	74.0	88.5	112	0.0	191	52.0					
3	15.7	3.21	2.79	6.00	1.15	0.8	3.04	0.23	0.08	50	0	0	0	50	0	0	28.9	11.1	118	9.0	201	12.0					

GLUCOSE EXCRETION IN BRIGHT'S DISEASE

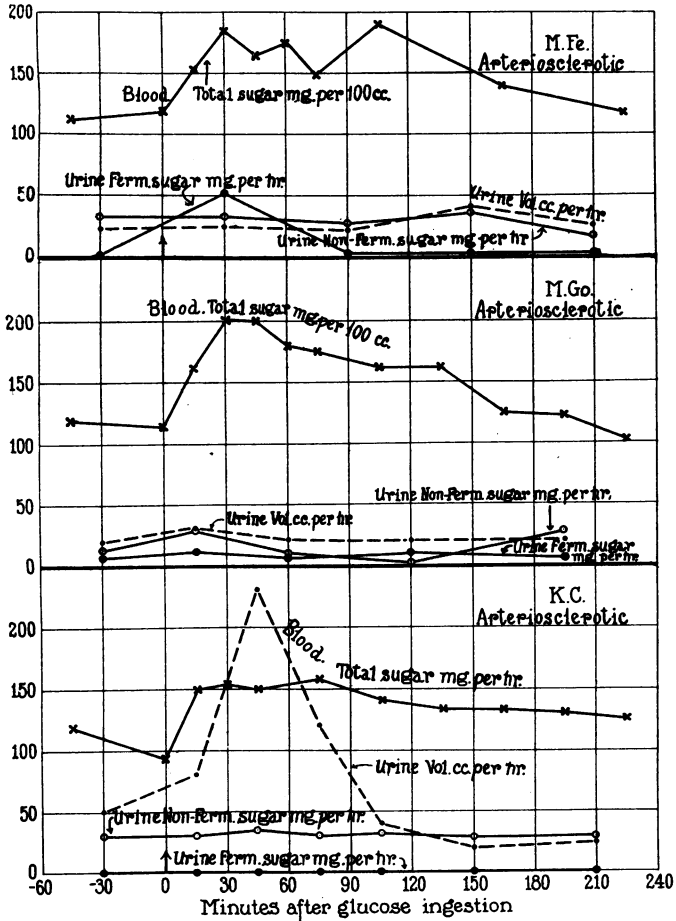


FIG. 11. DATA ON SUBJECTS WITH ARTERIOSCLEROTIC HEMORRHAGIC NEPHRITIS

SUMMARY

Excretion of fermentable sugar has been studied, together with blood sugar curves after glucose ingestion, in normal subjects and in patients with hemorrhagic, degenerative, and arteriosclerotic Bright's disease.

Excretion of fermentable sugar exceeding that observed in the normal control subjects was found to be frequent in all types of the disease. In the degenerative and advanced hemorrhagic types it occurred in all the cases we examined. In half the degenerative cases it amounted to gross glycosuria, the urine containing more than 0.3 per cent of fermentable sugar during fasting and more than 1.0 per cent after glucose ingestion.

The blood sugar values observed before and after glucose ingestion indicated that in all our cases the glycosuria was renal rather than diabetic.

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