KETOGENIC DIET IN THE TREATMENT OF PYURIA IN CHILDHOOD*

BY

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In October, 1931, Helmholtz¹ published results of the treatment of pyuria in children by means of the ketogenic diet. This form of treatment was suggested to him by the observation that the urine of a patient being treated for epilepsy by ketogenic diet remained free of bacterial cloudiness after being kept for a week. He quotes Neilson², who in 1920 gave cream to patients with urinary infection and claimed good results due to increased acidity of the urine. In spite of previous in vitro experiments showing that the colon bacillus can grow in a medium of an acidity of pH 5.0 Nielson stated that in the absence of obstruction mere inhibition of growth is sufficient to cure a urinary infection. Even before this Shohl and Janney³ in 1917 reported that the growth of bacillus coli was inhibited in urine of a pH of 4.6.

At the same time and from the same clinic, Clark⁴ reported a series of adult cases of urinary infection treated by ketogenic diet with good results.

Helmholtz postulates two conditions which must be fulfilled for the effective employment of this mode of treatment. First, there must be a state of ketosis induced; and secondly, the urinary pH must be below 5.6. In a test series of four normal cases ammonium chloride was given, resulting in a urinary pH varying from 4.8 to 5.3. The growth of micro-organisms after inoculation and incubation of the urine of these patients was abundant. Again, in a test series of normal cases on ketogenic diet only those urines with pH 5.6 or below were rendered sterile after inoculation with micro-organisms and incubation. Ketosis was present.

More recently Wilson⁵ was completely successful in treating himself with ketogenic diet for a urinary infection which had lasted seven months.

Present investigations.

The object of this communication is to report the results of this form of treatment in a series of six cases. Each patient was investigated on admission with regard to renal function by the ability to excrete phenolsulphonephthalein and to concentrate urea. The non-protein nitrogen of the blood was estimated and intravenous pyelography performed. The patients were then started on the ketogenic diet which was constructed by use of the formula

$$\frac{\text{Ketogenic units (K)}}{\text{Anti-ketogenic units (A.K.)}} = \frac{\text{Fat} + \frac{1}{2} \text{ Protein}}{\text{Carbohydrate} + \frac{1}{2} \text{ Protein}}$$

* The work was carried out during the tenure of a Carnegie Research Scholarship.

Table 1 shows the method of recording the daily observations. The first diet (A) was constructed to have K : AK ratio of 2 : 1 and this was steadily increased to 5 : 1 (Diet D) or even 6 : 1. Actually details of the diet are omitted for the sake of brevity but a diet of this nature can be easily constructed by reference to tables. Twenty-four hour specimens of urine, kept under oil, were examined in the side-room of the ward, Universal indicator being used for estimation of pH and Rothera's test for acetone. The duration of the course varied from 14 to 22 days. Cultures of the urine were made on the first and last days of the treatment.

Table 2 gives a summary of the results. Clinical details and results of the renal function tests are to be found in the summaries of the case reports. The acidity and ketonuria were considered to be satisfactory if the pH was 5.5 or lower and a very definite reaction to Rothera's test was obtained.

Results.—Four of the six cases had sterile urine free from pus at the end of the period of dietetic treatment. Cases 1 and 2 appeared to be cured, their urine being sterile one month after treatment had ceased, but Case 3 relapsed one week after the diet was stopped and Case 4 two weeks after. Case 5 was improved, there being no pus present in the urine and only a slight growth on culture, but a week after cessation of diet relapse occurred. In the sixth case, the urine was quite unaffected by the diet.

From these results it seems allowable to conclude that a state of ketosis accompanied by a highly acid urine does render the urine bactericidal, but that relapse is prone to occur. It is interesting to note that in each case in which relapse occurred some abnormality in the pyelogram was found. In these cases the urine became temporarily sterilized, but when treatment was stopped, either reinfection occurred, or a latent focus of infection became active once more.

Discussion.

In these six cases renal function tests all showed a poor result. In Case 5 where renal function tests had been performed in 1931, the lapse of a year showed a very considerable fall in the percentage excretion of phenolsulphonaphthalein and in concentration of urea. Of all the patients this child showed the worst renal function, and it is interesting to note that the response to ketogenic diet was very poor both as regards acetonuria and acidity. Clark suggests that in a patient with diminished renal function the kidney is unable to excrete a urine of a low pH. He quotes a case of unilateral hydronephrosis in which urine from the normal kidney had pH 5.0, that from the affected one pH 7.0. In Case 6 renal function was also diminished, but had not reached the low level of Case 5.

By intravenous pyelography with uroselectan B an abnormality of the urinary tract was demonstrated in three of the uncured cases (Cases 3, 5 and 6). One or both kidney pelves were dilated with clubbing of the calices. In Case 4 the picture suggests an early deformity of the right renal pelvis. In contra-distinction, the two patients whose urines remained sterile and

TABLE 1.
CASE 4: A. M., FEMALE, 11½ YEARS.

Date	Diet	K Units	AK Units	Fat gm.	CHO gm.	Prot. gm.	Daily cal. intake	Urine			Remarks
								pH	Ketone bodies	Pus	
16-17 Oct.	A	94	47	80	32	29	960	7.5	Tr.	+	CaCl ₂ gm. xv 4x daily
17-18 "	B	110	37	97	24.5	26	1087	6.5	Tr.	+	
18-19 "	C	133	35	120	23	25	1282	4.5	+	+	
19-20 "	D	150	32	137	18.5	27	1415	4.5	+	—	
20-21 "	"	"	"	"	"	"	"	4.5	+	—	
21-22 "	"	"	"	"	"	"	"	4.5	+	—	
22-23 "	"	"	"	"	"	"	"	4.5	+	—	
23-24 "	"	"	"	"	"	"	"	4.5	+	+	
24-25 "	"	"	"	"	"	"	"	4.5	+	+	
25-26 "	"	"	"	"	"	"	"	4.5	+	—	
26-27 "	"	"	"	"	"	"	"	4.5	+	—	Culture sterile. No pus
27-28 "	"	"	"	"	"	"	"	4.5	+	—	
28-29 "	"	"	"	"	"	"	"	4.5	+	—	
29-30 "	"	"	"	"	"	"	"	4.5	+	—	
								4.5	+	—	

TABLE 2.

Case	Age Years	Dura- tion of illness. Years	No. of days on ketogenic diet	Acidity and ketonuria	Results		Remarks
					Immediate	After 1 week	
1	2	6/52	16	Poor	Pus — Culture —	Pus — Culture —	Pyelogram normal
2	8	2/12	15	Satisfactory	Pus — Culture —	Pus — Culture —	Pyelogram normal
3	7½	7/12	22	Satisfactory	Pus — Culture —	Pus + Culture +	Pyelogram abnormal
4	11½	1	14	Satisfactory	Pus — Culture —	Pus — Culture —	Pyelogram ? abnormal
5	11	3½	15	Very poor	Pus — Culture —	Pus + Culture +	Relapsed after 2 weeks Pyelogram abnormal NH ₄ Cl for 2 days; vomited, discontinued
6	12	1,1/12	15	Satisfactory	Pus + + + Culture +	Pus + + + Culture +	Pyelogram abnormal

free from pus one month after the cessation of treatment, showed no abnormality on intravenous pyelography.

Neale⁶ contends that chronic non-tuberculous pyuria is nearly always associated with deformity of the urinary tract. Of 56 cases which he followed up, 7 with persistent pyuria had also a deformity of the urinary tract. The above observations are in agreement with this, as the two patients who recovered on ketogenic diet had a relatively short history of infection and showed no X-ray evidence of abnormality of the urinary tract. Again in an investigation of cases of pyuria admitted to the Royal Hospital for Sick Children in the years 1920–1930, most of whom were under Professor Leonard Findlay's care, of a total of 435 admissions to hospital, only 7 over the age of 3 years died. In 6 of these cases abnormality of the urinary tract was demonstrated, in 5 at autopsy and in 1 at operation. In the seventh case no post-mortem examination was allowed.

If no abnormality is present ketogenic diet is probably an efficient method of clearing up a urinary infection, but it is questionable if it has any advantage over the older forms of treatment. Its use would appear to be limited to older children. In the acute stage of the disease when fever is present it seems unwise to give a diet so deficient in carbohydrate. Further, the diet can only be used satisfactorily in hospital, and even there co-operation on the part of the patient is required. The diet is unpleasant and, as in treating epilepsy, considerable difficulty is encountered when the higher K : AK ratios are given.

Summary.

1. Six cases of chronic pyogenic infection of the urinary tract were treated with ketogenic diet.
2. At the end of treatment the urine was sterile in four cases and growth on culture scanty in a fifth, but three relapsed within three weeks. The sixth case showed no change in the condition.
3. In the two cases who were permanently cured the duration of the disease was short and no abnormality of the urinary tract was observed. In each of the four cases in which treatment failed abnormality of the urinary tract was demonstrated by pyelography.
4. It would appear that ketogenic diet is of little value as a curative agent in pyuria associated with abnormality of the urinary tract.

I wish to acknowledge my indebtedness to Dr. Stanley Graham who suggested this investigation and in whose wards the work was done.

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Appendix.

Summaries of case reports.

Case 1.—B. C., female, aged 2 years. B. coli infection of urinary tract of 3 weeks duration. Febrile on admission. Physical examination negative. Tuberculin skin reactions negative. Ketogenic diet started in sixth week of illness and continued for 16 days. The amount of acetone present in the urine and pH level varied considerably in spite of the addition of NH_4Cl grm. 15 every 4 hours. This was discontinued because of vomiting on the third day of administration. Urine at end of treatment was sterile and was still sterile 3 weeks later. Non-protein nitrogen 29.2 mgrm. per cent. Urea concentration test:—before urea, 2.02, first hour, 1.96, second hour, 1.20 per cent. Phenolsulphonephthalein excretion 34 per cent. in 2 hours. Intravenous pyelography showed no abnormality.

Case 2.—H. Y., female, aged 8 years. In hospital in 1931 with B. coli infection of urinary tract which cleared up on a course of injections of protosil into the bladder. Readmitted in October, 1932, with a staphylococcus albus infection of one month's duration. Ketogenic diet given for 15 days. Urine sterile at the end of treatment and still sterile 3 weeks later. Tuberculin skin reactions positive but no tubercle bacilli found on 2 examinations of the urine. Intravenous pyelography revealed no abnormality. Non-protein nitrogen 33.7 mgrm. per cent. Urea concentration test:—before urea 1.64, first hour 2.3, second hour 2.2 per cent. Phenolsulphonephthalein excretion 44 per cent. in 2 hours.

Case 3.—M. J., female, aged $7\frac{1}{2}$ years. B. coli infection of the urinary tract of 7 months duration. Physical examination negative. Tuberculin skin reactions negative. Cystogram negative. Intravenous pyelography showed both kidney pelves and ureters to be dilated, the left more than the right. Ketogenic diet given for 14 days. Urine sterile at the end of treatment but relapse occurred a week later. Non-protein nitrogen 22 mgrm. per cent. Urea concentration test:—before urea 0.96, first hour 1.19, second hour 1.61 per cent. Phenolsulphonephthalein excretion 48 per cent. in two hours.

Case 4.—A. M., female, aged $11\frac{1}{2}$ years. B. coli infection of 1 year's duration. Physical examination negative. Tuberculin skin reactions positive, but no tubercle bacilli found on 1 examination of the urine. Ketogenic diet given for 14 days with sterilization of the urine. Relapse occurred about 2 weeks later. Intravenous pyelograph showed doubtful early dilatation of right kidney pelvis and 1 calyx. Non-protein nitrogen 27 mgrm. per cent. Urea concentration test:—before urea 1.69, first hour 1.13, second hour 0.71 per cent. Phenolsulphonephthalein excretion 54 per cent. in two hours.

Case 5.—H. M., female, aged $10\frac{1}{2}$ years. Pyuria diagnosed in 1929, since when she has been in hospital on 6 occasions. Physical examination negative. Tuberculin skin reactions positive, but examination of the urine for tubercle bacilli was negative on five occasions. Retrograde pyelography by Mr. Matthew White in 1930 showed clubbing of calices of the right kidney. In 1931 non-protein nitrogen was 31.5 mgrm. per cent. Urea concentration test:—before urea 1.64, first hour 1.66, second hour 1.86 per cent. Phenolsulphonephthalein excretion in two hours 62 per cent. Retrograde pyelography by Mr. Matthew White showed both kidney pelves and ureters to be dilated. In October, 1932, ketogenic diet was given for 16 days with improvement, there being no pus and only a slight growth on culture of the infective organism, a gram-negative cocco-bacillus. In this case pH of the urine was never below 6.5 and acetonuria was not marked. A week after diet was stopped relapse occurred. Non-protein nitrogen 43 mgrm. per cent. Urea concentration test:—before urea 0.87, first hour 0.84, second hour 0.88 per cent. Phenolsulphonephthalein excretion 8 per cent. in 2 hours.

Case 6.—I. D., female, aged 12 years. *B. coli* infection of urinary tract since January, 1931. Tuberculin skin reactions negative. Physical examination negative. Cystogram negative. Cystoscopic examination by Mr. Matthew White revealed a dilated bladder with marked cystitis and double 'golf hole' ureter. Non-protein nitrogen 31 mgrm. per cent. Urea concentration test:—before urea 1·17, first hour 1·19, second hour 1·87 per cent. Phenolsulphonephthalein excretion 43 per cent. in 2 hours. In January, 1932, intravenous pyelography showed enlargement of right kidney pelvis and ureter. In October, 1932, ketogenic diet given for 16 days with no effect on the urine in spite of a constant low pH and adequate acetonuria. Non-protein nitrogen 35·5 mgrm. per cent. Urea concentration test:—before urea 0·97, first hour 1·35, second hour 1·28 per cent. Phenolsulphonephthalein excretion 43 per cent in 2 hours.