

KETOGENIC DIET IN PERSISTENT PYURIA

BY

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The ketogenic diet as a treatment of persistent pyuria was first introduced by Clark and Helmholz in 1931¹. They found that when the acidity of the urine was increased below pH 5.4 the urine became bacteria-free in a short time and in conjunction with this the pus disappeared from the urine. Later Clark² (1932) demonstrated that this sterilization was not due to the acidity of the urine. In 1933 Fuller³ showed experimentally that the principal factor inhibiting the growth of bacteria in the urine was due to the alpha-beta-hydroxy-butyric acid. This ketone body is inactive at a reaction more alkaline than pH 5.6. Gray⁴ has reported that he found the ketogenic diet helpful in pyelitis caused by staphylococci. Bell⁵ discussed the value of the diet as a therapeutic measure. Clark⁶ reported beneficial results in every one of fifty-three cases which he treated. Rennie⁷ on the other hand in six cases of pyelitis in children found that ketogenic diet cured two, caused temporary cessation of symptoms with later relapse in three, and was valueless in one. He cites a cure in one adult case. He considers ketogenic diet of little value as a curative agent in pyuria associated with an abnormality of the urinary tract.

Since the spring of 1932, fourteen cases of persistent pyuria have been treated by means of the ketogenic diet. The ages of the children, all girls, were from four to twelve years. In this present series there were three children with bilateral hydronephrosis, one with a prolonged pyuria but no anomaly, while the remainder had a unilateral hydronephrosis. All those with an anomaly had an obstruction either at the uretero-vesical orifice, in the ureter or at the pelvo-ureteral junction due to an aberrant artery. One child had a left renal calculus as well.

The routine followed was that outlined by the Mayo Clinic⁸. The patients were started on a $\frac{\text{fatty acid}}{\text{glucose}}$ ratio $\frac{1.6}{1}$ and over a period of a week the ratio was increased to $\frac{3.0}{1}$. In a few cases this ratio was increased to $\frac{3.3}{1}$. Later cases were given ten grains of ammonium chloride three times a day to hasten the formation of an acid urine. When possible these cases were discharged from the hospital on a modified ketogenic diet which consisted of low percentage vegetables and fruits, no bread, sugar, pastry, candy; bran substitutes for bread stuffs; normal protein and high fat consisting of half a pint of 32 per cent. cream and a liberal allowance of butter.

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Urines were cultured frequently, bacterial counts made and the urinary pH determined by the colorimetric method. The bacterial species found in this group of cases included *B. coli*, *B. coli communior*, *Bacillus dispar*, *staphylococcus haemolyticus* and non-haemolyticus, *C. xerosis* and streptococci.

Before the introduction of the ketogenic diet, surgical treatment was used as the treatment of persistent pyuria. This consisted of dilating or removing the cause of obstruction which allowed the kidney to drain more freely. In chart I is seen the effectiveness of surgical treatment in seven cases, over a period of eight months to four years. In these cases the hydronephrosis had not increased in size in any case, and in the majority it was either smaller or had disappeared. In one case there was a recurrence of the pyuria and in all cases there was bacilluria. In hope of

CHART I.

NAME	AGE IN YEARS	ANOMALY	DURATION OF ILLNESS PREVIOUS TO TREATMENT	TREATMENT	BACTERIAL SPECIES	FOLLOW-UP
M. R.	4	Rt. hydronephrosis, stricture rt. ureter	3 mth.	Surgical dilation of rt. ureter	<i>B. coli</i> communior to <i>b. dispar</i>	In 4 yr. hydronephrosis disappeared, urine culture positive for micro-organisms. No pus cells
G. G.	6	Bilateral hydronephrosis bilateral ureterovesical obstruction	3 mth.	Surgical	<i>B. coli</i>	In 4 yr. left side normal, rt. side has decreased. Culture urine, <i>b. coli</i> . Occasional pus cell
F. S.	6	Rt. hydronephrosis, obstruction rt. ureterovesical orifice	18 mth.	Surgical	<i>B. coli</i>	In 3 yr. hydronephrosis no larger. Urine culture positive and still contains pus cells
H. C.	4	Rt. hydronephrosis, obstruction rt. ureter	2 mth.	Surgical	<i>B. coli</i> to <i>b. coli</i> communior	18 mth. after surgical treatment hydronephrosis smaller. Urine positive and recurrence of pyuria
M. B.	5	Rt. hydronephrosis due to double rt. ureter	2 mth.	Surgical	<i>B. coli</i> to <i>b. coli</i> communior	3 yr. later occasional pus cell in urine; hydronephrosis not as large. Urine culture positive
R. K.	3	Rt. hydronephrosis, obstruction rt. ureterovesical orifice	3 wk.	Surgical	<i>B. coli</i> communior	2 yr. later very slight hydronephrosis, no pus in urine. Urine positive for bacteria
D. M.	4	Rt. hydronephrosis, aberrant vessel. Left renal calculus	3 mth.	Surgical	<i>B. dispar</i> to streptococci	8 mth. later left hydronephrosis no larger. Culture urine positive

clearing up this bacilluria, four of the seven children were placed on the ketogenic diet (chart II). Two of these children did not become bacteria-free. One child became bacteria-free in six month's time and has remained so for twelve months. The other child became bacteria-free in seven days but had a recurrence eight months later of pyuria with bacilluria.

CHART II.

NAME	TREATMENT	DURATION OF KETOGENIC TREATMENT IN HOSPITAL	RANGE OF pH	TIME FOR BACTERIA FREE	DURATION OF TREATMENT IN OUT-PATIENT DEPARTMENT	FOLLOW-UP
H. C.	Dilatation of obstruction. 18 mth. later put on ketogenic diet	13 days	5.4-5.2 from onset	7 days	No treatment for 8 mth. then modified ketogenic diet	8 mth. after discharge from H. S. C. no treatment. Urine bacteria free. At this time recurrence of pyuria and bacilluria. Modified ketogenic diet for 10 mth. No recurrence of pyuria. Occasional pus cell in urine and bacteria present in urine
M. B.	Relief of obstruction. 3 years later put on ketogenic diet	10 days	6.8-5.6	not free	Modified ketogenic diet for 10 mth.	In 10 mth. pH of urine never below 5.6. No symptoms. Urine, occasional white cells. Bacteria still present.
A. K.	Obstruction dilated. Put on ketogenic diet 22 months after dilation	8 days	6.4-5.4	not free	Modified ketogenic diet for 11 mth.	In 11 mth. pH of urine 5.8-6.2. No symptoms. No pyuria. Urine still bacteria positive
D. M.	Relief of obstruction. 8 mth. later put on ketogenic diet	16 days	7.6-5.4 in 16 days	Bacilluria for 6 mth. then sterile	Modified ketogenic diet for 12 mth.	In 12 mth. no pyuria, no bacteria and no symptoms

Chart III shows the results of the ketogenic diet in ten children who had no previous surgical treatment. In nine of these cases the urine became sterile. In the one patient's urine that did not become sterile there was a mixture of bacteria and though the B. coli were killed in thirty-four days the staphylococci persisted. That there is a definite relationship between the acidity of the urine and its bactericidal effect is clearly seen in charts II and III. The urine did not become bacteria-free till the urinary pH became 5.4. It took from one to twelve days to obtain this degree of acidity, but as a rule the time required was from four to six days. Sterile urines were obtained in from two to seven days except in three cases when it was found necessary to prolong the diet over a considerable time. One of these patients became bacteria-free in seventy-four days, one in four months

NAME	AGE IN YEARS	ANOMALY	DURATION OF ILLNESS	PREVIOUS TREATMENT	LATER TREATMENT	DURATION OF TREATMENT IN HOSPITAL
E. H.	8½	Rt. hydronephrosis, obstruction rt. ureter	4 mth.	None	Ketogenic diet	7 days
A. M.	4½	Rt. hydronephrosis, obstruction rt. ureter	2 yr.	None	Ketogenic diet and ammon. chloride	4 days
M. C.	6	Left hydronephrosis, obstruction left ureter	2 days	None	Ketogenic diet	10 days
J. M.	3¼	Bilateral hydronephrosis, obstruction uretero-vesical orifices	2 yr.	None	Ketogenic diet and ammon. chloride	40 days
M. L.	8	Rt. hydronephrosis, obstruction rt. ureter	1 yr.	None	Ketogenic diet	28 days
M. B.	11	Prolonged acute. No anomaly	3 days	None	Ammon. chloride and ketogenic diet on 30th day of illness	25 days
M. L.	10	Bilateral hydronephrosis, obstruction uretero-vesical orifices	4 yr.	None	Surgical and ketogenic diet	1 mth.
D. H.	12	Bilateral hydronephrosis, obstruction uretero-vesical orifices	1 yr.	None	Surgical and ketogenic diet	42 days
M. M.	6	Left hydronephrosis, obstruction at junction of double ureters.	2 wk.	None	Ketogenic diet and ammon. chloride	10 days
L. M.	9½	Rt. hydronephrosis, obstruction rt. ureter	6 days	None	Ketogenic diet	10 days

III.

DURATION OF TREATMENT IN OUT PATIENT DEPARTMENT	BACTERIAL SPECIES	RANGE OF pH	TIME FOR BACTERIA FREE	FOLLOW-UP
Mod. ketogenic diet 6 mth. with ammon. chloride	Staph. aureus	6·0-5·4 in 1 day	Intermittent bacilluria for 4 mth.; then sterile	2 mth. later no symptoms. No pyuria, no bacteria
Mod. ketogenic diet with ammon. chloride	Staph. aureus	6·6-5·4 in 4 days	2 days	8 mth. later no pyuria, no symptoms, no bacteria
Ammon. chloride	B. coli	5·4-5·2 from onset	6 days	6 mth. free from pyuria and bacteria, then recurrence of pyuria
None	Staph. aureus and b. coli communior	6·0-5·4 in 12 days	34 days B. coli communior gone. Staph. remained	3 mth. later occasional pus cell in urine and staph. present in urine
None	B. coli	6·4-5·4 in 6 days then 5·2-5·4	11 days	18 mth. later no pus cells. Urine sterile
None	B. coli	6·6-5·8 in 12 days	21 days	1½ mth. later no pus in urine and urine sterile
Mod. ketogenic diet 6 mth.	Staph aureus haem. and strept. faecalis	5·4 from onset	Staph. disappeared in 9 days and strept. faecalis 74	In 12 mth. no symptoms, no pyuria, urine sterile
Mod. ketogenic diet 1 year	Staph. aureus haem. C. xerosis. After 1 mth. b. coli communior	8·4-5·4 in 6 days	Staph. gone 8 days. C. xerosis 7 days. B. coli communior 6 days	In 18 mth. no symptoms, occasional pus cell in urine. No bacteria
Mod. ketogenic diet for 4 mth.	Staph. aureus, haem. Staph. aureus non haem. C. xerosis	6·2-5·2 in 1 day	6 days	No symptoms, no cells, no bacteria after 8 mth.
Mod. ketogenic diet for 5 mth.	Staph. aureus	5·8-5·2	5 days	No symptoms, no cells, no bacteria after 8 mth.

and the other in six months. In three patients the urines did not become bacteria-free, but in one of them this was due to the fact that her urine pH did not go below 5.6 and she was discharged before a more acid urine could be produced. In regard to the second of these three children, though the acidity reached pH 5.4 she still had a bacilluria eleven months later. The third case had both staphylococcus and *b. coli* in the urine and, although the *b. coli* disappeared in thirty-four days, the staphylococcus was present on the patient's discharge from hospital and also three months later when she was re-admitted. In conjunction with sterile urine the pus cells usually disappeared.

Following discharge from the hospital these cases were followed in the out-patient department over periods of from two to eighteen months. Some of these children were sent home on a modified ketogenic diet as has already been described.

Generally speaking, the health of these children has been very good. Most of them have gained weight and have had the minimum of upper respiratory tract infection. The three children who did not become bacteria-free in hospital have had a persistent bacilluria up to the present, though one gives consistently negative results for examination for albumin and pus cells while the third still shows occasional pus cells. This child had also had dilatation of her obstruction and one year later the hydronephrosis had decreased considerably in size. The other case has already been described above. In the remaining eleven cases the patients have had sterile urines over a period of two to eighteen months, but in two of these cases there was a recurrence of pyuria over a period of six months and eight months in which there were numerous pus cells and bacteria again present in the urine. In addition, an unsuccessful attempt was made to treat two infants fourteen and four months of age. This was due to their inability to tolerate the high fat diet.

Comment.

To compare the ketogenic diet with the surgical treatment of this type of case is difficult as the principle of surgical treatment is to relieve the obstruction to allow free drainage and to reduce the pressure atrophy on the kidney, aiming at some restoration of kidney tissue if no further obstruction occurs. With this treatment⁹ these children usually do well but in seven patients who have had their urine cultured for from eight months to four years after the relief of the obstruction, micro-organisms were still found to be present. With ketogenic diet and the production of sterile urine it can well be argued that kidney infection is eliminated but just how rapidly or to what extent the hydronephrosis will progress is not known. This will have to be controlled with further intravenous pyelography and cystoscopic examinations. That this form of treatment is not always effective is shown by the fact that 21 per cent. did not become bacteria-free, though one case was not under observation long enough for a fair trial. In 14 per cent. there

was a recurrence of the pyuria in six months and eight months and in the remaining 65 per cent. of cases the results are good.

Surgical treatment of chronic pyelitis serves merely to relieve the anatomical irregularity with the idea that the establishment of adequate drainage will remove the focus of infection. No bactericidal principle is provided to hasten the return of proper healthy function. The ketogenic diet does not correct anatomical anomalies but does provide the bactericidal agent. From a study of the two types of treatment it would appear that a combination is to be recommended to obtain the best results.

Conclusions.

By means of the ketogenic diet urine can be made both bacteria- and pus-free in 65 per cent. of the chronic pyelitis cases. This had been tested over periods ranging from two to eighteen months.

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