

ASTHMA IN CHILDREN

X. THE RÔLE OF KETOGENIC AND LOW CARBOHYDRATE DIETS IN THE TREATMENT OF A SELECTED GROUP OF PATIENTS *

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With the introduction of the protein skin tests in the past decade considerable progress has been made in the study and care of children suffering from bronchial asthma. A practical method of classification of asthma along etiologic lines is now possible and is of extreme value since it leads directly to rational therapy. As a result of modern therapy, the percentage of children definitely improved or relieved from asthma ranges widely, according to the reports in the literature, from 40 to as high as 90. Thus, between 10 and 60 per cent of the patients who have received accepted standard modern investigation and treatment continue to have asthma. Within this class of unimproved patients there exists, in our experience, a subgroup of children in whom the asthma remains severely chronic from the point of view of intensity, frequency and long duration of the attacks. In these cases little can be done to give relief until nature itself restores the "physicochemical balance." In a recent communication,¹ it was concluded that until newer methods are advanced that will successfully control the asthma of this group of children or free them from it, a "home" prepared to accommodate children with chronic asthma of the refractory type for at least six months is a humane and economic necessity, as well as a therapeutic measure of definite value.

In an attempt to decrease the number of children recommended for treatment by a change of environment for relief from chronic asthma, a form of therapy consisting only of ketogenic and low carbohydrate diets was tried, and the results are recorded in this communication.

MATERIAL AND METHOD

The material for this study is based on observations of fifteen children afflicted with chronic asthma (twelve sensitive and three nonsensitive to protein), ranging

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1. Peshkin, M. M.: Asthma in Children: IX. The Rôle of Environment in the Treatment of a Selected Group of Cases; a Plea for a "Home" as a Restorative Measure, *Am. J. Dis. Child.* **39**:774 (April) 1930.

in age from 3 to 15 years. The average age for the onset of asthma was 3.73 years, and the average age of the patients when first seen was 6.5 years. The average duration of asthma prior to treatment with the ketogenic diet was approximately five years.

Eleven of the fifteen children commenced the special dietary regimen in the winter, a season during which the symptoms of asthma are generally aggravated. The remaining four children began it in the spring of the year. The patients were under observation for periods ranging from five to ten months.

Six of the fifteen children gave a history of having, or of having had, eczema. Another four had recurrent urticaria, and one had intestinal allergy.

METHOD

The procedure employed in this investigation was as follows: The age, the weight and the total and sitting heights of each child were determined. It was found that the estimation of the food requirement in any given case was more easily and quickly determined from a formula used in the Pirquet² or "Nem" system of feeding than with any other method.

Every effort was made to include in the diet the amounts of calcium, phosphorus,³ iron and vitamins necessary for growth and development. In the diets with a ketogenic-antiketogenic ratio of 3:1 in which only 15 or 20 Gm. of carbohydrates was allowed, some difficulty was encountered. At least one-half glass of milk and one-half orange were included in each diet. Milk, cheese and vegetables were given for their high calcium content. Plenty of vegetables were allowed. Calcium in the form of calcium lactate or vitamins in the form of cod liver oil were not added. No drugs were permitted. Changes in environment were not recommended, for obvious reasons. A history of intolerance or the exhibition of positive skin reactions to various food substances prompted the exclusion of these foods from the diets of the children not only for some time prior to the institution of the special dietary treatment but also throughout the period of ketogenic diet. The ketogenic diet should not be confused with the elimination diets of Rowe⁴ and Dale and Thornberg⁵ which have for their

2. Pirquet, Clemens: *An Outline of the Pirquet System of Nutrition*, Philadelphia, W. B. Saunders Company, 1922. The Pirquet system of feeding has for its unit the "nem," which is equivalent to 1 cc. of human or cow's milk. One ounce of milk (20 calories) is equivalent to 30 nems. One nem is therefore the equivalent of two thirds of a calorie. The food requirement in the diet is determined by multiplying the square of the sitting height (in centimeters) by the desired number of decinems. Thus, a diet of 3.5 decinems (0.35 nems) for a child whose sitting height is 70 cm. is calculated as follows: $70 \times 70 = 4,900$ nems; $4,900 \times 0.35 = 1,715$ nems. The corresponding number of calories is $1,715 \times \frac{2}{3} = 1,143$. A maintenance diet for children is calculated at 4.5 decinems and a basal requirement diet at 3 decinems. Some children, because of overactivity, require diets of higher caloric value (from 5 to 6 decinems).

3. Sherman, H. C.: *Chemistry of Food and Nutrition*, New York, The Macmillan Company, 1928. The average growing child requires approximately 1 Gm. of calcium and 1.4 Gm. of phosphorus in the daily diet.

4. Rowe, A. H.: *Food Allergy, Its Manifestations, Diagnosis and Treatment*, J. A. M. A. **91**:1623 (Nov. 24) 1928.

5. Dale, J., and Thornberg, H. D.: *Diets for the Identification of Food Allergies*, J. A. M. A. **93**:505 (Aug. 17) 1929.

purpose the identification of food allergies in a patient refractory to the skin tests along with a history negative for food intolerance.

Detailed instructions were given to the mother by the dietitian concerning the preparation of the diet menus, i. e., the size of the portions, the weights and volume of food, substitution formulas, etc. The diets were made as appetizing as possible.

From several days to one week prior to the institution of the dietary treatment, an account of the quantity and kind of food eaten daily by the child was recorded in detail. From this record were calculated the carbohydrate, protein, and fat values in grams, the total caloric value and the ketogenic-antiketogenic ratio.⁶ These results are set forth with other details in table 1.

$$\frac{\text{Fatty acids}}{\text{Dextrose}} = \frac{\text{Ketogenic}}{\text{Antiketogenic}} = \frac{0.44 \text{ P} + 0.9 \text{ F}}{\text{C} + 0.58 \text{ P} + 0.1 \text{ F}}$$

TABLE 1.—*Estimated Daily Food Intake by Children with Chronic Asthma Prior to the Institution of Treatment with the Ketogenic Diet*

Patient	Age, Year	Weight, Kg.	Total Height, Cm.	Sitting Height, Cm.	Decinems*	Carbohydrate, Gm.	Protein, Gm.	Fat, Gm.	Total Calories	Ketogenic-Antiketogenic Ratio*
1	10	25.9	132.5	71	3.6	120	45	60	1,200	1:2
2	10	31.3	136.0	71	4.2	167	47	63	1,423	1:2.5
3	15½	42.7	147.5	79	4.2	196	60	80	1,740	1:2.5
4	15½	41.3	162.5	87	3.0	160	45	70	1,450	1:2
5	3½	17.7	101.0	58	6.0	180	40	50	1,330	1:3
6	5	20.4	115.0	61	6.0	165	55	65	1,465	1:2.5
7	13	59.9	155.0	82	3.2	135	50	80	1,460	1:2
8	14¾	48.2	157.5	81	3.6	175	45	75	1,555	1:2.5
9	4¾	16.3	102.5	57.5	3.7	92	20	41	817	1:2.5
10	10	21.3	127.5	70	5.0	175	40	90	1,670	1:2
11	8½	28.8	125.0	70.5	4.0	135	40	70	1,330	1:2
12	8½	24.0	127.5	71	5.0	150	60	90	1,650	1:2
13	4	17.7	100.0	59	6.0	150	40	70	1,390	1:2
14	6	21.8	120.0	64	3.2	85	29	46	870	1:2
15	2¾	14.5	92.5	54	5.7	100	44	59	1,107	1:2

* Figures are approximate. For the determination of decinem, see footnote 2, and for the diet ratio see footnote 6.

From table 1 it may be seen that nine children were living on diets the daily rations of which were below the maintenance requirement (4.5 decinems). Seven of the children in this series were found to be underweight. It is of interest, however, to note that all of these children were taking a diet relatively high in carbohydrate. Nine children were on a diet with an approximate ketogenic-antiketogenic ratio of 1:2, five were on diets with a ratio of 1:2.5 and one was on a diet with a ratio of 1:3.

Routine Employed in the Treatment with the Ketogenic Diet.—With the sitting height of the child determined, a diet of 3.5 decinems was computed and converted into calories. The child was placed on this calculated diet with a ketogenic-antiketogenic ratio of 1:1.5 for two days. At the end of this time, the ratio was changed to 1:1. In another two days, the caloric intake was increased to 4 decinems, and the diet ratio to 1.5:1. Several days later, the child was placed on a maintenance diet (4.5 decinems) with a ratio of 2:1. Again in a few days, the ratio was increased to 2.5:1 and finally to the maxi-

6. Woodyatt has proposed a formula based on the equimolecular weights of dextrose and fatty acids.

mum of 3:1, while the caloric intake was kept at the maintenance level. Ten per cent protein was allowed.

The diets of all the children were maintained for periods ranging from four to ten months. One child was placed on a diet of 5 decinems with a ratio of 2:1, and at the end of the second week the ratio was reduced to 1:1, which was maintained throughout the dietetic experiment (five months). This was done in order that we might observe the effect on the asthma of a diet relatively low in carbohydrate in the absence of ketosis. In this instance, the ratio of the original home diet was 1:2. In three cases, diets of the maximum caloric value were given from the start for the purpose of determining whether or not the initial diets of low caloric value were essential in obtaining satisfactory results.

EFFECTS OF THE DIETS ON ASTHMA

Table 2 is a summary of the results of treatment of fifteen children with the ketogenic and low carbohydrate diet, with other essential data.

Prior to the institution of this special dietary regimen these children (table 2) were under observation and treatment for varying periods as follows: two children for five years, two for four years, six for from one to three years, and five for less than one year.

Table 2 shows that slight improvement from asthma occurred in nine children at the end of the first week under the special dietary regimen. At the end of the second week of treatment, ten children showed moderate improvement and three marked improvement or relief from asthma. At the end of the third week, fourteen children, or 93 per cent of the series, manifested moderate to marked improvement or relief from asthma.⁷

The subsequent month to month progress of each child under the dietary regimen is readily obtained from table 2. Of the two children observed for ten months, one showed moderate to marked improvement and the other only slight improvement. The latter child was the only one (no. 4) of the series who failed to show a favorable response during the first month of treatment. Three children were observed for nine months; one of these children showed continued marked to moderate improvement, while the other two had an aggravation of the asthma in the fifth and the eighth months, respectively. Of the two children observed for eight months, one continued to show moderate improvement, and the other manifested a return of symptoms ("slipping") in the fourth month. The three children observed for seven months continued to show marked improvement or relief from asthma. Of the five children under treatment for periods ranging from four to six months, three showed evidences of "slipping" in the third, fourth and fifth months,

7. In a series of unpublished observations, marked improvement from asthma was elicited at the end of the first week in cases in which diets with ratios of 1:1, 2:1 and 3:1 were given at intervals of two days, respectively. The sudden shift from a home diet to one with a ratio of 3:1 is also under investigation.

TABLE 2.—Results of the Treatment with the Ketogenic and Low Carbohydrate Diet in Fifteen Children with Chronic Asthma of the Refractory Type

Patient	Age,* Year	Age First Seen, Year	Age of Onset of Asthma, Year	Dura- tion of Asthma, Year	Results of Treatment**												Weight, Kg. At Onset At End of Diet of Diet Treat- Treat- ment ment
					Subsequent Months												
					First Month												
1 w†	2 w	3 w	4 w	1	2	3	4	5	6	7	8	9	10				
1	10	9	1	9	+	+	+	+	+	+	+	+	+	0	25.9	27.7	
2	10	9½	9	1	+	+	+	+	+	+	+	+	+	+	31.3	36.3	
3	15½	11	7	8½	0	+	+	+	+	+	+	+	+	0	42.7	45.4	
4†	16½	12	7	8½	0	+	0	+	+	+	+	+	+	+	41.3	44.9	
5	3½	1	½	3	+	+	+	+	+	+	+	+	+	+	17.7	20.4	
6	5	4	3	2	+	+	+	+	+	+	+	+	+	+	20.4	20.0	
7	13	8	4	9	+	+	+	+	+	+	+	+	+	0	59.9	55.0	
8	14½	13	6	8½	0	+	+	+	+	+	+	+	+	+	48.2	51.4	
9†	4½	4	3	1½	+	+	+	+	+	+	+	+	+	+	16.3	17.7	
10	10	4½	4	6	0	+	+	+	+	+	+	+	+	+	21.3	32.2	
11†	8½	7½	4	4½	+	+	+	+	+	+	+	+	+	+	28.8	30.9	
12	8½	8	2½	6	+	+	+	+	+	+	+	+	+	+	24.0	26.4	
13‡	4	1	½	3½	0	+	+	+	+	+	+	+	+	+	17.7	19.0	
14	6	4	3½	2½	+	+	+	+	+	+	+	+	+	+	21.8	22.7	
15	2½	2	2	2	0	+	+	+	+	+	+	+	+	+	14.5	15.9	

* Age when dietary regimen was begun.

** Slight improvement = +; moderate improvement = ++; marked improvement or relief from asthma = +++, and no improvement = 0.

† w = week.

‡ For the first two weeks the diet ratio was 2:1; thereafter, the ratio was reduced and maintained at 1:1.

§ Taking home diet.

¶ Protein nonsensitive.

Sent to "convalescent home" for four months, where he was free from asthma and gained 1.8 Kg.

respectively; and the remaining two continued to manifest marked improvement or relief from asthma.⁸

It is thus apparent that the marked control of the asthmatic condition noted at the end of the third and fourth weeks in the fourteen cases was not permanent. After this period, six patients maintained their improved condition for periods varying from two to seven months before relapses ensued. The asthma in the latter cases, as a rule, was not so severe and prolonged as in the period prior to the special dietary treatment. The cause and prevention of a relapse to the asthmatic state warrant further investigation. The remaining eight patients, or 53 per cent of the series, continued to maintain moderate to marked improvement or relief from asthma for periods varying from four to ten months.

The first signs of improvement noted were the diminution or disappearance of dyspnea and heaviness in the chest. Wheezing was soon less noticeable, and the attacks of asthma were milder and less frequent. The cough was less troublesome or gone. The child looked better, and the pinched appearance was replaced by a pleasant facial expression. The nocturnal wheeze was slightly present, if at all, and sleep was undisturbed. Later the cheeks became noticeably pink, and the posture was improved. The child became more alert and active and could run up and down the stairs without inducing a wheeze or dyspnea. Such striking improvement from severe asthma of the refractory type was observed with no other treatment, except hospitalization or change of environment.¹

The case to be reported is of special interest because of the marked gain in weight and because of the intensity and long duration of the asthma, which was finally controlled with the ketogenic dietary regimen.

REPORT OF CASE

M. W. (patient 10, table 2), a girl, was first seen on May 15, 1923, when 4½ years of age, with a history of asthma the onset of which occurred eight months previously. There was no personal history of eczema, urticaria or angioneurotic edema. The antecedent family history was positive for allergy, the paternal grandfather having had asthma. When first seen, the patient appeared malnourished and weighed 31½ pounds (14.3 Kg.). The results of physical examination were otherwise negative except for the usual signs of asthma in the chest. Roentgenoscopy of the chest showed no definite abnormality in the lungs. A complete series of protein skin tests (scratch and intradermal technics) showed positive reactions to barley, radish, mustard and house dust. The Pirquet test was negative. The intradermal test was negative up to a concentration of 1 mg. of tuberculin. The blood count was normal. The patient was given appropriate dietetic and environmental treatment. Tonsillectomy and

8. The ketogenic diet treatment was administered to two adults with severe chronic asthma, of the type nonsensitive to protein, with no improvement. Acetonuria, however, resulted.

adenoidectomy were performed during the first year of observation, with no apparent benefit. Later, attacks of asthma became progressively more frequent, prolonged and intense. A series of nonspecific injections of sterile skimmed milk was administered, with little or no improvement. Ten months after the patient's admission to the clinic, she contracted acute lobar pneumonia with involvement of both lower lobes. During this illness of three weeks and for a subsequent month, she remained free from asthma. Then attacks recurred at intervals of from two to three weeks with spells of wheezing intervening. Another course of nonspecific injections (milk) was given. Later, a stock house dust was employed, as well as the extract made from the dust collected in the patient's home. General irradiations of the body by ultraviolet ray were also employed. Finally, injections of *Crotalus atrox* (nonspecific therapy) up to a concentration of 1.5 mg. were administered. In spite of all of these various forms of therapy, the patient continued to have severe asthma.

This condition existed for six years. The child was unable to attend school. On Feb. 14, 1929, she reported with a history of having had continual asthma for the three previous months.

On March 9, treatment with the ketogenic dietary regimen was commenced. The child was 10 years of age, the total height 127.5 cm. (51 in.) and the sitting height 70 cm. She was emaciated, weighing 47 pounds (21.3 Kg.), being 15 pounds (6.8 Kg.) underweight. Her posture was poor, and she appeared chronically ill. The anteroposterior measurement of the chest was increased above the normal.

The "home" diet that she had been taking was estimated to consist of 175 Gm. of carbohydrate, 40 Gm. of protein and 90 Gm. of fat, or 1,670 calories (5 decinems) with a ketogenic-antiketogenic ratio of 1:2. She commenced the dietary regimen with a diet of 1,275 calories (3.5 decinems) with a ratio of 1:1. Within a week, the diet was increased to 1,310 calories (4 decinems) with ratios of 1.5:1 and 2:1, respectively. At the end of two and one-half weeks, the patient was on a daily ration of 1,480 calories (4.5 decinems) with a ratio of 3:1.

At the end of the third week of dietary treatment, the child showed remarkable improvement. She was free from attacks of asthma and was able to get about with ease. At the end of the first month, she had no wheeze and had gained 2 pounds (0.9 Kg.). It may be mentioned here that for the entire year prior to this treatment, she showed a gain of only 1 pound (0.5 Kg.). The urine showed a moderate reaction to acetone with the diet ratio of 2:1 and a marked reaction with ratios of 2.5:1 and 3:1. Improvement continued during the second month; at this time, the patient was put on a diet of 1,660 calories (5 decinems) with a ratio of 3:1, with a resultant gain in weight of 7½ pounds (3.4 Kg.). Acetonuria persisted. It is of interest to state that this child previous to the dietary regimen was subject to frequent spells of "acidosis" with and without attacks of asthma. Now, with a ketosis induced by the ketogenic diet, she remained free from symptoms of "acidosis" and asthma.

The total period of observation of this patient under the treatment with the ketogenic diet was seven months. She had no attacks of asthma during this time, but had an occasional spell of wheezing at night. On October 8, she weighed 71 pounds (32.2 Kg.), showing a gain of 24 pounds (10.9 Kg.). Beginning with the seventh month, the diet ratio was reduced to 2:1, after which no acetone in the urine could be demonstrated. She was still on this diet at the time of writing, felt well and was attending public school for the first time in her life.

Table 3 shows, with other essential data, three of the menus with different ketogenic-antiketogenic ratios given to the patient in the case reported.

EFFECT OF THE DIET ON ACETONE IN THE URINE

The time of appearance of acetone in the urine (qualitative estimation) varies with the child. At some time during the first month of

TABLE 3.—Three of the Menus Given to Patient M. W. (10, Table 2) * During Treatment with the Ketogenic Diet

1:1 Ratio		2:1 Ratio		3:1 Ratio	
Grams	Food	Grams	Food	Grams	Food
Breakfast					
50	½ orange	50	½ orange	50	1 egg
200	1 Uneda cracker	100	½ glass milk	100	½ glass milk
	1 glass milk	50	¼ glass cream 40%	12	1 square butter
Dinner					
1	cup broth	1	cup broth	1	cup broth
100	½ cup vegetables	70	½ cup meat, fish 70 or chicken	70	½ cup meat, fish 70 or chicken
	3-5%	75	½ cup vegetables	75	½ cup vegetables
12	1 square butter	12	1 square butter	18	1½ squares butter
200	1 glass milk	50	¼ glass cream 40%	50	¼ glass cream 40%
3 P.M.					
200	1 glass milk	100	½ glass milk		3 P.M.
		50	¼ glass cream 40%		
Supper					
1	cup broth	1	cup broth	1	cup broth
20	¼ pkg. cream cheese	30	½ pkg. cream cheese	30	½ pkg. cream cheese
100	½ cup vegetables	75	½ cup vegetables	75	½ cup vegetables
	3-5%		3-5%		3-5%
18	1½ squares butter	12	1 square butter	18	1½ squares butter
200	1 glass milk	50	¼ glass cream 40%	50	¼ glass milk
50	¼ glass cream 40%			50	¼ glass cream 40%
1	Uneda cracker				
Summary		Summary		Summary	
Ratio.....	1:1	Ratio.....	2:1	Ratio.....	3:1
Carbohydrate...	70	Carbohydrate...	30	Carbohydrate...	15
Protein.....	35	Protein.....	35	Protein.....	35
Fat.....	86	Fat.....	125	Fat.....	145
Calories.....	1,194	Calories.....	1,385	Calories.....	1,505
Decinems.....	3.5	Decinems.....	4	Decinems.....	4.5
Calcium.....	1.319	Calcium.....	0.795	Calcium.....	0.689
Phosphorus.....	1.046	Phosphorus.....	0.769	Phosphorus.....	0.753
Iron.....	0.00527	Iron.....	0.00550	Iron.....	0.00669
Vitamin A.....	+++	Vitamin A.....	+++	Vitamin A.....	+++
B.....	++	B.....	++	B.....	++
C.....	+	C.....	+	C.....	+

* Sitting height 70 cm.

treatment, eleven children showed the presence of acetone. Of these children, six gave slightly positive reactions on a diet with a ketogenic-antiketogenic ratio of 1.5:1, three on a diet with a ratio of 2:1 and the remaining two on a diet with a ratio of 2.5:1. Only five (1, 2, 10, 12 and 14, table 2) of these eleven children showed moderate to marked reactions to acetone during the first month with the maximum diet ratio of 3:1. These five children and one other (7, table 2) ate only the foods permitted on the diet menus. The other children adhered less rigidly

to the prescribed diets, taking an extra Uneda cracker or a slice of toast and at times additional fruit.

During the subsequent months, six children (1, 2, 5, 10, 12 and 14, table 2) showed repeatedly moderate to marked traces of acetone in the urine, while four children (6, 11, 13 and 15) showed none. In the latter cases, no attempt was made to induce acetonuria with higher diet ratios (3.5:1 and 4:1).

It was observed that when the children with acetonuria began to have a return or an aggravation of the symptoms of asthma, a diminution or disappearance of the acetone took place. When a child recovered from a spell of wheezing or a mild attack of asthma, the return of acetone in the urine was delayed. One child (no. 1), with a persistent acetonuria, failed to show acetone when severe asthma returned early in the ragweed pollen season, in spite of the fact that a diet with a ratio of 3:1 was continued for another month.

The experiment of reducing the diet ratio from 3:1 to 2:1 was tried on three children who were markedly improved or relieved from asthma and in whom marked acetonuria had existed for several months. The marked improvement or relief from asthma continued in all three patients in spite of the elimination of ketosis. This observation seems to be of clinical importance, for if satisfactory results can be maintained with reduced ratios (2:1 or even 1:1), the difficulty of getting children to continue these diets over extended periods of time will be largely overcome. A diet relatively low in carbohydrate (50 Gm.) is more readily taken than a ketogenic diet (15 Gm. of carbohydrate) with a ratio of 3:1.

It seems evident from the urinary observations that acetone, per se, does not wholly account for the marked relief from asthma, experienced by the majority of the patients in this series. It is evident, also, that some of the children who were supposed to be on a diet ratio of 3:1 were taking not more than a ratio of 2:1. In other words, they were actually on a diet relatively low in carbohydrate and high in fat.

EFFECT OF THE DIET ON WEIGHT

At the end of the first month of the dietary regimen, six children showed unchanged weights. Three children had gained approximately 2 pounds (0.9 Kg.) each and two had lost weight. Four children showed a loss of from 1 (0.4 Kg.) to 2 pounds (0.9 Kg.) during the first two weeks, but regained the loss by the end of the first month. During the subsequent months, thirteen of the children showed substantial increases in weight, the average increase being 6.6 pounds (3 Kg.). One girl, 13 years of age, who was 23 pounds (10.4 Kg.) overweight, showed a loss of 9 pounds (4.1 Kg.) in eight months on

a diet above maintenance level (5.5 decinems) with a ratio of 3:1 and improvement from asthma. However, gain in weight, as a rule, accompanied clinical improvement. When a child began to "slip" and the symptoms of asthma returned or became aggravated, loss of weight and appetite followed. Subsequent experience justifies the statement that the use of maintenance diets or diets of higher caloric value with a ketogenic ratio in the treatment of a child with chronic asthma who is underweight, usually results in an appreciable gain of weight by the child after a period of four months, while in the case of a child who is obese, the use of such diets usually leads to a loss of weight in spite of the fact that both types of children have improved or have been relieved from asthma. Further investigations are being carried out for the purpose of ascertaining, if possible, an explanation for this interesting seeming paradox.

EFFECT OF THE DIET ON POLLEN SENSITIVENESS

Four of the children of this series were sensitive to ragweed pollen, in addition to being sensitive to food and other inhalant substances; two of these children were also sensitive to timothy. A ketogenic diet with a ratio of 3:1 was maintained before and during the pollen seasons and in each instance asthma returned or became aggravated and were accompanied by symptoms of hay-fever during the season. None of these children received pollen treatment during 1929.

One child, not included in this series, was sensitive to many substances besides ragweed pollen. Preseasonal treatment against ragweed pollen was commenced in April, 1929. In May, the patient developed a troublesome cough with nocturnal wheezing which could not be accounted for. These symptoms became progressively worse, and in July the ketogenic diet was commenced and continued with pollen therapy to the end of September. The patient was relieved from all symptoms and continued to remain so after the first week of the dietary regimen.

Three children, with only hay-fever of the ragweed type, not included in this series, were also studied. One boy of 12 years was previously treated for three years with preseasonal injections of pollen extract, with satisfactory results. On Aug. 6, 1929, the child was placed exclusively on the dietary regimen, receiving at intervals of two days, ratios of 1:1, 2:1 and 3:1, respectively. The latter ratio was continued through August and part of September. There was moderate to marked acetonuria. However, severe hay-fever ensued, and pollen treatment was instituted to control the symptoms. Another child, a younger brother, was given the ketogenic diet at the same time and also did poorly during the pollen season. A third child, a boy of 9 years, commenced on the dietary regimen during the height of the hay-fever season

(August 29). He was taking a diet above the maintenance level (5 decinems) with a ratio of 3:1, which was maintained for one month. The urine showed marked traces of acetone. The mother said that the boy showed some improvement over the previous year, when no treatment of any kind was given.

From these results it appears that the ketogenic diet alone does not offer much promise of relief in hay-fever with or without asthma, but no final statement can be made until a larger number of cases is studied. However, the suggestion of administering specific pollen treatment in conjunction with the ketogenic diet in certain cases of asthma, may be borne in mind.

EFFECT OF THE DIET ON THE DERMATOSES

Six children in this series gave a history of eczema occurring during infancy. In three, the eczema had cleared several years before the dietary treatment was started, and in the other three, the eczema was recurrent in type. In two of the latter, the eczema became definitely aggravated on the diet high in fat. These two children demonstrated sensitivity to many substances, particularly to foods. The eczematous condition was treated with the usual ointments, with good results in spite of the existing ketosis.

Four of the children had recurrent urticaria. With the clearing up of the asthma, the itch and rash in two became aggravated. Later, an impetigenous eruption developed in one of these children.

Observations were made on three children with reference to the effect of ketosis on the protein skin reactions. No change in the skin reactions to food, inhalant substances and pollen in any of these children was observed even though they were markedly improved or relieved from asthma.

EFFECT OF THE DIET ON ASTHMA DURING INTERCURRENT INFECTIONS AND IN OTHER CONDITIONS

Intercurrent infections, such as grip and other respiratory infections, in some cases precipitated symptoms of asthma, milder, however, than those occurring in the prediet period.

Two children indulged in food to which they were specifically sensitive, and an attack of asthma resulted in each instance in spite of the ketogenic diet.

Two other children after having shown moderate to marked improvement from asthma for six and seven months, respectively, were at the end of these periods placed back on their original home diets. In one, symptoms of asthma became definitely aggravated, while in the other there was no change.

MISCELLANEOUS OBSERVATIONS

No untoward effects were observed in the children of this and subsequent series while under the ketogenic dietary regimen. Several children complained of hunger, which was readily relieved with an increase in the caloric value of the diet. Nausea and vomiting did not occur. Four children became constipated. Several others complained when the high fat diet was continued over a period of months, in spite of the fact that menus were changed and foods made more palatable. This diet is rather costly for this class of patients because of the daily requirement of large quantities of sweet cream and butter.

COMMENT

The reason for the beneficial effect resulting from the ketogenic diet in the treatment of certain conditions is not known. Several theories have been advanced making different mechanisms responsible for the favorable results obtained, but none of these theories has been generally accepted. In recent years, the ketogenic diet has been largely employed in the treatment for epilepsy in childhood. The literature is replete with comprehensive communications on this special dietary treatment of epilepsy; it includes reports by Wilder,⁹ Peterman,¹⁰ Talbot and his associates,¹¹ Lennox and Cobb¹² and Helmholz.¹³

In certain cases, idiopathic epilepsy is regarded by some workers as an allergic phenomenon and is referred to by Schick¹⁴ as an "asthma of the brain." The application of the ketogenic diet in the treatment for asthma in childhood in certain cases appears therefore not to be without foundation.

All of the children in this series, prior to the dietary treatment, were living on diets with ketogenic-antiketogenic ratios ranging from 1:2 to 1:3 (high in carbohydrate, low in fat). The change to a diet ratio of 3:1 (low in carbohydrate, high in fat) shifted the balance in the opposite direction. The rapid improvement or relief from asthma observed following treatment with the ketogenic diet exclusively in

9. Wilder, R. M.: The Effects of Ketonuria on the Course of Epilepsy, *Mayo Clin. Bull.* **2**:307, 1921.

10. Peterman, M. G.: The Ketogenic Diet in the Treatment of Epilepsy, *Am. J. Dis. Child.* **28**:28 (July) 1924.

11. Talbot, F. B.; Metcalf, K. M., and Moriarty, M. E.: A Clinical Study of Epileptic Children Treated by Ketogenic Diet, *Boston M. & S. J.* **196**:89 (Jan. 20) 1927.

12. Lennox, W. G., and Cobb, S.: Epilepsy from the Standpoint of Etiology and Treatment, *Medicine* **7**:105 (May) 1928.

13. Helmholz, H. F.: The Treatment of Epilepsy in Childhood; Five Years' Experience with the Ketogenic Diet, *J. A. M. A.* **88**:2028 (June 25) 1927.

14. Schick, Bela: Personal communication to the authors.

children with chronic asthma of the refractory type is possibly brought about by some mechanism which involves a physicochemical change in the cells and blood of the patient thereby inducing a partial or completely restored "physicochemical"¹⁵ or "allergic balance."¹⁶ This physicochemical balance may be associated with changes in the surface tension of various colloids, hydrogen-ion concentration, calcium, phosphorus, cholesterol, sodium chloride and other chemical elements. McQuarrie and Keith¹⁷ found that in children under treatment with the ketogenic diet, attacks of epilepsy diminished or disappeared when the p_H of the blood was between 7.33 and 7.41 or lower. The attacks, however, returned with the administration of alkalis or after the withdrawal of the diet or when p_H was above 7.41 (on the alkaline side). In a recent communication, McQuarrie¹⁸ emphasized the importance of the water balance and favored a diminution of the water intake in the treatment for this condition. These chemical changes may be nothing more than secondary observations incident to the disease and may be expressions of a physicochemical change.

Patients with certain diseases have been successfully immunized with specific vaccines via the alimentary tract. Early immunization of infants against tuberculous infection by the ingestion of the Calmette preparation (B.C.G.) has been carried out with apparent success. Peptone, ingested by patients with food allergy for purposes of nonspecific desensitization, is not without value. The ketogenic diet, on account of its extreme formula, is a dietary "stranger" to the allergic person; and, in our opinion, this diet can be considered, for children, at least, as a form of nonspecific therapy capable of inducing physicochemical change via the alimentary tract.

CONCLUSIONS

1. In a series of fifteen children (twelve sensitive and three non-sensitive to protein) ranging in age from 3 to 15 years, the asthma remained severe, persistent and of long duration in spite of treatment according to accepted standards of modern investigation and management. These children had been under observation for an average of two and one-fifth years when selected for treatment with the ketogenic

15. Peshkin, M. M.: Asthma in Children: III. The Incidence and Significance of Various Diseases and Infections, and of Tonsillectomy and Adenoidectomy, *Am. J. Dis. Child.* **33**:880 (June) 1927.

16. Vaughan, W. T.: Interaction of Specific and Nonspecific Factors in Allergic Disease, *Virginia M. Monthly* **51**:472 (Nov.) 1924.

17. McQuarrie, I., and Keith, H. M.: Experimental Study of the Acid-Base Equilibrium in Children with Idiopathic Epilepsy, *Am. J. Dis. Child.* **37**:267 (Feb.) 1929.

18. McQuarrie, I.: Epilepsy in Children; the Relationship of Water Balance to the Occurrence of Seizures, *Am. J. Dis. Child.* **38**:451 (Sept.) 1929.

(and low carbohydrate) diets. No drugs, injections or other therapeutic measures were employed. However, the various foods known to cause symptoms of allergy in these patients were eliminated not only from their former diets, but also from the ketogenic diets.

2. The estimated daily amount of food consumed by these children prior to the institution of the ketogenic diet regimen showed that they were all living on diets relatively high in carbohydrate. The approximate ketogenic-antiketogenic ratios of the home diets ranged from 1:2 to 1:3.

A maintenance diet or one of higher caloric value with a maximum ketogenic ratio of 3:1 was reached in all the cases (except one) within three weeks, and thereafter this level was maintained for periods ranging from four to ten months. Ten per cent protein was allowed.

3. At the end of the third week of treatment with the dietary regimen, fourteen children, or 93 per cent of the series, manifested moderate to marked improvement or relief from asthma. These improved states were maintained for another two months. Thereafter, and up to the tenth month, 53 per cent of the patients were considered moderately to markedly improved or relieved from asthma.

4. The ketogenic and low carbohydrate diets alone do not appear to offer much promise of relief from pollen asthma (four cases in this series) or hay-fever (three cases not included in this series). However, in pollen asthma, the administration of pollen treatment in conjunction with the ketogenic diet may prove of value.

5. Ketosis, per se, apparently does not account for the results obtained, since definite improvement or relief from asthma also occurred in some children in whom acetone in the urine could not be demonstrated.

Some of the children who were doing well on a ketogenic ratio of 3:1 were later actually taking ratios as low as 1.5:1 with continued benefit. In other words, they were finally on a relatively low carbohydrate-high fat diet, below the threshold of ketosis.

6. The use of a maintenance diet or one of higher caloric value with a ketogenic ratio of 3:1 in the treatment of a child with chronic asthma who is underweight usually results in an appreciable gain in weight by the child after a period of four months, while in the case of a child who is obese, the use of such a diet usually results in a loss of weight, in spite of the fact that both types of children have been improved or relieved from asthma. This is an interesting seeming paradox.

7. Children with asthma and recurrent eczema on a ketogenic diet showed definite improvement from asthma but aggravation of the eczema. However, the children who have been free from eczema for

several years prior to the institution of the low carbohydrate-high fat diet do not have a recurrence of the rash in spite of prolonged ketosis.

Two of the four children with recurrent urticaria had an aggravation of the rash as a result of the dietary regimen.

8. The estimation of the food requirement in any given case was more easily and quickly determined from a formula used in the Pirquet² system of feeding than with any other method.

9. The rapid control of asthma or relief from it observed following treatment with the ketogenic diet exclusively is possibly brought about by some mechanism which involves a physicochemical change in the cells and blood of the patient thereby inducing a partially or completely restored "physicochemical"¹⁵ or "allergic balance."¹⁶ Recent experimental evidence lends support to this conception.

The ketogenic diet, on account of its extreme formula, is a dietary "stranger" to the allergic person and, in our opinion, may be considered, for children, as a form of nonspecific treatment capable of inducing physicochemical change via the alimentary tract.

10. In this series of selected children with chronic asthma refractory to various forms of modern treatment, the ketogenic and relatively low carbohydrate-high fat diets alone have proved efficacious to the extent that the chronic asthmatic state in the majority of instances was controlled or entirely cleared up, at least for a sufficient period of time to permit such a child to get its bearings.

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