THE RELATION OF THE REACTION OF THE URINE TO THE DIET IN INFANTS AND CHILDREN *

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In the treatment of diseases of children there are many indications for changing the reaction of the urine. To bring about this change is often a matter of great difficulty. I believe the majority of failures are due to a lack of a proper dietary regulation, without which drugs may prove of no avail, much to the surprise of the physician.

INDICATIONS FOR CHANGING THE REACTION OF THE URINE

1. The principal indication for changing the reaction of the urine in children is pyelitis, the treatments for which are nearly all founded on these changes. The principles of such treatments are:

(a). *Render the urine alkaline*, because it is less irritant to the inflamed mucous membranes and helps to dissolve the mucous and pus.

(b) The use of hexamethylenamin, which is considered one of the best antiseptics for the urinary tract. But hexamethylenamin acts only by splitting into ammonia and formaldehyd, the formaldehyd having the antiseptic action; this splitting occurs in appreciable amounts only when the urine is acid.

(c). The alternation of these two treatments (a and b); that is, the changing from alkaline to acid and then from acid to alkaline, etc., hexamethylenamin being given or not during the acid periods.

These changes are supposed to make the surroundings unsuitable for the growth of bacteria, and have the advantage of avoiding the continuous irritative action of the formaldehyd on the urinary tract.

2. *Destroying and preventing crystals and calculi*. The most frequent, and perhaps the only crystals found in children's urine are those formed by uric acid or urates.

(a). The urate crystals are formed in acid urines, and some of them, particularly sodium urate, are apt to cause hematuria. An alkaline urine might prevent their formation.

(b). *Calculi*. Alkalinity cannot dissolve calculi, but it prevents the precipitation of uric acid and urates, which may occur to a serious extent only in acid urines.

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In a few instances it has been observed that alkalinity caused the breaking up of large stones into small fragments. This cannot be attributed to the solution of the uric acid; the explanation probably is that the calculi were composed of small fragments glued together by mucous, and that the alkalies merely caused the solution of the latter.

3. Acid urine is, as already stated, irritating to the mucous membranes and somewhat to the external genitalia, which often is the cause of masturbation in female children. Acid urine may also possibly cause enuresis. A change to alkalinity will usually relieve the irritation and dissolve any mucus that may be present.

4. An excess of uric acid in the urine may cause abdominal pains which would be very difficult to diagnose without an examination of the urine. Rendering the urine alkaline might prevent the further formation of the uric acid, or at least make it less troublesome.

5. Alkaline urine has a diuretic action, which, with its antiirritative action, has to be considered in the treatment of nephritis.

6. In cases of acidosis the acid in the urine is a consequence of the excess of acids in the blood. The change of the reaction of the urine is an index of the results of treatment and the progress of the disease.

METHOD FOR TESTING THE REACTION OF THE URINE

The real acidity of the urine, that is, the number of hydrogen ions, can be determined by the indicator method, or by the gas chain method, the former being the simpler.

I used the method of titrating the acidity by means of a tenth-normal or hundredth-normal solution of sodium hydrate which is added up to neutralization, phenolphthalein being used as the indicator. This is a very simple method and seems to have been sufficiently accurate as far as the final results are concerned.

If one desires to compute the number of grams of hydrogen in each 100 c.c. of urine it is necessary to multiply by 0.1 the number of cubic centimeters of tenth-normal sodium hydrate solution used in neutralizing the 10 c.c. of urine.

Dry potassium oxalate must be previously added to the urine in order to precipitate the lime salts which otherwise would precipitate the phosphates when the hydrate is added. Six grams should be added for each 10 c.c. of urine used.

When litmus is used, it must be remembered that the urine may be found alkaline, while it may be acid to phenolphthalein.

In testing the degree of alkalinity of a urine, I used a sulphuric acid solution equivalent to the strength of the sodium hydrate, with the same indicator.

HOW TO CHANGE THE REACTION BY DIETARY PROCEDURE

In studying the relation of diet to urinary reaction, I have considered the following phenomena, which, in part, were responsible for this investigation:

1. The urine of the carnivora is acid, and that of the herbivora is alkaline.

2. The acidity of the urine of the carnivora depends especially on the products of protein metabolism. Sulphur occurs in an unoxidized condition. Phosphoric acid occurs in nucleic acid, in nucleoproteins, in pseudonucleins and in lecithin. During metabolism these are oxidized into sulphuric acid or set free as phosphoric acid, thus accounting for the acidity of the urine.

3. There are also organic acids such as phenylacetic, benzoic, uric, urocyanic, etc., which are formed by oxidation of certain protein constituents, and contribute also to the acidity of the urine.

Nitrogen from the proteins is eliminated in the unoxidized form as urea for the most part, but this is a very weak base, practically neutral in reaction, and hence is not capable of neutralizing the acid produced.

4. The alkaline reaction of the urine of the herbivorous animals is due to the fact that vegetables and fruits contain salts. Some of these salts are neutral; others are acid salts of dibasic or polybasic acids or other carboxylic acids, as, for example, acid potassium malate, citrate, acetate, tartrate, etc.

On oxidation in the body these salts are burned to carbonates. Some of them are excreted through the lungs in the form of carbonic acid, leaving the disassociated base—usually sodium or potassium—to reunite with the very weak acid, carbonic acid, and in this form is excreted in the urine. These carbonates have an alkaline reaction owing to their giving rise to free alkali by hydrolysis. This explains why lemonade or orange juice makes the urine alkaline.

The vegetable proteins, on the other hand, are not absorbed as well as the animal proteins, and their products of metabolism are more apt to be found in the stools.

5. In starvation, the acidity of the urine increases, owing to the breaking down and digestion of the tissue proteins, which of course are animal in origin.

6. During the infectious diseases, also, the absorption of protein products is increased, especially those of the nucleic group, giving rise to an especially acid urine.

From all these facts, I arrive at two theoretical conclusions:

1. The more protein in the food (especially of the nucleic type) the more acid the urine.

2. A diet of vegetables, especially of those poor in proteins, diminishes the acidity of the urine.

With these theories as a starting point, the following experiments were undertaken, first on babies, and then on older children. Bottle fed babies rather than breast fed babies were used because of the impracticability of changing the percentage of the elements of the breast milk. This was readily done with the bottle feedings. The three babies used were on formulas of which the exact percentages of fat, carbohydrate and protein were known. These percentages were changed at will during the course of the experiments.

The results are shown in Charts 1, 2 and 3. The circles represent the grams of protein in the diet per kilo of body weight; the solid dots represent the number of cubic centimeters of tenth-normal sodium hydrate or sulphuric acid solution necessary to neutralize 10 c.c. of the whole twenty-four-hour amount of urine.

Chart 1.—The relation of feeding and other factors on the reaction of the urine in an infant: A, infant lost 100 gm.; B, lost 150 gm.; C, regained 100 gm.; otitis media.

EXPERIMENTS

Baby 5 months old (Chart 1). Started on a formula containing fat, 2 per cent.; dextrimaltose, 6 per cent.; protein, 2.50 per cent. (880 c.c.). As the baby weighed 4,620 gm., it was getting 4.7 gm. of protein per kilo of body weight. The acidity of the urine on the first day was 4; that is, it took 4 c.c. of tenth-normal sodium hydrate solution to neutralize 10 c.c. of urine. The next few days, although the percentage of protein in the food was not changed, the baby's daily total food intake and weight necessarily varied a little, thus accounting for the irregularity in the curve representing the relation of grams of protein in the food to the kilo of body weight. This variation holds throughout all these experiments.

Chart 2.—The relation of feeding and other factors on the reaction of the urine in an infant: A, infant fed cereal soup; B, cereal soup omitted.

Chart 3.—Irregular acidity of the urine on an unchanged diet.

December 8, the acidity suddenly rose to 7 c.c. with no change in the food. It happened that the baby lost 110 gm. of weight on that day, due to a nasopharyngitis accompanied by a slight fever. December 9, there was a further loss of 150 gm.; the acidity rose again. December 10, the baby was better and gained back 100 gm.; the acidity immediately dropped to the level at which it was before the onset of the fever and remained there.

December 17, the protein in the food was dropped from 2.50 per cent. to 0.90 per cent. This protein represented 1.9 gm. per kilo of body weight on December 18. The urine became alkaline, so that 2.2 c.c. of tenth-normal sulphuric acid was necessary to render 10 c.c. of it neutral.

December 26, an otitis media developed. The acidity of the urine rose immediately. A transfer of the baby to another bed made further experimentation impossible.

Baby 8 months old (Chart 2), weight 5,110 gm., November 3 was given a formula representing fat 2.50 per cent., lactose 5.50 per cent., protein 3.20 per cent. The baby took about 1,170 c.c. of food a day; this afforded 7.3 gm. of protein per kilo of body weight. The acidity of the urine remained at about 9 or 10 c.c. until November 27, when a sharp drop in the acidity was noted. I learned that on the day before, cereal soup had been ordered twice a day. Two days later I asked to have the cereal omitted, and without it the acidity again rose to its former level.

December 3, the protein was diminished from 3.20 per cent. to 2 per cent. This new formula gave about 2.9 gm. of protein per kilo of body weight. The acidity decreased immediately to 2 or 3 c.c., but the urine did not become alkaline. As a matter of interest, the cereal soup was started again December 6, and a marked degree of alkalinity resulted—over 2 c.c.

Baby 8 months of age (Chart 3), was started, November 23, on a formula containing 3 per cent. protein, representing 6.6 gm. of protein per kilo of body weight. It is to be noticed how irregular the acidity was in this urine, although the food was unchanged. The acidity began at 8 c.c. and oscillated widely, rising as high as 20 c.c. I cannot explain this wide variation.

December 18, the protein was reduced from 3 per cent. to 1 per cent., giving about 2 gm. of protein per kilo of body weight. The acidity of the urine dropped immediately to 2 c.c. and remained at about the same level during the remainder of the experiment. The addition of a vegetable soup would in all probability have turned the urine alkaline, but the baby left the hospital before this was tried.

These three charts show well what it was hoped the experiments would prove—the effects on the reaction of the urine of infection, starvation, loss of weight, vegetable and protein diets. It is to be noted that the proteins were never fed below the physiologic needs of the body; that is, 1.5 gm. per kilo of body weight. Emphasis must be placed on the fact that it is possible to change the reaction of the urine in bottle fed babies by a simple change in the formula, but that in the presence of fever or loss of weight, it is more difficult to make it alkaline by these same means.

The second series of experiments was made on two children, 5 and 5½ years old. In their diets, of course, the amount of proteins could not be regulated as accurately as with the babies, but in order to make them as accurate as possible, four types of diet were used: 1, vegetable diet; 2, mixed or "House Diet"; 3, milk diet; 4, animal diet. The accompanying table shows the average food percentage and calories of each diet.

TABLE SHOWING FOOD PERCENTAGE AND CALORIES OF VARIOUS DIETS

I. VEGETABLE DIET *				
	Amount, Gm. or C.c.	Fats, Gm.	Carbohyd., Gm.	Proteins, Gm.
Breakfast				
Cereal (rice)	100	1.50	2.00	8.00
Bread	15	0.50	15.00	3.00
Butter	5	5.00		
Dinner				
Bread	30	1.00	30.00	6.00
Tomato	30	0.07	1.40	0.42
1 potato.....	...	1.00	20.00	1.70
Asparagus	30	0.30	0.80	0.45
Cereal	100	1.50	2.00	8.00
Butter	...	5.00		
Supper				
Toast	15	0.50	15.00	3.00
Peas	40	0.40	1.20	8.00
Orangeade	120	0.25	21.25	1.50
Apple sauce.....	125	1.00	46.50	0.25
Total		18.02	155.15	40.32
Total calories, 1,008.03				

* 3 gm. protein per kilo; 80 calories per kilo.

II. MIXED DIET †				
Breakfast				
Potato	...	1.00	20.00	1.70
Milk	120	4.80	5.40	3.80
Bread	30	0.50	15.00	3.00
Dinner				
Chicken	45	4.50		10.00
Soup	100		0.60	3.48
Bread	30	0.50	15.00	3.00
Butter	...	5.00		
Potato	...	1.00	20.00	1.70
Supper				
Milk	200	8.00	9.00	6.40
		1.20	1.60	6.40
		0.50	15.00	3.00
Total		27.00	101.60	42.48
Total calories, 913.05				

† 72 calories per kilo; 3.5 gm. protein per kilo.

III. MILK DIET ‡				
Milk	1,000	40.00	45.00	32.00
Total calories, 687.8				

‡ 2.56 gm. of protein per kilo; 55 calories per kilo.

IV. ANIMAL DIET §				
Breakfast				
1 egg.....	...	5.00		7.00
Milk	180	7.20	8.10	5.76
Bread	15	0.25	8.00	1.50
Dinner				
1 egg.....	...	5.00		7.00
Milk	210	8.45	9.45	6.72
Broth	90	0.50		10.00
1 chop.....	60	6.00		14.00
Supper				
Milk	180	7.20	8.10	5.46
Bread	15	1.50	10.00	1.50
1 egg.....	...	5.00		7.00
Total		46.10	43.65	65.94
Total calories, 880.55				

§ 5 gm. protein per kilo; 70 calories per kilo.

The weight of the two children was about the same (12,400 and 12,550 gm.); therefore, they were getting about the same number of calories and the same amount of protein per kilo. The proportions were as follows:

	Calories Per Kilo	Proteins Per Kilo, Gm.
I. Vegetable Diet.....	80	3.0
II. House Diet.....	72	3.5
III. Milk Diet.....	55	2.6
IV. Animal Diet.....	70	5.0

The number of calories per kilo changed very little with the different diets excepting with the milk diet, because the children never took the amount required. The vegetable diet gave the greatest number of calories and the animal diet the greatest amount of protein per kilo.

As what I desired to determine in these experiments was the acid concentration of the urine, as well as the total acidity in twenty-four

Chart 4.—Influence of diet on the reaction of the urine in a child aged 5½ years: A, house diet; B, vegetable diet; C, milk diet; D, animal diet.

hours, especial care was necessary in giving the children the same amount of water every day, because it is evident that with the same diet the total acid eliminated in twenty-four hours ought to be about the same; but the concentration of the same quantity of urine taken from the whole twenty-four-hour amount would vary with the total volume eliminated; in other words, with the amount of water ingested.

The curves in Charts 4 and 5 show the changes in the acidity of the urine in the two children on the four diets given. The acidity represented by the dots denotes the number of cubic centimeters of tenth-normal solution of sodium hydrate required to neutralize 10 c.c. of urine taken from the total twenty-four-hour amount.

The changes in the diets were made twenty-four hours before testing the urine.

The curves do not show as wide changes as in the babies, because the changes in the amount of protein in the diet could not be regulated as well. While in the babies the protein changed from 2 to 8 gm. per kilo, in these children they could be changed only from 2.6 to 5 gm. per kilo of body weight.

The two curves (Charts 4 and 5) are remarkable for their similarity, although with some minor differences. The first decrease after changing from the "house diet" to the vegetable diet, is wider in Curve 4 than in 5; and, on the other hand, the small increase after changing from the vegetable to the milk diet is more marked in Curve 5 than in 4. The noteworthy points in these curves are:

1. The acidity of the urine decreased on the vegetable diet and rose more and more on adding food of animal origin. This change is very noticeable in both curves between February 9 and 11, when the vegetable diet was changed to an animal diet.

Chart 5.—Influence of diet on the reaction of the urine in a child aged 5 years: A, house diet; B, vegetable diet; C, milk diet; D, animal diet.

2. The difference in effect of the vegetable diet and milk diet was practically none. Theoretically, the acidity ought to increase with the milk diet (although not as much as with the animal diet), but the children only took on an average of 1,000 c.c. of milk daily, which only represented 2.6 gm. of protein per kilogram, being the smallest amount of protein taken during the experiment.

THE USE OF DRUGS

Only a superficial study was made of the drugs generally used to change the reaction of the urine, as it requires a great deal of time and hardly comes within the scope of this paper.

For making the urine acid, either acid sodium phosphate or sodium benzoate is generally used. The former is eliminated in its acid form

and the latter combines in the body with glycocoll, forming hippuric acid, which is excreted in the urine.

The curves representing the acidity and alkalinity of the urine as the result of the administration of drugs, do not represent the acidity or alkalinity of a fixed volume, but the acidity or alkalinity of each micturition, because in these experiments it was intended to study, not the daily changes, but rather the changes at frequent intervals during the twenty-four hours, on account of the fleeting action of the drugs.

Curve 6 shows that 2 grains (0.13 gm.) of acid sodium phosphate made the acidity increase to 12.5 c.c. It then decreased immediately after stopping the drug, reaching nearly the initial point (5.2 c.c.) eight hours after the last dose.

Curve 7 shows that the acidity remained the same for two hours after the first dose of 2 grains of sodium phosphate, which was probably due to a slower absorption, as three hours after the second dose the acidity rose from 2 c.c. to 14 c.c. As with the acid sodium phosphate, it dropped after the drug was stopped and reached 1.6 c.c. (a little under the initial point) eight hours after the last dose.

Curves 8 and 9 show that a single dose of 5 grains (0.33 gm.) of sodium benzoate had a similar effect, which began to diminish six hours after the dose had been administered.

From these experiments it seems conclusive that the acid sodium phosphate and the sodium benzoate must be given in frequent and repeated doses in order to maintain their action.

For making the urine alkaline potassium citrate or sodium bicarbonate is generally used. The indications for making a urine alkaline are more frequent in therapeutics than making it acid.

The following are two experiments which I think are worth mentioning:

One dose of 20 grains (1.25 gm.) of potassium citrate was given to a 5-year-old child with an ordinary "House Diet" to which about 15 gm. of extra meat were added. Then the same dose of the same drug was given while the child was taking a vegetable diet, adding as an extra, about 100 c.c. of orange juice (see Charts 10 and 11).

The results were that in the first part of the experiment the urine was acid and turned alkaline when the diet was changed.

The same experiment was made with the same diets, but giving 40 grains of sodium bicarbonate instead of the potassium citrate, and the same results were obtained (see Charts 12 and 13).

These last experiments are alike in results to those of the babies and demonstrate clearly the importance of the diet when it comes to changing the reaction of the urine.

Very often the potassium citrate and the sodium bicarbonate cause, especially in babies, digestive disturbances because of their action on the stomach. Such is the case in pyelitis and cystitis when one is

Chart 6

Chart 7

Chart 6.—Action of sodium acid phosphate in a child aged 5½ years, on a house diet. Arrows point to administration of 2 grains of the drug.

Chart 7.—Action of sodium acid phosphate in a child aged 5 years, on a house diet. Arrows point to administration of 2 grains of the drug.

Chart 8

Chart 9

Chart 8.—Action of sodium benzoate in a child aged 5 years, on a house diet. Arrow points to administration of 5 grains of the drug.

Chart 9.—Action of sodium benzoate in a child aged 5½ years, on a house diet. Arrow points to administration of 5 grains of the drug.

Chart 10

Chart 11

Chart 10.—Action of potassium citrate in a child aged 5 years, on a house diet. Arrow points to administration of 20 grains of the drug.

Chart 11.—Action of potassium citrate in the same child as in Chart 10, on a vegetable diet. Arrow points to administration of 20 grains of the drug.

Chart 12

Chart 13

Chart 12.—Action of sodium bicarbonate in a child on a house diet. Arrow points to administration of 40 grains of the drug.

Chart 13.—Action of sodium bicarbonate in the same child as in Chart 12, on a vegetable diet. Arrow points to administration of 40 grains of the drug.

obliged to give very large doses of the drug. Hole has said: "The citrate of potash in this condition [pyelitis] is apt to cause diarrhea or vomiting. It is therefore wise to give no more than 5 or 10 grains."

The two following cases will illustrate this a little better:

S. M., 2½ months old, in the Massachusetts General Hospital with acute pyelitis, was fed on modified milk and a small amount of breast milk. He was treated in the beginning with hexamethylenamin, but on account of a suspicion of nephritis the treatment was changed to rendering the urine alkaline. For this purpose he was given 15 grains of potassium citrate every four hours.

After three days of this new treatment I examined the urine before the morning dose of the medicine was given, the acidity of which was 4.2 c.c.; in the evening, two hours after the third dose, the acidity was 1.2 c.c. By that time the baby had taken a little more than 1.11 gm. of potassium citrate per kilo, which is a larger dose than is ordinarily given, even when a large dose is intended.

The baby was getting in his food, 4.27 gm. of protein per kilo. Perhaps if the protein had been diminished the urine would have become alkaline, but I did not have the opportunity to follow up this case.

M. M., 2 years old, having pneumonia and laryngitis, following the removal of a foreign body from a bronchus, had pyelitis. In order to render the urine alkaline, she was given 30 grains of potassium citrate every 2½ hours.

The urine was examined in the morning, before the first dose, and the acidity was found to be 6.6 c.c., and after taking 120 grains of the potassium citrate it was still acid (4.3 c.c.).

It is evident from these cases how difficult it is to turn the urine alkaline, when there is an infection in the urinary tract, without regulating the diet according to the schemes described.

CONCLUSIONS

1. The difficulties which one often encounters in changing the reaction of the urine in children are very much diminished when a suitable diet is prescribed.

2. Diminishing the amount of protein in the diet to 2 gm. and sometimes to 3 gm. per kilo will often in itself render the urine alkaline without using a drug.

3. In cases in which the amount of protein reaches the lowest physiologic limit without turning the urine alkaline, one may continue to diminish the acidity by adding vegetables to the diet.

4. In older children with whom the food is more varied, one can do much by regulating the diet in accordance with the principles outlined in this article.

5. In cases in which vegetables are used to turn the urine alkaline, one must use, if possible, vegetables in which the amount of protein is smaller in proportion to the salts, like fruits, rice, wheat, etc., rather than those which have a large amount of protein like pease, beans, etc. Vegetables which contain purins, like coffee, tea and cocoa, may increase the acidity, because they may produce uric acid.

6. In cases of infection, especially in infections of the urinary tract, and in cases of starvation, the urine tends to become more acid than in other conditions; therefore it is more difficult to render it alkaline.

7. When drugs are used without the proper diet, the doses necessary to make the urine alkaline are much larger than is ordinarily believed.

8. The action of drugs (either acid or alkaline) is very fleeting; therefore they should be given in large and frequent doses.

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