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CHANGES IN THE ACID-BASE BALANCE IN METABOLIC TREATMENT FOR PAIN

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In an earlier study (Lindahl 1966), the author introduced a new type of metabolic treatment for diffuse pain (varialgia) and reported the results obtained with this form of treatment in 100 patients. The therapy consists in the administration of medicine which neutralizes 50–100 mEq of hydrogen ions a day. Although the results were surprisingly good in these chronic cases where there was a resistance to therapy, with 69 per cent of the patients showing a partial or complete alleviation of varialgic pains, it was considered of interest to know whether the improvement might be associated with the intended change in the acid-base balance. An account is given here of the examination of the acid-base balance in 50 patients receiving this form of treatment.

MATERIAL

At an orthopaedic out-patient department a large number of patients seek advice for pains in various parts of the body. In many cases the pain is associated with local changes such as osteo-arthritis, disc hernia, or rheumatoid arthritis, but the pain is often of a fairly diffuse nature and can hardly be ascribed to such local conditions. The pain in these cases may vary in severity and move from one region to another; it may change with the weather, keep the patient awake at night in spite of a comfortable posture, and result in stiffness in the mornings. It may be localized in the long bones, in the joints or muscles, and may often render the patient nervous. In severe cases attempts at treatment are often unsuccessful, and the patients are not infrequently regarded as neurotic by the physician, who is unable to find objective features. This may often increase the patient's nervousness and irritability. Patients with some or all of these characteristics were considered by the author to be suffering from varialgia. The patients were selected for the above metabolic form of treatment, usually after a long period in which all conventional treatment such as medical therapy, radiotherapy, short-wave, and physiotherapy had proved unsuccessful. In some of the cases the varialgia was accompanied by a local orthopaedic disease or condition, for instance osteoarthrosis of the hip or the supraspinatus syndrome. This local disease was then not regarded

as part of the syndrome, and it was disregarded in assessing the effect of the treatment, only the other, general, symptoms being considered. After successful treatment these patients may thus be rid of the diffuse pain in various joints and the back, no longer be aware of changes in the weather, be able to sleep at nights, and have no morning stiffness. Pain in the hips after walking 100 metres due to osteoarthritis may, however, remain unchanged, as may the restriction of mobility in the hip-joint. A more detailed account of this morbid picture is presented in the earlier paper (Lindahl 1966). The present series comprised 50 patients.

METHODS

Because of the highly subjective nature of the symptoms, registration is dependent entirely on the patient's own assessment. At the beginning of the treatment an ordinary record was made in which special attention was devoted to the severity and site of the pains and aches. In the evaluation of the treatment the patient was questioned with respect to the pain and aches. It was often found that patients that had perhaps not experienced any major change still declared that there had been an improvement (perhaps through politeness to the physician), while patients that had in fact found an improvement declared that they were just as bad as ever.

The former group usually stated that there had been quite minor improvements, whose value is always open to discussion. They were then always asked: "Is it certain that there has been an appreciable improvement or is your condition perhaps no better than before?" In the discussion along these lines, with the plea for the plain truth, even if it should mean that the treatment had been worthless, it is usually possible to obtain a good impression of the reliability of the information. The latter group may sometimes be more difficult to penetrate. For when the patient states that he feels as bad as ever he may be referring to the pain in one particular region—say lumbar area. When questioned on his earlier headache and pain in shoulders and arms, which often kept him awake for a large part of the night, he will admit immediately, "Yes, indeed, the pains are in fact almost gone but the pain in the lower part of my back is severe". Further discussion on the lumbar pain may elicit the reply "Yes, compared with 4 months ago it is, of course much better, for it was then hardly supportable". In the conversations with the patient it is thus essential to mention the earlier symptoms.

TESTS OF THE ACID-BASE BALANCE

Our knowledge of the acid-base balance of the body is in certain respects extremely good, but still leaves much to be desired. The methods used for assessing this balance for the most part involve the detection of changes in the blood. The methods used have successively developed from alkali reserve, standard bicarbonate, blood pH, buffer base to base excess (Astrup 1961). The values for base excess may be said to reflect the excess or deficit of protones in the blood, but little is

known of how this factor is related to the storage of protones in the rest of the body or of how, and in what quantity, protones are stored. A number of authors (Daughaday 1961, Lobeck & Forbes 1958, Post & Shoemaker 1962, Reidenburg 1961) have shown that in acute and chronic acidosis, both in laboratory animals and man, there is an accumulation of protones not only in the blood and extracellular liquids, but also in the cells and collagen tissues where up to 50 per cent can be stored (Daughaday 1961). The collagen system functions as an ion exchange (a resin) and can store large amounts of protones. As regards the skeletal system, it has been shown that in acidosis 20–28 per cent of the sodium ions disappear from the skeleton and are replaced by protones (Lobeck & Forbes 1958, Post & Shoemaker 1962, Reidenburg 1961). In the erythrocytes and muscle cells the protones replace potassium and sodium, which decrease in concentration. Although we thus have some knowledge about which tissues are involved in the buffering mechanism in acidosis, we are not so well informed on the extent to which such changes can arise or the period required to reach equilibrium. On the connection between excess base in the blood and the buffer capacity of the various tissues, we also know little, although it would seem logical to suppose that there is a direct relationship between them. The kidneys are extremely sensitive to all kinds of changes in the homeostasis of the body, even in respect of changes in the protone balance. It is, in fact, the kidneys that finally take care of and excrete the excess protones that are derived from food, medicines, and acid metabolites, and that cannot be stored or excreted as carbon dioxide from the lungs. The pH of the 24-hour urine can therefore provide an impression of the acid-base status—provided there is no renal disease. On the other hand, a pH determination alone does not furnish a quantitative measure of the acid balance; and when ammonium carbamate and/or carbonate are excreted, the pH can sometimes be directly misleading. In addition to a determination of the pH, the total acid-base excretion in 24 hours should be recorded.

In various connections attempts have been made to form an opinion of the acid-base balance by loading with bases or acids (de Wardener 1961). Böttner & Lindén (1949) have reported a less pronounced alkalinization of the urine after supplying alkali to patients with chronic acidosis such as in diabetics, cases of ulcer, and hypertension.

In the present study the following tests were used:

1. Determination of pH in the 24-hour urine.

Table 1. pH in the 24-hour urine; mean of 50 patients

	pH	Standard error	Range
Before treatment	5.8	0.4	5.1–7.0
After treatment	7.6	0.5	6.9–8.0

observed, but with large individual variations. The means are presented in Table 1. The increase in pH after the treatment is statistically significant ($P < 0.001$). A division of the patients according to improvement or not showed that the pH of the urine was raised considerably more in the former group (Table 2, Figure 1). The difference between the two groups is significant ($0.001 < P < 0.01$). The number of patients not recording a pH above 7.4 was considerably greater in the unchanged than in the improved group (11 out of 19 against 4 out of

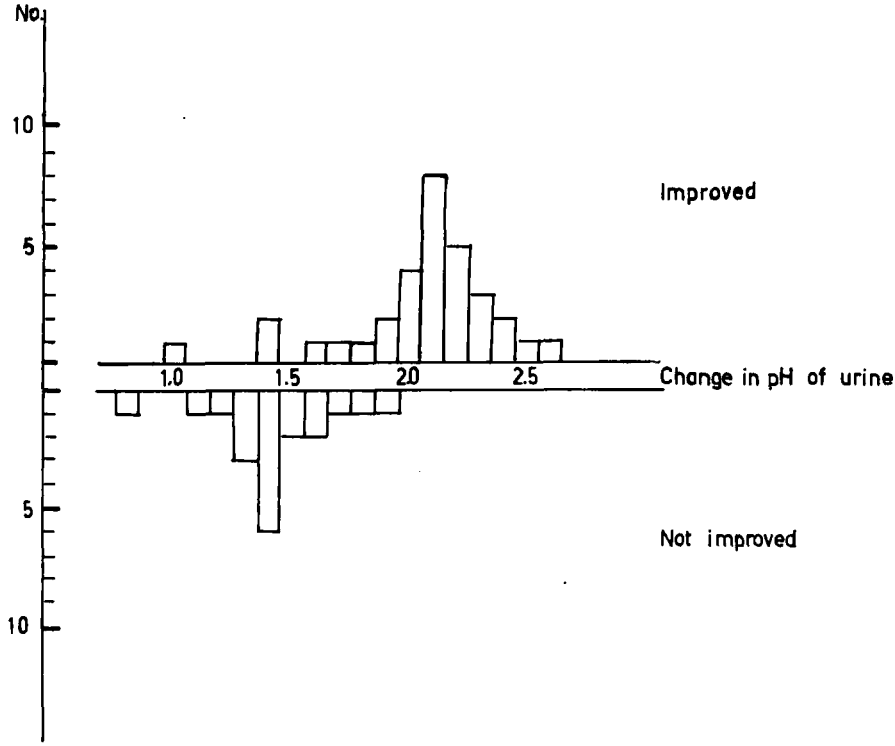

Figure 1. Histogram showing the individual change in pH of urine after treatment. The mean change is bigger in the improved group.

2. Determination of the total excretion of acid or base in the 24-hour urine by Jørgensen's method (1957).
3. Acid-loading: The bladder was emptied at 7 a.m. and 0.1 g of ammonium chloride per kg body-weight was given, followed by 1–2 litres of water. Every hour up to 2 p.m. the urine was collected and the volume measured. The pH was then determined on the different portions and the highest value used.
4. Alkali-loading. The procedure was the same as for the acid-loading except that 0.1 g of sodium bicarbonate per kg body-weight was given.
5. Determination of base excess in the blood.

Test 1 was performed without any change in diet. Tests 2–5 were performed at hospital after supplying a neutral diet for 2 consecutive days (the diet was reckoned to be neutral from the aspect of formation of acid and base). The diet for all the patients was exactly the same, and it was identical on both days. If this standardization is not performed, the differences in the diet can result in considerable displacements in the acid-base balance. The determinations were performed by standard methods, and small amounts of toluol were added to the urine to prevent bacterial decomposition pending analysis.

RESULTS

Subjective Improvement

In the previous study (Lindahl 1966) the patients were divided according to subjective improvement into the groups: nearly complete, marked, slight, and none. Because of the small size of the material the two best and the two worst groups were combined. The results were assessed after 4 or, more frequently, 6 months. Sixty-two per cent of the patients showed improvement and in 38 per cent no essential change was found.

Determination of pH of the 24-Hour Urine

Normally the pH of the urine is on the acid side, with a mean of 6.0. Only when large amounts of alkali have been given, or in the case of "extreme" diets or disturbance of the fluid balance does the urine become alkaline.

In all 50 subjects the pH was determined at the beginning of the treatment and 4–6 months afterwards. A rise in the pH was invariably

31). An improvement thus became significantly more common when it was possible to change the acid-base balance so that the urine became alkaline.

Table 2. Mean increase in pH of 24-hour urine after alkalinization treatment

	Change in pH of urine			
	No.	Value	Standard error	Range
Improved	31	2.1	0.1	1.0–2.6
Not improved	19	1.4	0.2	0.8–1.9

Determination of Total Excretion of Acids and Bases in the 24-Hour Urine

Normally, 50–100 mEq of protones are excreted in 24 hours (Pitts 1950, Pitts & Alexander 1945). In 23 patients in whom this excretion was determined before treatment the excretion was on average 78 mEq/day. In the subjects in whom the same examination was made after 4–6 months of treatment the same value was on average —14 mEq/day (that is to say, an excretion of bases). A division into improved and deteriorated here, too, showed a smaller change in the total excretion of acid in the patients not responding to treatment (Table 3). The difference was not significant.

Acid-Loading

It has been reported by de Wardener (1961) that in the case of acid-loading the pH should normally fall to about 5.3. In the 21 subjects where this test was performed the pH fell to a mean of 5.0, with a range of 4.6–5.5. The test was not performed after the treatment.

Table 3. Mean reduction in the total protone excretion in the 24-hour urine after treatment

	Reduction in excretion of H^+, mEq		
	No.	Value	Range
Improved	31	114	11–182
Not improved	19	72	15– 93

Alkali-Loading

The literature would appear to contain no report of an alkali-loading test. In 10 "normal subjects"—ones not reporting varialgic pains—who were admitted for foot and knee complaints and in whom the alkali-loading test was performed, the pH rose to a mean of 8.5 (range 8.0–9.6).

In all 21 subjects in whom the acid-loading test had been performed this alkali-loading test was also carried out; the pH increased to a mean of 8.9 with a range of 7.6 to 9.6. There was no significant difference between the normal and the test group.

Base Excess

For the base excess a normal range of —2.3 to +2.3 mEq/l has been given by Astrup (1961). In 24 subjects where this value was determined it was on average —2.2, with a range of +1.8 to —9.3. No determination was performed after the treatment.

DISCUSSION

As only a few, if any, studies of the acid-base balance have been performed along these lines it is difficult to evaluate the results, and it is obvious that further studies of the relationship between the various tests and the total body acid-base equilibrium are required to elucidate this difficult and obscure area. It would, however, seem to be established that the fairly simple examination of the pH of the 24-hour urine reflects in a fairly satisfactory manner the reaction of the body to administered protones or proton acceptors. The total excretion of acids or bases followed largely the same patterns as the pH, but it is difficult on the basis of present series to predict whether measurement of the total acid or base excretion, which is quantitative, provides a more accurate view of the body's reaction. The acid- and base-loading tests appear not to reflect the acid-base balance of the body, as in practically all the subjects normal values were obtained; these tests would seem rather to indicate the actual renal function. The difference between the normal and "acidotic" persons obtained by Böttner for the alkali-loading was not confirmed in this study; it may possibly be ascribed to a large difference in method.

The values for the base excess in these patients were definitely on the acid side, with most of them outside Astrup's normal limit of —2.3. Although this departure from the normal points to charging with pro-

tones in most of these patients, it is difficult to evaluate statistically. While the average urine pH for the series was certainly on the acid side (5.8), it cannot be said to differ essentially from that of a normal series. The most important result of this study is probably the difference in the metabolic reaction to the treatment observed in the improved and unimproved groups. The view that with this treatment it is possible to influence the patient's condition, and also the fact that in most of the subjects showing no improvement there was no alkalinization of the urine, finds strong support in this result. After a change in the medication, an alleviation of the symptoms and also the desired metabolic change were observed in 6 subjects (not reported here as improved). To be effective the recommended treatment must thus be followed-up with a regular check of the acid-base balance. An examination of the pH in the 24-hour urine and determination of the total acid-base excretion therein would thus appear at present to be the most suitable method.

SUMMARY

To 50 patients an oral dose of 50–100 mEq of protone acceptors was administered daily during 4–6 months (alkalinization) with the object of examining the value of this measure in diffuse and varying pain conditions, designated varialgia. The acid-base balance was also examined by determining the pH, and the total acid or base excretion in the 24-hour urine, by loading with acid and base, and by determining the base excess in the blood.

A significantly greater number of the patients showing an improvement displayed a metabolic swing to the alkaline side, whereas in most of those not improving with the treatment this intended metabolic effect was not observed. The various types of test of the acid-base balance are discussed. The determination of pH and total excretion of acids or bases in the 24-hour urine is recommended as a check on the efficacy of the treatment.

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