

Latent Acidosis: Overacidification as a Cause of Chronic Diseases

The physiological importance of a well-balanced acid-base equilibrium and preventive aspects of a diet rich in bases

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The regulation of the pH value inside and outside of the cells is an essential precondition for the functional ability of the enzyme-controlled metabolic processes of our body. The ratio of acids to bases is not only important for a healthy metabolism, it also determines the structure and function of proteins, permeability of cell membranes, distribution of electrolytes, and functioning of connective tissue. On the basis of the present state of scientific knowledge, long-term disturbances of the natural acid-base balance are receiving increasing attention as a risk factor for the pathogenesis of chronic diseases like, for example, osteoporosis - particularly since in the past, the pH regulation was medically taken for granted and the required buffering capacity of the organism was considered as almost inexhaustible. Nowadays, latent acidosis resulting from a gradual reduction of the buffer reserves, mainly due to nutritional influences, is increasingly becoming the focus of scientific studies.

Keywords: acid-base balance, latent acidosis, buffering capacity, osteoporosis, connective tissue, minerals

In the healthy human being, the blood has a pH value of 7.4. Even slight deviations from this value lead to severe disturbances in metabolism which can sometimes be life-threatening. That is why the blood pH is kept within very narrow limits between 7.37 and 7.43 by extensive buffer systems. The buffer systems bind and neutralize the additional protons (H^+ ions) or hydroxide ions (OH^- ions) associated with the excessive acidity or alkalinity respectively and thereby prevent them from immediately influencing the metabolism. In order to maintain the functional ability and therefore the buffering capacity of the system on a long-term basis, the organism is also dependent on the constant regeneration of the buffer systems.

Regulation of the acid-base balance

This presupposes a precise regulation of the acid-base balance which involves many factors (Fig. 1). Apart from the buffering characteristics of the blood and the extracellular and intracellular compartments, the gas exchange in the lungs and the excretion mechanisms of the kidneys are essential components of this regulatory system which are all in a functional equilibrium with one another.

The soluble buffer bases of the bicarbonate system are of primary importance for maintaining a constant blood pH. But plasma proteins as well as the red blood pigment hemoglobin and the phosphate buffer also play a role as H^+ or OH^- scavengers. The particularly rapid responsiveness of the buffer systems produces an extremely rapid and constant regulation of the blood pH.

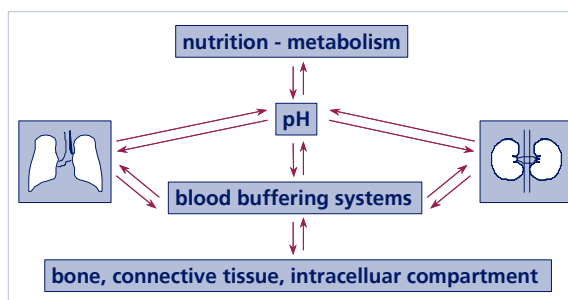


Fig. 1: Regulation of the acid-base balance.

Apart from water, transient carbon dioxide, the intermediate product from the protonation of bicarbonate (HCO_3^-), is produced as a dissociation product of carbonic acid; it is expired via the lungs and as a result, H^+ ions are effectively eliminated. But since HCO_3^- is also removed at the same time, a net acid excretion does not occur. Even though acute acidosis can usually be avoided via carbon dioxide expiration, the buffer systems of the kidneys are primarily responsible for the net

excretion of the H^+ ions released from the breakdown of various acids. This excretion is necessary because the production of protons (e.g. via metabolizing sulfur-containing amino acids from protein) exceeds the absorption of basic substances from a normal mixed diet. In the modern diet, mainly the proportionately high consumption of protein, compared with that of base-supplying fruit and vegetables, contributes to the daily acidification of the body. Phosphoric acid-containing beverages, for example, are also one of the particularly acidifying foods. Fasting increases the acidification of the body via the increased formation of keto acids from the breakdown of fatty acids, and so does the increased production of lactic acid under anaerobic conditions as the end product of glycolysis during sports activities.

With regard to the buffering of H^+ ions, major importance is attributed to the organic salts of minerals and trace elements. During the dissociation of these salts, organic anions are released which can then – according to the dissociation constant of the acid group – accept H^+ ions. The organic acids produced are neutrally metabolized to water and carbon dioxide (CO_2) and ensure in this way that protons are eliminated from the organism. As is shown for the example of sodium citrate (Fig. 2), the remaining cations (e.g. Na^+) in exchange for H^+ ions are available for reabsorption from the primary urine in the kidney. By this means, the charge neutrality is maintained and acid is eliminated from the body. Therefore, the level of intake of organic anions represents a major factor for the regulation of the acid-base balance.

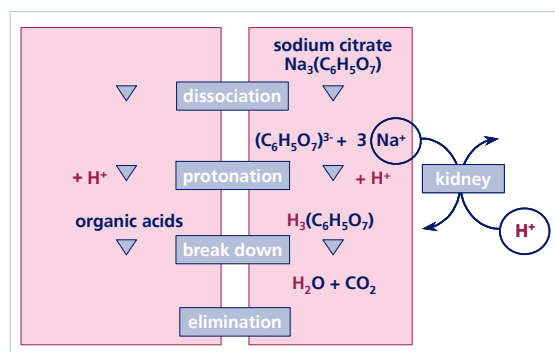


Fig. 2: Function of organically bound minerals in the elimination of acids.

Latent acidosis

Compared with the clinically rather rare manifest respiratory or metabolic acidosis, which are characterized by a decrease in the blood pH, latent acidosis is much more commonly observed. In most cases, there is a slight shift of the blood pH in the acid direction within the normal range and the buffering capacity of the blood is reduced. The term "latent" refers to a chronic condition which is without specific symptoms and is only clinically detectable via determination of the intracellular and extracellular buffer capacity as well as the renal net acid excretion.

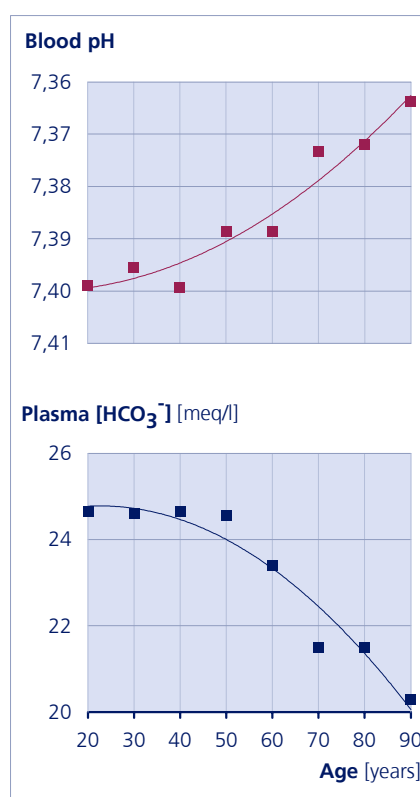


Fig. 3: Relationship between blood pH or plasma bicarbonate concentration and age [modified from [3]].

The cause of the increased acidification is above all the high protein content in food which, when coupled with the declining renal function associated with increasing age, leads to latent acidosis [1]. This in turn results in an increased consumption of buffering minerals from the bone reservoir. The ability of the kidneys to excrete acids progressively decreases with advancing age [2]. As is shown in Figure 3, the blood pH declines within the normal range over the years, but at the same time the concentration of bicarbonate buffer

bases also decreases. With a constant diet with a high protein content, increased acidification therefore occurs with detrimental effects on various metabolic functions like, for example, the increased muscle breakdown which is frequently observed in old age [3].

Compensation mechanisms of latent acidosis

The pathobiochemical effects of latent acidosis with osteoporosis, diabetes mellitus, hyperuricemia, gout or restricted renal function are undisputed today. These connections were ultimately recognized via the very efficient homeostatic counter-regulation of the organism to maintain the bicarbonate and proton concentrations and therefore the pH value of the blood; its mechanisms have been partially explained in recent years [4]. The adaptation mechanisms of the kidney play an essential role in the compensation of nutrition-induced latent acidosis. They are schematically depicted in Figure 4.

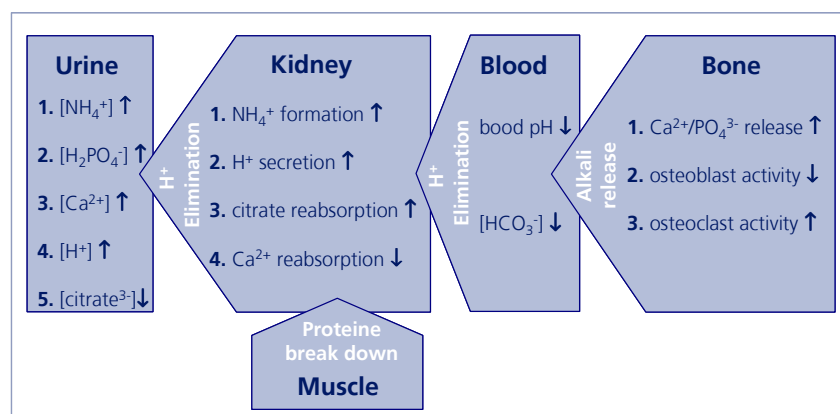


Fig. 4: Compensation mechanisms for latent acidosis (modified from [4]):

1. Increased excretion of ammonium ions (NH_4^+):

Ammonia (NH_3), which is produced in the tubular cells and can freely diffuse through membranes, combines with H^+ ions in the primary urine to form ammonium (NH_4^+) which can hardly diffuse back and is excreted with the urine. NH_3 is formed in the tubular cells from the breakdown of the nitrogenous amino acid glutamine. With acidosis, the activity of the glutamine-decomposing enzymes is increased. Accordingly, there is an

increased consumption of glutamine and subsequently other nitrogen-supplying amino acids. Therefore, latent acidosis also leads to an increased activity of the protein-decomposing systems in the muscular system with a corresponding loss of myoprotein.

2. Increased H^+ ion secretion in the renal tubules:

Even with mild acidosis, the quantity and activity of the Na^+/H^+ ion exchanger in the kidney is increased, whereby an increased excretion of H^+ ions with simultaneous Na^+ reabsorption occurs.

3. With latent acidosis, the citrate excretion in the urine is significantly reduced:

The relative reabsorption of citrate³⁻, the anion of citric acid, from the primary urine is increased with acidosis. The adaptation occurs via two mechanisms: the absorption of citrate³⁻ in the tubular cells occurs mainly in the protonated form H-citrate^{2-} . The activity of the citrate transporter is therefore increased with reduced pH. Intracellularly, citrate³⁻ is converted via accepting of additional protons to uncharged citric acid, which is then pH-neutrally broken down into carbon dioxide and water. Via the absorption of one molecule of citrate³⁻ from the primary urine, 3 H^+ ions can therefore be eliminated. As a

result, the concentration of citrate in the primary urine decreases. However, citrate is also able of complexing calcium ions (Ca^{2+}). This lack of Ca^{2+} complex formation increases the concentration of free Ca^{2+} ions and therefore the risk of the formation of renal calculi.

4. Increased release of minerals from the bones:

On the one hand, mild acidosis leads to a physical removal of minerals from the bone matrix. On the other hand, acidosis results in an increase in the activity of the bone-decomposing osteoclasts and an inhibition of the activity of the bone-forming osteoblasts (also see Fig. 8). All in all, an increased renal excretion of Ca^{2+}

ions takes place with the consequence of an increased risk of calcium renal calculi already described under point 3.

Diet-specific effects on the calcium and bone metabolism

With an experimentally produced acidosis, first a reduction of the buffer capacity of the blood occurs, then with further increases of the acidification a reduction of the intracellular buffering capacity and a strain on the buffering capacity of the bone, and finally with continuing acidification to buffering by the release of minerals from the bone [5]. This and comparable studies led already in the sixties to the hypothesis that one of the significant causes of osteoporosis is a high acid load in diet [6].

In the meantime, there are numerous epidemiological studies on the possible connections between the type of diet and the development of osteoporosis. The influence of a vegetarian diet on the bone density is based on a significant effect of the acid and base content in the diet, whereby a higher base content is correlated with a higher bone density [7].

intake in both groups, the women who ate a mixed diet showed not only a significantly higher excretion of acid but also a significantly higher excretion of calcium. A correlation between the intake of basic foods and the bone density was also described in premenopausal women [9]. Although the intake of basic-acting food components, especially potassium and magnesium, and a high consumption of fruit and vegetables were correlated in a study on elderly subjects with an increased bone density, this was not the case for the calcium content of the consumed food [10]. No associations with other food components like, for example, the calcium intake or the total caloric intake were found. On the whole, the epidemiological data clearly point to a connection between the amount of basic vital substances from fruit and vegetables ingested over the years and the effects on the calcium and bone metabolism observed with osteoporosis.

Intervention studies largely confirm the physiological effects of latent acidosis. Figure 5 shows the results of a study [11] in which an artificial acid excess was caused only by an increase in the protein intake. As expected, an increased renal excretion of calcium was first observed.

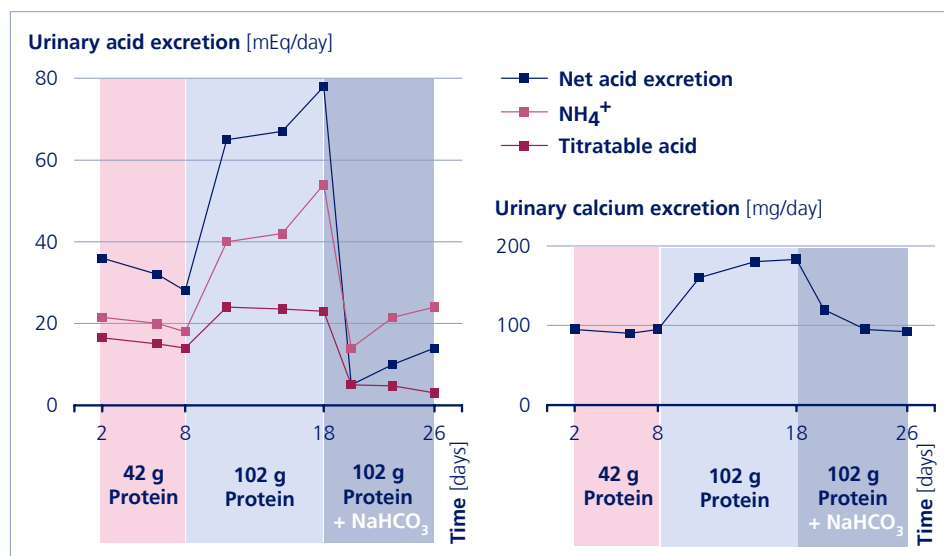


Fig. 5: Renal acid and calcium excretion with different protein intakes [g/day] or sodium bicarbonate substitution [70 mEq/day] (modified from [11]).

A comparative study on omnivorous and vegetarian women [8] showed that a high proportion of basic-acting foods lead in vegetarians to a clearly improved calcium balance; that is, in spite of an equal calcium

However, via the concomitant intake of sodium bicarbonate as a base supplier, a negative calcium balance could be prevented and the protein-induced overacidification of the organism was neutralized.

Via the specific intake of bases, the calcium release from the bone in young

women who had developed ketoacidosis as a result of fasting could be prevented [12]. In postmenopausal women, the increased intake of potassium bicarbonate (KHCO₃) brought about both a reduction of the breakdown of bone and an increase in bone formation [13]. Due only to a reduction of the protein intake, the calcium excretion and therefore the risk of renal calculi could be reduced in hypercalciuric patients [14]. In animal experiments as well, it was shown that due only to a high-protein

diet, the bone formation in young rats was impaired [15].

Animal protein as an acid-forming substance

According to the most recent studies, food protein from different sources seems to have different effects on bone metabolism. Elderly women who have a high proportion of animal protein in their diet showed a more rapid loss of bone density and a higher risk of hip fractures than women with a low proportion [16]. In the group with a low animal protein proportion, clearly fewer women sustained a hip fracture during the period of observation of 7 years. Animal foods contain predominantly acid-forming substances whereas protein in vegetable foods is accompanied by base-forming substances.

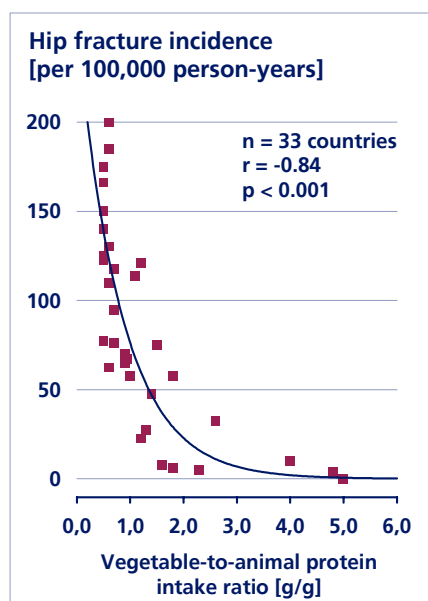


Fig. 6: Worldwide relationship between the incidence of hip fractures and the ratio of vegetable to animal protein intake [modified from [17]].

The vegetable basic substances in the form of metabolizable organic anions can neutralize the acid produced from protein metabolism.

The protective function that an increased consumption of vegetable as opposed to animal protein may have has also been confirmed in international studies. The incidence of hip fractures differs in the populations of different countries, and it is directly correlated with the level of consumption of animal protein of the different

cultures. The analysis of the data on the incidence of hip fractures in 33 countries in relation to the respective country-specific characteristics of the per capita consumption of animal and vegetable foods (Fig. 6) showed that the incidence of hip fractures is the lowest in countries with a low intake of animal protein [17].

The effects of acid on bone

The homeostasis for the maintenance of a stable physiological pH environment often functions only at the expense of the bone mineral content because latent acidosis causes the release of calcium from bone, and by means of this process the additional protons are buffered. Metabolic acidosis first stimulates a physicochemical release of minerals (decrease of the sodium, potassium, carbonate, and phosphate content of bones) and subsequently the cell-mediated absorption of bone, as is schematically depicted in Fig. 7. Acidosis results in an increase in the activity of bone-decomposing cells (osteoclasts) and inhibition of the bone-forming cells (osteoblasts). Genes that regulate the early "immediate reaction" of the osteoblasts are inhibited as are genes that control the formation of bone matrix, which causes an overall reduction of bone remodeling and formation. Several in vitro studies with artificially cultured bone cells confirmed their characteristics as potent acid buffers [18].

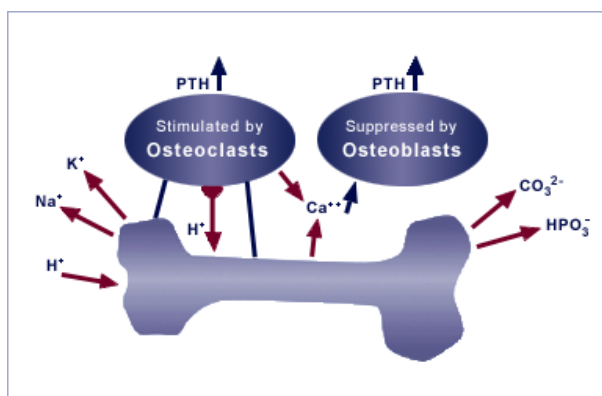


Fig. 7: Schematic diagram of the effects of latent acidosis on bone [modified from [18]].

For example, Figure 8 shows the dependence of the net calcium flux of cultured bone cells on the pH value of the surrounding medium. With a pH value below 7.4, calcium flows out of the bone cells into the medium, whereas a net absorption of calcium was only detectable with a pH value above 7.4.

Other pathophysiological consequences of latent acidosis

Even slight changes of the blood pH lead to a change of the physicochemical characteristics of the proteoglycans, the branched protein-saccharide constituents of connective tissue. These proteoglycans exchange with the extracellular fluid. Proteoglycans are composed of a protein component and a glucosaminoglycan component, which contains a multitude of charged functional groups (e.g. sulfate residues $R\sim O-SO_3^-$). The binding of extracellular matrix proteins to glucosaminoglycans is primarily charge-dependent. In cartilage as well, proteoglycans with the hyaluronic acid molecules that are bound to them represent a high-molecular-weight polyanionic complex that forms the important compressible component of cartilage due to the high water-binding capacity [19]. The water-binding capacity of the extracellular matrix proteins is considerably determined by the degree of dissociation of the functional acid residues, which is again highly pH-dependent. Effects of latent acidosis on the function of cartilage can be explained in this way. However, the complex structure of the extracellular matrix does not presently allow a direct measurement of the function of cartilaginous tissue with different degrees of dissociation.

For almost all syndromes involving the gastrointestinal tract, musculoskeletal system, cardiovascular system, tendency to exhaustion, and skin, a considerable improvement of the symptoms has been shown in a placebo-controlled study comparing treatment with basic minerals to a placebo group [20]. Also laboratory parameters (e.g. acid excretion, serum cholesterol etc.) were significantly improved by means of the base therapy.

Patients with chronic low back pain also profited from a 4-week substitution therapy with alkaline minerals: Both the pain as well as the physical movability improved significantly, and the consumption of antiphlogistic antirheumatic drugs could be clearly reduced [21].

Mild chronic metabolic acidosis affects the muscle protein metabolism as described above (see Figure 4). By increasing the intake of bases, the loss of nitrogen caused by mild latent acidosis could be prevented in postmenopausal women [22].

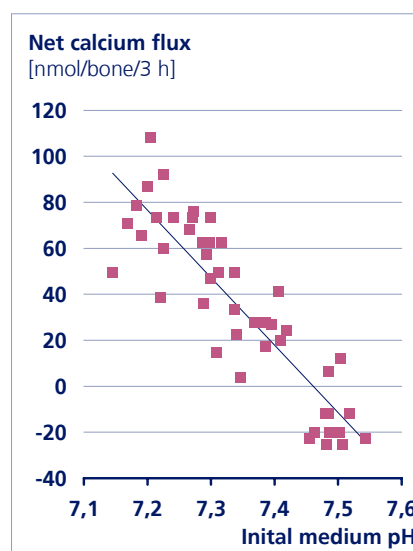


Fig. 8: Effects of the medium pH on the net calcium flux in cultured bone cells. A positive value shows a net calcium flow out of the bone cells into the surrounding medium [modified from [18]].

Conclusions

To what extent the diet can affect the acid-base balance has been the subject of controversy for many years. Acute acidosis or alkalosis cannot be produced by the consumption of certain foods. However, the pathobiochemical effects of latent acidosis with diseases like impaired renal function, diabetes mellitus, hyperuricemia, or gout are undisputed. Based on new scientific findings, causal evidence has also now been furnished for the positive effects of a well-balanced acid-base equilibrium empirically established in naturopathy. Although a diet-induced latent acidosis does not produce major changes in the blood pH due to the compensation mechanisms of the kidney, the compensation leads necessarily to the consumption of endogenous buffer reserves and, therefore, predominantly to a loss of bone substance if the increased acidification caused by a surplus of animal protein and a shortage of basic substances in the diet exists for a long period of time. A disturbance of the muscle protein metabolism as well as the structure and function of cartilage are other negative consequences of the endogenous compensation, which can also aggravate degenerative diseases like, for example, arthrosis or rheumatism.

Our Stone Age ancestors preferred a more or less mixed diet which in spite of containing a high proportion of animal protein was also

characterized by a surplus of base-forming substances. In contrast, the diet in today's Western industrial nations is characterized by a large quantity of acid-forming nutrients, above all due to the surplus of animal protein. On the other hand, a high proportion of fresh fruit and vegetables in the diet contributes to the formation of the surplus of bases in the body.

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