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Research Article

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Osteoporosis as a Process Conducive to Tissue Biomineralization

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Summary

Presented results were obtained in the years 1990-2020, during studies which were carried out with the use of various methods, including mineralogical. Studies on tissue biomineralization (calcification) show connection between developing osteoporosis and tissue biomineralization. This article presents the mechanisms of both osteoporosis and mineralization of selected human tissues. The relations between these processes were presented.

Introduction

Osteporosis is known as the process of bone destruction – reduction of their strength parameters, which in turn leads to their fragility, brittleness and lowering of osteogenic properties, i.e. reduction of the ability of forming bone fusion after fractures. In studies of these phenomena with the use of densitometry and other research techniques, no attention is paid to what happens with the elements removed from bone in the course of developing osteoporosis. Where do they go?

With the aging of organisms, calcification of various types of tissues and organs develops (1-29). The phenomenon is lethal for the organisms and in many cases may lead to death.

Tissue mineralization does not necessarily involve the presence of grains or crystals. When we can observe them, for example with the use of microscopes, we are talking about overt mineralization.

However, tissues can also be affected by hidden mineralization. In that case, mineral concentrations are not visible, but the chemical analyzes of the tissues affected by such mineralization clearly show higher contents of various elements. It is similar to mineral water, which does not contain crystals and yet contains high levels of many elements.

In the case of hidden mineralization, the elements occur in the atomic structures of organic compounds that build tissues, where they replace various atoms. That usually happens in areas where tissues have been damaged for various reasons. These damaged sites may be affected by hidden mineralization – the first stage on the way to overt mineralization.

This phenomenon, which includes the relationship between osteoporosis and tissue mineralization, is discussed in this article.

Biomineralogy of osteoporosis

Understanding osteoporosis is difficult without knowing the process of bone collagen mineralization. Collagen fibers present in bone trabeculae have centers of carbonate hydroxyapatite crystallization systematically arranged along their length. This mineral crystallizes in such crystallization centers from a chemical compound called alkaline phosphatase, which is generated in osteoblasts. Crystallization centers are endowed with electric charges that "trap" Ca^{2+} and PO_4^{3-} ions from the flowing alkaline phosphatase, building lamellar hexagonal crystals in the bones. After apatite crystallizes, an aggregate of collagen fibers overgrown with mineral plaques is formed.

Osteoporosis develops in the bones in very different places. This is confirmed by densitometric examinations of the femoral head in its subsequent sections. Dark – "decalcified" – zones create fanciful shapes in the heads of the femur (Photo 1, A). Observations made with a binocular microscope confirm disappearance of bone trabeculae in these places (Photo 1, B).

The functioning of bone cells located in the pits in the bone trabeculae involves a number of life processes, including nutrition and excretion of metabolic products. Nutrition is, generally speaking, the breakdown of polysaccharides, as a result of which cells receive vital energy.

The products of metabolism are excreted outside the cells, from where they migrate to blood vessels based on the concentration gradient (Fig. 2, A).

In this process, carbon dioxide, a product of cellular metabolism, and other products are removed from the bone cells into the microvessels embedded in the Haversian canals. Penetrating into microvessels through the systems of microholes in their walls, they enter the bloodstream. In studies conducted with a scanning microscope, crystallizing substances were observed in those microvessels (Fig. 2B),

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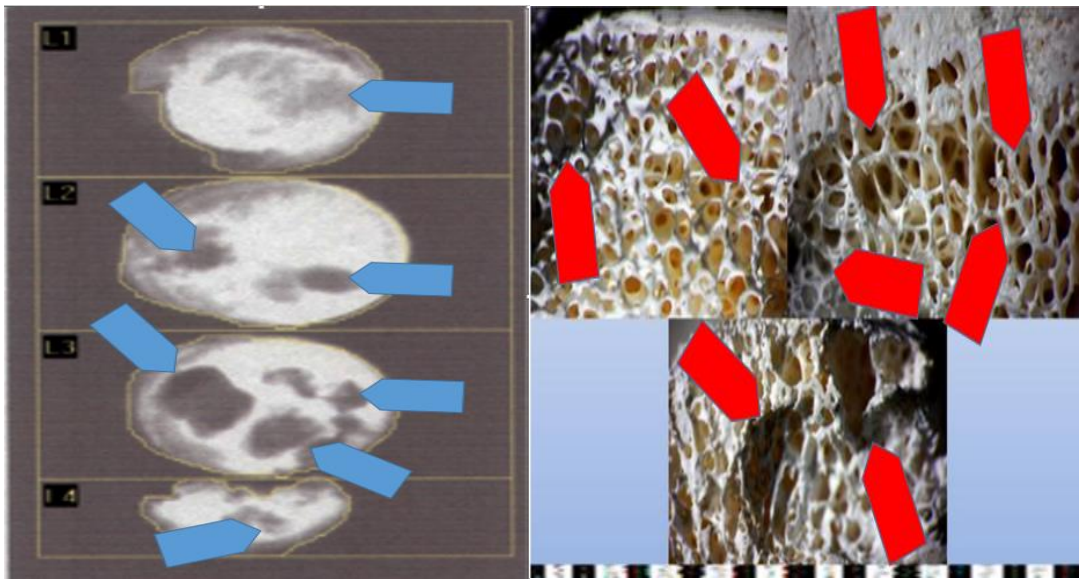
which, apart from calcium phosphates, may also contain organic compounds that are difficult to identify (Fig. 3, C). Their crystallization causes clogging of the vessels and makes it difficult for the excess carbon dioxide to be removed through them. Another effect is the local formation of increased amounts of carbonic acid and then an acidified environment with a pH <7.

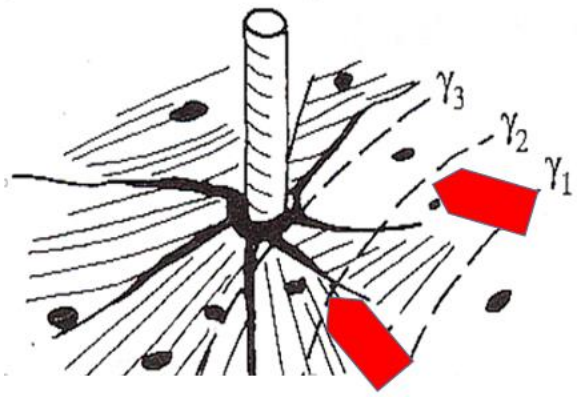
Bone apatite in collagen fibers is unstable in acidic environment and begins to dissolve. It also causes destruction of the structure of collagen fibers and, consequently, further deterioration of the bone trabeculae.

Since "clogging" of microvessels in bones is random and involves various microvessels, osteoporosis develops in an irregular manner.

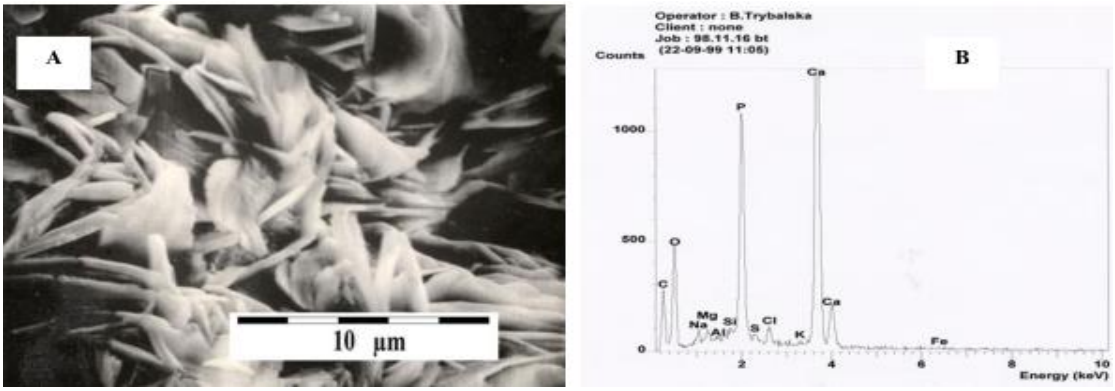


A **B**

Figure 1: A-densitometry images of slices of dissected femoral head. The arrows show the places with bone trabecular structure loss; B-bone loss zones (arrows). Binocular microscope, scale-20 mm.



A



B **C**

Figure 2: A-diagram of migration of the products of bone cell metabolism (arrows) towards the vessels in Haversian canals; B-phosphate microcrystals on the wall of the artery near the site affected by osteoporosis. SEM, magnification according to scale; C-EDS energy spectrum of phosphates shown in photo 2B.

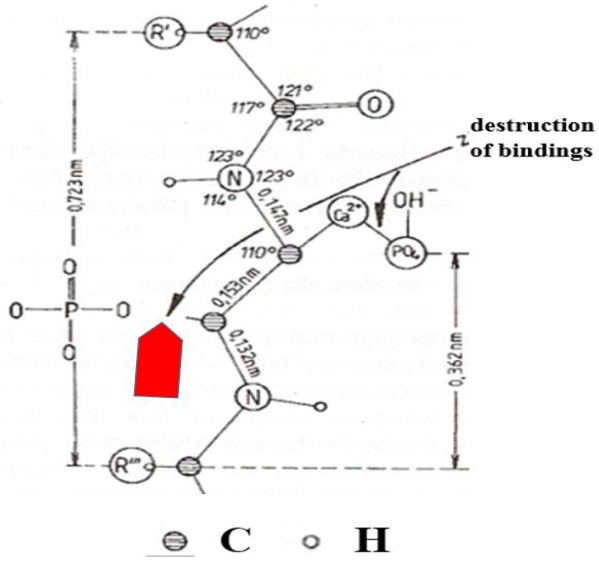


Figure 3: Diagram of destruction of atomic bonds between bone collagen and calcium phosphate (carbonate hydroxyapatite) in the process of osteoporosis.

Diagram of the migration of Ca^{2+} and PO_4^{3-} ions released as a result of osteoporosis through the circulatory system

Calcium and phosphorus, removed from bone in the process of osteoporosis, enter the venous blood (Fig. 4, A). Because of the CO_2 supplied to the blood, weak, easily dissociating carbonic acid is formed, which slightly acidifies the venous blood. As phosphates, including apatite, crystallize in alkaline environment, in venous blood of pH <7 they have no chance of crystallization. The venous blood travels to the lungs, where CO_2 is exchanged with O_2. Oxidizing the blood and removing the acidifying CO_2 makes it slightly alkaline (Fig. 4, B). That creates the conditions for phosphate crystallization in the arteries. The process takes place in spots called crystallization centers, which are areas where tissues have been damaged. For example, in arteries those sites may mark damage to the endothelium (Fig. 4, C, D) or the inside of the wall.

Crystallization centers are found not only in arteries, but also in other tissues. If the tissue environment is slightly alkaline and there is any damage (crystallization centers), biomineralization may also develop here – not only with calcium phosphates, but also with organic substances (cholesterol, fats, etc.).

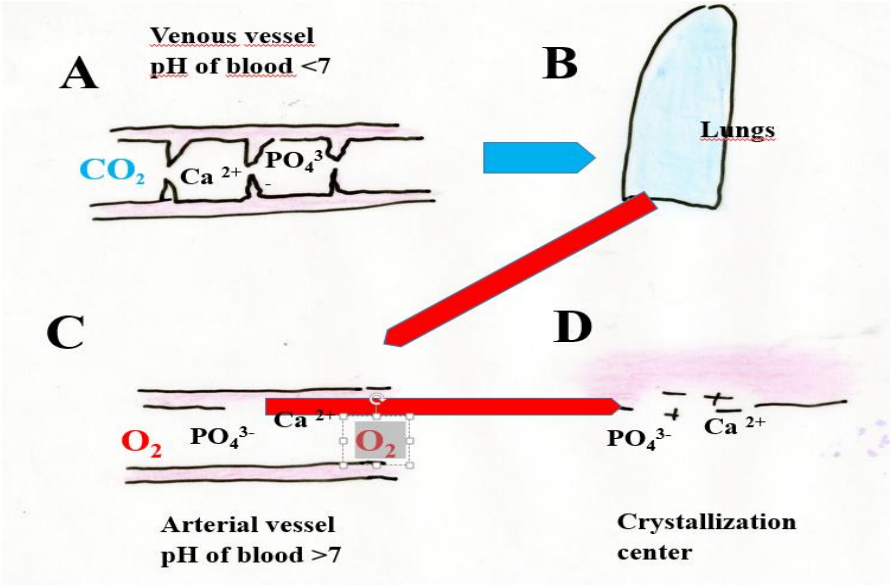
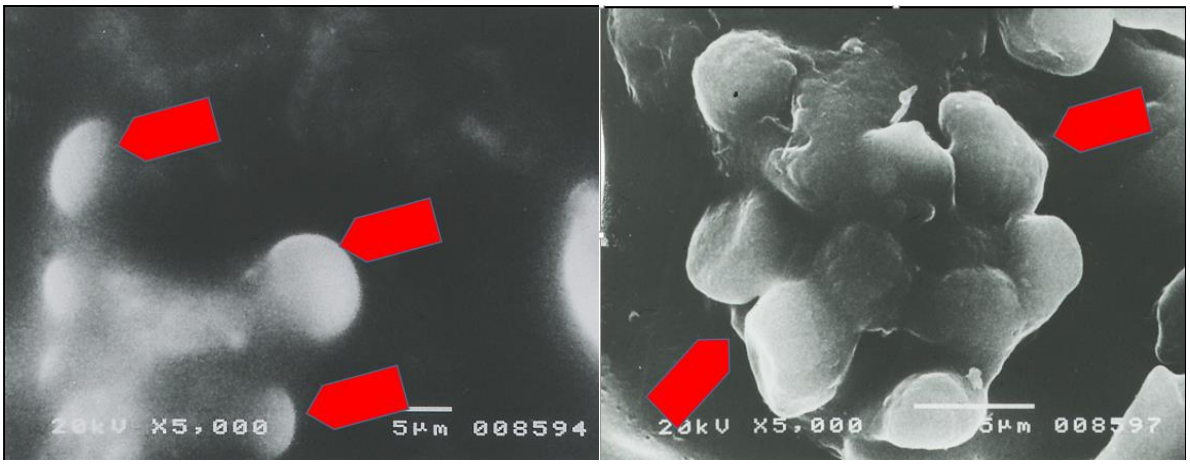


Figure 4: A-diagram of the migration of ions removed from bone in venous blood at pH <7; B-venous blood migration to the lungs where CO_2 is exchanged with O_2 and arterial blood is formed. This causes an increase in blood pH> 7, i.e. conditions for crystallization of phosphates are created; C-initiation of phosphate crystallization on the artery wall, at the site of endothelial damage (in the center of crystallization); D-enlarged crystallization center, in which calcium phosphates crystallize, derivatives of osteoporosis as well as Ca and P taken with food and fluids.

Biomineralization of arteries

It begins with hidden biomineralization and may or may not evolve to overt mineralization, which can be observed with the naked eye.

Initial biomineralization is only manifested by an increased content of mainly calcium and phosphorus, which can only be detected with sensitive chemical analysis methods. As it progresses further on the endothelium, but also in the artery wall, phosphate microcrystals appear (Fig. 5 A, B), which grow, typically together with cholesterol, to form the so-called "atherosclerotic plaque". Its presence in the artery reduces its internal diameter (cross-section). A consequence of this phenomenon is an increase of blood pressure.

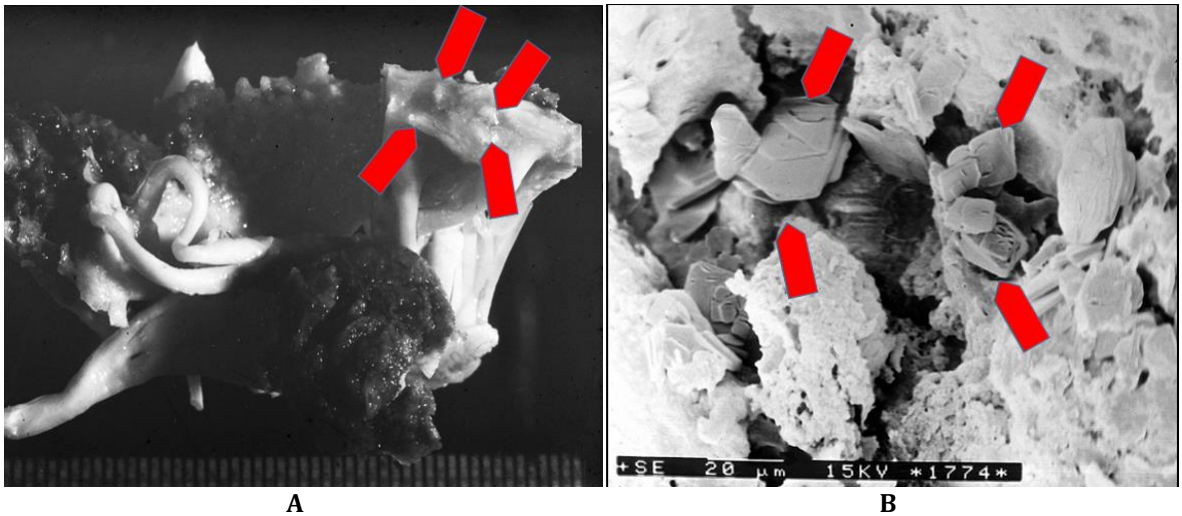


A **B**

Figure 5: Microscopic image of phosphate microcrystals on the endothelial surface. A-initial stage of transformation of hidden mineralization into overt mineralization. Phosphate concentrations appear in the crystallization center (arrows); B-further crystallization of aggregates of hexagonal apatite crystals (arrows) on the endothelial surface. SEM, magnification according to scale.

Biomineralization of the heart valves

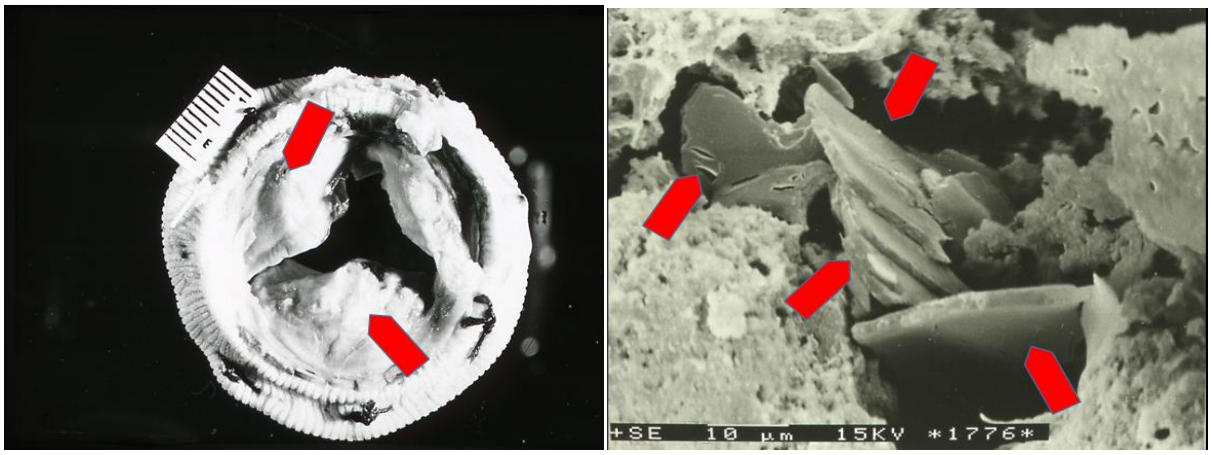
A special case of biomineralization is the so-called calcification of the heart valves. They affect both the aortic and mitral valve (Figs. 6A, B), and often also artificial valves (Fig. 6, A, B). They are usually located in places where valve tissues are damaged, which may result from various phenomena.



A **B**

Figure 6: A-mineralization of the atrioventricular (mitral) valve. The arrows indicate the "mineral grains" represented by phosphates; B-hexagonal platelets of apatite crystals in the cavity (damaged area) of the mitral valve.

The phosphate concentrations can take the form of irregular grains (Fig. 7, A) or even beautiful idiomorphic crystals whose edges are so sharp that they can easily cut and damage the valve tissues made of collagen fibers. The damaged valve leaflets also show mixed phosphate-cholesterol crystals (Fig. 7, B).

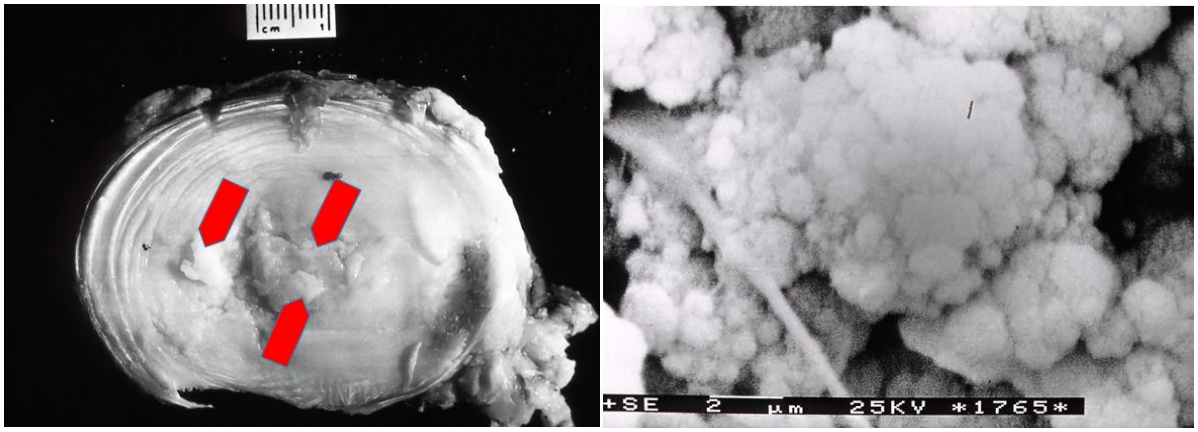


A B

Figure 7: A-aortic valve prosthesis-leaflets made from pig's valve; ring made of synthetic collagen (visible dark threads from the valve being sewn in). The arrows show the sites of superficial biomineralization of the valve leaflets with hydrated calcium phosphate; B – enlarged area of mixed phosphate-cholesterol biomineralization at the site of damage to the leaflet surface of the aortic valve prosthesis. Arrows show aggregates of crystals. SEM.

Cartilage biomineralization

More recent studies also indicate biomineralization of cartilage located in various parts of the body. A special case is the mineralization of spinal discs (Fig. 8, A). When it is hidden, it causes hardening of the disc cartilage, which may contribute to disc deformation. When overt mineralization occurs, visible within the discs, cauliflower-shaped micro-grains are observed, which may even form specific colonies (Fig. 8, B). This type of mineralization may apply to joints were, additionally, idiomorphic crystals, e.g. oxalates, may be present in the synovial fluid.

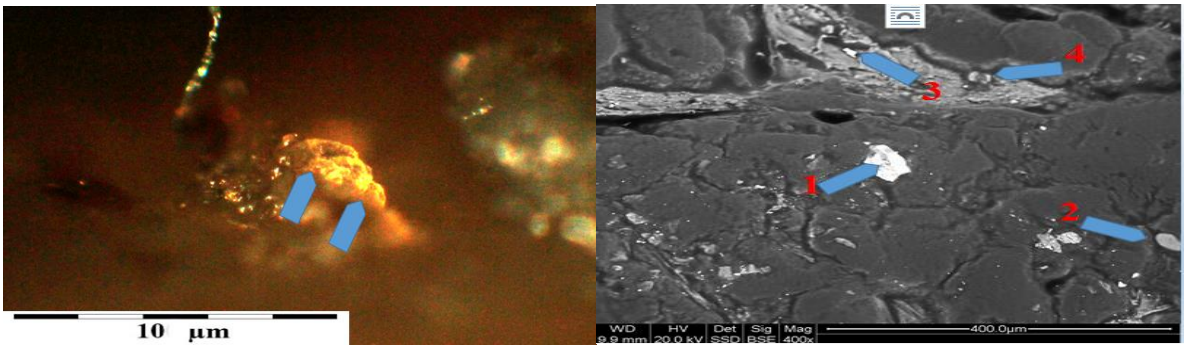


A B

Figure 8: A-spinal disc with phosphate concentrations (arrows); B-concentrations of "cauliflower-shaped" micro-grains of phosphate in the outer zone of the spinal disc. SEM.

Tendon biomineralization

Mineral grains were also found in the areas of tendon damage (Fig. 9, A). Their size, observed microscopically, does not exceed several dozen micrometers (Fig. 9, B). The presence of this type of grains – most often phosphate – undoubtedly hinders the proper functioning of the tendons and thus the mobility of the whole body.



A B

Figure 9: A-phosphate mineral grain (arrows) in tendon tissue. Polarizing microscope, partially X polaroids; B-mineral grains (arrows) observed in tendon. The numbers show the places where chemical analyzes were performed using the EDS method. SEM.

Summary of research results and conclusions

1. Osteoporosis develops mostly in places where blood vessels “clog”, which causes local acidification of the environment and dissolution of bone apatite.
2. The conducted research shows connection between osteoporosis and tissue biomineralization.
3. The process affects especially places where tissues are damaged. Such damages are the centers of crystallization.
4. The initial stage of biomineralization is hidden mineralization, recognizable only using sensitive chemical methods.
5. Hidden biomineralization may or may not evolve to overt mineralization, represented by phosphate grains and crystals. They can coexist with organic concentrations, e.g. cholesterol.
6. Both phosphate and phosphate-cholesterol concentrations hinder, and often even prevent the proper functioning of tissues and organs.
7. Osteporosis usually increases with age, and it is the “source” of mineralization of tissues and organs with calcium and phosphorus derived from the bones.
8. Therefore, introducing these elements into the body through diet (e.g. dairy) seems to be disadvantageous from the point of view of biomineralization (“calcification”) of tissues.

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