Archives of Health Science
Research Article

Atherosclerosis Types of Biomineralization Centers in the Circulatory System

Maciej Pawlikowski*

AGH - Univ. of Science and Technology, Dept. Mineralogy, Petrography and Geochemistry, al. Mickiewicza 30, 30-059 Cracow, Poland

***Corresponding author:** Maciej Pawlikowski, AGH - Univ. of Science and Technology, Dept. Mineralogy, Petrography and Geochemistry, al. Mickiewicza 30, 30-059 Cracow, Poland

Abstract

High blood pressure is caused by substances that build up in the arteries and reduce their internal diameter. Because of that,thesame volume of blood must fit into narrower arteries. The result is an increase in blood pressure.

This article presents the causes, manner of formation and types of biomineralization (mineralization of biological tissues) centers, i.e. the formation of the so-called atherosclerotic plaque on arteries and heart elements.

Presented examples of this phenomenon are based on the author's own research. Causes of biomineralization of transplanted elements of the heart are indicated, andan example of self-healing of some arterial damageis presented.

Introduction

Hypertension, which results in various diseases, is one of the leading causes of death. Millions of people around the world die because of it every year, which is why research progress in this area is so important (1-74).

Presented research results broaden our knowledge on the causes and manners of formation of atherosclerosis.

Findings

1. **Why does biomineralization affect elements of the circulatory system carrying oxygenated blood, and not venous blood?**

Studies of calcifications of the arteries and elements of the heart indicate that they are mainly represented by calcium phosphates of varying crystallinity, from amorphous (non-crystalline) substances with significant hydration to crystalline substances. Crystalline calcifications are represented by calcium hydroxyapatite, in which some of the components may be replaced by other ions. Experimental studies on the synthesis of this type of apatite indicate that it crystallizes and is stable at pH >6.6–6.7 (Fig. 1).

This means that the apatite crystallizing from the blood in the blood vessels can only form in the arteries, because the pH of arterial blood exceeds 7.0, while venous blood typically has a pH of 6.7. This situation results from the transport of carbon dioxide by the venous blood, which easily dissociates,to form with water a weak carbonic acid (H_2CO_3).

Because carbon dioxide is removed during the gas exchange in the lungs, oxygenated blood is free of carbon dioxide. This increases the pH of oxygenated blood. As a result, the solubility product of phosphates is exceeded, and they crystallize in the form of the so-called calcifications.

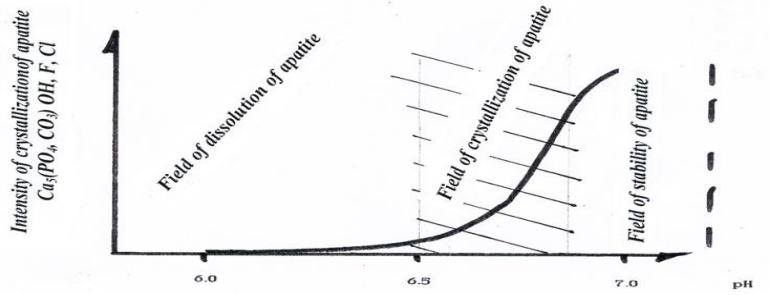


Fig 1. Stability fields of phosphates from the apatite group

2. What is a biomineralization center and what does it do?

An extremely important starting point for the biomineralization of arteries and heart elements are so-called crystallization centers. These are the places where the process of formation of atherosclerotic plaque begins.

Biomineralization centers are often areas where tissue has been damaged. Their formation can be caused by many reasons.

Damage sites (biomineralization centers) are endowed with electric charges, which results from the damage of interatomic bonds in the process of tissue destruction (Fig. 2a, 2b). The electric field occurring in the crystallization centers is a place where electrically charged ions can very easily attach. This applies to both "organic" and inorganic ions.

Their attachment to the crystallization center initiates the biomineralization of the arteries and elements of the heart. This process can develop, leading to the formation of "atherosclerotic plaque", or it can be stopped. Completion of suchbiomineralizationcan take place at an early stage, after all the electrical bonds of the damaged tissue have been ''saturated''. Then, hidden biomineralization is formed, one that is not visible and can be revealed only through chemical analyses, performed with the use of the most sensitive methods.

However, it can also develop further, resulting in overt biomineralization that can be observed both microscopically and macroscopically.

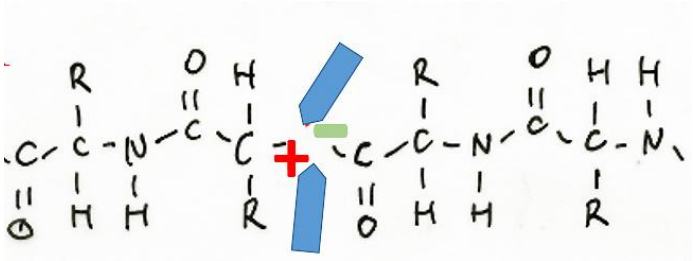


Fig 2.a. The initial phase of biomineralization of a biological structure defect (hidden mineralization). Attachment of single ions.

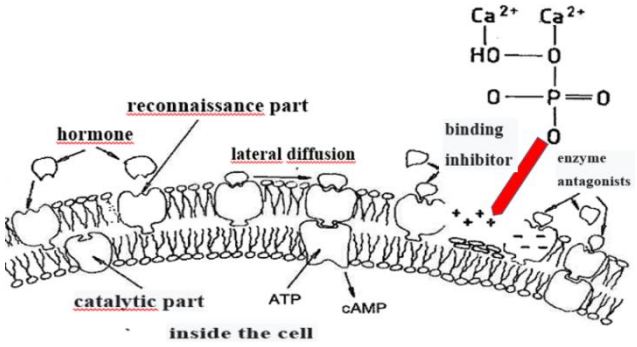


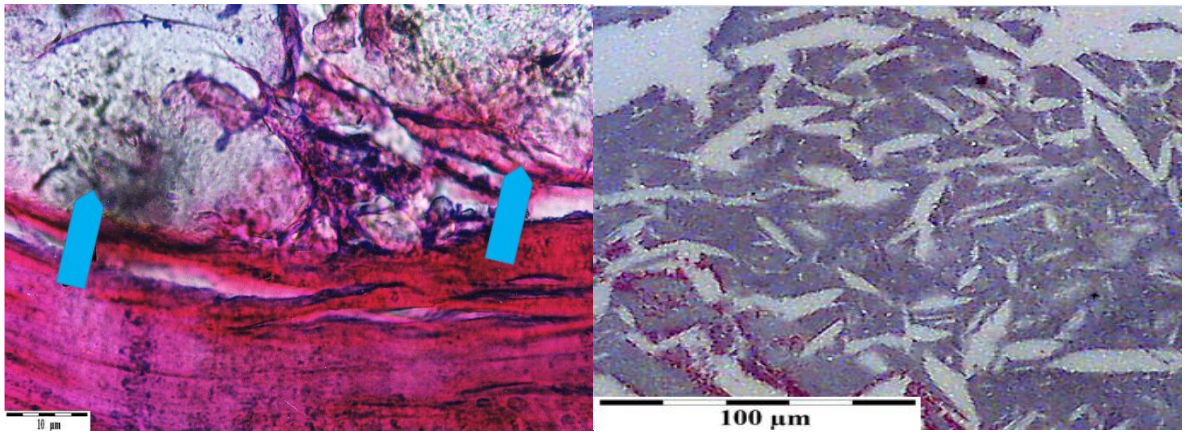
Fig 2.b. Schematic picture of the structure of endothelial cell membrane (intima). The damaged zone (arrow) is the center of biomineralization developing on the surface of the inner wall of the artery.

(After: M. Pawlikowski, 1995, Sekrety mineralizacji tkanek. PAN. Kraków).

3. Biomineralization of arteries and heart with organic substances

3.a. Cholesterol and Fats

Since cholesterol is an organic, yet crystalline substance, it is subject to mineralogical laws similarly to the crystals of inorganic substances. This also applies to the arteries, both on their inner wall (the endothelium) and in the arterial wall. In both places it forms polycrystalline clusters (Fig. 3.a) that reduce the diameter of the artery and contribute to the increase in arterial pressure.

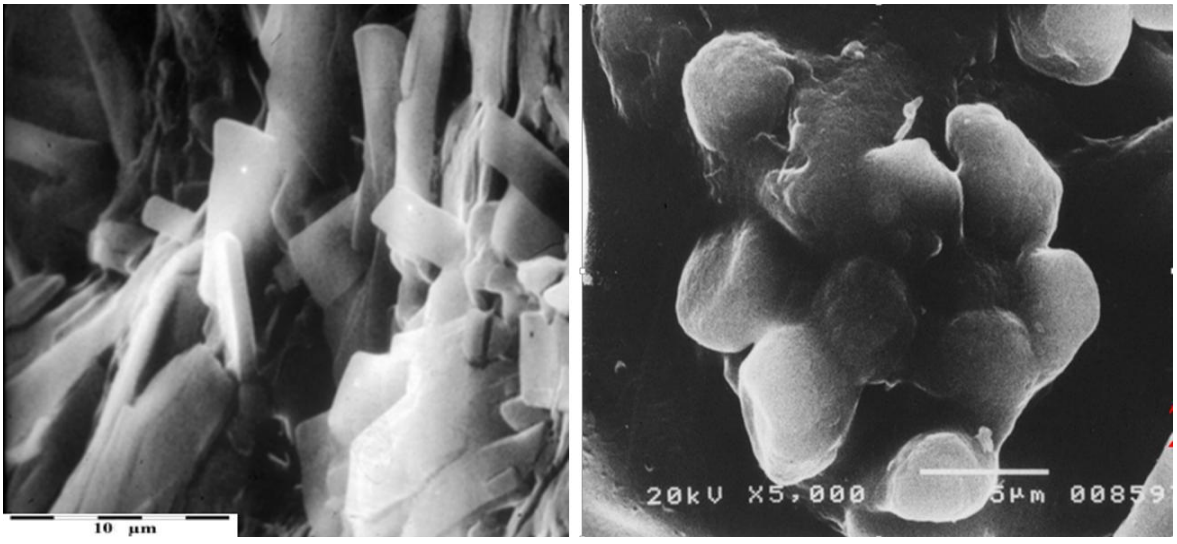


A **B**

Fig 3.a. Organic compounds crystallizing in the artery wall. A – cholesterol aggregates (arrows) in the artery wall. B – bright cholesterol crystals stuck in the shape of boats in the organic mass of the substance.

3.b. Phosphates

Studies indicate that at least some of the phosphates crystallizing in the arteries are derived from osteoporosis. Calcium and phosphorus ions removed from the bones in the course of osteoporosis flow with blood through the blood vessels, and when they encounter a crystallization center, they start the process of biomineralization of the arteries. That results is the so-called calcifications crystallizing both on the endothelium (Fig. 3.b) and in the arterial wall. Unlike cholesterol, these phosphates, mainly represented by apatite, are not flexible and can detach from the endothelium when the blood pressure increases. Detached, they travel with the blood and can block arteries, leading to clots and heart attacks.



A **B**

Fig 3.b. A, B – phosphates (mainly hydroxyapatite) crystallizing on arterial endothelium. SEM.

Crystalline atomic structure of this type of phosphates was confirmed through X-ray diffraction performed on grains removed from the artery wall (Fig. 3.b.1.)

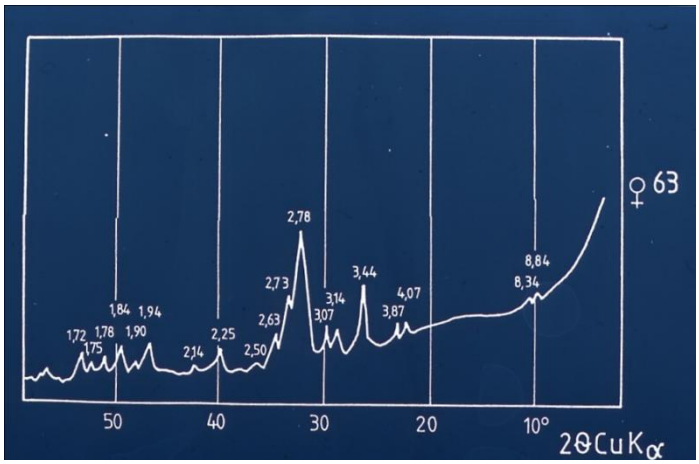


Fig 3.b.1. X-ray pattern of grain ofcrystalline hydroxyapatiteseparated from wall ofartery.

3.c. The Most Common, Mixed Biomineralization of the Arteries by Organic Compounds and Phosphates

The most common type of biomineralization of the arteries is a mixed organic-inorganic biomineralization with different proportions of both components (Fig. 3.c, A, B). This type of biomineralization proves variable amounts of cholesterol and phosphates in the arterial blood.

Each of the listed types of arterial biomineralization should be adressed with a different pharmacological treatment, as it is the cause of various phenomena outside of the circulatory system.

Fig 3.c. Examples of the most common type of arterial biomineralization – mixed inorganic-organic. A – cross-section of the neck artery with atherosclerotic plaque (arrow). B – cholesterol-phosphate aggregate from the surface of the endothelium of the artery. SEM.

4. Mechanism of Biomineralization of Crystallization Centers

The most common phenomenon of crystallization is the result of exceeding the so-called solubility product of the crystallizing substance. This occurs when there is an "excess" of solute in the solution, which causes the process to start.

In the case of biomineralization of the arteries, such a situation is impossible because such a high concentration of cholesterol or phosphates in the blood would stop the functioning of the entire circulatory system.

Biomineralization of crystallization centers in the arteries takes place in a different way, namely by equalizing concentrations and the phenomenon of ionic currents.

In the biomineralization center formed in the artery (Fig. 4 A, B), interatomic bonds are broken (destroyed). As a result, a place is created in the artery with free bonds endowed with electric charges (plus and minus).

These electrical charges attract oppositely charged ions that travel with the arterial blood. After these wandering ions are bound in the crystallization center

(biomineralization), near the center there is a lower concentration of ions "captured" by the crystallization center. At this point, an "ionic current" is created towards the crystallization center (biomineralization of the artery), which functions by equalizing the ion concentrations (Fig. 4C).

It works like in the following example.

When we spray a fragrance in one of the corners of the room, after some time the whole room will smell equally, based on the equalization of concentrations.

When the number of mineralizing ions in the blood decreases in the artery, near the center of biomineralization (because some of them have been captured and built into the artery), an ionic current will be created (to equalize concentrations). By equalizing concentrations, it will transport ions towards the center of biomineralization. That will result in the development of mineral concentrations in this area (Fig. 4, D and E). This phenomenon can take place in one or more places. In the final stage, it leads to the formation of the so-called atherosclerotic plaque.

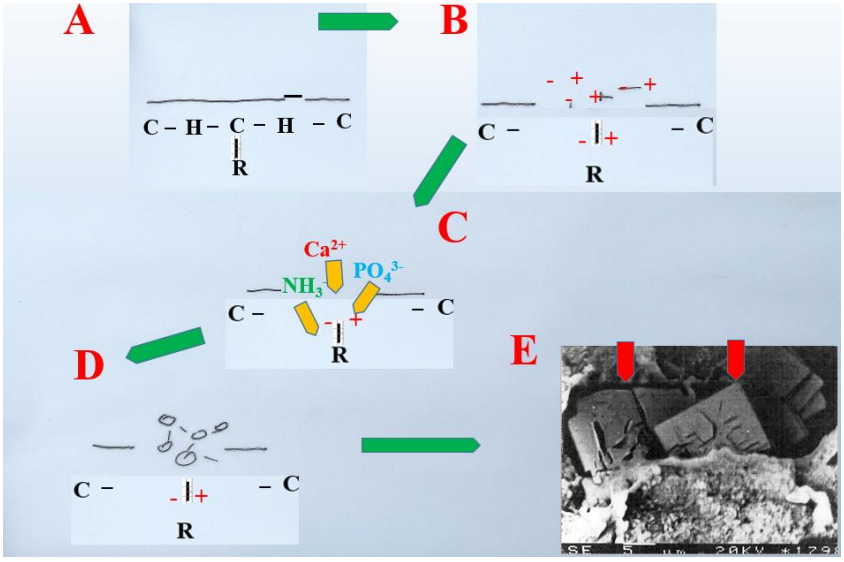


Fig 4. Diagram of the phases of development of biomineralization in arteries and heart elements. A – schematic image of the tissue before the formation of the center. B – the phase of formation of the crystallization center. C – initial phase of biomineralization, attachment of individual ions to damaged biological structures (hidden mineralization). D – further development of biomineralization (overt mineralization). E – mineralization of the surface of the aortic valve (arrows). SEM.

Thus, two factors are necessary for the biomineralization of arteries to occur, i.e. the presence of crystallization centers in the arteries and the presence of artery mineralizing substances in the blood.

The presence of only one of these elements is insufficient for biomineralization of the arteries – and as such, indirectly, for atherosclerosis and an increase in blood pressure – to occur.

5. Formation of Biomineralization Centers

Although the damage to the arteries and heart elements (the formation of biomineralization centers) has various causes, their structure looks similar. Such places where organic and inorganic mineral concentrations are formed have a common feature: it is the occurrence of an electric field caused by the destruction of interatomic bonds in tissues.

Some of the most common types of biomineralization center will be discussed below, mainly those affecting arteries and elements of the heart.

5. a. Primary (genetic) biomineralization centers

These are places in the organic structures of tissues that are defective. These defects are passed down from generation to generation, causing biomineralization of e.g. coronary arteries. Such structural defects may occur in different elements of arteries and heart (Fig. 5.a). Their biomineralization proceeds in the same way as in structural defects caused by other factors, e.g. external ones.

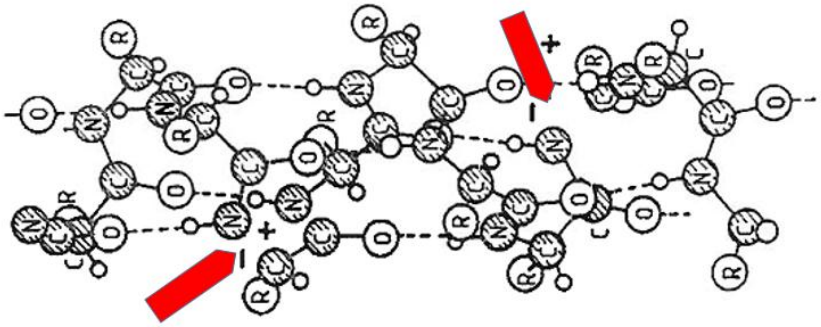


Fig 5.a. Electrically charged biomineralization centers (red arrows) associated with primary, genetic defects in the atomic structure of the polypeptide chain.

5.b. Secondary biomineralization centers

5.b.1. Crystallization centers (biomineralization) arising as a result of mechanical tissue damage, caused, for example, by excessive physical effort

This type of damage to biological structures is observed in people who work hard physically and in high-performance athletes. Interatomic bonds in biological structures have a certaindurability. After crossing its limits, they are destroyed (broken). Along with other tissues, this kind of damage affects the elements of the heart and arteries. It frequently occurs in the structure of collagen fibers.

Biomineralization grows extremely quickly in damaged collagen, not only in the muscular layer of the arteries (Fig. 5.b.1) but alsoin tendons and joint cartilage, etc.

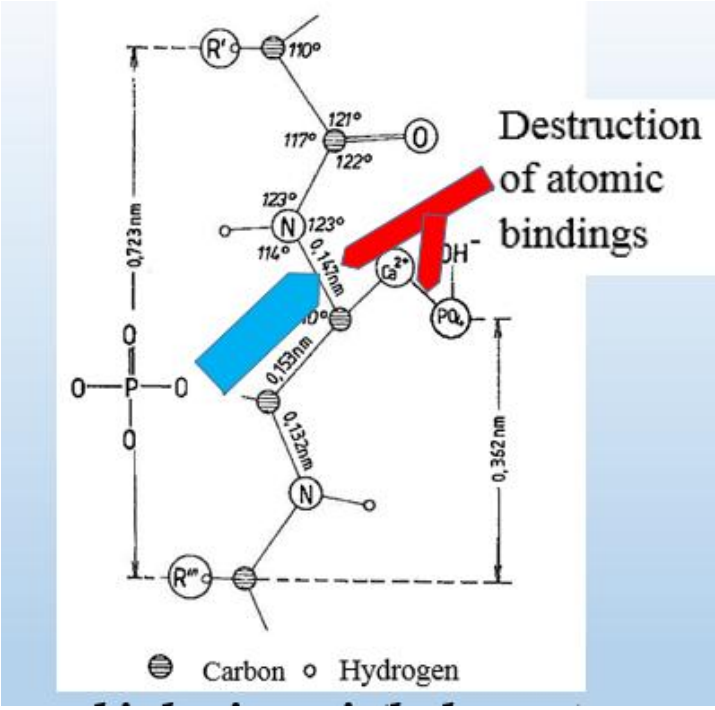


Fig 5.b.1. Destruction of the biological structure (collagen) caused by physical effort (red arrows). At the damaged site, a phosphate biomineralization center is formed (blue arrow)

5.b.2. Biomineralization centers formed as a result of mechanical destruction of biological structures by solids penetrating the body

The carcinogenic properties of asbestos are well known. Chrysotile asbestos fibers embedded in the biological structures of the lungs lead to destruction of these structures and creation of electric fields around the embedded fibers (Fig. 5.b.2). Such areas are particularly easily affected by calcifications, which can be revealed on chest x-rays.

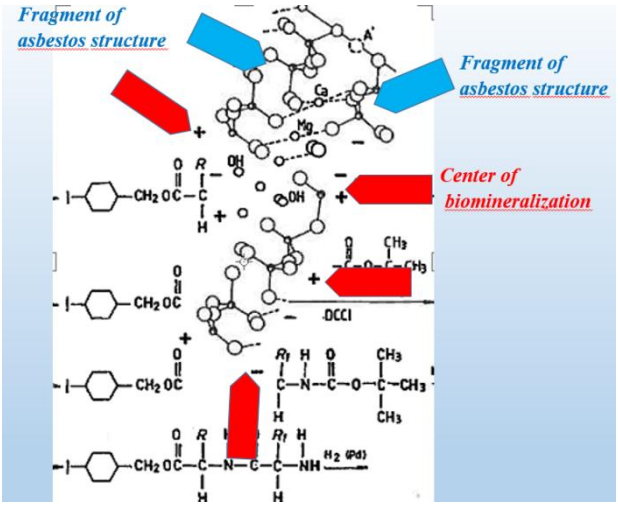


Fig. 5.b.2. Asbestos fiber (blue arrows) embedded in a polypeptide structure. Destroyed bonds in the polypeptide (red arrows) create an electric field (biomineralization center). Synthetics and minerals penetrating the lungs work in a similar way

Quartz grains in silicosis and coal dust in pneumoconiosis, diagnosed in coal miners, have a similar effect on biological structures, as dosynthetic substances, e.g. slags, synthetic silicates, etc.

5.b.3. Crystallization centers caused by chemical compounds produced by microorganisms infecting the human body, as well as chemical substances entering the body from the outside

Infectious diseases are caused by various types of microorganisms (bacteria, viruses, fungi, etc.). Infecting organisms produce a number of toxins in their life processes,whichcause disease symptoms. Each infection has its own particular symptoms. In other words, each of these types of toxins causes these symptoms.

The toxins produced by infecting microorganisms are, generally, toxic chemicals. Their aggressiveness manifests itself in the lysis of tissues, i.e. damagingtissues. Such damaged places are areaswhere interatomic bonds in biological structures are broken, i.e. biomineralization centers (Fig. 5.b.4).

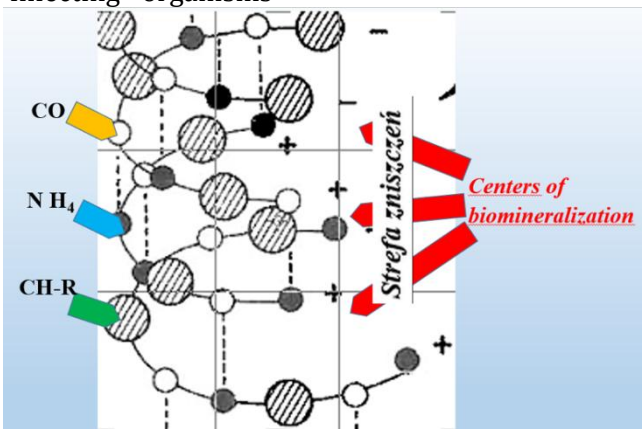


Fig 5.b.4. Fragment of the peptide chain destroyed by toxins produced by infecting microorganisms during an illness. Chemicals entering the body from the outside (in the form of gases, solutions and solid toxins – e.g. some preservatives) work in a similar way

Chemical substances entering the body from the outside have a similar effect on the formation of biomineralization centers in the arteries and elements of the heart.

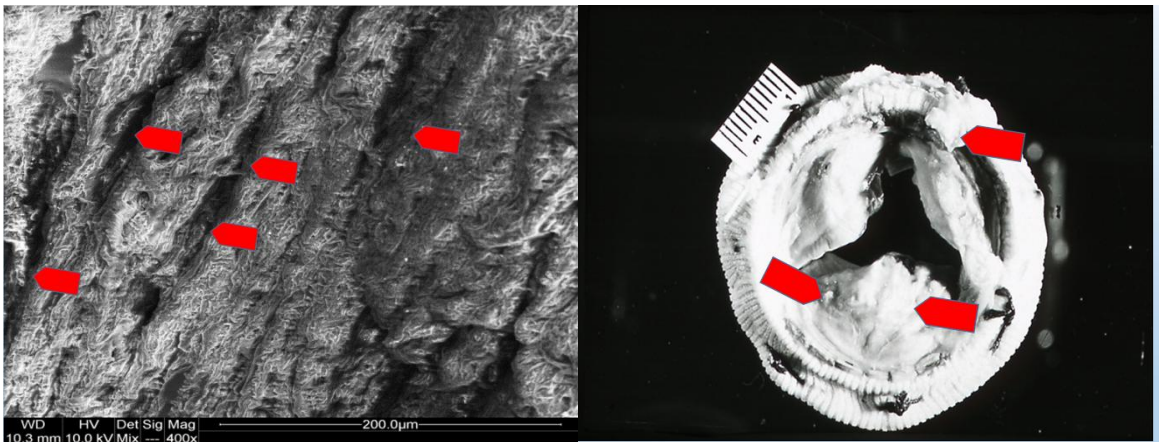
Depending on the aggressiveness of the substances and the duration of their impact, tissue damage (biomineralization centers) can be of various sizes. Therefore, it is important to shorten the time of this impact as much as possible

6. Centers of Biomineralization in Transplants

It has been observed that "calcifications" may appear quite quickly in transplants of the heart, its elements and in

the so-called bypasses. Studies of heart valves from a valve bank indicate that long-term storage at low temperatures causes delamination of collagen structures. Spots affected by such process are the sites of the valve's potential biomineralization after its implementation (Fig. 6A).

This biomineralization phenomenon was observed in valves implanted and then removed (Fig. 6B). A connection was found between the delamination of the valve structure and the time of its storage in deep freezing.



A **B**

Fig 6.A. split (delaminated) collagen fibers (arrows) of an aortic valve leaflet from a valve bank. These places are the centers of future biomineralization of the transplant. B – transplanted and removed aortic heart valve with biomineralization (arrows).

7. Self-Healing Processes

While examining the surfaces of the arteries' inner walls, a self-repair (healing) process was observed in damaged spots. It is manifested by the development of endothelium in damaged places (Fig. 7).

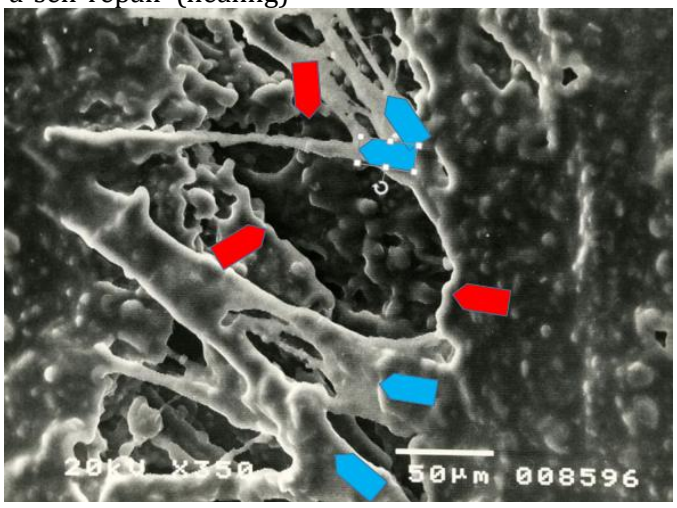


Fig 7. Self-healing of arterial damage. Overgrowth of the damaged arterial wall (red arrows) by the proliferating endothelium of the artery (blue arrows). SEM.

Observed phenomenonindicates that self-repair processes of damaged arteries are present in the body. Studying and use of this phenomenon will lead to discovery of breakthrough methods in the treatment of atherosclerosis in the future.

Summary

The most common types of crystallization centers (biomineralization of circulatory system elements) are presented, which do not cover all cases.

The presented diagrams show the formation of biomineralization centers in parts of the circulatory system.

Simultaneous occurrence of several causes of tissue destruction and formation of biomineralization centers leads to many diseases, including those resulting in death.

Some damage to the arteries and heart the body can heal by itself (self-healing). The importance of studying this process in terms of treatment cannot be overestimated.

Formation of atherosclerotic plaque in damaged areas of arteries and heart elements can also be considered a form of self-healing. On the one hand, it "closes off" the damage sites, but on the other, it causes accumulation of harmful substances that increase blood pressure.

The problem is damage that the body is unable to heal on its own. In this case, it is advantageous to use biomineralization center blockers. They close the way to the development of biomineralization of the arteries and the heart.

A separate and difficult problem are the methods of removal, including dissolution, of already formed deposits, because different "solvents" must be used for different types of crystallizing substances.

References

[1] Abedin M., Lim J., Tang T.B., Park D., Demer L.L., Tintut Y. 2006 N-3 fatty acids inhibit vascular calcification via the p38-mitogen-activated protein kinase and peroxisome proliferator-activated receptor-gamma pathways. Circ. Res., 98: 727–729.

[2] Allison M.A., Criqui M.H., Wright C.M., 2004 Patterns and risk factors for systemic calcified atherosclerosis. Arterioscl. Thromb. Vasc. Biol., 24: 331–336.

[3] Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD2005 Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study.

[4] J. Am. Coll. Cardiol., 46(1):158-65.

[5] Bas A., Lopez I., Perez J., Rodriguez M., Aguilera-Tejero E., 2006 Reversibility of calcitriol-induced medial artery calcification in rats with intact renal function. J. Bone. Miner. Res., 21: 484–490.

[6] Bostrom K., Watson K.E., Horn S., Wortham C., Herman I.M., Demer L.L, 1993; Bone morphogenetic protein expression in human atherosclerotic lesions. J. Clin. Invest., 91: 1800–1809.

[7] Callaway M.P., Richards P., Goddard P., Rees M.,1997 The incidence of coronary artery calcification on standard thoracic CT scans. Br. J. Radiol., 834 :572-574.

[8] Campbell G.R., Campbell J.H., 2000 Vascular smooth muscle and arterial calcification. Z. Kardiol., 89 (suppl 2): 54–62.

[9] Canfield A.E., Sutton A.B., Hoyland J.A., Schor A.M., 1996 Association of thrombospondin-1 with osteogenic differentiation of retinal pericytes in vitro. J. Cell Sci., 109 (pt 2): 343–353.

[10] Cowell S.J., Newby D.E., Prescott R.J., Bloomfield P., Reid J., Northridge D.B., Boon N.A., 2005; A randomized trial of intensive lipid-lowering therapy in calcific aortic stenosis. N. Engl. J.Med., 352: 2389–2397.

[11] El-Abbadi M., Giachelli C.M., 2007 Mechanisms of vascular calcification. Adv. Chronic. Kidney Dis., 14 :54–66.

[12] Huang H., Virmani R., Younis H., Burke A.P., Kamm R.D., Lee R.T., 2001The impact of calcification on the biomechanical stability of atherosclerotic plaques. Circulation., 103: 1051–1056.

[13] Iribarren C., Sidney S., Sternfeld B., Browner W.S., 2000 Calcification of the aortic arch: risk factors and association with coronary heart disease, stroke, and peripheral vascular disease. JAMA., 283(21):2810-5

[14] Jono S., McKee M.D., Murry C.E., Shioi A., Nishizawa Y., Mori K., Morii H., Giachelli C.M., 2000 Phosphate regulation of vascular smooth muscle cell calcification. Circ. Res., 87: E10–E17.

[15] Keelan P.C., Bielak L.F., Ashai K., Jamjoum L.S., Denktas A.E., Rumberger J.A., Sheedy I.P., Peyser P.A., Schwartz R.S., 2001 Long-term prognostic value of coronary calcification detected by electron-beam computed tomography in patients undergoing coronary angiography. Circulation., 104: 412–417.

[16] Lomashvili K.A., Cobbs S., Hennigar R.A., Hardcastle K.I., O'Neill W.C., 2004 Phosphate-induced vascular calcification: role of pyrophosphate and osteopontin. J. Am. Soc. Nephrol., 15: 1392–1401.

[17] Luo G., Ducy P., McKee M.D., Pinero G.J., Loyer E., Behringer R.R., Karsenty G., 1997 Spontaneous calcification of arteries and cartilage in mice lacking matrix GLA protein. Nature., 386: 78–81.

[18] Matsushita M., Nishikimi N., Sakurai T., Nimura Y., 2000 Relationship between aortic calcification and atherosclerotic disease in patients with abdominal aortic aneurysm. Int Angiol., 3:276-9.

[19] Nadra I., Mason J.C., Philippidis P., Florey O., Smythe C.D., McCarthy G.M., Landis R.C., Haskard D.O., 2005 Proinflammatory activation of macrophages by basic calcium

phosphate crystals via protein kinase C and MAP kinase pathways: a vicious cycle of inflammation and arterial calcification? Circ. Res., 96:1248–1256.

[20] Neves K.R., Graciolli F.G., dos Reis L.M., Graciolli R.G., Neves C.L., Magalhaes AO, Custodio. MR, Batista DG, Jorgetti V, Moyses RM. 2007 Vascular calcification: contribution of parathyroid hormone in renal failure.Kidney Int.,71: 1262–1270.

[21] Nicholls S.J., Tuzcu E.M., Wolski K., Sipahi I., Schoenhagen P., Crowe T., Kapadia S.R., Hazen S.L., Nissen S.E., 2007 Coronary artery calcification and changes in atheroma burden in response to established medical therapies. J. Am. Coll. Cardiol., 49: 263–270.

[22] Niskanen L., Siitonen O., Suhonen M., Uusitupa M.I., 1994 Medial artery calcification predicts cardiovascular mortality in patients with NIDDM. Diabetes Care., 11:1252

[23] Orita Y., Yamamoto H., Kohno N., Sugihara M., Honda H., Kawamata S., Mito S., Soe N.N., 2007 Yoshizumi M. Role of osteoprotegerin in arterial calcification: development of new animal model. Arterioscler. Thromb. Vasc. Biol., 27: 2058–2064.

[24] Parhami F., Morrow A.D., Balucan J., Leitinger N., Watson A.D., Tintut Y., Berliner J.A., Demer L.L., 1997 Lipid oxidation products have opposite effects on calcifying vascular cell and bone cell differentiation: a possible explanation for the paradox of arterial calcification in osteoporotic patients. Arterioscler. Thromb. Vasc. Biol.,17: 680–687.

[25] Parhami F., Basseri B., Hwang J., Tintut Y., Demer L.L., 2002 High-density lipoprotein regulates calcification of vascular cells. Circ. Res., 91: 570–576.

[26] Pawlikowski M., 1987 Mineralizacja organizmu człowieka żyjącego (Mineralization of human living organism). Prace Mineral., 79:121.

[27] Pawlikowski M., Ryskala Z., 1991 Charakterystyka mineralogiczno-chemiczna fosforanowej mineralizacji wybranych naczyń tętniczych człowieka. (Mineralogical-chemical characteristic of phosphate mineralization of human arteries). Roczniki Nauk Dyd, WSP w Krakowie Prace Fizjologiczne.: 81–104.

[28] Pawlikowski M., 1991 Mineralizacja nowotworowa (Mineralization of cancer). In: Biomineralizacja i biomateriały. PWN, Warszawa., : 84–92.

[29] Pawlikowski M.1993 Kryształy w organizmie człowieka, (Crystals of humanorganism). Secesja.:132.

[30] Pawlikowski M., 1995 Sekrety mineralizacji tkanek (Secrets of tissue mineralization). PAN Kraków., : 97.

[31] Pawlikowski M., 1999 Preliminary results of dissolution of substances mineralizing human arteries. Arch Mineralog., 52 :195.

[32] Pawlikowski M., Pfitzner R, 1995 Zastosowanie metod mineralogicznych w badaniach tkanek człowieka. I. Sposoby badania mineralizacji. (Mineralogical methods useful for examination of human tissues). Przegl. Lekarski.;52:119–123.

[33] Pawlikowski M., Pfitzner R. 1995 Zastosowanie metod mineralogicznych w badaniach tkanek człowieka. II. Mineralizacja struktur serca. (Mineralogical methods useful for examination of human tissues. Mineralization of heart structures). Przegl. Lekarski., :52:24–27.

[34] Pawlikowski M., Pfitzner K., Skinner C., 1995. Cholesterol-mineral concentrations of the aneurysmatic wall. Acta Angiologica., :. 1–15.

[35] Pawlikowski M., Pfitzner R., 1999 Mineralizacja serca i dużych naczyń, (Mineralization of heart and big blood vessels). Wyd IGSMiE PAN Kraków, :142

[36] Pawlikowski M., 2003 Minerals in human blood vessels and their dissolution in vitro. In: Skinner HCW, Berger AW, editors. Geology and health. Oxford University Press., :155–158.

[37] Pawlikowski M. 2011 Biomineralization of cancer tissues. 20th Int. Symp. Molecular and Physiological Aspects of Regulatory Processes of the Organism. Cracow, H Lach editors. Wyd Abaton Kraków. :190–191.

[38] Pawlikowski M., 2014 Osteoporosis as a source of tissue mineralization. Research on osteoporosis therapy and dissolution of arterial mineralization. Jour. Life Science.;8:610–625.

[39] Pawlikowski M. 2017 Biomineralogy of angiogenesis. Arch. Clin. Biomed. Res., 1 :161–167.

[40] Pawlikowski M., 2017a Centers of Human Tissue Biomineralization (Calcification). Cardiol. Cardiovasc. Med., 1 :252–262.

[41] Pawlikowski M., 2017bBiomineralogy of Angiogenesis.Arch. Clin. Biomed. Res.1 (4): 161-167.

[42] Pawlikowski M., 2017c Centers of Human Tissue Biomineralization (Calcification). Cardiol.Cardiovasc. Med.1 (6): 252-261.

[43] Pawlikowski M., 2018aThe Phenomenon of Joint Hip Cartilage Biomineralization Archives of Clinical and Biomedical Research- http://archclinbiomedres.com/ - Vol. 2 No. 5 - Oct 2018. [ISSN 2572-5017]

[44] Pawlikowski M., 2018b Problems of Biomineralization Dissolution in Human Arteries. Adv. Card. Res. 1(4) -. ACR.MS.ID.000118

[45] Pawlikowski M., 2018c Biomineralogical Phenomenon of Mineralization (Calcification) of Arteries. Int. J. Cardiac and Pulmonary Rehabilitation: IJCPR-102.

[46] Pawlikowski M., 2018d Biomineralogical Phenomena in Hip Joint Endoprostheses.J. of Biotech.Bioeng. V2,I4: 31-37.

[47] Pawlikowski M.,2019a Biomineralization of Heart Valves.J. Clin. Rev. Case Rep, V4: 2– 6.

[48] Pawlikowski M., 2019c Phenomena in Frozen Valves from A Valve Bank.Sur. Cas. Stud. Op. Acc. J. 2(5): 208-2013.

[49] Pawlikowski M., 2019c Phenomena in Frozen Valves from A Valve Bank.Sur. Cas. Stud. Op. Acc. J. 2(5): 208-2013.

[50] Pawlikowski M., Bozecki P.,2019Tendon Biomineralization. Glob J Ortho Res. 1(3): GJOR.MS.ID.000515.

[51] Pawlikowski M. 2020 Artery biomineralization and its dissolution. ES J Cardiolog. ; 1(1): 1006.

[52] Pawlikowski M., 2021 Centers of Biomineralization. J Surg Open Access 7(5): dx.doi.org/10.16966/2470-0991.253.

[53] Price P.A., Faus S.A., Williamson M.K.. 2000; Warfarin-induced artery calcification is accelerated by growth and vitamin D. Arterioscler. Thromb. Vasc. Biol.,20 :317–327.

[54] Price P.A., June H.H., Buckley J.R., Williamson M.K., 2001. Osteoprotegerin inhibits artery calcification induced by warfarin and by vitamin D. Arterioscler. Thromb. Vasc. Biol.,21: 1610–1616.

[55] Price P.A,, Faus S.A., Williamson M.K., 2001 Bisphosphonates alendronate and ibandronate inhibit artery calcification at doses comparable to those that inhibit bone resorption. Arterioscler. Thromb. Vasc. Biol.,21: 817–824.

[56] Proudfoot D., Skepper J.N., Shanahan C.M., Weissberg P.L., 1998Calcification of human vascular cells in vitro is correlated with high levels of matrix Gla protein and low levels of osteopontin expression. Arterioscler. Thromb. Vasc. Biol.,18: 379–388.

[57] Qiao J.H., Xie P.Z., Fishbein M.C., Kreuzer J., Drake T.A., Demer L.L., Lusis A.J., 1994 Pathology of atheromatous lesions in inbred and genetically engineered mice: genetic determination of arterial calcification. Arterioscler. Thromb., 14 : 1480–1497.

[58] Qiao J.H., Fishbein M.C., Demer L.L., Lusis A.J., 1995 Genetic determination of cartilaginous metaplasia in mouse aorta. Arterioscler. Thromb. Vasc. Biol., 15: 2265–2272.

[59] Qiao J.H., Mertens R.B., Fishbein M.C., Geller S.A.,2003 Cartilaginous metaplasia in calcified diabetic peripheral vascular disease: morphologic evidence of enchondral ossification. Hum. Pathol., 34: 402–407.

[60] Rajamannan N.M., Subramaniam M., Stock S.R., Stone N.J., Springett M., Ignatiev K.I., McConnell J.P., Singh R.J., Bonow R.O., Spelsberg T.C., 2005 Atorvastatin inhibits calcification and enhances nitric oxide synthase production in the hypercholesterolaemic aortic valve. Heart., 91: 806–810.

[61] Reaven P.D, Sacks J.,2005. Coronary artery and abdominal aortic calcification are associated with cardiovascular disease in type2 diabetes. Diabetologia., 48: 379–385.

[62] Rennenberg R..J., Schurgers L.,Stehouwer C.,D.,A., 2010 Arterial calcifications. J. Cell. Mol. Med., 14: 2203–2210.

[63] Reynolds J.L., Joannides A.J., Skepper J.N., McNair R., Schurgers L.J., Proudfoot D., Jahnen-Dechent W., Weissberg P.L., Shanahan C.M,. 2004; Human vascular smooth muscle cells undergo vesicle-mediated calcification in response to changes in extracellular calcium and phosphate concentrations: a potential mechanism for accelerated vascular calcification in ESRD. J. Am. Soc. Nephrol., 15: 2857–2867.

[64] Sangiorgi G., Rumberger J.A., Severson A., Edwards W.D., Gregoire J., Fitzpatrick L.A., Schwartz R.S., 1998 Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. J. Am. Coll. Cardiol., 31: 126–133.

[65] Shanahan C.M., Proudfoot D., Farzaneh-Far A., Weissberg P.L., 1998 The role of Gla proteins in vascular calcification. Crit, Rev, Eukaryot, Gene, Expr., 8: 357–375.

[66] Shao J.S, Cheng S.L., Charlton-Kachigian N., Loewy A.P., Towler D.A., 2003 Teriparatide (human parathyroid hormone (1–34)) inhibits osteogenic vascular calcification in diabetic low density lipoprotein receptor-

deficient mice. J. Biol .Chem.,278: 50195–50202.

[67] Steitz S.A., Speer M.Y., McKee M.D.,Liaw L., Almeida M., Yang H., Giachelli C.M., 2002; Osteopontin inhibits mineral deposition and promotes regression of ectopic calcification. Am. J. Pathol.,161: 2035–2046.

[68] Schmermund A., Achenbach S., Budde T., Buziashvili Y., Forster A., Friedrich G., Henein M., Kerkhoff G., Knollmann F., Kukharchuk V., Lahiri A., Leischik R., Moshage W., Schartl M., Siffert W., Steinhagen-Thiessen E., Sinitsyn V., Vogt A., Wiedeking B., Erbel R., 2006 Effect of intensive versus standard lipid-lowering treatment with atorvastatin on the progression of calcified coronary atherosclerosis over 12 months: a multicenter, randomized, double-blind trial. Circulation.,113: 427–437.

[69] Tanimura A., McGregor D.H., Anderson H.C., 1983Matrix vesicles in atherosclerotic calcification. Proc. Soc. Exp. Biol. Med.,172: 173–177.

[70] Tse J., Martin-McNaulty B., Halks-Miller M., Kauser K., DelVecchio V., Vergona R., Sullivan M.E, Rubanyi G.M., 1999 Accelerated atherosclerosis and premature calcified cartilaginous metaplasia in the aorta of diabetic male Apo E knockout mice can be prevented by chronic treatment with 17 beta-estradiol. Atherosclerosis., 144: 303–313.

[71] Wada T., McKee M.D., Steitz S., Giachelli C.M., 1999 Calcification of vascular smooth muscle cell cultures: inhibition by osteopontin. Circ. Res., 84: 166–178.

[72] Wang L., Jerosch-Herold M., Jacobs D.R. Jr, Shahar E., Detrano R., Folsom A.R., 2006 Coronary artery calcification and myocardial perfusion in asymptomatic adults: the MESA (Multi-Ethnic Study of Atherosclerosis). J. Am. Coll. Cardiol.,48: 1018–1026.

[73] Weiss R.M., Ohashi M., Miller J.D., Young S.G., Heistad D.D., 2006Calcific aortic valve stenosis in old hypercholesterolemic mice. Circulation.,114: 2065–2069.

[74] Vliegenthart R., Oudkerk M., Hofman A., Oei H.H., van Dijck W., vanRooij F.J., Witteman J.C., 2005 Coronary calcification improves cardiovascular risk prediction in the elderly. Circulation.,112: 572–577.

Citation: Maciej Pawlikowski, (2023), "Atherosclerosis Types of Biomineralization Centers in the Circulatory System", Arch Health Sci; 7(1): 1-12.

DOI: 10.31829/2641-7456/ahs2023-7(1)-007