# 23

# Geochemistry and Vertebrate Bones

H. Catherine W. Skinner
*Department of Geology and Geophysics*
*Yale University, New Haven, Connecticut*

### *Introduction*

The human body has been a focus of attention for thousands of years. The ancients wished to mummify it to assure transposition to the life hereafter. Today we expend a lot of effort and money to forestall the effects of aging of such a complicated machine. The mineralized portion of the body, the skeleton, is the most permanent portion of the body and records the basic size and shape of the individual. Underscoring the wish for properly functioning bones and teeth, we today have a medical 'spare parts' industry that provides substitute knees, hips, or an entire denture. The need to accomplish these implants/transplants successfully has aligned physicians and dentists with cell and molecular biologists, materials scientists, bioengineers, and mineralogists. All wish to create faithful replicas of the mineralized parts, but any substitutes must be in harmony with the internal dynamic biochemical environment, and be part of a viable functioning skeleton.

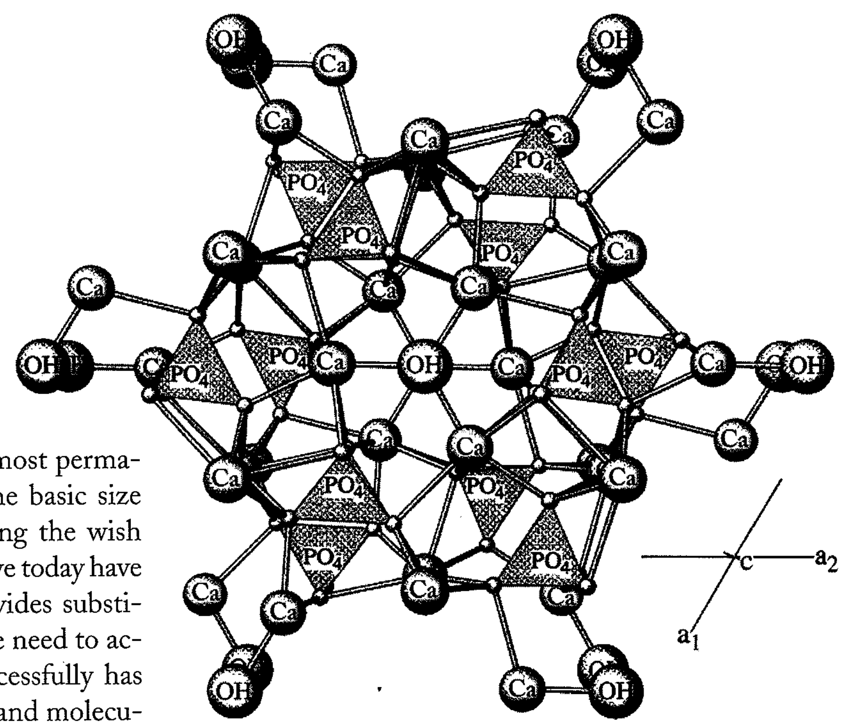


*Figure 23.1: Hydroxylapatite:* $Ca_5(PO_4)_3(OH)$

The general health of every human is a response to the local, regional, and global environment. The interaction noted in the scientific literature almost 50 years ago (Warren 1954) continues (Hopps and Cannon 1972, Ross and Skinner 1994). There is burgeoning interest as many scientists, with ever increasing abilities to detect and measure extremely small amounts of certain elemental species or potentially hazardous substances, focus on the relationships of the environment and health. The roles of the skeletal mineral substance as a participant and faithful recorder in this crossover are outlined here.

### *Bone Tissues, Cells and Molecular Biology*

"Bone" can refer to any one of the more than 200 individual organs with distinctive shapes that make up every human skeleton or to the tissue that is present in each of these organs. The tissues of bone, and teeth, are composites of organic matrix, mineral matter, and specialized cells (Skinner 1987, Albright and Skinner 1987). The cells not only form but also maintain, reconstruct, and repair the bone tissues as required. Cells known as osteoblasts produce a protein and polysaccharide matrix in and on which mineral is deposited. The cells become embedded in this extracellular mineralized matrix but continue to assist and sustain the viability of their products. They have a programmed life cycle and, aided by the concomitant development of arterial and venous systems, respond to the intake of nutrients that are required to sustain all body tissues. Essential elements — or as they are unfortunately labeled on many vitamin supplement containers 'minerals' — and all precursor molecules required for tissue production are transported by the vascular system to the osteoblasts. These cells orchestrate the form of the organ, setting out an appropriate disposition of matrix and mineral, just as the specialized cells in other tissues form the non-mineralized organs of the body. Another specialized bone cell, the osteoclast, reworks the mineralized tissue. These giant multinucleate cells resorb and reorganize the deposits during growth or repair, maintaining the architecture and the function of the organ (Jee 1983, Nijweide et al. 1986).

### *Bone Biochemistry*

All of the separate activities that combine in the formation and reshaping of the mineralized skeletal tissues require a constant chemical flux between the tissues and the blood. Hormones and other biomolecules influence the status and the rates of exchange at all stages of tissue turnover (Canalis 1996). These biochemicals may be generated locally by the bone cells or arrive via the blood from many different organs. For example, some are derived from the food ingested, broken down, and absorbed via the intestine (Turnberg and Kumar 1993). Others, such as parathyroid hormone, derived in the thyroid gland and assisted by actions of the kidney (Suki and Rouse 1996), maintain the level of ionized calcium in the blood at around 5 mg/dL and the total level of calcium in the serum between 9 and 11 mg/dL (Bowers et al. 1986). The concentration of circulating calcium in the blood and serum has as its ultimate source the composition and amount of the calcium-containing mineral per unit area of bone tissue. The hormones are the means by which the various calcium pools keep the blood and serum at the required levels. An adult human body may contain 1 kg of calcium but less than 1% is outside the skeleton (Bronnar 1997). Formation and maintenance of skeletal tissue with its important mineral constituent are homeostatic, a balance served by a series of checks and balances, a feedback system of chemical reactions that are totally integrated and internal.

The health of humans is intimately connected with the ingestion of adequate nutrients. The elements essential for all living forms — oxygen, carbon, nitrogen and hydrogen — are never in short supply (Kohn 1999), but some cations can be rate-limiting in converting these elements into the molecules of life. The list of the essential elements in addition to C, N, O, and H is presented (Table 23.1) in groups of macro, micro, and trace elements, to illustrate the present understanding of the amount of each element required daily for adequate nutrition (O'Dell and Sunde 1997).

### *Bone Mineral*

The list contains a large proportion of the naturally occurring elements found in the Periodic Table. At the top of the list of macronutrients are Ca and P. They are essential to the formation and deposition of hydroxylapatite, $Ca_5(PO_4)_3(OH)$, the main constituent of the mineral matter of bones and teeth (Skinner 1973). Many of the elements in the list form stable solid solutions in the apatite crystal structure (Fig. 23.1), as has been shown from study of the natural occurrences of apatites in igneous, metamorphic, and sedimentary rocks (Deer et al. 1992, Skinner 1997). Carefully extracting the mineral from the organic/cellular fraction of bone shows that all of these elements occur as part of this essential inorganic constituent of the tissues. Table 23.2, an analysis of the mineral found in the dense portion (the cortex) of a leg bone of a cow, is presented to illustrate the amount of each element found in normal, heavily mineralized tissue. The

Table 23.1: Elements for adequate nutrition

Macro:
Elements with daily requirements more than 100 mg
Ca, P, Na, K, Cl, Mg, S

Micro:
Elements with daily requirement less than 1 mg up to 100 mg
Fe, CU, Zn, Mn, I, Mo, Se, F, Br, Cr, Co, Si

Trace:
Elements whose requirements are not as yet adequately determined, but whose presence in microgram quantities is thought to be necessary. As and Pb are potentially hazardous in excess.
As, B, Sn, Ni, Ge, V, W, Pb

Table 23.2: Composition of the mineral of bovine cortical bone after ethylenediamine extraction

| *Element* | *Content (Percent by Weight)* | *Element* | *Content (Percent by Weight)* |
|---|---|---|---|
| Ca | 33.50 ± 0.13 | P | 15.53 ± 0.05 |
| Ag | 0.001 | Mn | <0.001 |
| Al | 0.01–0.1 | Na | 1–10.0 |
| Ba | 0.001–0.01 | Pb | 0.001–0.01 |
| Cr | 0.001–0.01 | Si | <0.001 |
| Cu | 0.01–0.1 | Ni | <0.001 |
| Fe | 0.1–1.0 | Sn | 0.001–0.01 |
| Mg | 0.1–1.0 | Sr | 0.01–0.1 |
| K | <1.0 | $H_2O$ | 3.5 |

Spectrographic semiquantitative analysis from Spectrochemical Analysis Section, Analytical Chemical Division, National Bureau of Standards, U.S. Department of Commerce.
Other elements looked for but not detected: As, Au, B, Be, Bi, Cd, Ce, Co, Ga, Ge, Hf, Hg, In, Ir, La, Mo, Nb, Os, Pd, Pt, Rh, Ru, Sb, Sc, Ta, Te, Th, Tl, U, V, W, Y, Zn, Zr.
[Skinner (1987) p.201]

composition of human bone tissue would be very similar. Each sample of cortical bone submitted to such detailed analysis will show small differences in trace element composition based on the diet and metabolism of the specific individual.

With extreme insolubility over a range of pH, hydroxylapatite usually forms as very small crystallites, on the order of 5 x 50 micrometers, when precipitated in any biological tissues (Skinner 2000b). The crystallites, therefore, have large surface areas on which other elements and ligands can be absorbed.

The mineral in bone plays important roles in the dynamic equilibrium between the intake of elements and their availability locally and systemically. As a storehouse of elements, and an intermediary, bone mineral makes a very important chemical contribution to the viability of all tissues in the body. The deposition of hydroxylapatite in bone acts to conserve phosphorus, the most important element in the energy cycles of all living forms. We literally carry around with us our private fuel source. In light of the distinctive chemical and physical attributes of this mineral, it is not surprising that vertebrate hard tissues are mineralized with apatite (Skinner 2000a).

Strontium affords us a prime example of one of the cations that cross over from the environment into the bone mineral system. We learned about its transposition in a most direct and, indeed, urgent manner. The radioactive isotope, $^{90}$Sr, was generated during the tests on the hydrogen bomb in the early 1950s. The expectation that the radioelement would be deposited in mineralized tissues led to outcries across the U.S. and elsewhere for the military to stop testing. The focus of concern was the potential immediate, and long term, harm to children whose rapidly growing bones and teeth would incorporate the radioactive form of Sr. Numerous scientific reports were published elucidating the distribution of $^{90}$Sr, as well as non-radioactive forms of Sr, in soils, milk and other foods (Hoopes 1962, Knapp 1961), as well as the uptake in humans and specifically in teeth (Bjornerstedt et al. 1957, Pennington and Jones 1961). Detailed effects of the inhalation and ingestion of $^{90}$Sr-laden foods at the cellular and tissue level followed (Bustad and Goldman 1972). The data generated on the relationship of dose to response could not have been gathered without the enormous public interest in the radioactive hazard. Fortunately, the ingestion of large amounts of Ca in the children's diets prevented an excessive uptake of the radioactive form of Sr. As the tests ceased, a relieved populace moved away from worries about future cancers in their youngsters. Because of these adventitious circumstances we obtained valuable insight into the interaction of Sr and health.

## *Conclusions*

The mineral deposited and sequestered in the skeleton reflects the composition of food ingested. Bone tissue is, in effect, a mirror of the global environment in which it forms. The importance and influence of some anions and cations on bone tissue, bone mineral, and the mechanisms of biomineralization continue to be investigated (Bronnar 1996). Studies of the many other living vertebrates, all of whom derive their nutrition directly and ultimately from the geological environment, although occasionally manipulated by humans, can also be relevant to, and increase our understanding of, the effects of a range of elements on our skeletal tissues and ultimately our total health. In addition, it seems prudent that research detailing the composition of bone mineral by biomedical scientists be correlated with the data becoming available through geochemical studies on the environment (**Plant et al.**, and **Selinus**).

### References


Albright, J.A. and H.C.W. Skinner (1987) Bone: Structural organization and remodeling dynamics. Chapter 5, p.165–198 in The Scientific Basis of Orthopaedics. Edited by J.A.Albright and R. Brand. Appleton and Lange, Norwalk, CT.

Banfield, J.F and K.H. Nealson (1997) Geomicrobiology: Interactions between microbes and minerals. Reviews in Mineralogy 35, 448 pages. Mineralogical Society of America, Washington, D.C.

Bjornerstedt, R., A, Engstrom, C-J Clemendson, and A. Nelson (1957) Bone and Radiostronium. John Wiley & Sons, Inc. New York.

Bowers, G.N., C. Brassard and S. Sena (1986) Measurement of ionized calcium in serum with ion-selective electrodes. A mature technology that can meet daily service needs. Clinical Chemistry 21: 1437–1447.

Bronnar, Felix (1996) Metals in Bone: Aluminum, boron, cadmium, chromium, lead, silicon and strontium. Chapter 22 in Principles of Bone Biology Edited by Academic Press, New York.

Bronnar, Felix (1997) Calcium Chapter 2, p.13–61 in Handbook of Nutritionally Essential Mineral Elements. Edited by B.L. O'Dell and R.A. Sunde. Marcel Deker, Inc., New York

Canalis, E. (1996) Regulation of bone remodeling. p. 29–34. in Primer on Metabolic Bone Diseases and Disorders of Mineral Metabolism. 3rd Edition Edited by M. J. Favus. Lippincott-Raven Publishers, Philadelphia.

Centeno, Jose A. (this volume) Examination of tissues by chemical microscopy and biophysical techniques. P. ?.

Deer, W.A., R.A. Howie and J. Zussman (1992) An Introduction to the Rock-Forming Minerals. 2nd Edition. Apatite p. 663–669 Longman Scientific & Technical, Essex, England.

Goldman, M & L.K. Bustad (1972) (Eds) Medical Implications of Radiostrontium Exposure.. Proc. of symposium held in Davis, CA, Feb 22–24, 1971. US Atomic Energy Committee, Office of Information Services, Oak Ridge, Tenn.

Hoffman, P.E. and D.P. Schragg (2000) The snowball earth. Scientific American 282:68–75.

Hoopes, Roy (1962) A Report of Fallout in Your Food. Signet Books, New York

Hopps, H.C. and H.L. Cannon (1972) Editors of Geochemical Environment in Relation to Health and Disease. Annals New York Academy of Sciences 199, 352 pages.

Jee, W.S.S. (1983) The skeletal tissues p. 200–255 in Histology, Cell and Tissue Biology. Edited by L. Weiss, Elsevier Biomedical, New York.

Kohn, Matthew J. (1999) You are what you eat. Science, v. 283, p.335–336.

Knapp, H.A. The Effect of Deposition Rate and Cumulative Soil Level on the Concentration of Strontium –90 in U.S. Milk and Food Supplies. US Atomic Energy Commission, Division of Technical Information.

Nijweidie, P., E.H. Burger, and J.H.M. Feyen (1986) Cells of bone; proliferation, differentiation and hormonal regulation. Physiological Reviews v.66, p.855–886

O'Dell, B.L. and R.A. Sunde (1997) Editors of Handbook of Nutritionally Essential Mineral Elements. Marcel Dekker, Inc., New York

Pennington, J.A.T. & J. W. Jones (1987) Molybdenum, Nickel, Cobalt, Vanadium and Strontium in Total Diets. J. Amer. Dietetic Assn. v.897, p.1646–

Plant, Jane, David Smith, Barry Smith, and Shaun Reeder (this volume) Environmental Geochemistry for Global Sustainability.

Ross, M. & Skinner, H.C.W. (1994) Geology and human health. Geotimes v.39(1), p.13–15.

Schidlowski, M. (1988) A 3,800-million-year isotopic record of life from carbon in sedimentary rocks. Nature, v.333, p.313–318.

Selinus, Olle (this volume) Biogeochemical Monitoring in Medical Geology.

Skinner, H. Catherine W. (1972) Preparation of the mineral phase of bone using ethylene diamine extraction. Calcified Tiss. Res. v.10, p.257–268.

Skinner, H. Catherine W. (1973) Studies in the basic mineralizing system CaO-P2 O5-H2O. Calcified Tissue Research v.14, p.3–14.

Skinner, H. Catherine W. (1987) Bone: Mineral and mineralization. Chapter 6, p.198–212 in The Scientific Basis of Orthopaedics. Edited by J. A. Albright and R. Brand. Appleton and Lange, Norwalk, CT.

Skinner, H. Catherine W. (1997) The Apatite Group p. 854–863 in Dana's New Mineralogy 8th Edition. Edited by R. V. Gaines, H.C.W. Skinner, E. Foord, B. Mason and A. Rosensweig. John Wiley & Sons, New York.

Skinner, H. Catherine W. (2000a) In praise of phosphates or why vertebrates chose apatite to mineralize their skeletal elements. International Geological Review 42:232–240.

Skinner, H.Catherine W. (2000b) Minerals and human health. Chapter 11, p.383–412 in Environmental Mineralogy. Edited by D.J. Vaughan and R.A. Wogelius, European Mineralogical Union Notes in Mineralogy, Eotvos University Press, Budapest, Hungary.

Suki, W.N. and Rouse, D. (1996) Renal transport of calcium, magnesium and phosphorus. p. 472–515 in The Kidney. 5th Edition, Ed. by B.M. Brenner, WB Saunders, Philadelphia.

Turnberg, L.A. and R. Kumar (1993) Digestion and absorbtion of nutrients and vitamins. p.977–1008. in Gastrointestinal Disease: Pathophysiology, Diagnostics, Management. 5th Edition. Edited by Sleisenger, M.H., J.S. Fordtran et al., W.B. Saunders, Philadelphia.

Warren, H.V. (1954) Geology and Health. The Scientific Monthly 78(6):339–345.