CHAPTER 8

WATER HARDNESS IN RELATION TO CARDIOVASCULAR DISEASES AND URINARY STONES

One of the most intriguing, yet, not very well defined geochemistry-health correlations is the incidence of cardiovascular diseases (CVD) in connection with water hardness of a particular area (Crawford et al., 1977; Comstock, 1979; Bernardi et al., 1995). One of the earliest studies on the relationship between water hardness and the incidence of vascular diseases was by a Japanese chemist Kobayashi (1957). He showed on epidemiological grounds higher mortality rates from cardiovascular diseases (strokes) in the areas of Japanese rivers with softer water compared to areas with hard water used for drinking purposes. Kožíšek (2003) has summarized the beginnings of research that led to the health significance of water hardness. He mentions that among the best known studies is that by Schroeder (1960) who showed a correlation between mortality from CVD in males (ages 45-64) and water hardness in 163 largest cities of the USA and who summarized his results under the caption **"soft water, hard arteries".**

Within the first two decades of research into water hardness in association with cardiovascular diseases, more than 100 papers had been published (Hewitt and Neri, 1980). In several countries and areas, a negative correlation has been observed between water hardness and death rate due to heart diseases (Masironi, 1979; Pocock et al., 1980; Teitge, 1990). Even though a definite causal effect still cannot be ascribed to this geochemical correlation, the effect of trace elements in drinking water on heart diseases has caused great interest among medical geologists. It is of particular interest to note that such a negative association between water hardness and cardiovascular pathology is evident in both industrialized and developing countries in the tropics.

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It should, however, be mentioned that not all studies confirm such a relationship. Miyake and Iki (2004) for example, in a recent study, observed that there is a lack of association between water hardness and coronary heart diseases (CHD) mortality in Japan. These authors observed that in males, after adjustment for age, an inverse dose-response relationship between water hardness and mortality from CHD was significant (p=0.004). However, the relationship virtually disappeared after further adjusting for socioeconomics status and health care status. In females they found no association between water hardness and coronary mortality. Nonetheless, a large number of studies covering many countries suggest such a correlation and geochemically it is worthy of serious study.

WATER HARDNESS

Water hardness has been defined in the literature in a variety of ways with multiple units being used to express it, such as German, French and English degrees; equivalent $CaCO_3$ or CaO in mg/L. Even though initially water hardness was rather vaguely defined as a measure of the capacity of water to precipitate soap, it is now generally accepted that hardness is defined as the concentrations of calcium and magnesium ions or as $CaCO_3$ equivalent in mg/L. General guidelines for classification of water are given below:

$CaCO_3$ mg/L	Water hardness
0-60	Soft
61-20	Moderately hard
121-180	Hard
>180	Very hard

Most natural water supplies contain at least some hardness due to dissolved calcium and magnesium bearing carbonates and silicates. Elements such as iron may contribute to the hardness of water, but in natural water, they are generally present in low quantities. The total hardness of water may range from trace amounts to milligrams per litre.

Cardio-protective Role of Calcium and Magnesium

The `*water factor*` in the heavily discussed association of water hardness with the low incidence of cardiovascular diseases (CVD) has been the

most intriguing question. What is it in the hard water that is really responsible for the cardio-protective role? Based on a large number of research investigations, the increasing evidence is indicative of magnesium as the `*candidate element*` with calcium playing a sub-ordinate supportive role (Eisenberg, 1992).

The presence of calcium and magnesium in natural water results from the decomposition of calcium and magnesium aluminosilicates and, at higher concentrations, from the dissolution of limestone, magnesium limestone, magnesite, gypsum and other minerals. In most waters, Ca and Mg are present as simple ions Ca^{2+} and Mg^{2+} with the Ca levels varying from tens to hundreds of mg/L and the Mg concentrations varying from units to tens of mg/L. The crustal abundance of Mg is much lower as compared to Ca and hence the lower abundance of Mg in the natural waters, the average Ca/Mg ratio being 4.

It is well known that both Ca and Mg are essential for the human body. Apart from being a major component of bones and teeth, they both play a role in the decrease of neuromuscular excitability, myocardial system, heart and muscle contractility, intracellular information, transmission and blood coagulability. Among the common manifestations of Ca-deficiency is osteoporosis and osteomalacia, while hypertension is also thought to be linked to Ca-deficiency.

Mg is a vital cofactor and activator of more than 300 enzymatic reactions including glycolysis, ATP metabolism, transport of elements such as Na, K and Ca through membranes, synthesis of proteins and nucleic acids, neuromuscular excitability, muscle contraction (Kožíšek, 2003). Mg-deficiency is known to be linked to e.g. vasoconstrictions, hypertension, cardiac arrhythmia, acute myocardial infarction.

An important point to note is that although only two out of three studies have shown correlation between cardiovascular mortality and water hardness (Figure 8.1), studies carried out on the water magnesium alone have all shown an inverse correlation between cardiovascular mortality and water magnesium level (Durlach et al., 1985).

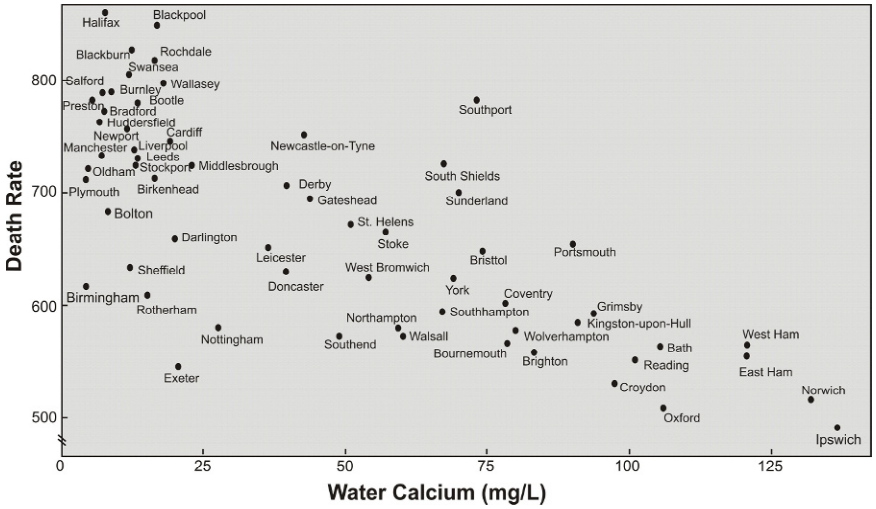


Fig. 8.1. Water Ca in some areas in England and Wales in relation to cardiovascular death rate (per 100,000 men), age 45-64 years during 1958-64 (Gardner 1973; Keil, 1979)

Neri et al. (1975, 1977) who carried out a nation-wide survey of 15 elements present in 575 drinking water samples were of the opinion that Mg was the element most-likely to show the cardioprotective role. They based their conclusions on the following evidence as reported by Marier (1978).

(i) It was present in more than 10% of sampled waters.

(ii) Mg has a consistent function of the softness-hardness gradient.

(iii) Mg represents a significantly high proportion of the daily intake from other sources.

(iv) The known metabolic effects of Mg are consistent with the hard water mortality trend.

(v) Analysis of 350 tissue samples from 161 autopsy cases revealed that myocardial Mg was 6% lower in "*cardiac death*" patients from soft-water localities in comparison with hard water regions.

(vi) Myocardial Mg in all "*cardiac death*" tissues averaged 22% lower than in the group of non-cardiac fatalities.

In the search for the "unknown water factor" associated with hard water, trace elements beneficial to health (Li, Zn, Co, Cu, Sn, Mn) and toxic (Pb, Cd, Hg) had also been investigated. No significant correlation between the content of these elements in water with CVD morbidity had been ob-

served. Attention had been paid also to the higher corrosive potential of soft water known to support higher leakage of toxic compounds from water pipes.

Rubenowitz et al. (2000) studied the correlation between the drinking water Mg and Ca levels and morbidity and mortality from acute myocardial infarction (AMI) in 823 males and females aged 50-74 years in 18 Swedish districts. Their findings supported the hypothesis that Mg prevents sudden death from AMI, rather than all ischaemic disease deaths.

Maier (2003) observed that there is a link between low magnesium and atherosclerosis. It was shown that Mg-deficiency caused by poor diet and/or errors in its metabolism may be a missing link between diverse cardiovascular risk factors and atherosclerosis. The latter is described as a form of chronic inflammation resulting from interaction between lipoproteins, monocyte-derived macrophages, T cells and the normal components of the arterial wall.

Apart from Mg-deficiencies promoting inflammation, it is also known to be frequently associated with hypertension, diabetes and aging - known risk factors of atherosclerosis.

It has been shown (WHO, 1978; Oh et al., 1986), that soft water markedly reduces the content of different elements (including Mg and Ca) in food if used for cooking vegetables, meat and cereals. For Mg and Ca this figure could be as high as 60%. As against this if hard water is used for cooking, this loss was estimated to be much lower. Kožíšek (2003) was of the view that in areas supplied with soft water, one needs to take into account not only a lower intake of Mg and Ca from drinking water, but also a lower intake of Mg and Ca from food due to their loss during cooking in such water.

Several attempts have been made to quantify the protective effect of water magnesium (Figure 8.2). The study by Schroeder (1960) in USA estimated that an increase of the water Mg level by about 8 mg/L led to reduction of mortality from all CVD by about 10%. Teitge (1990), in his extensive

German study reported that if drinking water Mg is reduced by about 4.5 mg/L, the incidence of myocardial infarction increases by 10%.

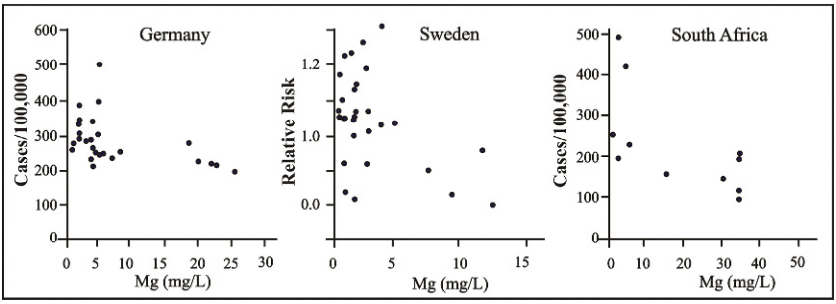


Fig. 8.2. Relation between cardiovascular death among men and drinking water magnesium levels in Sweden, Germany and South Africa (Rylander, 1996)

Even though the role of Mg in cardiovascular diseases has been more important, the Ca/Mg ratio has also been a subject of interest (Figure 8.3). However, there are no well defined values for such a ratio, bearing in mind, the still hypothetical nature of the importance of Ca and Mg in drinking water in CVD.

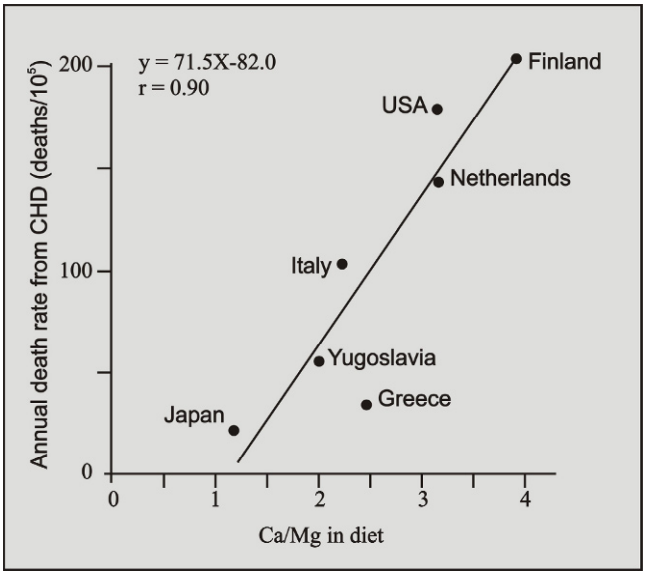


Fig. 8.3. Relationship between death rates from Coronary Heart Diseases (CHD) and the average calcium to magnesium ratio of the diet in different Organization for Economic Co-operation and Development (OECD) countries (Karppanen et al., 1978)

GEOCHEMICAL BASIS FOR TROPICAL ENDOMYOCARDIAL FIBROSIS (EMF)

Endomyocardial fibrosis (EMF) is an idiopathic disorder of people living in the tropical and subtropical regions of the world and characterized by the development of restrictive cardiomyopathy. It is sometimes considered to be a part of a spectrum of single disease processes that includes Löffler endocarditis (non-tropical eosiniophilic endomyocardial fibrosis). EMF displays a growth of a thick meshwork of fibrous tissues (collagen and elastin) within the endocardium and heart valves (Fergeson, 2002; Smith et al., 1998). EMF has been observed in Uganda, Nigeria and India among other tropical countries.

The aetiology of EMF is uncertain. One of the suggested reasons for tropical EMF is the influence of the element cerium (Eapen, 1998; Smith, 1998). The presence of elevated levels of dietary Ce and deficient levels of Mg, notably in South India have been considered as potential cofactors in the aetiology of endomyocardial fibrosis. Figure 8.4 shows the concentration of EMF in the equatorial region.

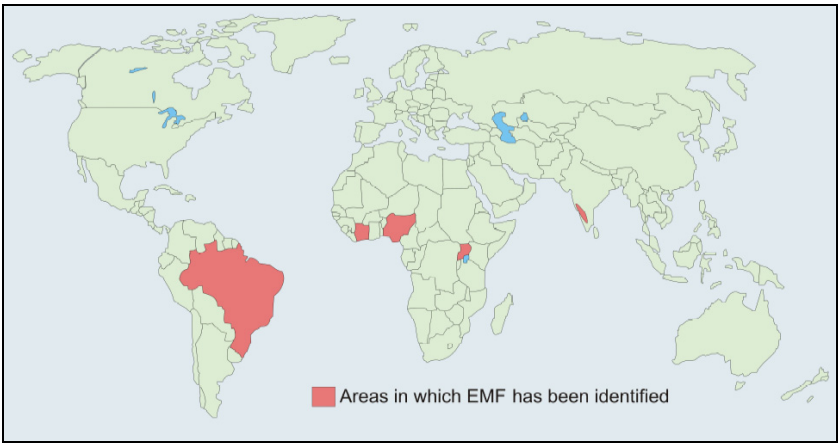


Fig. 8.4. World wide distribution of endomyocardial fibrosis (EMF) (Smith el al., 1998, Valiathan et al., 1993)

Valiathan et al. (1993) pointed out that the geochemistry of these tropical countries has common characteristics and it is the geochemistry that is perhaps responsible for tropical EMF. These authors studied the tropical EMF of Kerala in South India and made several observations. The major-

ity of the tropical EMF cases were concentrated in the coastal areas where the Ce-rich mineral monazite was also concentrated (Fig 8.5). The monazite from the coastal sands from 2 sites of Kerala had cerium contents ranging from 34 to 37%. Cerium is the most abundant element in monazite and shows the highest solubility among all rare-earth metals. It is now known to be toxic to humans.

Valiathan et al. (1993) hypothesised that the non-random distribution of EMF in Kerala and its spatial coincidence with latosolic soils is indicative of geochemical factors having a causal association with the disease.

Kartha et al. (1993), in an attempt to develop an animal model for EMF based on the geochemical hypothesis, carried out experiments on rats using Mg and C. They claimed that there is evidence for the possible connection of EMF with myocardial levels of these two elements. The supportive data were the preferential accumulation of Ce in cardiac tissues compared to skeletal muscle, enhancement of cerium levels in tissues in Mg deficiency and the synergistic effect of Mg-deficiency, and the severity of myocardial lesions.

The presence of Th and Ce in conjunction with Mg-deficiency was indicative of the possibility that EMF could be the "cardiac expression of an elemental interaction that causes a toxic metal to replace an essential element at the cellular level" (Valiathan et al., 1993). An interesting observation made by these authors was that children suffering from helminthiasis and anaemia in Kerala were known to consume sand. The radioactivity of urine measured in children of Kerala between 5 and 9 was 21+2±7.1 pCi/L. They also refer to a case study in Minas Gerais, Brazil, where human ingestion of Th and REE based on their contents in faeces revealed a tandem relationship between Th and Ce (Linslata et al., 1986).

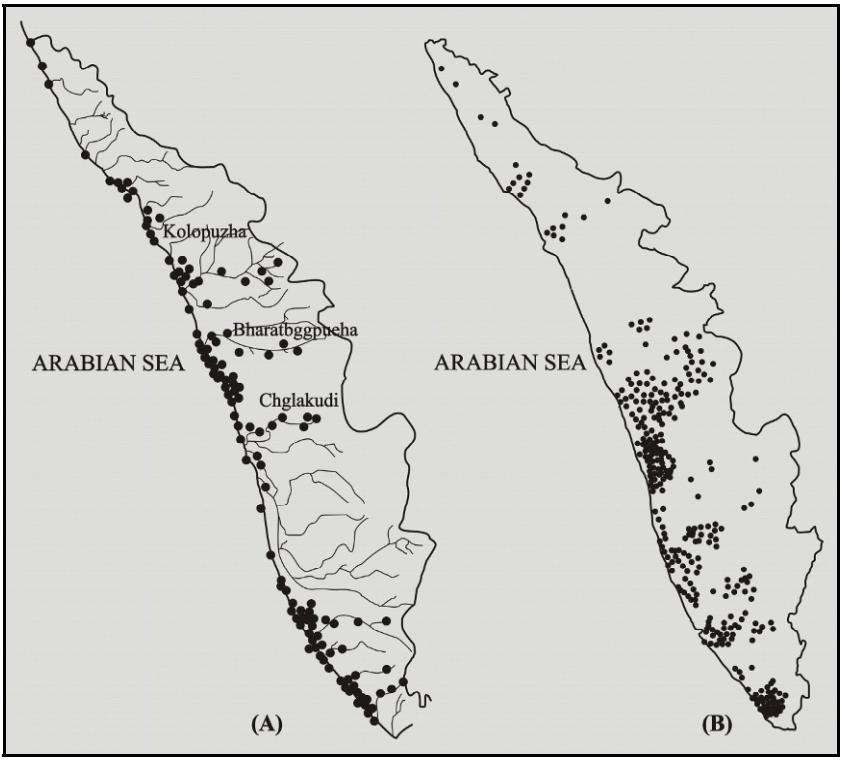


Fig. 8.5. (A) Distribution of monazite sand along Kerala coast, India and (B) Distribution of places of origin of 300 patients with endomyocardial fibrosis in (Valiathan et al., 1993)

The role of Mg was considered to be synergistic insofar as it enhances the adsorption of Ce and provides binding sites for the toxic element in the myocardium. If this geochemical hypothesis is correct, then similar over exposures to Ce must occur in other environments where EMF is prevalent. Smith et al. (1998) tested this hypothesis in Uganda where EMF is endemic and which represents the most common form of infantile heart condition. In Uganda, the presence of elevated Ce and lack of Mg in the surface environment was associated with the presence of highly weathered ancient granites and gneisses that form latosolic soils over large tracts of central and northern parts. Mineralogical and analytical examinations revealed the presence of a Ce-bearing non-phosphate mineral (with no significant La or P) possibly carbonate, oxide or hydroxide. Smith et al. (1998) were of the view that the occurrence of Ce without La and other REE indicates a mineral formed at low temperatures at the near-surface environment. Cerium present in the finer fractions of dust increases its

mobility, bioavailability in the human gastrointestinal tract and the direct absorption through the skin (Price and Henderson, 1981) or scavenging cells within the gastrointestinal tract (Powell et al., 1996).

The work of Smith et al. (1998) substantiated the observations made in south-western India, and showed that Ce within the Ugandan environment is controlled by the presence of <20 μm particles in the soil.

EFFECT OF WATER HARDNESS ON URINARY STONE FORMATION (UROLITHIASIS)

The mineral and electrolyte content of drinking water varies markedly depending on the geology, soil chemistry and hydrology of the terrains concerned. The effect of these minerals and electrolytes on the human physiology has been the subject of many investigations. Urinary stone formation is common in many countries and particularly in some of the tropical countries (Singh et al., 2001). Figures 8.6 and 8.7 show some urinary stones and their internal structures.

Stones which form in the kidneys are made of different types of crystals.

There are made up of:

(a) calcium oxalate
(b) calcium phosphate
(c) combination of calcium oxalate and calcium phosphate
(d) magnesium ammonium phosphate (known as struvite or infection stones)
(e) uric acid
(f) cystine
(g) miscellaneous types which may occur with drug metabolites.

Fig. 8.6. A kidney stone with a diameter of about 6 cm

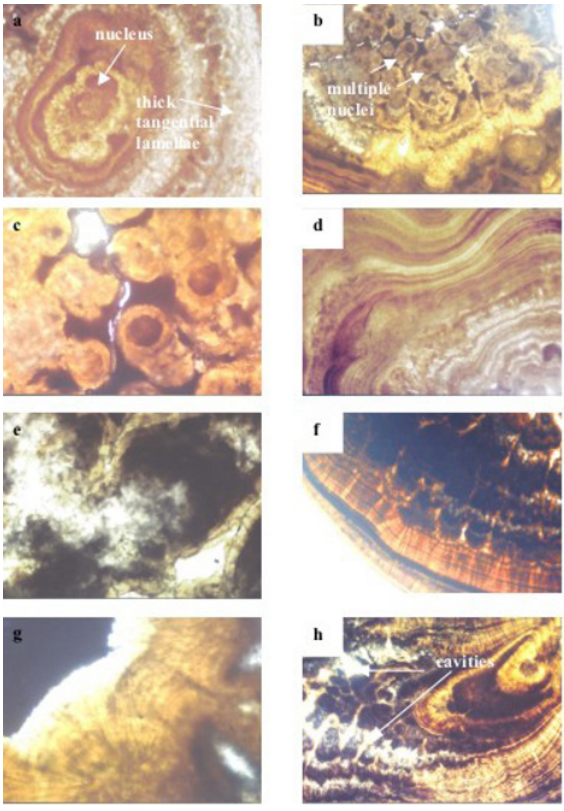


Fig. 8.7. Internal structures of kidney stones (Wijewardana, 2005)

Types of Stones

Calcium oxalate

This is the most common type of stone, and forms due to excessive amount of calcium oxalate in the urine. They are of two types namely (i) monohydrate (ii) dihydrate. While calcium oxalate dihydrate stones break easily with the treatment procedure lithotripsy, monohydrate stones are among the most difficult to break. These stones usually develop when the urine is acid (pH <6.0) (Leonard, 1961; Gibson, 1974; Kadurin, 1998; Sokol et al., 2005).

Calcium phosphate

Calcium phosphate develops in alkaline urine (pH >7.2) and often occur in people with urinary tract infection, hyperparathyroidism, medullary sponge kidneys or Renal Tubular Acidosis (RTA). Citrate is known to play an important role in calcium stone formation. It forms a soluble salt with calcium and inhibits the formation of calcium oxalate and calcium phosphate crystals. Low levels of urinary citrate therefore increase the chances of developing stones. However, when urine pH is less that 5.5, uric acid crystals develop and calcium crystals then form layers around the crystal to form a calcium oxalate stone.

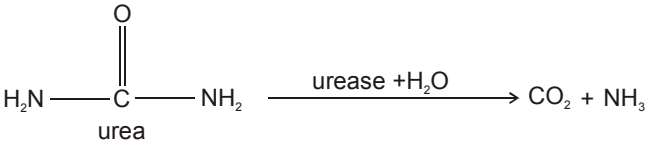
Uric acid

In their pure form these stones do not contain calcium. Uric acid is an end product of urine metabolism and the crystals cause gout, an arthritic condition. In acid urine (pH <5.5) uric acid crystals precipitate leading to stone formation. When urine is alkaline, uric acid remains soluble.

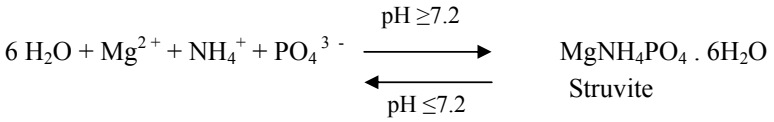
Magnesium ammonium phosphate stones (struvite)

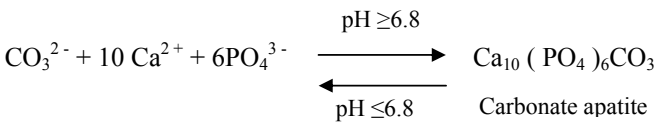
These stones are termed infection stones or struvite. They make up approximately 15% of the urine stones and are thus an important group. The basic precondition for the formation of infection stones is a urease positive urinary tract infection. Urease splits the urea to ammonia and CO_2. Alkaline urine also develops and struvite and carbonate apatite crystals develop (Bichler et al., 2002).

The following reactions take place in the formation of carbonate apatite and struvite in ureas positive infection. Urea is hydrolysed in the presence of urine.



Ammonia and carbon dioxide hydrolyze to ammonium ions and bicarbonate. Binding with available cations produces magnesium ammonium phosphate (2) and carbonate apatite.





Cysteine

These stones are different from the others since they do not have a protein matrix due to excess amounts of the amino acid cysteine in the urine (cystinuria). Due to the protein matrix, these stones are difficult to fragment.

The urinary stones, as discussed above are minerals and can be studied by techniques such as X-ray diffraction and optical microscopy. Among these minerals are:

(a) Apatite	$Ca_5(PO_4,CO_3)_3$ (F,OH,Cl)	calcium phosphate
(b) Whewellite	$CaC_2O_4.H_2O$	calcium oxalate
(c) Weddellite	$CaC_2O_4.2H_2O$	
(d) Struvite	$Mg(NH_4)PO_4.6H_2O$	magnesium ammonium phosphate
(e) Brushite	$CaHPO_4.2H_2O$	calcium hydrogen phosphate
(f) Whitlockite	$Ca_9(Mg, Fe)H(PO_4)_7$	calcium phosphate(more common as prostate stone)
(g) Newberyite	$MgHPO_4.3H_2O$	magnesium hydrogen phosphate

Kajander and Ciftcioglu (1998) in a controversial theory attributed stone formation and calcification in the human body to nanobacteria. These authors found nanobacterial culture systems that allow for reproducible production of apatite calcifications in vitro. Depending on the culture conditions, tiny nanocolloid-sized particles covered with apatite, forming various sizes of aggregates and stones were observed. They considered nanobacteria as important nidi (microcrystalline centres) for crystal formation. They concluded that bacteria- mediated apatite takes place in humans just as in the case of aqueous environments and geological materials, notably sediments. This theory however was criticized by Cisar et al. (2000) who proposed that biomineralization was caused by the non-living, nucleating activities of self- propagating microcrystalline centres (nidi) which form crystalloid macromolecules of calcium carbonate phosphate apatite. Photographs of these non-living structures taken by electron microscopy were identical in appearance to those previously described by Kajander and Ciftcioglu (1998).

Studies carried out on the effect of water hardness on urinary stone formation (Schwartz et al., 2002) appear to indicate a lack of any significant association between water hardness and the incidence of urinary formation. Bellizia et al. (1999) in their studies on effects of water hardness on urinary risk factors for kidney stones in patients with idiopathic nephrolithiasis observed that, as compared with both tap and soft water, hard water was associated with a significant 50% increase of the urinary calcium concentration in the absence of changes of oxalate excretion.

Many early investigators have documented an inverse relationship between drinking water hardness and calcium urolithiasis (Churchill et al., 1978; Churchill et al., 1980; Shuster et al., 1982). The reason for such an inverse relationship was not well known. As pointed out by Schwartz et al. (2002), increased mineral content, most notably calcium, in hard water is the biggest concern of most patients. However, these authors contend that no studies support the premise that ingesting hard water increases the risk of urinary stone formation. Singh et al. (2001) studied the role of fluoride in urinary stone formation in humans using case studies in India. They selected two areas, a fluoride endemic area and a fluoride non-endemic area. They observed that the prevalence of urolithiasis was 4.6 times higher in the endemic area as compared to the non-endemic area. Furthermore, they noted that the prevalence was almost double in subjects with fluorosis as against those without fluorosis in the endemic area. However, the effect of fluoride in drinking water on urinary stone formation is still not sufficiently well known.