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Evolutionary events culminating in specific minerals becoming essential for life

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Summary The environment in which living organisms evolved was apparently a primary determinant of which elements became essential for life. The first organic materials and, ultimately, life forms most likely were formed in an ancient sea containing minerals that provided structural integrity and catalytic ability to the first complex organic substances. The site at which life began has been suggested to be at the edge of the sea near sediments, or around a hydrothermal system. The strongest circumstantial evidence supports a hyperthermophilic beginning. Regardless of the site, the biological importance of elements tends to parallel oceanic abundance, but in higher forms of life this parallelism apparently has been mitigated by a natural selection process that resulted

in some elements becoming more important because of their superior abilities over other elements to perform vital functions. The converse to biological importance is that toxicity of elements and oceanic abundance tends to be inversely related. The basis for this relationship may be that the efficiency of homeostatic mechanisms to cope with a high intake of a specific element probably reflects upon the exposure of an organism to the element during its evolution. Thus, a study of evolutionary events may be helpful in predicting and comprehending the essential and toxic nature of mineral elements in humans.

Key words Essential elements – toxic elements – minerals – evolution – trace elements – homeostasis – life

Introduction

Essential or not essential, that is the question – when one considers the significance of mineral elements for life. In other words, this is the only incontrovertible method of classification of mineral elements in respect to their biological behavior. Often, however, one hears mineral elements being classified in other ways. ‘Toxic minerals’ is a grouping quite often encountered in the nutritional and toxicological literature. Although this term is usually recognized as referring to specific minerals, it can, in reality, be applied to all mineral elements because all minerals are toxic if they are present in living organisms in sufficiently high quantity. As Paracelsus stated almost 500 years ago, “it is the dose that

makes it poison or remedy.” Of course, the dose at which specific minerals become toxic varies greatly.

Why are some elements essential and others not? Why are some elements so much more toxic than others? These are questions that have been pondered by a number of scientists including Shaw [1], Frieden [2, 3], Egami [4, 5], McClendon [6], Schroeder [7], Ochiai [8], Osterberg [9], Christie and Williams [10], and Nisbet and Fowler [11]. The conclusion most often reached is that the environment in which life first began was the preeminent factor in determining the ultimate pre-dominant biological behavior of each mineral element in living organisms.

The first organic materials and, ultimately, life forms most likely were formed in the presence of water containing minerals that provided structural integrity and catalytic

ability to the first complex organic substances; this water probably was a part of an ancient sea. The mineral elements incorporated in the first primitive organisms, therefore, most likely reflected the mineral element concentrations in the sea water where they evolved. This is supported by the finding that most primitive modern invertebrates that live in the present oceans have tissue fluid composition that is very similar to the composition of the sea water around them [1]. The location in the sea where life evolved can only be hypothesized.

Early discourses [1–4, 7] on evolution stated that life probably originated in a tidal basin, at the edge of the sea, or in sediments because here the concentration of phosphates and other minerals was much higher than in the primitive oceans. Such a location could account for the enrichment in the content of carbon, nitrogen, phosphorus and sulphur in living organisms. Establishment of life under such conditions, however, needs an explanation for why iron is so prevalent in later biochemical systems despite its high dilution in sea water. One such explanation is that when life began, the earth's atmosphere was not strongly oxidizing; thus, iron would have been present in the more soluble Fe^{2+} form [2, 3].

In 1960, Shaw [1] divided essential elements into three groups; Division I was the essential alkali and alkaline earth metals, Division II was the essential transitional metals, and Division III was the essential non-metals. He stated that within a periodic group, biological importance tended to parallel oceanic abundance. Thus, in Division I, Group 1a elements hydrogen, sodium and potassium are biologically most important and are found in the greatest abundance in sea water; similar conclusions can be made about group 2a elements magnesium and calcium. In Division II, within a periodic Group, parallelism also is found between biological importance and oceanic abundance. Shaw [1] stated that Division III elements provide good tests of the oceanic beginnings of life. For example, aluminum is much more abundant than boron in the cosmos and the earth's crust, but aluminum has not been shown essential to life while boron has. Boron is a hydrophilic element. Also, oceanic abundant carbon is biologically more important than crustal abundant silicon.

In 1960, on the basis of his thoughts about the evolution of the importance of elements to life, Shaw [1] made the following predictions. "Vanadium will become a well-established trace element. Nickel will be found to play a role in a nutritionally significant co-ordination compound – probably associated with an enzyme. Chromium will be similarly implicated. The neglected element, titanium, may soon be recognized as essential to the life of plants and animals." Shaw [1] also thought that aluminum, silicon and, especially, arsenic would be assigned hitherto unsuspected roles in living organisms, and that rubidium and lithium merited further investigation. Based upon the findings with the ultra trace elements since 1970, many of Shaw's predictions may become realities.

Discovery of life near thermal vents on the bottom of oceans has spawned another suggestion as to where life began. According to Nisbet and Fowler [11], there is a wide variety of independent clues indicating that the first living community existed around a hydrothermal system. One clue is that key mineral elements that are important to life today would have been found near hydrothermal or volcanic systems. On the Archaean planet, black smokers and other hydrothermal emissions on young oceanic plates were probably more vigorous than today. At Archaean ridges, as today, sulfide vent chimneys would have formed that emitted fluids, compared to sea water, highly enriched in iron, manganese and sulfur; other locally enriched minerals would have been copper, zinc, molybdenum, selenium, nickel, magnesium and phosphorus. Vent gases at modern ridges include carbon dioxide, methane, hydrogen sulfide and hydrogen. On prebiotic earth, it is likely that similar gases were emitted as well as hydrogen cyanide made by high temperature reactions in the hydrothermal systems near magma. Nitrogen would have been present as ammonium minerals. All of these elements are essential for life.

Another clue for a hydrothermal beginning presented by Nisbet and Fowler [11] is that all of the ancient branches of life share a common hyperthermophile character of subsisting at temperatures between 80 and 100 °C. The first communities of life that existed in the Archaean period were Archaea and Bacteria; the higher Eucarya evolved in the Proterozoic period. These three communities can be traced back to a hyperthermophilic ancestor on the basis of 16S rRNA sequence comparisons.

Further evidence for a hyperthermophilic beginning of life is that the heat shock proteins and their analogues apparently are of the deepest antiquity [11]. Heat shock proteins and analogues occur in all three domains of life and are diversely involved in modern biochemical processes such as photosynthesis, mitochondrial function, nuclear membrane operation, and spermatogenesis. Other important enzymes most likely of hydrothermal origin include the nickel enzymes urease and hydrogenase, and the molybdenum (sometimes vanadium) enzyme nitrogenase.

Sulfur, iron, manganese and magnesium are mineral elements crucial to life today; this probably occurred because the first living organisms utilized these elements which are characteristic of hydrothermal environments, and thus were readily available without sophisticated processes. The wide variety of other mineral elements that assumed essential functions for various forms of life could also have been introduced to simple early organisms sited on a hydrothermal-associated environmental substrate which made them more highly concentrated and reactive. By analogy with modern hydrothermal systems the essential participation of zinc, copper, molybdenum, selenium and magnesium in life may have first evolved around systems above subduction zones, possibly in andesitic or andesite-like areas, perhaps in shallow seas on early continental crust or around island arcs [11].

Regardless of the exact location, it seems quite evident that life began in the sea. Among the first molecules formed from components of the pre-biotic environment were pyrrole rings and their protoporphyrin condensation products [12]. Such molecules could have rapidly complexed with dissolved transition metals to carry out the first catalytic actions in life. One of the most important events in the evolution of life was the formation of a molecule with the ability to absorb the energy of light for use in forming carbohydrates from carbon dioxide in water or air while releasing oxygen. This porphyrin molecule called chlorophyll contained magnesium in its center. This allowed organisms to move away from chemical and thermophilic mechanisms to obtain energy to sustain life as we know it; organisms could move to cooler and more diverse environments. It also resulted in the conversion of a carbon dioxide-rich atmosphere to an oxygen-rich atmosphere in which animal life could exist.

Although most of the elements important for early microorganism and plant life remain important today, the relative importance of some elements, especially the essential trace and ultra trace elements, was modified when organisms moved to different, sometimes hostile, environments. Evolution of mechanisms to protect and sustain life resulted in the formation of semipermeable membranes, closed circulatory systems, and mechanisms for concentrating needed elements for specialized functions and for disposing of unnecessary or potentially toxic elements. During the formation of these systems natural selection resulted in the prevalence of one element with superior ability to perform a function over others with the ability to perform the same function [2, 3, 10]. For example, nickel and cobalt were of considerable importance as catalysts in the early stages of life when reducing gases such as hydrogen, ammonia, methane, and hydrogen sulphide were abundant in the environment. Nickel was especially good as a catalytic metal in oxidation/reduction reactions providing energy from hydrogen and carbon monoxide. However, when the atmosphere became rich in nitrogen, oxygen and carbon dioxide, there was a need for better catalysts in this electron-poor environment and living organisms switched from cobalt and nickel to copper, iron, and zinc. Nickel and cobalt can still activate many enzymes by replacing the preferred element at the active site. However, an enzyme reconstituted with cobalt or nickel usually is not as efficient as the element normally used; this indicates that the usual transition element for that enzyme was found to be optimal during evolution. As a result, nickel and cobalt became generally less important in modern, compared to primitive, organisms.

Another example of natural selection was put forth by Schroeder [7]. Most molluscs use copper for their oxidation-reduction systems and for carrying oxygen in their blood. Copper has considerable disadvantages because it has only half the oxygen carrying capacity of iron and this probably was a major reason that molluscs did not become

evolutionary ancestors to advanced forms. Worms use iron to carry their blood oxygen; this element, being more efficient than copper, apparently allowed the evolution of these organisms to the vertebrates and the prime vertebrate, humans. The first chordate fish, the ancestor of humans that used iron in many life processes, had a notochord, a spinal column with a bulge on the front end from which developed the most complex organ on Earth, the human brain. Another organism at this time was less conservative and more adventurous; it used vanadium to carry blood oxygen. Vanadium was the wrong metal, for instead of ending up as a human, this organism ended up as a sea squirt which has green blood cells full of vanadium. Interestingly, sea squirt larvae have a notochord, but as they grow, they lose their nervous systems, degenerating into an animal with only a single nerve ganglion which lacks the first faint capacity for thought. Thus, the use of vanadium led to an evolutionary regression, an experiment which came to a blind end because of the chemical limits of this element as a versatile catalyst for living organisms.

It took about 250 million years for fish to evolve into amphibians and then into reptiles. This evolution occurred on the littoral, or in estuaries and swamps. When the first terrestrial reptilian vertebrate left the littoral to walk or slither on land, the problems it met were enormous. Its internal composition was established by the environment from which it came, but this reptile no longer could return to the sea to replenish it. As stated by Schroeder [7], this reptile went from an environment of evenly distributed plenitude to one of uneven superabundance and deficiency. For example, zinc, copper, iron and manganese were plentiful wherever there was vegetation. Cobalt, molybdenum, fluorine and boron were not distributed uniformly. Therefore, to survive, this land-based animal had to adapt not only to conserve essential elements, but to reject excesses of both essential and non-essential elements which could be toxic. Exquisite homeostatic mechanisms have evolved to achieve this.

Homeostasis, or the maintenance of a steady optimal concentration of an element in the body, involves the processes of absorption, storage and excretion [13]. The relative importance of these three processes varies among the mineral elements. The amount absorbed from the gastrointestinal tract is often the controlling mechanism for positively charged transition elements such as iron, manganese and copper. With these trace elements, if the body content is low, or if intake is low, the percentage of the element absorbed from the gastrointestinal tract is increased and vice versa. Trace elements that exist mainly as negatively charged ions or oxyanions, such as arsenic, boron and fluoride, are usually absorbed quite freely and completely from the gastrointestinal tract. Excretion through the urine, bile, sweat and breath is, therefore, the major mechanism for controlling the amount of these trace elements in an organism. Elements essential to life as electrolytes such as magnesium, calcium and sodium are con-

trolled both through absorption and excretion mechanisms. By being stored at inactive sites (e. g., fluorine in bone) or in an unreactive form (e. g., iron as ferritin), some elements are prevented from causing adverse actions when present in the body in high quantity. Release of an essential element from a storage form also can be important in preventing deficiency.

Toxicity of both essential and non-essential elements occurs when an organism is exposed to amounts that overwhelm homeostatic mechanisms. The efficiency of homeostatic mechanisms to deal with a specific element most likely depends upon the exposure of an organism to the element during its evolution. Thus, exposure to elements in concentrations found in sea water is not likely to be toxic to living things. The corollary to this is that exposure to elements at concentrations well above that to which living organisms were exposed while evolving in the sea or on the pre-human earth crust often will be found toxic to life. Arsenic and mercury are elements that can be used to exemplify this concept. Arsenic ($3 \mu\text{L}$) is found in higher concentrations than mercury ($0.03 \mu\text{g/L}$) in sea water (Table 1), and especially so near hyperthermal vents. This may be why arsenic can induce the formation of certain heat shock proteins and apparently is essential in low amounts [14]. However, arsenic was not the best element for performing most essential functions and thus exposure to its reactive forms came to be limited by efficient homeostatic mechanisms. In other words, arsenic is a relatively non-toxic element (although human activity has increased the amount in the modern environment) because animal life in the sea acquired a mechanism through which the more reactive, and thus toxic, inorganic form was made into a non-toxic methylated form. This ability was retained by most higher animals including humans which readily excrete methylated arsenic via the kidney [14]. On the other hand, because exposure to mercury was limited, early life probably did not develop good methods to handle the amounts that are sometimes encountered through activities of humans. Thus, mercury is a relatively toxic element.

Generally, the preceding discussion indicates that for evolutionary reasons, the most toxic elements to humans are those that are non-essential and are present in sea water in very low concentrations. Thus, based on Table 1, it is not surprising that elements such as mercury, cadmium, antimony, beryllium, silver, and gold in the ionic form are often referred to as the “toxic” mineral elements. One element that is often referred to as a toxic element, but does not seem to have the characteristics of these elements is lead. There is evidence that this element has beneficial, perhaps essential, properties in low amounts [15] and is present in sea water in relatively high quantity, equaling iron and arsenic (Table 1). The reason for the categorization of lead as toxic element, however, is actually the same as the other “toxic” elements. That is, environmental exposure to lead through human activity has resulted in intakes much above any requirement level and in frequent circumstances

Table 1 Trace elements in seawater^a

Essential		Possibly Essential	
Element	Sea Water concentration $\mu\text{g/L}$	Element	Sea Water concentration $\mu\text{g/L}$
Arsenic	3	Aluminum	1200
Boron	4600	Bromine	65000
Chromium	2	Cadmium	0.03
Cobalt	0.1	Fluorine	1300
Copper	10	Lead	4
Iodine	50	Lithium	100
Iron	3.4	Rubidium	120
Manganese	1	Strontium	8000
Molybdenum	14	Tin	3
Nickel	3	Titanium	5
Selenium	4	Non-Essential	
Vanadium	5	Beryllium	?
Zinc	15	Gold	0.004
		Mercury	0.03
		Niobium	0.01
		Silver	0.15
		Zirconium	0.02

^aAdapted from Schroeder [7]

well above the amount that homeostatic mechanisms developed through evolution are able to handle. This exposure has come about from the use of dishes and utensils containing lead materials, lead water pipes, lead-containing paints and lead additives to gasoline.

Because essentiality implies the presence of good homeostatic mechanisms, and thus a means to prevent toxicity over a wide range of intakes, knowing which elements are essential for higher forms of life and establishing the requirements for these elements are important in the establishment of toxicological risk of any mineral. Essential elements for humans beyond those needed to form organic molecules and to perform electrolyte functions are calcium, cobalt, copper, iodine, iron, magnesium, manganese, molybdenum, selenium, and zinc [16]. Recently, rather conclusive evidence has come forth to include boron and chromium on this list [17]. Circumstantial evidence, including essential functions in lower forms of life, for the essentiality of arsenic, nickel, silicon, and vanadium for humans is very strong [17]. The possibility that other elements are essential remains. This statement is supported by the existence of limited circumstantial evidence for the essentiality of aluminum, bromine, cadmium, fluorine, germanium, lead, lithium, rubidium and tin [18]. Moreover, evolutionary aspects of some of these elements suggest that they will be established as essential elements.

In summary, the environment in which living organisms evolved was a primary determinant of which elements became essential for life. The biological importance of elements tends to parallel oceanic abundance, but in higher

forms of life this association has been mitigated by a natural selection process which resulted in some elements becoming relatively more important (e. g., iron and zinc) because of their superior abilities over other elements (e. g., nickel and vanadium) to perform vital functions. The converse to biological importance is that toxicity of elements and oceanic abundance tend to be inversely related. Thus,

an examination of evolutionary events is helpful in understanding the essentiality and toxicity of elements for life.

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