review article
received: 2011-12-20

UDC: 612.751:1(37)

BONE COMPOSITION AND THE BIRTH OF QUANTITATIVE CHEMISTRY

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ABSTRACT

Bone is an important tissue for space specialists since it undergoes significant changes under microgravity conditions and its healing is slow. Bone has been considered a special tissue since the very inception of medical theories. In Acragas, according to Empedocles (493–432 BC), bone was made of two parts earth, two parts water and four parts fire, thus marking the beginning of quantitative chemistry.

Keywords: *osteoporosis, space, Empedocles, elements in bone, quantitative chemistry*

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SESTAVA KOSTI IN ROJSTVO KVANTITATIVNEGA RAZISKOVANJA V KEMIJI

IZVLEČEK

Kost je pomembno tkivo za specialiste na področju vesolja, saj gre v stanju mikrogravitacije skozi pomembne spremembe, njeno zdravljenje pa je počasno. Kost je bila obravnavana kot posebno tkivo že od začetkov medicinskih teorij. V Akragasu je Empedoklej (493–432 pr. n. št.) postavil hipotezo, v kateri je menil, da je kost sestavljena iz dveh delov zemlje, dveh delov vode in štirih delov ognja, kar označuje začetke kvantitativne kemije.

Ključne besede: *osteoporoza, vesolje, Empedoklej, elementi v kosti, kvantitativna kemija*

INTRODUCTION

Bone is an important tissue for space specialists. Bone, having adapted to gravity over the millennia, undergoes significant changes during space flight. These changes resemble those found in bedridden individuals and are long lasting and heal with difficulty. Bone loss from immobilized limbs can be observed in detail as a result of prolonged experimental bed rest and space flight, as well in clinical cases such as stroke or spinal cord injury. Bed rest in humans causes a loss of cortical bone in the legs. Skeletal bones with a thin cortex and a long cortical circumference are particularly at risk (Rittweger et al, 2009). Loss of bone mass is typical during space missions and is a limitation to missions of long duration. This is due to the lack of gravity. Bone changes cause secondary effects due to a disrupted equilibrium between the mineralization and demineralization of the bone matrix. Bed rest is used to investigate changes in bones here on Earth which are similar to those occurring in space (Cirillo M. and De Santo N.G., 2011). There is a strong interest in preventing bone disease in space flights, thus its structure is thoroughly scrutinized, as was the case at the very beginnings of science with the work of Empedocles.

The quest of the unifying principle

The quests for the answers to the basic nature and structure of the world originated in Miletus, (Table 1) in the Mediterranean, the unifying sea, where all great cultures originated. It was the quest for the ultimate material on the principle unifying the variety of phenomena (*Arché*). Thales identified water, Anaximander the limitless (*Apeiron*), Anaximenes, air. For Heraclitus, the principle was fire. At Elea, Parmenides rejected a single material and postulated the existence of two principles as the minimum economical explanation of the world. The proportions of the two principles, which he named Light and Night, made up the characteristics of objects and living organisms. As pointed out by Guthrie (1965a) "men were offsprings of Sun (father) and women of Earth (mother), thus Parmenides "composed a cosmic system mingling the elements Light and Night, out of and by means of these produced all phenomena. He has much to say by Earth and Sky and sun and moon, and recounts the origin of mankind". In the report of Plutarch (*Adversus Colotem /Against Colotes* 1114b) we read:

"you shall know the nature of aither and all the signs in the aither and the destructive effects of the shining sun's pure torch and from there they came to be. You shall learn the wandering accomplishment of the round moon and its nature. And you shall learn about the surrounding heaven, from where it grew, and how Necessity, leading it, constrained it to hold the limits of the stars". *(DK28B10)*

Table 1. Timeline, places and Archai of the Presocratic philosophers.

Philosophers	Location	BC	Archai
Thales	Miletus	c.600	Water
Anaximander	Miletus	c.580	*Apeiron* (limitless)
Anaximenes	Miletus	c.550	Air
Xenophanes	Colophon	540-537	Earth
Heraclitus	Ephesus	c.500	Fire
Anaxagoras	Clazomenae	c.500	*Nous* (Mind)
Parmenides	Elea	c.480	Fire(Light) and Night (darkness)
Democritus	Abdera	470-460	Atoms
Empedocles	Acragas	c.460	Air, Water, Earth and Fire

Empedocles of Acragas

Empedocles (492–432 BC) lived at Acragas at the time of the tyrant Theron, the man who defeated the Carthaginians at Himera. His *floruit* was about 444 BC. The list of his contemporaries includes Anaxagoras, Euripides, Glaucus of Rhegium, Hippodamus, Melissus, Pericles, Protagoras, Sophocles, and Socrates. Acragas was on the "yellow river" – defined by Pindar "the loveliest city of mortals" at that time was a stimulating city, inhabited by 300,000 people, rich in temples, among the largest of those days, probably second only to those of Ephesus.

Empedocles, who taught Pausanias and Acron of Locri, greatly contributed to the foundation of physiology and of medical theory, and is considered the founder of art in Sicily. He championed democracy, which came of age in Acragas after Theron's death. He authored two books: *On Nature* and *Purifications;* of the 5000 lines, more than 450 remain. The circumstances of his death is a well-kept mystery of Mount Etna fires and ashes. He was not immune to charlatanism since he promised remedies against old age and all kinds of disease, thus behaving as a healer. In fact as outlined in the fragment below, (DK31B111) he promises his fellows philosophers that they will learn about drugs for all diseases and even more against ageing:

"You shall learn the drugs that exist as a defence against illness and old age; for you alone will I accomplish all this" *(DK31B111).*

According to Empedocles, two elements (roots) were insufficient to form all known things, and he postulated four roots (Air, Water, Earth and Fire) as the minimum economical explanation of the world.

"Hear first the four roots of all things: bright Zeus, life-bringing Hera, Aidoneus and Nestis,

Who causes a mortal spring of moisture to flow with her tears" (*DK31B6*).

"Fire and Water and Earth and the boundless height of Air" *(DK31B17).*

"There is no creation of substance in any one of mortal existences, nor any end in execrable death, but only mixing and exchanges of what has been mixed, and the name 'substance' (*Phusis*, '*On Nature*') is applied to them by mankind" *(DK31B6).*

Empedocles gives divine names to the roots (Primavesi 2008). Fire is identified either with Hephaestus and /or with Zeus, the father of gods. Air is named Hera, Earth is Aidoneus (god of Hades) and Water, Nestis (Sicilian water-goddess). Interestingly there are two males (Zeus, Aidoneus), two females (Hera, Nestis), two divine (Zeus, Hera) and two terrestrial (Aidoneus, Nestis).

How do the roots mix?

Empedocles solves the puzzle with talent and originality by the mixing of the elements:

"How by the mixture of water, earth, air and sun (fire) there came into being the shapes and colours of all mortal things that are now in being, put together by Aphrodite" *(DK31B71).*

"For all of these – sun, earth, sky and sea – are at one with their own parts which are scattered far from them in mortal things". *(DK31B22).*

Thus according to Empedocles, the ordinary stuff around us is a determinate combination of the four roots. Aristotle supported Empedocles' originality in that he was the first to speak of four elements. Although Pythagoreans had also made use of four elements, only with the work of Empedocles did they become true *"Archai"*. In fact, none of the elements is more important to any other, none is more fundamental to any other, there is specificity:

"all these [elements] are equal and of the same age in their creation; but each presides over its office, and each has its own character, and they prevail in turn in the course of Time". (*DK31B17*).

"And earth happened in roughly equal quantity on these,/ Hephaestus, rain, and all-flashing *aithêr*/Anchored in the perfect harbors of Love, / Either a little more [of earth] or less in more of them,/ And from them came blood and other forms of flesh". (*DK 31B98*)

"[The elements] uncreated". *(DK31B7).*

"From these [elements] are all things fitted and fixed together, and by means of these do men think, and feel pleasure and sorrow" (*DK31B107*).

The roots are ungenerated, indestructible, unalterable, homogeneous, in motion, and divisible, thus anticipating the corpuscular nature of matter which also Galen attributed to Empedocles. In addition, according to Empedocles, perception occurs by similar means.

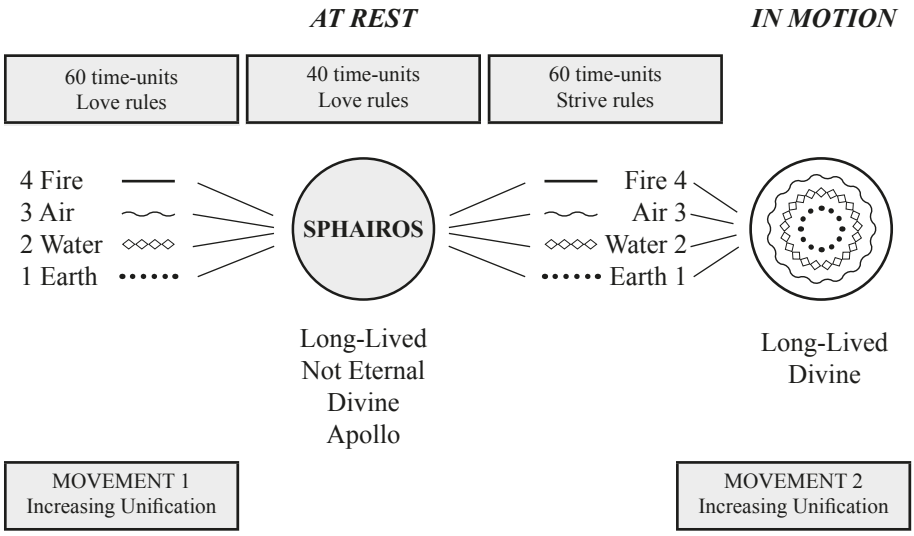
"We see Earth by means of Earth, Water by means of Water, divine Air by means of Air, and destructive Fire by means of Fire; Affections by means of affections, Hate by means of baneful Hate. (*DK31B109*).

Thus appropriately Hankinson (2008) stated that "here for the first time we have a fully developed element-theory, in which the stuffs of the world are supposed to be reducible to specific compounds of the fundamental elements, elements which do not transmute, but remain intact in the compounds and serve to explain reductively, the nature of those compounds".

Living organisms and inanimate things were made by the four roots (Air, Fire, Water and Earth) mixed under the influence of Love and Strife.

"When love dominates there is a motionless Sphere in which roots are thoroughly mixed that none can be discerned. Strife then gathers force and breaks up the sphere, under his power a separation of roots occur until they are completely segregated from one another". (Empedocles, *On Nature).*

The four roots were a tool to understand and to explain things (Primavesi O., 2008, De Santo NG et al, 2011). Thus the physical world is subject to rational explanation and can be understood (Figure 1). Four roots under the control of Love, adhesive Love (Aphrodite, Harmony, Cypris, Joy) and Strife (discord, hate, wrath). Four roots, irreducible, underived, imperishable, equal and of the same age, each ruling in its town-province.



"I shall tell of a double process: at one time it increased so as to be a single One out of Many; at another time again it grew apart so as to be Many out of One. There is a double creation of mortals and a double decline; the union of all things causes the birth and destruction of the one, the other is reared as the elements row apart, and then flies asunder. All these elements never cease their continuous exchange, sometimes uniting under the influence of Love, so that all become One, at other times each moving apart through the hostile force of hate". (*DK31B17*).

In this system the elements remain unaltered and follow the cyclic process described in Figure 1. Thus all is made of four roots immutable, indestructible, ingenerated, qualitative unalterable, homogenous, in motion, and divisible. Each element has its own individuality. No one element was superior to another. Elements capable of mutual transformation, sentient, immortal, everlasting, divine. They were gods, even in their mixture in the Sphairos. Having the capability of commuting one into another, having motion, being divisible, they mingled and the mixture had no birth, no death (Primavesi 2008).

"But in [the reign of] Wrath they are all different in form and separate, while in [the reign of] Love they come together and long for one another. For from these [elements] come all this that were and are and will be; […]. For these [elements] alone exist, but by running through one another they become different; to such a degree does mixing change them" (*DK31B21*).

Table 2. Tissue structure according to Empedocles. From De Santo NG et al.(2011) with slight modifications.

Eye	[is produced when] "the benevolent flame [of the eye] happened to obtain a slight admixture of the Earth".
Flesh	"is the product of an equal blend of the four elements".
Sinews	[are the product] "of Fire and Earth mixed with double amount of Water".
Sweat and Tears	"occur when blood is diffused in addition to thinning out".
Nails and Claws	are the "product of sinews cooled down by meeting Water".
The Ear	is[a kind of] bell. It is a fleshy shoot".
Blood	[is made of] "about equal proportions of Earth, Hephaestus, Moisture and Aeter". The ratio is 1:1:1:1:
Bone	[originated when] "Earth received two parts of the shining Nestis, four of Hephaestus". The ratio is 4:2:2 or 4:2:1.

Bone structure

In a previous paper dedicated to the roots of Empedocles (De Santo et al. 2011) we have discussed how they participate in the genesis of various tissues. For the purposes of this paper, we wish to depart from Aristotle, who in *De Anima* states that bone is made up of four elements mingled by chance, under the influence of Love, according

to a mathematical ratio named *lógos*, as explained by Aristotle in *De Anima:*

"The kindly earth received in its broad melting-pots two parts of the glitter of Nestis out of eight, and four of Hephaestus. And they became white bones, wondrously joined by the cement of Harmonia" (*DK31B96 96*).

"Bones are the product of two parts of water and earth, and four of fire when these parts have become mixed together inside earth" (Aetius, *DK31A78*).

"The spine [acquired its present form by being broken (divided into vertebrae) when the foetus turned its neck]" *(DK31B97).*

"Bone is by virtue of a ratio which is the essence and the reality" (Aristotle*, Metaphysics*).

On the hardening role of fire

Thus bone is made up of four parts fire, two parts water and two parts earth for a total of eight parts. Fire provides the whiteness and the dry hardness.

"Just then Cypris, busy about forms, after moistening the Earth mixed with water gave it swift fire to harden it up" (*DK31B73*).

"Fire the element that hardens the moon" *(DK31A54).*

"The element that hardens the rocks, stones and thermal waters (*DK1A68*).

W.K.C. Guthrie (1965b) acutely stressed that "Even in the eighteenth century the elements of the body were Earth, Water, Air and Fire. In fact J.F. Gmelin in his Einleitung in der Chemie of 1780 said that "we have very good reasons to allow the names of elements to fire, water, air and earth if we imagine them in their greatest purity."

Proportion, logos, chance and necessity

Organic substances are made by elements in various proportions. The proportion is a chance outcome of the interaction of Love and Strife. Proportion means *logos,* however *logos* may also mean thought as well as the result of thought. The most appropriate name seems chance, however it might be safe to speak of necessity. Simplicius (*Physica 331.10*) wrote that chance is found on many occasions in Empedocles' work, however, he never explains what it is. Of course chance was opposed by Plato and Aristotle who defined it as "a cause not manifest to human reason". (Guthrie W.K.C. 1965c).

Logos was used by Aristotle in explaining Empedocles' theory on bone (*De Anima* 409b32). The same happened when Simplicius spoke about bone (*Phys* 30.19). Furthermore, Aristotle (*Metaphysics, 993a17*) points out that "Empedocles says bone exists by *logos*, that is the essence and substance of things". In *De Partibus Animalium* (642a17) Aristotle says that for Empedocles

"the essence or nature is the *logos*, for instance when he explains what bone is, for he defines it not as one of the elements, or two or three or all of them, but as the *logos* of their mixture".

According to Plato, Empedocles' followers affirm: "fire, water, earth and air exist by nature and chance, none of them built as a work of art by an artisan, from those inanimate elements, earth, sun, moon and stars originate. Now these stars are in motion by chance, each of them according its own inclination, meet while falling down and adapt according to their qualities warm with cold bodies, dry with humid, soft with hard, and all of them in chance combination of contraries, are necessarily mixed" (Plato, *Laws* X899B).

Table 3. Chance and Necessity in Empedocles.

Chance	Necessity
But the benevolent flame [of the eye] happened to obtain only a slight admixture of Earth". *(DK31B85).*	"Ananke is Love/Strife". *(Plutarch)*
"By the whim of chance all things think". *(DK31B103)*	"The decree of Ananke" *(Fr 115)*, Hyppolitus)
"in so far as the finest bodies met by chance in their fall". *(DK31N104)*	"Ananke a third causative cause" (Simplicius)
	"The action of Love and Strife is a necessity" (Aristotle).
	"They make things happen "necessarily by chance"(Plato)
	"But he suggested no cause for necessity (Aristotle, *Methaphysics* 1000b12)
	"The internal motive powers of the roots themselves"(WKC Guthrie, 1965)

Aristotle quoted Empedocles on many occasions including *Timeus, Metaphysica*, *Poetica*, *Rethorica I:* "More than any other pre-Platonic philosopher, perhaps the coherence of Empedocles' doctrine, which was stronger than for any preceding thinker". (Gallavotti C, 1975). As pointed out by Kenny (2004) "Aristotle praised Empedocles for having realized that a cosmological theory must not just identify the elements of the universe, but must assign causes for the development and intermingling of the elements to make the living inanimate compounds of the actual world". Of course Aristotle rejected chance, he looked for design. However Empedocles had the last laugh when Darwin saluted him for foreshadowing the principle of natural selection".

CONCLUSION

In conclusion, according to Empedocles, air, water, earth and fire were used to start the study of body composition. The joining together of the roots occurred according to proportion, logos, chance and necessity. In this sense, bone is more than tissue, it marks the beginning of quantitative chemistry. Empedocles for the first time describes the fundamental elements of all materials which combined harmoniously according to principles governed by their differences.

ACKNOWLEDGEMENTS

For translations of the fragments, reference is made to:

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b) Warren J. Presocratics. University of California Press, Berkeley, 2007.

ABBREVIATIONS

DK = Diels H. Die Fragmente der Vorsokratiker, 3 vols. Kranz W. Ed., 6th Edition. Zurich, Weidman 1951–52. This book includes all extant writings of all Presocratic authors. Each author is assigned a number, of which, 31 is for Empedocles. Entries are numbered as (a) testimonia, that is ancient accounts of the author's life and doctrine, (b) ipsissima verba reporting the exact words of the author, and (c) imitations that false the author as a model.

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