

## The evolutionary approach: the lost dimension of medicine

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### Abstract

The results of a meta-analysis on the use of calcium supplements by women, “strongly suggest a relatively modest risk of myocardial infarction and stroke”. Although the authors acknowledge the inherent limitations in such studies, they recommend “a reassessment of the role of calcium supplements in the management of osteoporosis.” As possible underlying mechanisms, they suggest that a regulated vascular calcification process similar to osteogenesis occurs, and the possibility that excess calcium contributes to the risk of arterial thrombus formation.

This essay is not intended to recommend changes in the clinical use of calcium supplements or to suggest a deeper analysis of the mentioned and other mechanisms. It seeks to analyze the problem according to the principles of Darwinian medicine. It is important to bear in mind that the evolutionary approach tries to explain the vulnerability to disease of *Homo sapiens* as a species. Although there is no doubt that individual susceptibilities to virtually all diseases may be present, with very few exceptions, the expectations of the Human Genome Project, in terms of examples and of the relevance of predisposing genes, have been far from fulfilled. It is reasonable to assume that the interest in this forgotten dimension of biomedicine -entirely ignored in the aforementioned article- could help to better understand the origin of medical problems such as the one related to the use of calcium supplements by women, and even to guide research and application of “personalized medicine”.

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The results of a meta-analysis on the use of calcium supplements by women, “strongly suggest a relatively modest risk of myocardial infarction (MI) and stroke”<sup>1</sup> Although the authors acknowledge the inherent limitations in such studies, they recommend “a reassessment of the role of calcium supplements in the management of osteoporosis.” As possible underlying mechanisms, they suggest that a regulated vascular calcification process similar to osteogenesis occurs and the possibility that excess calcium contributes to the risk of arterial thrombus formation.

This essay is not intended to recommend changes in the clinical use of calcium supplements or to suggest a deeper analysis of the mechanism mentioned or of any other one. It seeks to analyze the problem according to the principles of Darwinian medicine (DM).<sup>2</sup> It is important to bear in mind that the evolutionary approach tries to explain the vulnerability to disease of *Homo sapiens* as a species. Although there is no doubt that individual susceptibilities to virtually all diseases may be present; with very few exceptions, the expectations of the Human Genome Project, in terms of examples and of the relevance of predisposing genes, have been far from fulfilled. It is reasonable to assume that the interest in this forgotten dimension of biomedicine- entirely ignored in the aforementioned article- could help to better understand the origin of medical problems such as the one related to the use of calcium supplements by women, and even to guide research and application of “personalized medicine”. It is important to remember that:

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**Abbreviations:** DM, Darwinian Medicine; MI, myocardial infarction; CVA, cardiovascular accident (stroke).

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DM is not intended to replace current biomedical research (proximal causes, mechanism, how?). Rather, both approaches complement and provide feedback to each other (evolutionary causes, why?)

The authors' analysis of the physiological and molecular mechanisms of the calcification process seeks to answer how; this is, the immediate or proximal cause of the problem. This is an example of the traditional approach of scientific medicine (Box). The evolutionary question is why; this is, the root or distal cause of the problem.

In order to analyse the case, it is necessary to take into account the following two postulates of DM:

- Natural selection does not design organisms so that they are healthy, unless health contributes to reproductive success.
- Vulnerability to disease may originate partly in antagonistic pleiotropy (George C. Williams), which means that genes barter beneficial traits at an early age for detrimental ones at older ages.

It is interesting to note that the authors of the article present some evidence that the mechanism of calcification in the arteries is similar to osteogenesis. Although there is no evidence yet of antagonistic pleiotropy in humans (despite being abundant in the case of other species), this essay portrays an inspiring hypothetical example of the action of a gene that provides adaptive value (ability to reproduce) by enhancing early fixation of calcium, thus allowing for more efficient repair of fractures at the price, however, of the possibility of coronary artery calcification at older ages.<sup>3</sup> The central issue is that around the Paleolithic period, when humans were hunters and gatherers, life expectancy was 35 to 40 years. Individuals were more likely to die early as a result of accidents and attacks by wild animals. Therefore, natural selection is "indifferent" to a greater risk of MI and other problems that occur mostly at older ages, which are beyond the "reproductive peak" (25 to 30 years old).

Since evolution is slow, the human genome is about the same as 10 000 years ago, when farming and domestication of animals began. It is reasonable to assume that during the period of hunters and gatherers, natural selection led to the emergence of genes that favoured a better assimilation of calcium because sources were scarce as dairy did not exist.

The article's authors point out that, according to experimental studies in rats, excess calcium can promote thrombus formation.

Taking this into consideration, it is possible to better visualise the context in which the problem of a likely increase in the risk of MI and stroke due to calcium supplements develops. Our adaptation occurred as a result of the selective

### Box. Determinism, teleology and evolution

Claude Bernard states in his work *An Introduction to the Study of Experimental Medicine*, that research in biology and medicine should be limited to the how and never to the why... of a phenomenon. In Darwinian medicine, the why is related to "what is the reason for" rather than "for what" (Mayr). Bernard dismissed this latter finalist connotation, "why", and it has been properly excluded from the hypotheses of experimental medicine. Natural selection has no direction or purpose. *Teleology*, or Aristotle's idea that there is a goal of human perfection (orthogenesis) that sets a direction to the evolutionary process has been definitely ruled out.

pressures of an environment very different from the one in which we live in today. It was selective to achieve an efficient repair of fractures and coagulation, which is obviously also beneficial to modern humans. However, with increasing life expectancy, the price paid is problems to which natural selection is indifferent. Given that apparently osteogenesis and calcification in arteries share a common mechanism, it is reasonable to question, why does it remain "selectively active in a perverse manner" at older ages, damaging the cardiovascular system, while allowing the development of osteoporosis. The evolutionary answer is that osteogenesis requires other factors and natural selection, which is sloppy, does not invest metabolic energy in keeping the body healthy at older ages, the "disposable soma" (Kirkwood).

Given these findings and hypotheses, it is valid to assume that the risk of MI and stroke that comes with calcium supplements may result from "fanning a flame" for which natural selection had no interest in turn it off, and that arose during evolution in very different environments.

It is crucial to remember that the human body is the result of thousands and even millions of years of evolution and not a machine that can simply be repaired in all cases.

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