The bone as a metamorphosis and the bisphosphonates!*

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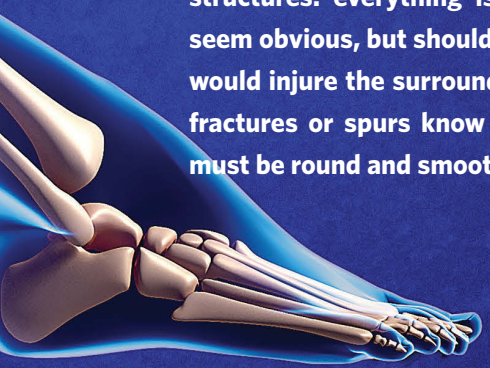
Raul Seixas, one of my favorite Brazilian singers, has continuously played in my iPod. One of his songs used to say: "I would rather be a wandering metamorphosis, than have the same old opinion about everything!" One of these days, a lady complained about the fact that her 35-year-old husband had left her four years before. After that, I heard that he had come back with an exciting talk: "Honey, I am back. Now, I am a new man, I have changed, everything is new!"

Although he was trying to deceive his lover, the man was right. The human skeleton has 206 bones, all of which are well and impeccably formed so as to meet our functional demands as well as absorb or exert forces when we move. Our bones, together with muscles and tendons, take us to every corner of the globe. If you go to a museum where human skeletons are displayed, you will see the shape of the bones, how they articulate or relate themselves with other parts of our body.

Our bones do not have corners, live edges or sharp structures: everything is smooth and round. It may seem obvious, but should our bones not be round, they would injure the surrounding soft tissues. People with fractures or spurs know how painful they are. Bones must be round and smooth.



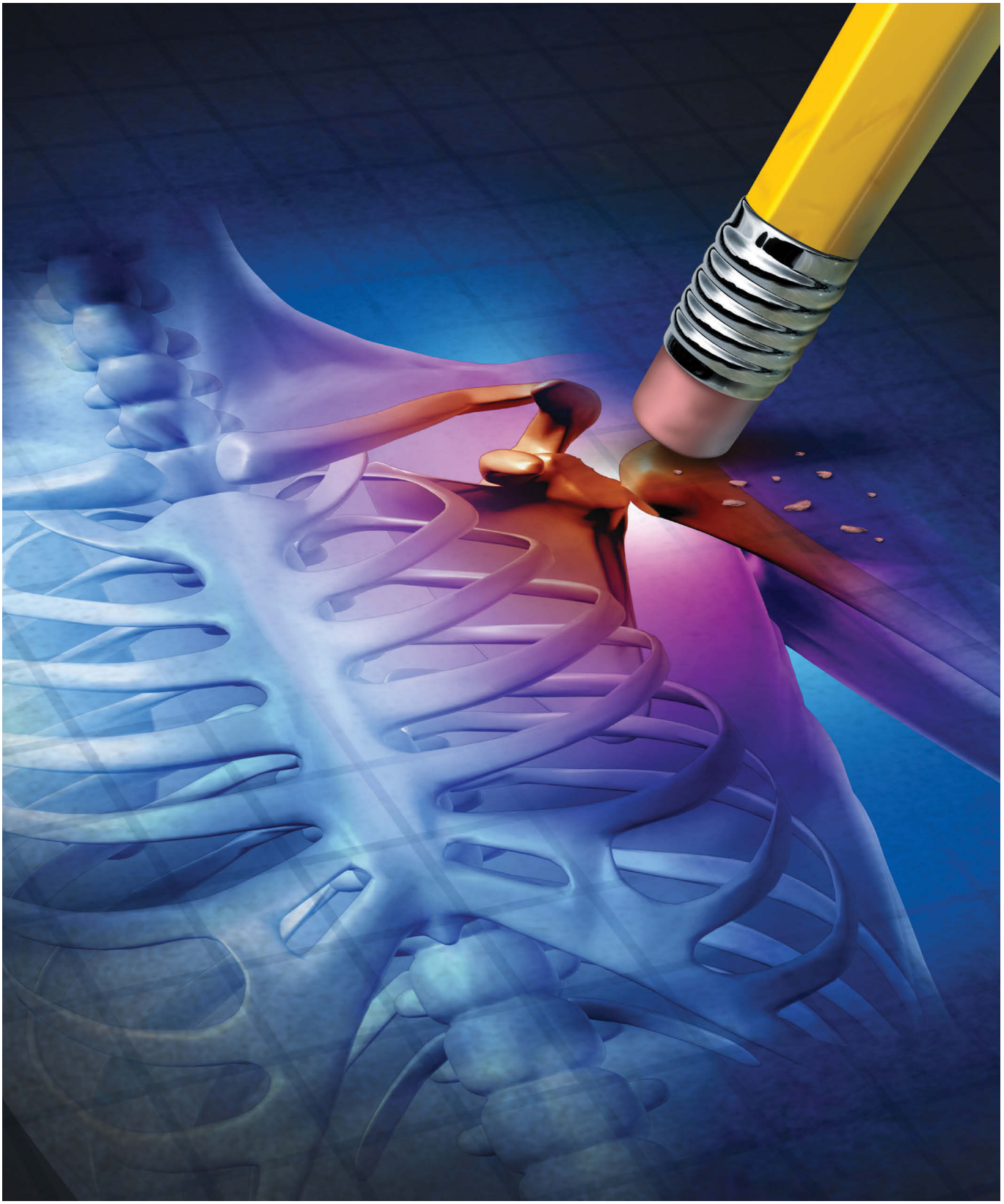
Whatever is vital is protected by bones: the brain, heart and lungs, as well as the marrow that produces the liquid responsible for giving us life and defense: the blood. Bones are dazzling structures with many different variables: cartilage, tendons and joints. They even come in a gift wrapping paper: their outer surface has a resistant and protective membrane, the periosteum.

Athletes' bones are thicker and more mineralized, with adjusted structure and design. Conversely, sedentary people's bones are thin, less dense and less mineralized. We tend to consider the bones as hard and resistant structures. But, in fact, they are flexible, adaptable structures that meet all our functional demands. The skeleton is an excellent partner, but we usually ignore that!

How can the bone be like that? A skeleton of a young adult renews itself every 4-5 years, in other words, our skeleton is under continuous transformation. The husband was right, he did not lie when he claimed to be a whole new man. At least his skeleton had changed.

Let's make it clear: the brain does not renew itself, and that must be the reason why that stubborn is known as hardheaded, in which case it is not the bone's fault!

* Extracted and adapted from the book 'Queremos Saber' (We want to know), Ed. Idea, Bauru, 2013.



The mineralized bone structure has millions of tiny little lacunae as small as spider-shaped cells. The osteocytes have from 20 to 50 cytoplasmic extensions randomly distributed along the hard surface of the bone. Each one of these cells are connected with more 20 to 30 cells. Try to imagine many spiders holding hands with more 20 to 30 spiders. The osteocytes form a network inside the bone. When we apply force while moving, a deformation process occurs due to stretching or compressing. The network formed inside the bone apprehends these changes in shape and immediately sends chemical products to the inner or outer surfaces with the following message: change your current shape; we need to adapt ourselves to the new situation, improve the design. Every day, bone design is adapted to use. A show of flexibility, adaptability and will to serve.

Bone surface cells resemble masons: the clasts demolish coatings and walls, whereas the osteoblasts build up and reinforce pillars and structures. Researches reveal that surface cells are more and more controlled by osteocytes. The same osteocytes scientists believed to be lost and isolated in the mineralized matrix: scientists were certainly mistaken!

If you wish to strengthen your skeleton, deform and stretch your muscles and tendons so as to deform and stimulate the osteocytes network to adapt its design as you wish! Should the osteocytes be discouraged and inactive, they will not be stimulated to renew the skeleton and adapt it to different lifestyles. Bones will become more and more fragile, less thick and less resistant: it is up to you to decide! Should you like it or not, at least your skeleton is a wandering metamorphosis! This process is known as bone remodeling or turnover.

Our machine is incredible: remodeling provides the blood with calcium, a vital ion. A balance is established in this wandering metamorphosis: blood calcium must be stable; the skeleton must have a structure that agrees with its function. What is hard as bone is flexible and adaptable; and balance arises of an ongoing and wandering metamorphosis! We always have a lot to learn with our body. It is incredible!

Bisphosphonates and bone biology

Calcium is present in most chemical reactions and plays an important role in most functions performed by our body. New cells need it and are at risk of dying if its levels in the blood are too low or too high. When its levels in the blood are low, the parathyroid glands release into the blood a substance known as parathormone which enhances the release of calcium from the bones, resulting in a transfer of calcium from bone fluid to the blood. When its levels in the blood are too high, thyroid cells release another hormone, calcitonin, which hinders bone resorption and reduces blood calcium.

It happens during the entire day: levels of calcium increase and decrease as we go on with our lives. To hinder bone resorption, calcitonin counts on the help offered by estrogen.

When the normal function of parathyroid and thyroid glands is no longer fulfilled, there may be more or less bone resorption. Should it be beyond normal conditions, the mineralized bone structures known as trabeculae and cortical become thin and fragile. This condition is known as osteopenia. In this condition, bones are subject to fracture in tiny areas or as a whole, and should it happen, osteopenia with fracture is defined as osteoporosis.

In menopausal women, there is loss of estrogen, a hormone that helps calcitonin to hinder bone resorption. In this case, daily bone remodeling is sped up, given that one of the elements that controls or hinders it, the estrogen, is absent. Women's skeleton may present osteopenia or even osteoporosis.

No consensus has yet been established with regard to the advantages and disadvantages of estrogen hormone replacement therapy. In the last few years, this subject has not been on focus due to the emergence of a group of drugs known as bisphosphonates. Millions of women make use of this medication to control or prevent osteoporosis. The type of bisphosphonates most widely used is the alendronate, under different trademarks.

Bisphosphonates reach the blood and easily combine with circulating calcium. Wherever calcium goes, the bisphosphonate molecule goes along, reaching the entire body within weeks. Women under use of bisphosphonates will never have bone calcium alone; it will always be followed by something else. When the clasts (bone resorption cells) absorb calcium, they also absorb bisphosphonates that promote or speed up apoptosis. Clasts that used to be found in large amounts in the skeleton subject to osteopenia and/or osteoporosis are now found in amounts lower than normal and remodeling reestablishes its normal flow, similarly to what happens to a non-fragile skeleton.

In other words, bisphosphonates prevent, reduce and even eliminate osteopenia and osteoporosis. Since millions of women use this type of medication, imagine all the money and financial interest involved. Laboratories that do not hold a patent seek other alternatives and continue raising doubts about the efficacy of bisphosphonates and spreading their potential side effects.

These are minor, occasional and questionable effects that include femur fracture, association with esophagus cancer and maxillary bone necrosis, especially when alendronate is used. Researchers with no commercial interests acknowledge that the benefits overcome the side effects.

After carrying out a number of studies, the FDA questioned the benefits of long-term use of bisphosphonates for more than five years. The main question is: How long should bisphosphonates be taken in order to prevent osteopenia and osteoporosis? Studies suggest that in women with high risks of fracture, the long-term use of bisphosphonates is more beneficial, in which case is worth taking the risk. When the risks of fracture are lower, the cost-benefit relationship must be carefully analyzed.

Should there be any doubts, ask your doctor how you should proceed, because some published work is opposed to many scientific reports and that is how science works: whenever there is truth, it is ephemeral and when it remains, it will always be questioned!

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