LETTERS

Osteoporosis: A Cautionary Note

Jean L. Marx, in her excellent article about osteoporosis (Research News, 8 Feb., p. 628), suggests that imbalance between two competing processes—resorption, in the form of dissolution of the calcium-containing mineral, and bone formation—could be at the heart of the osteoporotic puzzle. We would like to comment on some aspects of this pattern.

Morphological data characteristically show osteoporotic bone trabeculae to be less numerous and thinner than normal ones (*1*). However, this phenomenon is not the net result of a bare loss of mineral combined with a loss of organic matrix, it is accompanied by physical and chemical modifications of the mineral and organic phases of the bone.

Osteoporotic bone trabeculae (the inner part of bone, as opposed to cortical bone, the outer weight-bearing structure) have a higher specific gravity and a higher calcium content per unit weight (*2*) or volume (*3, 4*) correlating with higher calcium and phosphorous-to-hydroxyproline ratios (*5*). Thus, osteoporotic bone is more porous and more mineralized; this if anything, could account for its being more brittle.

In addition, components are more homogeneous in osteoporotic bone than in normal bone: magnesium content (*4*) and noncollagenous proteins (*4, 6*) both decrease with age and, in osteoporosis, show a negative correlation with specific gravity and calcium content (*4*); furthermore, the collagen molecules of the matrix become less extractable with age (*3*), suggesting stronger cross-links; hence a greater degree of homogeneity and a higher order of organization are achieved in osteoporotic trabecular bone, while the crystallinity of cortical bone has been shown to remain unaltered with age (*7*).

We can speculate therefore that, in order to reverse osteoporosis, any agent influencing the balance between bone deposition and resorption should also be able to reverse the time-dependent evolution of extracellular trabecular bone components toward a more compact and orderly structure.

Basic knowledge of the physics and chemistry of extracellular bone components in humans is still scanty with respect to age groups and in view of the vast problems arising from the mere effects of time [and weightlessness (*8*)] on bone components; more extensive studies of the latter are particularly indicated and caution is justified when optimistic statements are made claiming reversal of osteoporosis on the basis of an exclusively biological approach, no matter how well substantiated experimental results might be.

People in affluent societies expect to lead an active life beyond menopause or andropause. How much such expectations justify the needed heavy investments in view of the population explosion and the ever-widening gap between developing and affluent societies is a matter where self-interest, scientific interest, and worldwide policy are difficult to disentangle.

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The "Ellipsoid Algorithm"

Gina Bari Kolata's article (Research News, 2 Nov. 1979, p. 545) on the algorithm for linear programming (LP) published by L. G. Khachian was the first report on it to the general scientific community. Since then, amid a flurry of comment in the press, many applied mathematicians (and others) have studied it, tried it out, and proposed improvements. The Mathematical Programming Society (MPS) has received 42 technical papers written about the algorithm since Gács and Lovász presented their version at the Tenth International Symposium of the MPS in Montreal last August. These papers are listed in a bibliography (*1*), along with relevant previous work and some of the subsequent press coverage.

Eighty researchers attended the MPS "Workshop on polynomial-time algorithms for linear programming" held in New York on 8 February. The 17 reports presented and lively discussions added much to our knowledge of the subject. There are no written proceedings, but most of the short presentations were extracted from authors' longer written papers reviewed in (*1*).

We learned that most of the algorithm Khachian used is the work of other Soviet mathematicians: D. B. Yudin and A. S. Nemirovsky of Moscow, and N. Z. Shor of Kiev, whose article (*2*) states the algorithm in its clearest form and also its best form for practical computation—not only for LP, but for the much more general "convex programming" problem. Because of the multiple authorship and the basic idea—the generation of numbers which, geometrically, describe a sequence of ellipsoids which must all contain a solution and which shrink, so that it is eventually identified—we agreed to refer to it and its near relatives as the "ellipsoid algorithm" (EA). (Khachian showed that, for one EA variant, each step, and thus the whole algorithm, could in principle be executed in "polynomial time" on a suitable computer. That was the finding which excited theoretical computer scientists, since the simpler versions of the generally used method for solving LP problems, Dantzig's "simplex method," have been shown not to run in polynomial, but in exponential time, in the worst case. "Worst case" behavior is always the easiest to study; a theory of "average" behavior, which would explain the fact that, in practice, the simplex method acts like a highly efficient polynomial-time algorithm, does not exist. Misconceived as applying to the traveling salesman and other "NP-complete" problems, Khachian's result overexcited some journalists.)

There is agreement that Khachian's variant will not be used. In both theory and practice it can take thousands of steps to solve trivial problems. A typical real problem of good size might require, say, 1 hour of high-speed computer time to be solved by the simplex method. The computer time for Khachian's variant would be about 50,000,000 years (it is an algorithm for which the "worst case" and "average" behavior are not far apart).

The idea of the EA, though, is intriguing and admits a large number of possible improvements, to which most of the papers at our workshop were directed: the starting ellipsoid chosen can be much smaller than early work indicated; the sequence can often be made to shrink much more rapidly (the way of doing that was discovered independently by 16 of the 42 authors); there are better ways of formulating the LP problem for solution, ways to reduce its size as the EA progresses, improved "stop rules," and proposals for hybrid methods that would use the EA to locate a rough solution which could then be polished off by the simplex method.

Perhaps in combination these ideas will improve the computing speed by several orders of magnitude, and a few hope that, after enough development, the EA will overtake the simplex method for LP. Since the simplex method was invented in 1947, improvements in the algorithm itself are thought to have speeded it up by no more than a factor of 10; the more important development has been the exploitation of "sparseness," the fact that almost all the data in the large matrices used are zeroes and need not enter into the arithmetic. This could account for a factor of 100 in the problem mentioned above, which thus might require 1000 hours, or 0.1 years, using the original version of the simplex method (and 10,000 years on a 1947 model computer). It seems the EA would not have competed with the simplex method had it been available in 1947; what's worse, no one has yet seen how to use the valuable "sparseness" devices in the EA.

One can, however, say this for the EA: it solved a significant theoretical problem and can be used to solve others; it may still be practically useful for the difficult nonlinear problems that Shor deals with; and it certainly brought a new kind of excitement to one area of applied mathematics.

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A Second "Random Walk"

For a second edition of *A Random Walk in Science* (Crane-Russak, New York, 1974), I should welcome contributions of humor in science, historic and contemporary: anecdotes, witty accounts, cartoons, self-deceptions, and hoaxes. Especially sought are items which, while humorous, also have value for history and insight—in all fields of science. Please identify fully the sources of contributions.

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