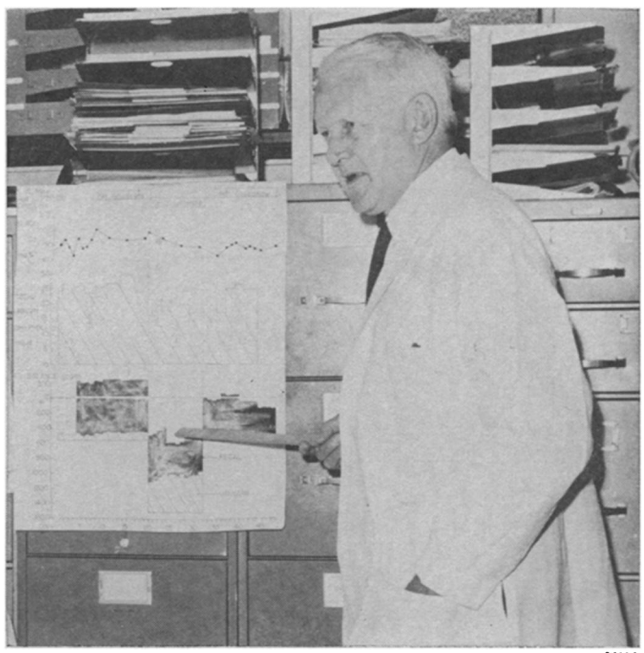
Repairing brittle bones

Calcium infusions appear to change the course of osteoporosis

by Barbara J. Culliton



NIH

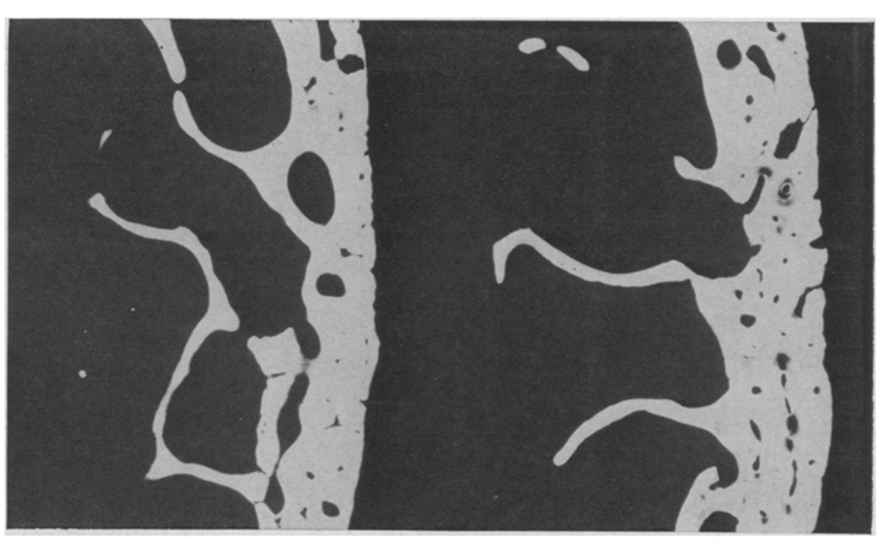
Dr. Frederic Bartter: Correcting the metabolic error.

Almost everyone who lives to be 80 develops osteoporosis, a condition that literally means porous bone. It is well known that the elderly are prone to broken bones under circumstances that pose no hazard to younger people. In some instances, ribs and other bones even fracture spontaneously.

While osteoporosis is generally associated with aging, it is a disease by no means confined to the elderly. When it occurs in young men and women, the diagnosis goes by the name of idiopathic osteoporosis, which is used to mean: "We don't know the cause." In any case, there has been very little physicians could do to ameliorate or reverse the course of bone thinning.

Some insights into the condition and a therapeutic approach to osteoporosis are emerging from studies by Dr. Frederic C. Bartter and his colleagues in the endocrinology branch of the National Heart and Lung Institute in Bethesda, Md.

Individuals with osteoporosis have too little bone, which means that they are experiencing too much bone dissolution, or calcium loss, or too little bone formation, or both. Dr. Bartter hypothesizes that this phenomenon is due to a metabolic error resulting in an imbalance in two key hormones. The first is parathyroid hormone, PTH. Secreted by the parathyroid glands in the neck, PTH dissolves bone, releasing calcium into the blood. The second is thyrocalcitonin, a hormone that prevents calcium loss. "When these hormones are out of balance," he speculates, "you get osteoporosis. The disease may represent a state in which you have relatively too much PTH secretion or relatively too little TCT secretion."



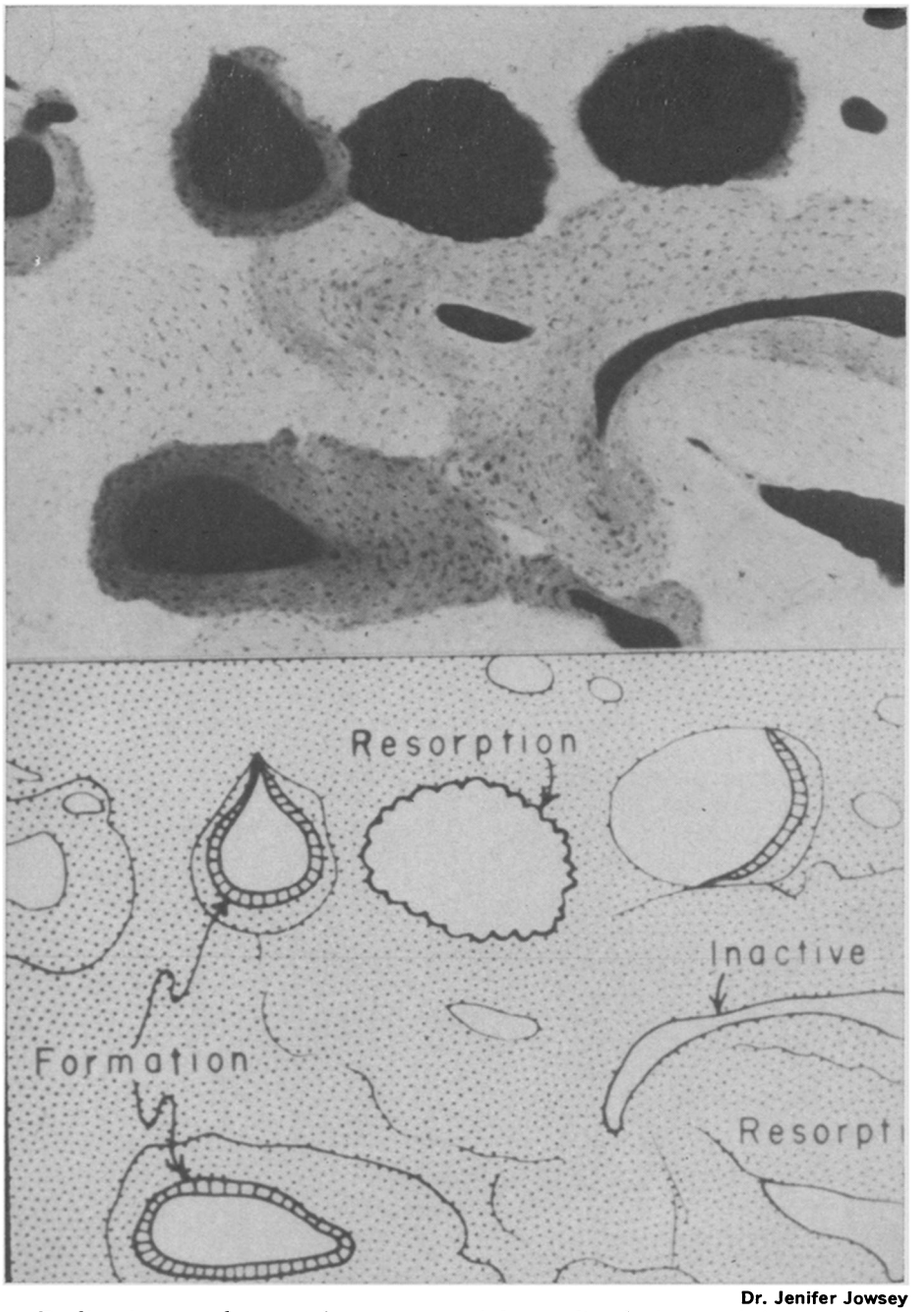
Dr. Jenifer Jowsey

Porous bone (left) begins to regenerate after a series of calcium infusions.

Conveniently, the secretion of both hormones is regulated by the concentration of calcium ions in the blood. When there is a decrease in calcium, PTH secretion is stimulated as a compensatory measure. The hormone dissolves some bone and calcium is released to raise the blood calcium to normal limits. A severe increase means overcompensation and abnormal bone loss. On the other hand, too much blood calcium triggers another compensatory action. High calcium levels, or hypercalcemia, stimulate thyrocalcitonin secretion. The TCT then blocks PTH activity and bone dissolution ceases.

Having identified what is probably the metabolic error in osteoporosis, Dr. Bartter, with Catherine Delea and Drs. Charles Pak and Myron Lifschitz, reasoned that the course of bone loss could be controlled by deliberately creating hypercalcemia in osteoporotic patients. Initial trials were conducted with six individuals, four of whom responded well. As of now, treatment has been applied to 12 individuals, all under 65 years of age.

Either consecutively for 12 days, or over a period of 21 days, these patients received infusions of calcium, each intravenous infusion lasting up to four hours. Almost immediately, most of these individuals, known to be free of other types of hormonal disease, began laying down bone. Improvement was measured by biochemical tests indicating a restoration of PTH-TCT balance; in clinical terms an absence of pain and a renewed ability to sustain normal physical activity without bone fracture was noted.



Dr. Jenifer Jowsey

Radiomicrographs reveal processes of bone dissolution and formation.

The effects of calcium infusions last for several months at least. One patient has been in hormone balance and clinically improved for two and a half years after a single series of calcium treatments. It is this as yet unexplained phenomenon that leads Dr. Bartter to presume that calcium, administered intravenously, somehow corrects the metabolic error that leads to the disease.

"It appears," he says, "that calcium infusions lead to a prolonged suppression of parathyroid hormone function and a comparably enhanced stimulation of thyrocalcitonin secretion. They may reverse the metabolic errors, resetting to normal the aberration in the biochemical mechanisms for calcium homeostasis and thereby correcting the imbalance in rates of PTH and TCT secretion."

The key to this effect seems to lie in the fact that infused calcium stimulates the body's own production and secretion of thyrocalcitonin. Orally administered calcium, poorly absorbed from the gastrointestinal tract, is ineffective. Likewise, administering TCT itself has no prolonged beneficial result because it stimulates the parathyroid glands to overactivity.

The challenge now, of course, is to determine the mechanism by which calcium infusions so profoundly alter the metabolic pathways involved in PTH and TCT activity. In the meantime, however, calcium infusions, which pose no apparent danger to the patient and which can be repeated if the effect wears off, constitute a new and promising approach to the treatment of a previously untreatable disease. □