Fluoride-Calcium Combo Builds Better Bones

Texas researchers have developed and tested a new fluoride and calcium therapy for spinal osteoporosis, a type of porous bone disease that afflicts 5 million people in the United States, predominantly elderly women. "It's a new form of treatment designed to restore lost bone in a safe manner," says Charles Y.C. Pak at the University of Texas Southwestern Medical Center in Dallas.

Although past studies demonstrated the bone-building prowess of fluoride and calcium, enthusiasm over the treatment waned with reports of serious side effects (SN: 8/27/88, p.134). Tablets that dump large doses of fluoride into the stomach can corrode its lining and cause bleeding. Fluoride also can trigger abnormal bone development and cause joint pain and swelling.

"Our treatment has been designed to overcome these problems," says Pak, who together with the Mission Pharmacal Co. of San Antonio, Tex., developed a tablet that releases its fluoride gradually, minimizing gastrointestinal problems.

The Texas research team gave 65 patients with spinal osteoporosis 25 milligrams of slow-release fluoride along with 400 milligrams of calcium supplements twice daily. After 3½ years, Pak's group found patients had heftier backbones, with spinal bone mass increasing by 3 to 6 percent each year they were treated. Spinal fractures declined as well. The average patient experienced one fracture every eight months prior to treatment and one fracture every 4½ years after treatment.

The slow-release form of fluoride seemed to perform well. "We have not seen anyone with bleeding," Pak reports. Fewer than 5 percent of patients showed gastrointestinal problems, and just 6 percent complained of joint pain or swelling. Pak and his colleagues report a trial involving 44 patients in the January JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM. They say they will describe their study of 65 patients in the spring JOURNAL OF BONE AND MINERAL RESEARCH.

Fluoride therapy builds bone mass by spurring bone-making cells called osteoblasts. The osteoblasts produce a protein matrix that fills up with calcium deposits, which harden to make bone strong. Patients must take calcium supplements along with their fluoride, or they could end up with weak new bones.

Pak says further research may show the treatment helps all victims of osteoporosis, not just those with porous spinal bones. Osteoporosis afflicts about 20 million people in the United States and can affect bones of the hip, wrist and other body parts.

Pak expects to submit the spinal treatment to the Food and Drug Administration this spring, but he notes that it can take three to five years for a new drug to wend its way through the approval process. Until then, people with the disease must make their way to clinical research centers to get the new treatment.

Bone researcher B. Lawrence Riggs at the Mayo Clinic in Rochester, Minn., calls slow-release fluoride "a definite improvement" in reducing side effects. Mayo researchers and a team at the Henry Ford Hospital in Detroit are studying an osteoporosis treatment that uses regular fluoride rather than the slow-release type. But Riggs says he worries that fluoride-stimulated bone may be brittle and prone to breaks. The only way to obtain proof of the treatment's efficacy, he adds, will be to study it for many more years.

– K.A. Fackelmann

Sunshine fuels a bacterial relationship

Courtesy of Boyce Thompson Inst.

Novel bacteria form nodules on the stem of a plant.

Scientists have identified a bacterium that lives with and "fixes" nitrogen for certain plants, but uses the sun's energy instead of the plant's to survive. The discovery, which highlights nature's unexplored biological diversity, could someday be used to increase the yield of certain crops, says Ralph W.F. Hardy, president of the Ithaca, N.Y.-based Boyce Thompson Institute for Plant Research, where the work was done.

Although other photosynthetic, nitrogen-fixing bacteria exist, Hardy says these are the first such bacteria known to form symbiotic relationships with leguminous plants, a family including soybeans, alfalfa and peanuts. He is continuing the work of plant physiologist Allan R.J. Eaglesham, who first isolated the novel bacterium and has since moved to Enichem Americas, a research facility in Monmouth Junction, N.J. The bacterium, tentatively named *Photorhizobium thompsonum*, belongs to the genus *Rhizobium*, whose members form nodules or swellings on the roots of leguminous plants and supply the plants with usable nitrogen.

Root-living rhizobia draw carbohydrates and other energy-supplying materials from the plant, decreasing the amount of seed or vegetation the plant produces. They use about 12 pounds of plant material for every pound of nitrogen they fix, Hardy says. Although rhizobia normally appear on roots, under certain conditions they live on stems instead. For instance, stem nodules may appear on plants in flooded areas, where water cuts off oxygen and nitrogen needed for root nodules.

If made to live on stems, *Photorhizobium thompsonum* uses sunlight instead of plant resources for energy. "The plant material saved could be redirected in producing seed or forage," Hardy suggests. Photosynthetic rhizobia provide "exciting [agricultural] potential that seems realistic based on what we know about these [leguminous] plants, but the reality remains to be proven."

The researchers discovered the bacteria serendipitously after transplanting some plants dying from nitrogen deficiency into some sand they took from Virginia. After flooding the dying plants' roots to make nodules appear on the stems, they found the nodules were produced by a bacterium not known to be living in the sand.

Plant-living bacteria are a more cost-effective and environmentally sound way to provide plants with nitrogen than are synthetic nitrogen fertilizers, Hardy says. Fertilizers require huge capital and labor costs and are inefficiently used by the plant, which takes up only about half the nitrogen. Unused fertilizer runs off or seeps into the soil, polluting the environment. In contrast, rhizobia deliver nitrogen directly to the plant, Hardy says.

In order to use these bacteria to increase the yield of leguminous crops, scientists will need a better understanding of stem nodulation – specifically, how to make stem nodules in plants that do not have them. "We now do this experimentally by flooding the roots, but undoubtedly there are other ways," Hardy says.

In addition to exploring how the bacteria form stem nodules, Hardy is trying to discover what gives this rhizobium its special characteristics, whether other photosynthetic rhizobia exist and when such organisms appeared in evolution. *– I. Wickelgren*