to be identified. "EMBL should honor its contract" with the staff.

But at the moment, a slim majority of current staff is in favor of compromising. In a vote conducted by EMBL's staff association last month, 54% of the staff said they would be willing to accept the 2.1% figure, while 46% insisted upon the 8% interpretation. In a 23 November letter to the council delegates, which *Science* has obtained, the staff association warned that despite this slim majority in favor of the less costly interpretation, "individual members of staff would continue the case" by appealing to the ILO, and went on to urge the council to "consider implementing the 8% salary adjustment." Such an outcome "will be a substantial financial challenge to the laboratory," Kafatos told *Science*. But he says that he will argue "forcefully" that EMBL's scientific program must go ahead despite the costs. "The focus has to be on science."

That scientific program will be put under more pressure next year by the need to make up for the withdrawal of the European Union as a funding partner for EBI. Until the council can get government approval to increase its funding to EBI next March, the MRC has offered to loan EMBL enough money to keep the center running. "EBI is not out of the woods yet," says Graham Cameron, co-head of the institute. Cameron adds that although the council "has expressed a clear intention to insure that the 2000 budget will be up to the 1999 level ... our [$8.3 million annual] budget is still less than half that of our peers in the United States"—namely the National Center for Biotechnology Information (NCBI) in Bethesda, Maryland, whose yearly budget is about $19 million. Catching up with the NCBI is a key component of EMBL's 5-year plan for 2001–05, a draft of which Kafatos presented at the council meeting.

Despite these uncertainties, many EMBL scientists expressed satisfaction that the council had acted quickly to deal with the crisis. "The council has taken the high road, and that is very good for EMBL," Cameron says.

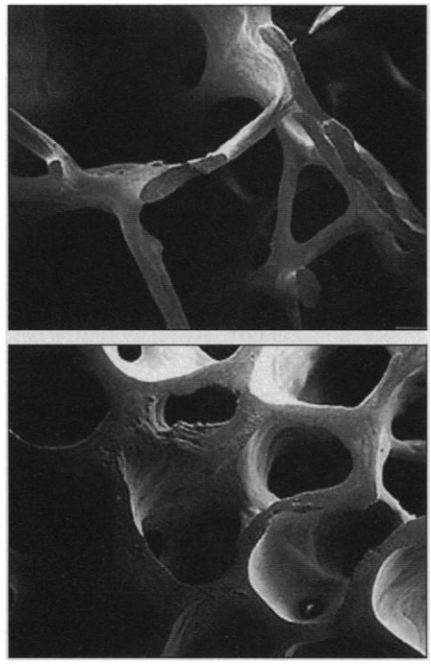
–MICHAEL BALTER

BIOMEDICINE

Cholesterol-Lowering Drugs May Boost Bones

Most drug side effects are unwanted, but a newly discovered "side effect" of the statins, drugs taken by tens of millions of people to lower their cholesterol levels and presumably their risk of heart disease, may in fact be beneficial. On page 1946, a team led by endocrinologist Greg Mundy of the biotech company OsteoScreen and the University of Texas Health Science Center in San Antonio shows that statins trigger bone growth in tissue culture and in rats and mice. If they have the same effect in humans, statins could be the first drugs able to increase bone growth in patients with osteoporosis, the bone-weakening condition that often afflicts postmenopausal women.

The observation could be "a real breakthrough" in osteoporosis treatment, says Lawrence Riggs, an endocrinologist at the Mayo Clinic in Rochester, Minnesota. "If you can thicken remaining bone, you could theoretically bring bone mass back to normal" in patients, he says. "We have not had effective treatment for that." Drugs available today can slow ongoing bone loss but cannot fully repair weakened bones.



Heartfelt aid. Cholesterol-lowering statin drugs might help restore bones weakened by osteoporosis *(top)* to normal density *(bottom)*.

CREDITS: (LEFT TO RIGHT) DEMPSTER *ET AL.*, *J. BONE MINER. RES.* 1, 15 (1986); DARESBURY LABORATORY

Statins lower blood cholesterol concentrations by blocking an enzyme called HMG Co-A reductase, which the body uses to synthesize the lipid. But there were already hints that the drugs might have broader effects. A meta-analysis published in the journal *Circulation* last year, for example, showed that people taking the drugs in large clinical trials had lower death rates from all causes, not just heart disease. Even so, Mundy says, finding an effect of statins on bone came as a "total surprise."

He and his team had been screening a library of 30,000 natural compounds to find potential bone-strengthening drugs. They tested the molecules in cultured mouse bone cells, looking for any that could increase the production of bone morphogenetic protein–2

ScienceScope

DESY Debate Researchers are contesting a one-man campaign to shutter Germany's flagship particle physics facility. In an article last month in the magazine *Der Spiegel*, physicist Hans Grassmann charged that the Deutsche Elektronen Synchrotron (DESY) in Hamburg conducts "irrelevant physics" and advocated making better use of its $140 million annual budget. In response, DESY's directors, led by physicist Albrecht Wagner, posted a four-page rebuttal on the lab's Web site, along with more than 50 endorsements from physicists around the world. In one, Fermilab director Michael Witherell calls DESY "one of the world's most important physics laboratories."

But Grassmann, a German who recently joined Italy's University of Udine, contends that DESY's scientific output has been poor. And he denies that his attack was motivated by his failure to win a job at DESY, where he worked briefly as a student. But Grassmann has found few allies so far. Because German scientists fear reprisals, he says, it is "almost impossible" to find physicists "who would make such criticisms in public."

Choices, Choices The saga of where to build DIAMOND, Britain's new $290 million synchrotron x-ray source, has taken some new twists. Just as he was expected to announce which of two sites had won the machine, Trade and Industry Secretary Stephen Byers last week told Parliament that he will put off the choice until next month pending the completion of two new government studies.

Along with the delay came word that the charitable Wellcome Trust, which is footing $184 million of DIAMOND's construction costs, favors one competitor: the Rutherford Appleton Laboratory (RAL) near Oxford (*Science*, 22 October, p. 655). Indeed, trust officials asserted in a statement last week that their discussions with Byers's department and the French research ministry, which is contributing $57 million to the project, "have been based on the understanding that the ... RAL site was the preferred location." Wellcome said DIAMOND would face engineering problems at RAL's rival, the Daresbury Laboratory near Manchester.

But such claims are "flimsy," charges physicist Graham Bushnell-Wye, who helps run the "DIAMOND at Daresbury" campaign. And he predicts Daresbury is going to do just fine in the new studies, which will weigh engineering issues and opinions in the scientific community.

(BMP-2), which stimulates bone growth. Only one compound had the desired effect. This was lovastatin, a molecule derived from a strain of the fungus *Aspergillus terreus* that Merck sells under the brand name Mevacor in the United States.

To find out if lovastatin's ability to stimulate BMP-2 production by cultured cells translated into increased bone formation in live animals, the team injected the drug into the tissue above the skullcap bones of young mice. After injecting the animals three times a day for 5 days, the researchers found that treated bone was nearly 50% larger than that in mice injected with a salt solution.

Another statin, called simvastatin (trade name Zocor), also had promising effects, this time in female rats whose ovaries had been removed to mimic the hormonal changes of menopause, when many women start to lose bone density. In rats that received oral doses of the statin for 35 days, the leg bones and vertebrae were nearly twice as dense as in rats that received a placebo.

Mundy and his colleagues don't know how the statins encourage bone growth. But cardiologist James Liao of Brigham and Women's Hospital in Boston, who has studied the molecular effects of statins on the cells that line blood vessels, suggests one possibility. He notes that by blocking HMG Co-A reductase, the statins also block the production of other lipids that attach to signaling proteins in the cell, allowing them to function properly. Disrupting these proteins might somehow trigger the cells to make BMP-2, he says.

It's also far from clear what the findings mean for people who take statins, which can cost hundreds of dollars a year. A few scientists who have conducted clinical trials on statins have searched their databases for signs that the drugs improved bone density. They saw some intriguing hints: Clinical researcher Steven Cummings of the University of California, San Francisco, for example, says patients taking statins seemed to have lower risk for bone fractures. But the numbers were too small to produce statistically significant results.

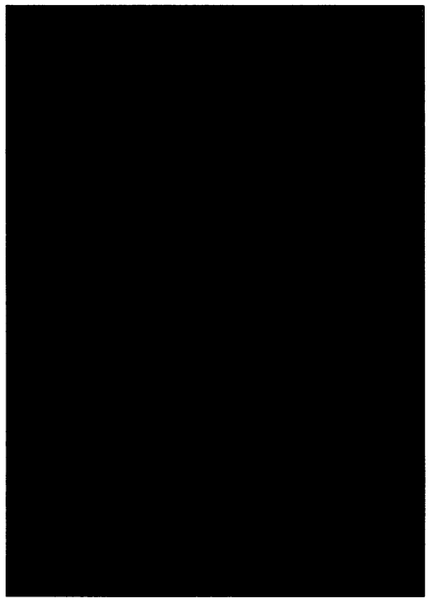
Indeed, the doses used to lower cholesterol levels may be too low to have much effect on bone density. Mundy and his colleagues gave their rats doses about 10 times higher than those typically taken by patients. The high doses may be needed, Mundy says, because the statins currently on pharmacy shelves were chosen for their ability to target the liver, the body's main site of cholesterol synthesis, rather than the bones. He and Cummings both think that similar compounds chosen for their ability to target bone would likely be more effective. "My guess is that the statins given for lipid lowering are not necessarily going to be ideal" for treating osteoporosis, Mundy says. But they might point to similar molecules that could encourage bone formation more effectively, he says—perhaps with the side effect of lowering high cholesterol levels. –GRETCHEN VOGEL

STEM CELLS

Rat Spinal Cord Function Partially Restored

Behind the controversy over research on primordial cells from early human embryos is a dream: using these versatile cells to repair a wide range of injured tissues in adults. Researchers at Washington University in St. Louis have now brought this dream a step closer to reality for the spinal cord.

In the December issue of *Nature Medicine*, neurologists Dennis Choi, John McDonald, and their colleagues report that when they injected immature nerve cells derived from mouse embryonic stem cells into rats whose hindlimbs had been paralyzed by blows to their spinal cords, the animals regained some mobility. What's more, because the animals were treated 9 days after they were injured, the results suggest that stem-cell therapies might someday lead to treatments for the hundreds of thousands of patients worldwide with spinal cord injuries they received long ago.



Spinal patches? Neurons such as these, grown from mouse embryonic stem cells, may help repair damaged spinal cords.

CREDIT: J. W. MCDONALD

Oswald Steward, a spinal cord researcher at the University of California, Irvine, College of Medicine, calls the work "compelling" and "an obligatory first step toward a transplantation therapy for spinal cord injury" based on embryonic stem cells. Still, he and others caution that no such therapy is anywhere near the clinic. The Washington University researchers do not yet understand how the transplants worked, and until they do, it will be hard to improve upon the results.

Choi and McDonald started their stem-cell experiments back in 1996, upon hearing that a colleague at Washington University, neurobiologist David Gottlieb, had chemically coaxed mouse embryonic stem cells to become nerve cells in a lab dish. Initially, Choi and McDonald simply wanted to test whether Gottlieb's mouse embryonic stem cells would survive in the rat nervous system, as a first step toward a workable therapy. After Gottlieb coaxed the cells to develop into precursors of nervous tissue, Choi's team injected the cells into the spinal cords of 22 adult rats with 9-day-old spinal cord injuries. Several weeks later, the researchers examined the animals to see what had become of the transplants.

By using fluorescent antibodies that home in on mouse tissue, the researchers could see that many of the implanted cells had survived and spread throughout the injured spinal cord area. Using antibodies that stick to specific cell types, they also detected clear signs that those cells had matured to form both nerve cells and support cells known as oligodendrocytes and astrocytes. "We're confident that the cells survive and differentiate," Choi says.

Meanwhile, the researchers checked the rats for any behavioral benefits of the transplants, not expecting to find anything dramatic. After all, no one had ever seen any improvement in locomotion from an attempt to repair damage to the spinal cord more than 24 hours after an injury. But within a month of performing the transplants, the Washington University team noticed that the rats could lift their rear ends and step awkwardly with their hindlimbs. By contrast, rats that had received sham injections simply dragged their behinds wherever they went. "We didn't believe the behavioral recovery when we first saw it," McDonald recalls. But after seeing exactly the same result with a second group of rats, the scientists knew it was real.

Exactly what accounts for the improvement is still unclear, however. One possibility is that the new mouse neurons made functional connections with rat neurons, thus partially restoring the spinal cord's ability to transmit nerve signals between the brain and the rear legs. Another is that the mouse-derived oligodendrocytes rebuilt the insulating myelin sheaths around battered spinal cord nerves, enabling them to conduct impulses again. And a third hypothesis is that the implanted cells simply secreted chemicals that acted on damaged cells in the rat spinal cord, either preventing them from