Medical Alchemy: Muscle Turned to Bone

In a modern twist on the alchemists' dream, a surgeon and a cell biologist have transformed shapeless muscle into hard, well-formed bone. The pair have just reported molding rat muscle into tiny leg and jaw bones. Their ultimate goal, however, is far loftier: production of genuine bone replacements for people injured in car accidents or crippled by disease.

"The beauty of our experiment is that the muscle melts away and everything turns into bone," says plastic surgeon Roger K. Khouri of the Washington University School of Medicine in St. Louis. Together with Hari Reddi of Johns Hopkins University in Baltimore, he has literally remolded soft tissue into firm bone.

The researchers isolated their starting material from the thighs of 23 rats. They cut into a piece of muscle and lifted out a flap of this tissue. They left it connected to an artery and a vein so that the muscle would continue to receive nourishment throughout the experiment.

In 18 animals, the researchers injected the muscle flap with osteogenin, a naturally occurring protein in bone that scientists believe may play an important role in the development of the fetal skeleton. Khouri's team then inserted the muscle flaps from the 18 osteogenin-treated rats into small rubber molds packed with pulverized bone. This pulverized bone probably contains additional growth factors, Khouri says. The five untreated flaps were packed into molds without the pulverized bone. Finally, the mold of muscle was surgically inserted into a pouch within each rat's abdomen.

After 10 days, the researchers reopened the pouches and withdrew the molds. All muscle treated with osteogenin had undergone a complete transformation to bone, Khouri and Reddi report in the Oct. 9 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. Depending on the mold, this tissue resembled long bones of the leg, the jaw's mandible or the ball-like tip of the femur (thigh bone). Despite a similar incubation, the five flaps without osteogenin retained the soft, formless texture and cell types characteristic of ordinary muscle.

"A lot of growth factors like osteogenin may actually be very important in terms of fetal development," Khouri says. In fact, this experiment was designed to mimic a process that goes on in the womb, when the tiny embryo's shapeless tissue starts to form a skeleton, Reddi explains. Although researchers believe osteogenin directs that early event, the body may use this protein later in life to heal broken bones, he says.

The researchers don't know whether the newly fashioned bones are as strong as normal ones. For instance, Khouri says the femur they created appears spongy, and perhaps weaker than normal. While scientists know that such spongy bone can become stronger with exercise, researchers must do additional studies before they can evaluate whether such manufactured hard tissue offers a suitable replacement for the leg bones, which must support a lot of weight, he says.

If scientists can identify and mass produce such substances as osteogenin, surgeons might one day garner the ability to build replacements for other types of damaged tissues, including heart valves, comments surgeon William Shaw of the University of California, Los Angeles. Indeed, he adds, "This is the beginning of a whole different approach to surgery."

Shaw speculates, for example, that bioengineers may one day use osteogenin to fashion the ball-like top of the thigh bone, an advance that could provide longer-lasting relief to people suffering from osteoarthritis, a degenerative disease affecting the hip. People with this condition often suffer excruciating pain from years of stress and inflammation that damage the hip's ball and socket. To fix the problem, surgeons usually replace the damaged femur tip with a metal ball-shaped prosthesis. However, a femur tip fashioned from the person's own muscle should last longer and induce fewer infections, Shaw says.

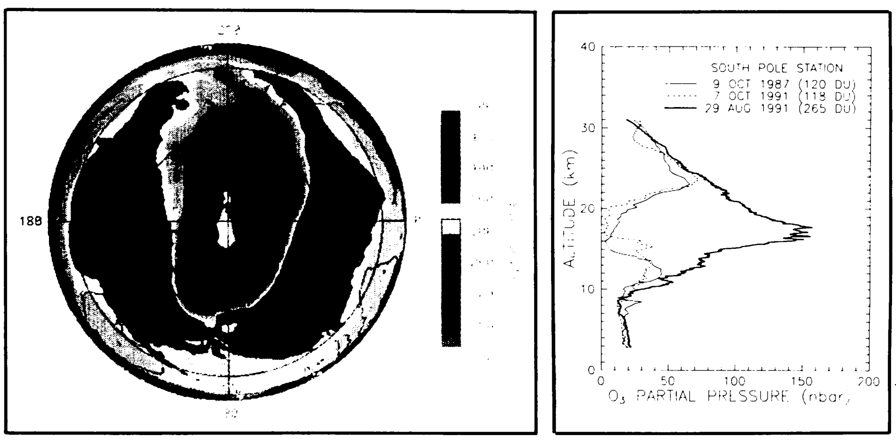
"It sounds like science fiction," acknowledges Khouri. Though cautioning that their data come only from rats, he says the team might extend the bone remodeling experiments to human tissues within a few years. Whether those studies provide humans with natural replacements for worn out parts remains to be seen. Clearly, Shaw says, the work has a long way to go. *— K.A. Fackelmann*

Antarctic ozone hole sinks to a record low

Atmospheric pollutants have again left their mark in the skies over Antarctica as this year's ozone hole reached maturity last week. The atmospheric concentration of ozone dwindled to its lowest recorded level, according to satellite measurements. The dramatic ozone depletion marks the third year in a row that a severe ozone hole has developed over Antarctica, in contrast to the 1980s when major holes formed only in alternate years.

"Three years in a row of low ozone leads one to wonder that maybe most years will be low in the future," says Charles H. Jackman of NASA's Goddard Space Flight Center in Greenbelt, Md.

The term ozone hole refers to a marked reduction in the number of stratospheric ozone molecules. Such a hole has formed over Antarctica each September since the late 1970s. Energized by the first faint rays of sunlight in the austral spring, chlorine chemicals in the atmosphere destroy



NASA

Oltmans/NOAA

Data from the Nimbus-7 satellite show the ozone hole over the Antarctic continent (outlined in black). The oblong blue ring marks the "edge" of the hole, while white patches over Antarctica represent areas of most severe ozone loss. White blotches over other parts of globe denote regions of missing data. Graph shows vertical measurements of ozone values taken by balloon-borne instruments. The thick solid line demonstrates normal ozone values, while the thin solid line shows the 1987 ozone hole. The hatched line from October 7, 1991, shows the main region of ozone loss from about 12 to 23 kilometers in altitude. Also visible this year is an upper region of ozone loss from 27 to 29 km in altitude.