Hormone may restore muscle in elderly

A preliminary study hints that a recombinant form of human growth hormone may boost muscle mass and skin thickness in some people over age 60 and perhaps improve their strength and endurance. However, scientists caution that the experimental treatment — so far tested in only 12 men — must undergo many more years of study before it can be declared effective or safe.

"These studies are very exciting," comments endocrinologist Mary Lee Vance of the University of Virginia in Charlottesville. But Vance advises against viewing human growth hormone as a potential cure for old age. "I just don't think you can make a global statement that this will improve everyone's life."

Human growth hormone, normally secreted by the pituitary gland, not only fuels children's growth but also helps promote leanness in adults by spurring cells to use stored fat for fuel. Scientists suspect that its production begins to taper off in many people after age 40, leading to some characteristic signs of aging, including increased fat deposition, decreased muscle mass and thinner skin.

"For many years it was thought that this progressive change in body composition was an inevitable consequence of aging," says Daniel Rudman of the Medical College of Wisconsin in Milwaukee. In the July 5 NEW ENGLAND JOURNAL OF MEDICINE, Rudman and his colleagues suggest that treatment with synthetic human growth hormone might help some older people counteract that steady decline.

The study involved 21 healthy men aged 61 to 81 who produced little or no growth hormone, as gauged by a marker in the blood called insulin-like growth factor I (IGF-I). All volunteers entered the study with deficient IGF-I blood levels of less than 350 units per liter. For six months, 12 of the men gave themselves subcutaneous injections of the synthetic hormone three times a week, while nine controls received neither treatment nor placebo. When therapy ended, the treated men had IGF-I levels of 500 to 1,500 units per liter — a concentration common among people aged 30 or less. Controls showed no rise in IGF-I blood levels.

The treatment group also showed an 8.8 percent increase in lean body mass (which includes muscle), a 14.4 percent decline in fatty tissue and a 7.1 percent increase in skin thickness. The investigators measured bone density before and after therapy, but Rudman says the study provided no conclusive results on whether the treatment built stronger bones. Nor can the researchers tell whether the skin and muscle changes will last.

Their hope is that growth hormone can strengthen muscle and perhaps bone enough to help elderly people avoid bone-breaking falls, which frequently result in disability and loss of independence, Rudman says. Although men taking the hormone said they felt more energetic after treatment, the researchers note that such self-reports are subjective and possibly biased. In addition, the team has yet to prove that a leaner body mass means improved strength. Rudman hopes to establish that connection in future studies.

Even if further research verifies that the experimental therapy can benefit the elderly, physicians and patients must treat this drug with extreme caution, Vance warns in an editorial accompanying the research report. "It's a double-edged hormone," she told SCIENCE NEWS, noting that extended treatment or large doses can lead to high blood pressure, diabetes and even heart disease. Rudman adds that some older people don't have deficits in growth hormone and thus wouldn't be eligible for the treatment.

Jeremy Rifkin of Washington, D.C., a vocal critic of recombinant DNA technology, says he worries that reports like Rudman's may inadvertently boost illegal use of the synthetic hormone, which is already abused by athletes and bodybuilders. The FDA has approved the drug only for very short children who completely lack the natural growth hormone, Rudman notes. — *K.A. Fackelmann*

Protecting tissue from inflammatory attack

A surgeon finishes the delicate repair of damaged cardiac tissue and signals an assistant to restore blood flow to the fist-shaped heart muscle. To their shock, the medical team realizes the heart has gone rigid, refusing to pump.

The deadly "stunned heart" phenomenon — caused by inflammation of heart tissue following the restoration of blood flow — was once an all-too-common aftermath of open-heart surgery. Today, surgeons avoid it by chilling the heart and bathing it in a chemical cocktail during surgery. This is a complicated and laborious procedure, and medical researchers admit they don't really know how it works. But the threat of catastrophic inflammation compels surgeons to accept an imperfect solution.

Now, in animal and *in vitro* studies using genetically engineered versions of proteins found in the human body, two research teams say they have found new ways to prevent or dramatically suppress the culprits behind inflammation. This work, they say, could have implications for a whole range of debilitating, inflammatory conditions — from rheumatoid arthritis and cystic fibrosis to skin burns and stunned heart.

The inflammatory culprits are some of the same blood-borne proteins and white blood cells that fight infection. Activated by an initial tissue injury, the normally helpful proteins — part of a network of substances called complement — attach to blood vessel walls at the damaged site. The activated proteins, in turn, attract white blood cells called neutrophils. As large numbers of neutrophils congregate outside the vessel walls, they begin eating away at surrounding connective tissue, destroying the very cells they were intended to protect.

Using a protein known to bind and inhibit the action of key members of the blood-borne complement network, researchers at the Johns Hopkins University School of Medicine in Baltimore and T Cell Sciences, Inc., in Cambridge, Mass., have blocked the cascade of events leading to the neutrophil invasion.

The recombinant protein, known as complement receptor type I (CR1), is a soluble form of a substance normally anchored to certain cell membranes in the body. CR1 strongly suppresses complement activation *in vitro,* Douglas T. Fearon and his co-workers report in the July 13 SCIENCE. Moreover, when the researchers clamped and reopened the coronary artery in rats — simulating a human heart attack and its aftermath — CR1 injections nearly halved the amount of heart muscle that died, they say.

These findings identify CR1 "as a potential agent for the suppression of complement-dependent tissue injury in autoimmune and inflammatory diseases," the researchers say.

In a separate effort, William G. Rice of Emory University in Atlanta and Stephen J. Weiss of the University of Michigan in Ann Arbor are working to halt inflammation by interfering with the neutrophils' tissue-degrading enzymes. In the same issue of SCIENCE, they describe *in vitro* experiments using a recombinant form of a human protein known as secretory leukoprotease inhibitor, or SLPI. This substance, normally found only in mucus, prevented neutrophils from attacking fibronectin and elastin — major components of connective tissue.

Rice and Weiss suggest that SLPI's newly discovered function might lead to the development of a novel class of anti-inflammatory agents. In experiments with hamsters, other researchers have shown that SLPI can prevent inflammatory damage to lung tissue. And human testing may not be far behind. Biochemist Robert C. Thompson of Synergen Inc. in Boulder, Colo., which makes recombinant SLPI, says his company plans to seek FDA permission this winter to administer the experimental compound to emphysema and cystic fibrosis patients. — *R. Cowen*