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ESTROGEN PLAYS KEY ROLE IN NORMAL BONE GROWTH IN MEN

DALLAS — July 10, 1997 — Estrogen, the hormone usually associated with women, plays an irreplaceable role in skeletal maturation and bone metabolism in men, according to scientists at UT Southwestern Medical Center at Dallas and colleagues at two other institutions. In a 38-year-old male patient who was still growing taller, estrogen treatment reversed abnormally low bone density that was much like that found in postmenopausal women, according to research published today in the *New England Journal of Medicine*. The hormonal protocol caused areas of unfused bone, which had allowed the prolonged growth, to fuse normally. Such bone maturation ordinarily occurs shortly after puberty.

Investigators found that the man had a mutation of the aromatase P450 gene. Aromatase is the enzyme that synthesizes estrogen in sex organs, adipose, bones and other parts of the body. "Because his aromatase was inactive, the bones were not maturing so the patient continued to sustain linear growth," said Dr. Evan Simpson, UT Southwestern professor of obstetrics and gynecology and of biochemistry and a researcher in the Cecil H. and Ida Green Center for Reproductive Biology Sciences.

The role of estrogen in this case may also help explain why most men don't get osteoporosis but women often do.

The patient was about 5 feet 7 inches tall at age 18; 6 feet 1.6 inches at 31; and 6 feet 2.8 inches at age 38. He was sent to the University of Modena, Italy, for observation because he had persistent growth in height, aching bones and apparent infertility. Doctors there consulted with UT Southwestern researchers who did the necessary genetic and chemical testing.

Tests showed that the man had an abnormally low sperm count. In addition, new

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sperm cells were not being produced. Low mineral density in his bones was evident, as were higher than normal levels of gonadotropins — hormones that promote function and growth of sex organs and sexual characteristics.

"Both men and woman have the capacity to produce estrogen in bone cells," Simpson said. "But it's possible one reason men have a higher level of mineralization in their bones when compared with women is that males have a precursor, circulating testosterone, that allows continued estrogen synthesis throughout life. This may be why men don't often get osteoporosis. It's a conceivable theory we are continuing to investigate."

The male patient in the study was treated with testosterone for six months with no effect on his symptoms. He then was treated with an estrogen patch for six months. His aching bones improved, the density of his bones normalized and the open areas of bone that permit continued growth in height experienced epiphyseal closure.

The scientists also discovered that his cholesterol and triglyceride levels, which were high before the treatment, improved.

Dallas researchers have studied one similar case, a New York man with a different aromatase mutation but similar bone problems. However, he did not have the infertility problems of the Italian patient. Scientists will continue investigating this area to determine if the genetic mutation plays any part in the sexual aspects of such cases.

Other authors of the study are Dr. Ke-nan Qin, UT Southwestern postdoctoral fellow; Dr. Cesare Carani, Department of Endocrinology, University of Modena; Stefania Serpente and Marco Fusini Faustini of the University of Modena; Dr. Kenneth Korach, Laboratory of Reproductive and Developmental Toxicology, National Institutes of Health; and Dr. Manuela Simoni, now at the Institute of Reproductive Medicine, University of Münster, Germany.

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