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New studies may explain fractures in some who take osteoporosis drugs

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Research with baboons at the Texas Biomedical Research Institute may help explain why some people who take bone-strengthening drugs like bisphosphonates are at-risk for atypical fractures in the long bones in their legs.

Texas Biomed scientist Lorena M. Havill, Ph.D. and colleagues at the Southwest Research Institute and Indiana University examined femurs of deceased baboons and found differences in the microstructure of their femurs that she traced to genetic variation among the animals. The study supports the theory that genetic variations may regulate bone remodeling , a natural process during which mature bone tissue is removed from the skeleton so that new tissue can be added. These genetic differences could explain why a small percentage of older women suffer a distinct type of fracture of their femurs when they take bisphosphonates, a type of medication prescribed for millions of people with the bone-weakening disease osteoporosis.

The study, funded by the Texas Biomedical Forum, the Texas Biomed Founder's Council, the San Antonio Area Foundation, and the National Institutes of Health (NIH), is published in the November issue of the journal *Calcified Tissue International*.

In osteoporosis, bone remodeling happens faster than the growth of new bone tissue to replace the lost bone. Bisphosphonates suppress remodeling, allowing the accumulation of bone tissue.

Havill and others have theorized that some women are genetically predisposed to slower remodeling in the absence of osteoporosis. This genetic difference could be causing the drugs to have a greater effect on them and weaken their bones in areas not typically prone to osteoporotic fractures.

In their study, Havill and her colleagues examined femurs from 101 baboons from the pedigreed colony at Southwest National Primate Research Center. All had died for reasons unrelated to this research project. Their bones were obtained during necropsy and preserved. The researchers did microscopic examinations and found differences in bone remodeling dynamics that were influenced by inherited differences among the animals.

"Baboons are anatomically and physiologically very similar to humans, and these animals live a long time, so they develop many of the same age-related diseases that we do," Havill said. "This makes them a good model for age-related diseases such as osteoporosis. The results of this study suggest an explanation for why some women respond differently to the widely prescribed bisphosphonates."

"This supports the potential for a scenario in which certain individuals who are genetically predisposed to cortical microstructure that is less mechanically advantageous may experience disadvantageous responses to remodeling suppression, such as being at higher risk for atypical femoral fractures," Havill wrote in the study.

Provided by Texas Biomedical Research Institute