

## Diabetes weakens your bones

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Current research suggests that the inflammatory molecule TNF- $\alpha$  may contribute to delayed bone fracture healing in diabetics. The related report by Alblowi et al, "High Levels of TNF- $\alpha$  Contribute to Accelerated Loss of Cartilage in Diabetic Fracture Healing" appears in the October 2009 issue of the *American Journal of Pathology*.

Diabetes, a condition where the body either does not produce enough, or respond to, insulin, affects at least 171 million people worldwide, a figure that is likely to double by 2030. Long-term complications of diabetes include cardiovascular disease, chronic renal failure, retinal damage that may lead to blindness, nerve damage, and blood vessel damage, which may cause erectile dysfunction and poor wound healing.

Diabetic patients often experience low bone density, which is associated with increased risk of bone fractures and delayed fracture repair. To examine how diabetes affects bone, Dr. Dana Graves and colleagues of the University of Medicine and Dentistry of New Jersey and the Boston University School of Medicine explored bone repair in a mouse model of diabetes. They observed increased levels of inflammatory molecules, including TNF- $\alpha$  during fracture healing. The diabetic animals had rapid loss of cartilage in the healing bones, which was due to increased numbers of osteoclasts, cells that remove bone and cartilage. Factors that stimulate osteoclast formation were regulated by both TNF- $\alpha$  and a downstream mediator, FOXO1. These results suggest that diabetesmediated increases in TNF- $\alpha$  and FOXO1 may underlie the impaired healing of diabetic fractures.



Alblowi et al suggest that "TNF- $\alpha$  dysregulation plays a prominent role in the recently identified catabolic events associated with diabetic fracture healing." In future studies, Dr. Graves and colleagues plan to "examine the effect of FOXO1 on mineralized tissue to examine how it may regulate factors that control bone resorption and osteoclastogenesis, in addition to effects it may have on osteoblastic cells."

More information: Alblowi J, Kayal RA, Siqueira M, McKenzie E, Krothapalli N, McLean J, Conn J, Nikolajczyk B, Einhorn TA, Gerstenfeld L, Graves DT: High Levels of TNF-α Contribute to Accelerated Loss of Cartilage in Diabetic Fracture Healing. *Am J Pathol* 2009 175: 1574-1585

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