Preventing early osteoporotic fractures after childhood chronic diseases

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Mary Leonard, MD, is pointing at a spine MRI scan of a young adult who had a bone marrow transplant in childhood. "That vertebra is compressed," said Leonard, a professor of pediatrics and of medicine who serves as an associate dean for maternal and child health research. "These patients who are in their teens or early 20s have little-old-lady kinds of fractures."

Preventing early osteoporotic fractures in those who have withstood childhood chronic diseases is a central aim of Leonard's research program. She and her colleagues have documented abnormal bone structure, muscle mass and muscle strength in children and teens with conditions ranging from cancer to Crohn's disease to organ transplantation. Immobility, inflammation, malabsorption of nutrients and treatment with radiation or steroids can all pose threats to developing bones.

"We believe that once you go through puberty, you're not getting that bone back," Leonard said. "I feel like we've described and described the problem, and now we need to do clinical trials to see what we can do to improve bone health in these patients. We just want to make sure they go into adulthood with the best, strongest skeleton possible—with bones to last a lifetime."

Clinical trials could assess the efficacy of exercise programs, compare kidney-transplant patients on a steroid-free protocol with those who are given steroids and, eventually, test pharmaceutical interventions. In a

new Stanford research center on Arastradero Road in Palo Alto, both kids with chronic diseases and healthy control subjects will undergo three assessments: a muscle-strength exam; a full-body DXA scan to quantify bone, muscle and fat; and ankle and wrist scans in the latest-generation XtremeCT machine. The total radiation dose from the three tests, Leonard says, is less than a week of background radiation exposure from living on Earth.

The XtremeCT is one of 10 in the United States, and one of only two being used to assess children with chronic diseases. "Its name is the HR-pQCT, but we call it the hokey-pokey machine, because you put your right arm in; you put your right arm out," said Leonard. As long as you don't actually shake it all about—children under 5, it seems, are too wiggly to be scanned—the high-resolution CT yields a fine-grained look at bone structure in those arms and legs. "DXA bone density scans tell you how much bone is there, but don't tell you enough about bone quality—its thickness, porosity and micro-architecture," she said. By comparing before-and-after scans from the HR-pQCT machine, "we can really look at what the treatment is doing to bone structure and strength."

Leonard sees two implications of her work. First, some children with chronic diseases may need to be treated more aggressively before and during puberty, to improve their overall health and enable them to build more bone. "If you wait to treat the Crohn's until their bones are done developing, or if they don't get their kidney transplant until their bones are done developing, that window of opportunity may be lost," she said. Second, as life expectancy improves for children with rare and once-fatal conditions, physicians need to anticipate the lasting effects of their illness and treatment.

"As patients with complex congenital heart disease or cancer are surviving well into adulthood, the focus of research has to shift from improving survival to understanding some of the long-term

complications," Leonard said. "And osteoporosis and fractures are part of it."

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