

approved indications in postmenopausal and male osteoporosis, we recommended that teriparatide be considered for patients at high risk for fracture who require sustained use of glucocorticoids and who have either osteoporosis or low bone mass with a prevalent fracture. In his editorial, Sambrook suggests the use of teriparatide as a first-line therapy. We believe that the gain in bone mineral density achieved with teriparatide may outweigh the potential drawbacks of higher cost and greater inconvenience in certain patients with or at risk for severe glucocorticoid-induced osteoporosis.

Nori and colleagues sound a cautionary note about the use of teriparatide in patients with chronic kidney disease and in kidney-transplant recipients with secondary hyperparathyroidism. Patients with kidney disease, defined as a serum creatinine level that, in the opinion of the investigator, indicated significant renal impairment or a creatinine clearance of 30 ml per minute or less were excluded from our trial. This is consistent with Food and Drug Administration labeling,

which states that there is limited information available to evaluate the safety of teriparatide in patients with kidney disease. We concur that clinical evaluation and judgment are needed before prescribing any medication.

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Atypical Fractures of the Femoral Diaphysis in Postmenopausal Women Taking Alendronate

TO THE EDITOR: The long-term safety of bisphosphonates for the treatment of osteoporosis has been questioned. Two case series have suggested a link between prolonged bisphosphonate therapy and atypical fractures. In one series, a small number of patients sustained low-energy nonvertebral fractures while receiving long-term alendronate therapy; three were fractures of the femoral shaft.¹ Bone biopsies in these patients showed evidence of severely suppressed bone turnover and fracture healing that was delayed or absent. In the other series, low-energy subtrochanteric fractures were found in nine women who had been receiving long-term alendronate therapy.² Theoretically, bisphosphonates suppress bone turnover and thus might be associated with accumulated microdamage in bone. To our knowledge, no study has demonstrated microdamage accumulation in patients treated with bisphosphonates, and data from studies in animals remain difficult to interpret be-

cause supranormal doses of bisphosphonates are used. Nevertheless, the possibility that bisphosphonates alter bone strength with prolonged use appears to exist.

We identified 15 postmenopausal women who had been receiving alendronate for a mean (\pm SD) of 5.4 \pm 2.7 years and who presented with atypical low-energy fractures, defined as fractures occurring in a fall from a standing height or less. All patients sustained subtrochanteric or proximal diaphyseal fractures. Bisphosphonate use was observed in 37% of all patients presenting with low-energy subtrochanteric or diaphyseal fractures. Fractures of the subtrochanteric or diaphyseal regions are relatively rare in postmenopausal women, representing 6% of all osteoporotic hip fractures in our patient population (unpublished data).

Ten of the 15 patients were found to share a unique radiographic pattern, defined as a simple transverse or oblique ($\leq 30^\circ$) fracture with beaking

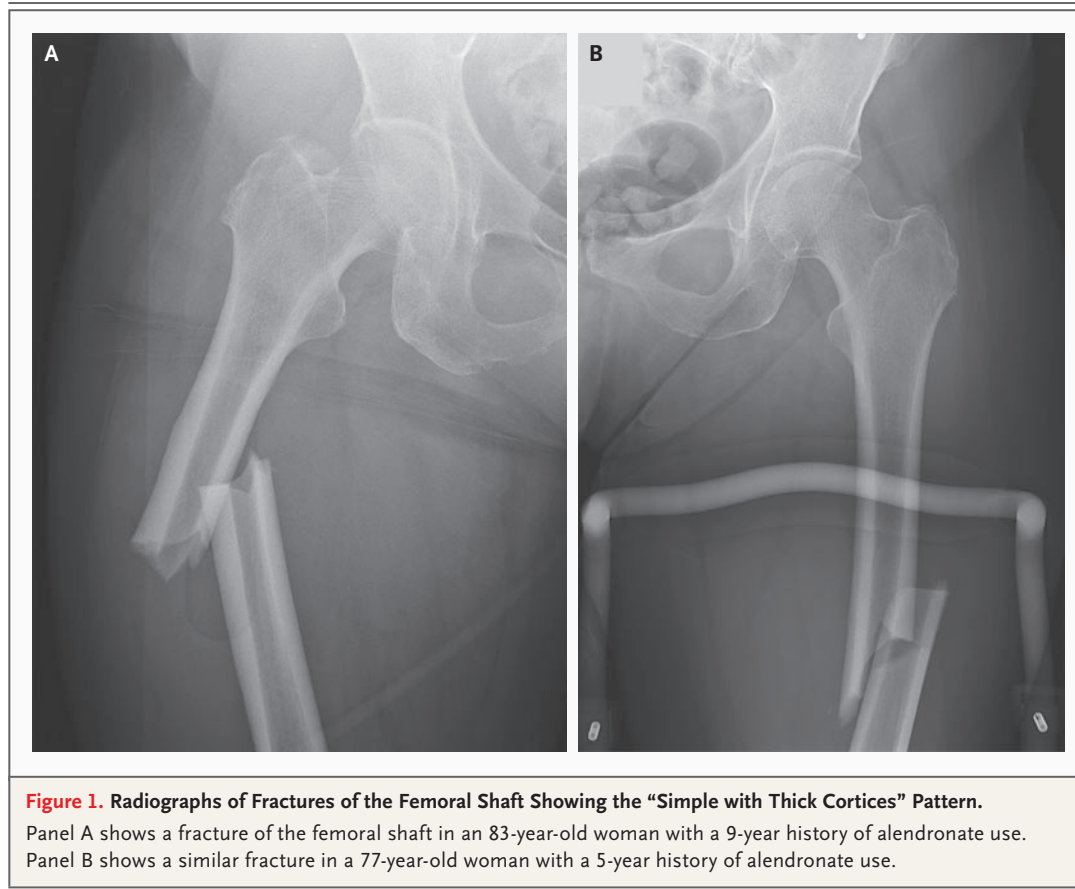


Figure 1. Radiographs of Fractures of the Femoral Shaft Showing the “Simple with Thick Cortices” Pattern.

Panel A shows a fracture of the femoral shaft in an 83-year-old woman with a 9-year history of alendronate use. Panel B shows a similar fracture in a 77-year-old woman with a 5-year history of alendronate use.

of the cortex and diffuse cortical thickening of the proximal femoral shaft. We call this pattern “simple with thick cortices” (Fig. 1). These patients had an average duration of alendronate use of 7.3 ± 1.8 years, which was significantly longer than the duration of 2.8 ± 1.3 years for the five patients without this pattern ($P < 0.001$). Cortical thickening was present in the contralateral femur in all the patients with this pattern. Three of the 15 patients had a history of femoral fractures, all in the contralateral femur, whereas no patients had a history of vertebral fractures. Vitamin D and parathyroid hormone measurements and bone densitometry were not performed during fracture care; therefore, we cannot determine the status of the patients with respect to metabolic bone disease.

Our results provide further evidence of a potential link between alendronate use and low-energy fractures of the femur. In light of the limitations

of our study, a prospective study is indicated. Although many possible explanations exist, patients with the unique radiographic pattern shown here may represent a subgroup of the population that is more susceptible to the effects of prolonged suppression of bone turnover. Additional studies are needed to characterize this subgroup and to establish a clear association between atypical fractures of the femur and prolonged bisphosphonate treatment.

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Airway Disease and Thaumatin-like Protein in an Olive-Oil Mill Worker

TO THE EDITOR: The olive fruit is frequently consumed as food and used as raw material to obtain olive oil. Olive oil is pressed in mills, where workers are exposed daily to inhalation of particles derived from this processing. Despite widespread consumption, allergies to olive fruit and derivative products have seldom been documented.¹⁻⁴

We report on a 41-year-old man who had been working since 1993 in an olive-oil mill. He was first seen in 2006, when the olive-oil mill was operating in Jaén, Spain; he had a 2-year history of episodic rhinitis, shortness of breath, chest tightness, and wheezing. Symptoms occurred within 30 minutes after he arrived at the workplace and partially improved immediately after he left it. He controlled the symptoms by using salbutamol as needed and formoterol-budesonide twice a day on a regular basis. Baseline spirometric measurements showed a forced expiratory volume in 1 second (FEV₁) of 3.74 liters (87% of the predicted value), with a ratio of FEV₁ to forced vital capacity of 76%. Methacholine challenge showed a 20% decrease in FEV₁ at 1.2 mg per milliliter. The peak expiratory flow (PEF) varied, depending on workplace exposure (Fig. 1A). The patient had a diurnal variation in PEF rates that was greater than 20% on 11 working days, whereas no significant changes were observed on days away from the workplace.

Olive pulp from the mill was lyophilized, powdered, and extracted with ether-ethanol (3:1 ratio). The pellet was extracted with phosphate-buffered saline (pH 7.0). The supernatant obtained by centrifugation was dialyzed against 0.05 M ammonium bicarbonate (pH 8.0), lyophilized, and stored at -20°C. All the steps were performed at 4°C. A skin-prick test with this extract at 6 mg per milliliter was positive in the patient (wheal

area, 50 mm²) and was negative in control subjects.

We investigated sensitization to olive-fruit allergens as possible causative agents. Immunoblotting with the patient's serum revealed a reactive 23-kD band in olive-fruit protein extract (Fig. 1B) that was purified by size-exclusion chromatography and reverse-phase high-performance liquid chromatography. The purified protein was IgE-reactive (Fig. 1C), and Edman degradation gave the amino acid sequence ATFXIVNQXTYT-VXAAASP, which showed homology to allergenic thaumatin-like proteins (TLPs) from plant foods and pollen.⁵

A skin-prick test with purified TLP at 1 μg per milliliter was positive in the patient (wheal area, 9 mm²) and was negative in control subjects. We performed a nasal challenge test in the patient by measuring nasal resistance with active anterior rhinomanometry, using TLP (0.1 μg per milliliter); the result was positive, with nasal obstruction, sneezing, and runny nose. A nasal challenge test with TLP (100 μg per milliliter) was negative in four healthy subjects and three patients who were allergic to olive pollen.

Our findings indicate that occupational asthma can be caused by a thaumatin-like protein from olive fruit.

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