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1. Newell-Price J, Bertagna X, Grossman AB, Nieman LK. Cushing's syndrome. *Lancet* 2006;367:1605-17.
2. de Bruin C, Pereira AM, Feelders RA, et al. Coexpression of dopamine and somatostatin receptor subtypes in corticotroph adenomas. *J Clin Endocrinol Metab* 2009;94:1118-24.
3. Schmid HA. Pasireotide (SOM230): development, mechanism of action and potential applications. *Mol Cell Endocrinol* 2008;286:69-74.
4. Boscaro M, Ludlam WH, Atkinson B, et al. Treatment of pituitary-dependent Cushing's disease with the multireceptor ligand and somatostatin analog pasireotide (SOM230): a multicenter, phase II trial. *J Clin Endocrinol Metab* 2009;94:115-22.
5. Pivonello R, De Martino MC, Cappabianca P, et al. The medical treatment of Cushing's disease: effectiveness of chronic treatment with the dopamine agonist cabergoline in patients unsuccessfully treated by surgery. *J Clin Endocrinol Metab* 2009;94:223-30.

Atypical Femoral Fractures and Bisphosphonate Use

TO THE EDITOR: Since 2007, there have been several reports suggesting a potential association between the use of bisphosphonates and the occurrence of subtrochanteric or so-called atypical femoral fracture.¹⁻⁴ However, a recent registry-based cross-sectional study did not show a greater frequency of such fractures in patients receiving alendronate.⁵ Thus, the association between atypical femoral fractures and bisphosphonate use remains an open issue.

We reviewed 152 femoral fractures (not including hip) that occurred in 152 patients who were admitted to a tertiary center during a 60-month period from June 2003 through May 2008. The mean (\pm SD) age of the patients was 78 \pm 5 years, and 132 of the patients were women. A senior orthopedic surgeon who was unaware of the patients' baseline characteristics and medication use reviewed the fracture radiographs of every patient in random sequence on two separate occasions (Cohen's $\kappa=0.8$), identifying those fractures that fit the criteria for an atypical fracture (i.e., a lateral transverse or <30-degree oblique fracture line in an area of cortical thickening with a medial uncortical beak), as described previously.^{3,4}

Twenty of the 152 fractures were classified as atypical. After unblinding of the database, 17 patients in this group were found to be receiving current oral bisphosphonate treatment. Of these patients, 15 were taking alendronate (mean treatment duration, 5.1 years), and 2 were taking risedronate (mean treatment duration, 3 years). Of the 132 patients whose radiographs did not fulfill the criteria for atypical fracture, 2 patients (1.5%) were taking alendronate, and 1 patient was taking risedronate (0.8%), with mean treatment

durations of 3.5 years and 1 year, respectively. The atypical fracture pattern appeared to be 96.7% specific to patients receiving bisphosphonates.

Several additional risk factors were associated with atypical femur fracture. These included a history of low-energy fracture (odds ratio, 3.2; 95% confidence interval [CI], 2.1 to 17.1; $P<0.001$), the use of glucocorticoid therapy for more than 6 months (odds ratio, 5.2; 95% CI, 1.3 to 31.0; $P=0.01$), active rheumatoid arthritis (odds ratio, 16.5; 95% CI, 1.4 to 142.3; $P<0.001$), and a level of serum 25-hydroxyvitamin D of less than 16 ng per milliliter (40 nmol per liter) (odds ratio, 3.5; 95% CI, 1.7 to 18.7; $P<0.001$).

Although there is an association between atypical subtrochanteric femur fracture and oral bisphosphonate use, clinicians should remember that bisphosphonates significantly reduce the risk of fragility fractures in patients with osteoporosis and that overall the antifracture effects of bisphosphonates far outweigh their potential risks.

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1. Lee P, van der Wall H, Seibel MJ. Looking beyond low bone mineral density: multiple insufficiency fractures in a woman with post-menopausal osteoporosis on alendronate therapy. *J Endocrinol Invest* 2007;30:590-7.
2. Lee P, Seibel MJ. More on atypical fractures of the femoral diaphysis. *N Engl J Med* 2008;359:317.
3. Neviaser AS, Lane JM, Lenart BA, Edober-Osula F, Lorch

DG. Low-energy femoral shaft fractures associated with alendronate use. *J Orthop Trauma* 2008;22:346-50.

4. Lenart BA, Lorich DG, Lane JM. Atypical fractures of the femoral diaphysis in postmenopausal women taking alendronate. *N Engl J Med* 2008;358:1304-6.

5. Abrahamsen B, Eiken P, Eastell R. Subtrochanteric and diaphyseal femur fractures in patients treated with alendronate: a register-based national cohort study. *J Bone Miner Res* 2009;24:1095-102.

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CORRECTION

Outcomes after Internal versus External Tocodynamometry for Monitoring Labor (January 28, 2010;362:306-13). A correction is described in the Correspondence section of this issue of the *Journal* (Internal versus External Tocodynamometry in Labor [May 13, 2010;362:1842-3]).

NOTICES

Notices submitted for publication should contain a mailing address and telephone number of a contact person or department. We regret that we are unable to publish all notices received. Notices also appear on the *Journal's* Web site (NEJM.org/meetings). The listings can be viewed in their entirety or searched by location, month, or key word.

NHS 2010 — BEYOND NEWBORN HEARING SCREENING: INFANT AND CHILDHOOD HEARING IN SCIENCE AND CLINICAL PRACTICE

The conference will be held in Cernobbio, Italy, June 8–10.

Contact the Organizing Secretariat, Meet and Work Srl, Piazza del Sole e della Pace 5, 35031 Abano Terme (Padova), Italy; or call (49) 860 1818; or fax (49) 860 2389; or see <http://www.nhs2010.org>; or e-mail nhs@polimi.it.

INTERNATIONAL PROBIOTIC CONFERENCE 2010 — IPC 2010

The conference will be held in Kosice, Slovakia, June 15–17.

Contact the organizing secretariat, Pamida International Ltd., Komenskeho 2656, 024 01 Kysucke Nove Mesto, Slovakia; or call (421) 904 837 153; or fax (421) 41 4000123; or e-mail info@probiotic-conference.net; or see <http://www.probiotic-conference.net>.

6TH INTERNATIONAL MUSCLE SYMPOSIUM

The symposium will be held in Vienna, Sept. 2–4.

Contact Hedwig Schulz, Vienna Medical Academy, Alserstrasse 4, A-1090 Vienna, Austria; or call (43) 1 405 13 83-19; or fax (43) 1 407 82 74; or e-mail hedwig.schultz@medacad.at; or see <http://www.musclesymposium2010.at>.

THOMAS L. PETTY ASPEN LUNG CONFERENCE

The 53rd annual meeting, entitled “Systems Biology of Lung Diseases — Progress in the ‘Omics’ Era,” will be held in Aspen, CO, June 9–12.

Contact Dr. Mark W. Geraci, c/o Jeanne Cleary, Thomas L. Petty Aspen Lung Conference, Anschutz Medical Campus, Research 2, Box C272, 9th Floor, 12700 E. 19th Ave., Aurora, CO 80045; or call (303) 724-6038 or (303) 358-2797; or fax (720) 851-1034; or e-mail jeanne.cleary@ucdenver.edu; or see <http://www.aspenlungconference.org>.

17TH WORLD CONGRESS IN CARDIAC ELECTROPHYSIOLOGY & TECHNIQUES

The congress, entitled “Cardiostim 2010,” will be held in Nice Acropolis, France, June 16–19.

Contact Reed Expositions France, 52-54 quai De Dion Bouton CS 80001, 92806 Puteaux CEDEX, France; or see <http://www.cardiostim.fr>.

AMERICAN SOCIETY OF EMERGENCY RADIOLOGY 2010 ANNUAL MEETING AND POSTGRADUATE COURSE IN TRAUMA AND EMERGENCY RADIOLOGY

The meeting and course will be held in Seattle, Aug. 11–14. It is jointly sponsored by the American Society of Emergency Radiology and Continuing Medical Educational Resources, Inc.

Contact the ASER Meeting Department, American Society of Emergency Radiology, 4550 Post Oak Place, Suite 342, Houston, TX 77027; or call (713) 965-0566; or fax (713) 960-0488; or e-mail asermeetingsdept@meetingmanagers.com; or see <http://www.erad.org>.

INTENSIVE MEDICAL SPANISH & CULTURAL COMPETENCY WORKSHOP

The conference will be held in the following cities: Denver (May 21–24); Phoenix, AZ (June 11–14, Nov. 5–8); Los Angeles (June 25–28); San Diego, CA (July 16–19, Nov. 19–22); San Francisco (Aug. 13–16, Nov. 12–15); Tucson, AZ (Sept. 17–20); La Paz, BCS, Mexico (Oct. 23–30); Las Vegas (Dec. 3–6); and Acapulco, GRO, Mexico (Dec. 10–17).

Contact Tamara Rios, Rios Associates, 3729 N. Bay Horse Loop, Tucson, AZ 85719; or call (520) 907-3318; or see <http://www.medspanish.org>.