



Osteoporosis Canada

Ostéoporose Canada

Summer 2009 • vol. 13 no. 2

# osteoporosis

**update**

a practical guide  
for Canadian physicians

## Depression and osteoporosis

Exploring the connection  
between two common  
conditions in elderly patients

### case study

The impact of glucocorticoids  
on bone health in children  
and adolescents

### questions & answers

How long to continue antiresorptive therapy

The role of vitamin C

Benefits and risks of vitamin K

### resources & announcements

page 10



*Osteoporosis Update* is published by

**OSTEOPOROSIS CANADA**

1090 Don Mills Road, Suite 301  
Toronto, Ontario, M3C 3R6  
Tel: (416) 696-2663 • Fax: (416) 696-2673  
Toll Free: 1-800-463-6842

**Julie M. Foley**, President & CEO  
**Dr. Famida Jiwa**, Vice-President, Operations  
**Ania Basiukiewicz**, Communications Manager

**PARKHURST**

400 McGill Street, 3<sup>rd</sup> Floor  
Montréal, Québec, H2Y 2G1

**Mairi MacKinnon**, Managing Editor  
Tel: (514) 397-8833 • Fax: (514) 397-0228  
Email: osteo@parkpub.com

**Susan Usher**, Corporate Editorial Director  
**Pierre Marc Pelletier**, Senior Art Director

**EDITORIAL BOARD**

**Richard G. Crilly**, MD, MRCP, FRCPC  
University of Western Ontario

**Sidney Feldman**, MD, FCFP  
University of Toronto

**Abida Sophina Jamal**, MD, PhD, FRCPC  
University of Toronto

**Heather McDonald-Blumer**, MD, MSc, FRCPC  
University of Toronto

**Suzanne Morin**, MD, MSc, FRCP  
McGill University

**Anne-Marie Whelan**, PharmD  
Dalhousie University

©2009 OSTEOPOROSIS CANADA

No articles may be reprinted without permission.  
Views expressed by the authors are not necessarily endorsed by Osteoporosis Canada.

*Osteoporosis Update* is made possible with the assistance of unrestricted educational grants from the following sponsors:

**Eli Lilly Canada Inc.**  
**P&G Pharmaceuticals Canada and**  
**sanofi-aventis Canada Inc.**

The financial support received from sponsors does not constitute an endorsement by OSTEOPOROSIS CANADA of any of the sponsors' products or services.

ISSN 1480-3119

Canadian Publications Mail Sales Product Agreement No. 40063730

Return undeliverable Canadian addresses to: Circulation, 400 McGill Street, 3<sup>rd</sup> Floor  
Montréal, Québec H2Y 2G1

# Multifaceted interventions for diverse patient populations



**Suzanne Morin**, MD, MSc, FRCP, is a physician in the Division of General Internal Medicine, MUHC — Montreal General Hospital, and Associate Professor, Department of Medicine at McGill University.

Numerous studies have demonstrated an association between antidepressant medications and osteoporosis-related fractures, and it has been suggested that depression itself may be a risk factor for osteoporosis (Takkouche B, Montes-Martinez A, Gill S et al. *Drug Safety* 2007;30:171-184; Cizza G, Ravn P, Chrousos G. *Trends Endocrinol Metab* 2001;12:198-203). Potential mechanisms for such an association include alterations in the hypothalamic-pituitary-adrenal axis, adoption of poor health behaviours, influences of comorbid health conditions and the use of medications that affect bone metabolism. Indeed, several observational studies have demonstrated a relationship between bone mineral density (BMD) and antidepressant use. In particular, selective serotonin reuptake inhibitor use has been found to increase the risk of low-trauma fracture independently of BMD and falls in Canadian women and men (Richards JB, Papaioannou A, Adachi JD et al. *Arch Int Med* 2007;167:188-94). In this edition of *Osteoporosis Update*, Dr. David Goltzman, Professor of Medicine at McGill University, examines the proposed links between depression, antidepressant use, BMD and fracture risk, and their implications in clinical practice.

Through case presentations, Drs. Anne Marie Sbrocchi and Leanne Ward review the important concepts of osteoporosis diagnosis and management in pediatric patients who require treatment with corticosteroids for chronic conditions. Also in this issue, Dr. Heather McDonald tackles the significant and clinically relevant question of drug holiday in patients who have been on antiresorptive treatment for a number of years. The role of vitamin C and vitamin K in bone metabolism is addressed in turn by Dr. Susan Whiting and Dr. Angela Cheung, who provide recommendations on how to respond to patients' questions on these topics.

The ultimate goal of osteoporosis management is to maintain skeletal integrity through multifaceted interventions. Dissemination of scientific knowledge is key in this area of medicine, as in others. We welcome your comments and questions (osteo@parkpub.com).

Beginning in the fall of 2009, a print subscription to *Osteoporosis Update* will no longer be offered free of charge to all readers. Formerly, all interested readers were able to request a free print subscription; unfortunately, due to unsustainable production and shipping costs, we are no longer able to offer this option to everyone. As a result of this change, some of our readers will no longer receive a copy of *Osteoporosis Update* in the mail; however, the publication will still be available on our website free of charge.

Further information about print subscription options will be available soon on our website ([www.osteoporosis.ca](http://www.osteoporosis.ca)).

# Osteoporosis in children with glucocorticoid-treated illnesses

**O**steoporosis remains a global problem in adults and is associated with significant morbidity. Recently, focus has shifted towards children, as it is now apparent that osteoporosis is not limited to the adult population. Glucocorticoid use in the context of childhood illnesses is one of the main risk factors for osteoporosis in children and adolescents. The following cases illustrate the negative impact of glucocorticoid therapy on bone health in the pediatric population.

**Anne Marie Sbrocchi, MD, FRCPC**, completed her pediatric endocrinology fellowship at the Montreal Children's Hospital in 2008. She has an interest in bone health in children and will pursue a clinical research fellowship under the supervision of Dr. Leanne Ward at the Children's Hospital of Eastern Ontario starting July 2009.

**Leanne Ward, MD, FRCPC**, is a Pediatric Endocrinologist, Director of the Pediatric Bone Health Clinical and Research Programs at the Children's Hospital of Eastern Ontario, and Associate Professor in the Department of Pediatrics at the University of Ottawa.

## CASE 1: adolescent male with muscular dystrophy

A wheelchair-bound, 13-year-old male with Duchenne muscular dystrophy had been treated with deflazacort for his underlying dystrophinopathy. After 6 years of deflazacort therapy, he presented to the bone health clinic with incapacitating back pain, which was unrelieved by acetaminophen or codeine. His intake of calcium and vitamin D had been adequate. On physical exam, he manifested short stature (less than the 5<sup>th</sup> percentile) and a Cushingoid appearance, consistent with long-term glucocorticoid therapy. He also complained of exquisite tenderness to palpation over the posterior spinous processes in the thoracic and lumbar regions. A radiograph of the spine revealed vertebral fractures at multiple levels including thoracic vertebrae T5, 7, 8, 11, 12, and lumbar vertebrae L1–L4 (**Figure A**). An areal bone mineral density (BMD) Z-score at the lumbar spine was  $-3.8$ . The spine volumetric BMD Z-score, used to account for short stature and small bone size, was  $-2.5$ .

The boy was diagnosed with glucocorticoid- and immobilization-induced osteoporosis resulting in multiple vertebral fractures. Given the impact of his vertebral fractures on quality of life, he was treated with cyclical



**Figure A**  
Pre-treatment



**Figure B**  
2 years post-treatment

intravenous pamidronate, consisting of a 3-day treatment of 1 mg/kg/day every 4 months for 2 years. At the same time, he was weaned from his deflazacort, since the side effects were deemed to have outweighed the benefits by that time. He experienced significant improvement in his symptomatology. In addition, areal BMD Z-score increased to  $-1.1$  and the spine volumetric BMD Z-score increased to  $+0.9$ . A striking finding was reshaping of the affected vertebral bodies, as noted on a spine x-ray taken two years following the initiation of pamidronate therapy (**Figure B**). No new vertebral fractures occurred during treatment.

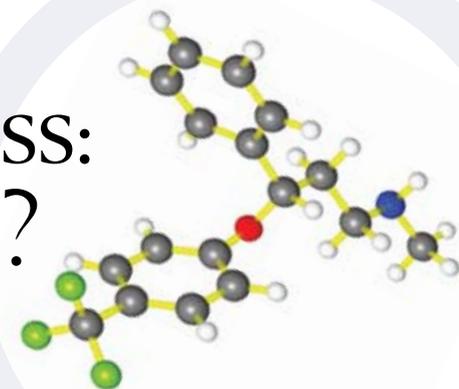
*Continued on page 6*

## Key points

- Glucocorticoid use is one of the main risk factors for osteoporosis in children and adolescents.
- In children, the diagnosis of osteoporosis does not rest on BMD alone; both clinical evidence for bone fragility (vertebral fractures and/or recurrent low-trauma extremity fractures) and low BMD must co-exist before a child is deemed to have osteoporosis. To test BMD in children, the spine is the most reliable skeletal site, and the age- and gender-matched Z-score is used rather than T-score as in adults. Recently, the International Society for Clinical Densitometry has suggested formal guidelines for the diagnosis of osteoporosis in children, with BMD an adjuvant tool in the diagnostic process (Gordon CM et al. Dual energy X-ray absorptiometry interpretation and reporting in children and adolescents: the 2007 ISCD Pediatric Official Positions. *J Clin Densitom* 2007;11[1]:43-58).
- Vertebral fractures can occur in the first 12 months of glucocorticoid therapy in children, despite normal intake of calcium and vitamin D.
- Initial management steps include: minimize glucocorticoid use (if possible); treat the underlying illness; encourage physical activity; optimize calcium and vitamin D intake.
- Bisphosphonates can be used in children with osteoporosis, particularly if risk factors are persistent and if conservative measures to enhance bone health have been insufficient to rescue the child from the osteoporotic state. Such agents should only be administered by pediatricians/bone health clinicians with expertise in their use for children with chronic illnesses.

# Depression and bone loss: What is the connection?

By David Goltzman, MD, FRCPC



In recent years, a relationship between depression and osteoporosis has become evident; postmenopausal women, younger women and men are all potentially affected. While effects of depression on lifestyle are contributing factors, e.g. potential failure of depressed people to get enough exercise and to ensure adequate dietary intake of bone-building nutrients, the relationship goes deeper than that. A series of studies over the last 10–15 years have looked at the effects of depression and antidepressants on fractures. Bone loss may be a potential side effect of selective serotonin reuptake inhibitor (SSRI) antidepressants, and may even result from physiological effects of depression itself.

## Linking depression, bone loss and fractures

Among elderly Canadians, about 9% of women and 3% of men suffer from depression.<sup>1</sup> Decreased bone mineral density (BMD) has been observed in depressed individuals, both women and men.<sup>2–4</sup> Depression itself has been associated with fractures. The presumed mechanism has been falls, since the association seems to disappear after correction for falls, although other processes may also be involved.<sup>5</sup> Animal studies suggest that depression may predispose to osteoporosis; suspected mechanisms include an impaired hypothalamic-pituitary-adrenal system with increased serum cortisol levels, and upregulation of the proinflammatory cytokines interleukin 6 and tumour necrosis factor.<sup>2,6,7</sup> Older men appear to be even more susceptible to the effects of depression on bone density than older women,<sup>8</sup> and younger women are also at risk.<sup>9</sup>

## The role of antidepressants

The data on the role of antidepressants in bone loss and fractures is much stronger than that on the impact of depression alone. Initially, studies on tricyclic antidepressant (TCA) medications showed an association with fractures,<sup>10</sup> but the mechanism was not clear. SSRIs became widely used to treat depression in the 1990s, and about a decade ago a study implicated SSRIs as a potential risk factor for hip fractures.<sup>11</sup> The data was from a large, administrative database designed to collect information relevant to healthcare administration in Ontario — not specifically osteoporosis — and the study did not correct for all the possible confounding factors. A subsequent study using the United Kingdom

General Practice Database associated the use of both types of antidepressants with increased fractures.<sup>12</sup>

## SSRIs: a specific risk?

Recent evidence indicates that increased fractures are a side effect of SSRIs, independently of BMD and the incidence of falls. In 2004, a group using data from the US Medicare Current Beneficiary Survey showed an increased relative risk of 1.8 (95% CI 1.5–2.1) of hip fractures with SSRI use after controlling for five potential confounding factors: body mass index, smoking, activities of daily living score, cognitive impairment and the Roslow-Breslau physical impairment scale.<sup>13</sup>

The Canadian Multicentre Osteoporosis Study (CaMos) research group conducted a prospective cohort study that followed 5008 randomly selected men and women (78% women) aged  $\geq 50$  years.<sup>14</sup> Participants were specifically assessed for factors potentially relevant to osteoporosis. About 12% reported symptoms of depression on the MMC and the MHI-5 scales of the Medical Outcomes Study 36-Item Short-Form Health Survey questionnaire. The data was adjusted for many potential covariates including age, total hip bone mineral density (BMD), falls, modified Charlson comorbidity index, prevalent vertebral deformity, prevalent fragility fractures at baseline, and cumulative lifetime estrogen use in women. Findings in the 137 people taking SSRIs daily at baseline (66 of these were also taking SSRIs at 5 years' follow-up) showed roughly twice the risk of fragility fractures (e.g. occurring with minimal or no trauma) (HR 2.1; 95% CI 1.3–1.4). Fracture sites included forearm, ankle, foot, hip, rib, femur and back. As well, BMD was reduced by 4% at the hip (statistically significant) and 2.4% at the lower spine (not statistically significant) in patients reporting daily use of SSRIs. While SSRI users were more likely to be also taking anticonvulsants or corticosteroids, other drugs known to be associated with lower BMD, the association with fractures persisted after consideration of these as covariates. SSRI users also had a higher risk of falling (odds ratio 2.2; 95% CI 1.4–3.5). Although the mechanism was unclear, SSRIs can induce hypotension, which may predispose to falls.

A non-statistically significant tendency towards increased risk of fractures was seen in individuals taking TCA antidepressants; however, it was not known how many of

David Goltzman, MD, FRCPC, is a Professor in the Departments of Medicine and Physiology at McGill University, Director of the McGill Centre for Bone and Periodontal Research, and Senior Physician and Director of the Clinical Bone Centre at the McGill University Health Centre (MUHC). He is National Principal Investigator of the CaMos Study and a member of the Scientific Advisory Council of Osteoporosis Canada.

these had switched to treatment with SSRIs. A greater risk of fractures (hazard ratio [HR] 1.5; 95% CI 1.1–2.1) was seen for each SSRI dose increase from the lowest daily dose — in other words, a dose-response effect was seen. Although the duration of SSRI use was unknown, the 66 patients taking the medication both at baseline and at year 5 of the study showed a similar risk (HR 2.1; 95% CI 1.1–4.0). Some limitations of this study were that the number of SSRI users was small (137) and that, as in all observational studies, SSRI use may be associated with unknown confounders that were not controlled for.

A subsequent study<sup>15</sup> compared hip BMD in 2722 women with a median age of 78.5 years, who were participants in the prospective Study of Osteoporotic Fractures. At follow-up of 4.9 years, after adjusting for many potential confounding factors (including age, race, health status, Geriatric Depression Scale score, Mini-Mental State Examination score, smoking status, body mass index, hip BMD and use of calcium supplements, vitamin D, estrogen, thiazide and bisphosphonates), the 198 women using SSRIs had a greater rate of reduction in hip BMD (0.82% per year) than those using TCAs or no antidepressant (both 0.47% per year). Results were similar in women scoring < 6 on the Geriatric Depression Scale.

### SSRIs may work directly to weaken bone cells and impair bone formation, or they may affect bone via neuronal input from the brain to the bone, or both

A study in men<sup>16</sup> showed that those taking SSRIs had 3.9% lower hip BMD and 5.9% lower lumbar spine BMD compared to those reporting trazodone, TCA or no antidepressant use. **Table 1** summarizes the associations between SSRI use and bone density observed in these three studies. The risk of lowered bone density with SSRI use appears to be similar to the risk with glucocorticoids,

## Practice tips

- Consider the possibility of increased risk of osteoporosis in depressed patients.
- Inform patients taking or considering taking SSRIs that these drugs appear to increase their risk of fracture by about 10%.
- Measure bone density and consider bisphosphonates therapy if appropriate.
- Ensure that depressed patients receive counseling on lifestyle measures to counteract bone loss: weight-bearing exercise, ensuring a diet rich in calcium and vitamin D, and avoiding smoking and alcohol.

which are considered a risk factor for osteoporosis, along with other drugs such as anticonvulsants, prolactin-elevating antipsychotics (e.g. risperidone and many first-generation antipsychotics) and anticoagulants.<sup>14</sup>

SSRIs may work directly to weaken bone cells and impair bone formation, or they may affect bone via neuronal input from the brain to the bone, or both.<sup>17</sup> In vitro and mouse studies indicate that bone has serotonin receptors, bone cell function is affected by serotonin,<sup>18</sup> SSRI-treated mice have reduced bone mass,<sup>19</sup> and the SSRI fluoxetine inhibits formation of osteoblasts and lowers osteoclast differentiation.<sup>18</sup>

### Clinical implications

None of the studies conducted to date were designed to determine the effects of dose or duration of SSRI use on bone loss. Prospective, longitudinal studies are needed to clarify the influence of antidepressant use on BMD, markers of bone turnover and fractures. A randomized controlled clinical trial comparing the effects of SSRIs

**Table 1**  
Reports of the association between SSRI use and BMD

|                              | Patients studied   | Number taking SSRIs | Reduction in BMD vs non-SSRI users   |
|------------------------------|--|---------------------|--|
| Richards et al <sup>14</sup> | <ul style="list-style-type: none"> <li>• n = 5008</li> <li>• 78% women</li> <li>• Median age: 65.1 years for SSRI users, 65.7 years for non-users</li> </ul> | 137                 | Hip: 4% decrease at hip<br>Lumbar spine: 2.4% decrease at spine, measured at baseline  |
| Diem et al <sup>15</sup>     | <ul style="list-style-type: none"> <li>• 2722 women</li> <li>• Mean age 78.5 years</li> </ul>  | 198                 | Hip: 0.82% per year rate of bone reduction vs 0.47% in non-SSRI users, measured 4.9 years after first examination<br>Spine: not measured |
| Haney et al <sup>16</sup>    | <ul style="list-style-type: none"> <li>• 5995 men</li> <li>• Mean age 73.7 years</li> </ul>  | 160                 | Hip: 3.9% decrease<br>Lumbar spine: 5.9% decrease, measured at baseline  |

and TCAs on bone, perhaps with an historical control arm, would be extremely helpful to guide clinical practice. Current guidelines for assessment of osteoporosis risk, including the 2002 Osteoporosis Canada guidelines<sup>20</sup> and the World Health Organization's FRAX model,<sup>21</sup> do not incorporate depression or antidepressants as a risk factor — both may bear revisiting pending such additional data.

In the meantime, physicians should be aware of the evidence supporting the increased likelihood of bone loss in patients with depression, especially in those taking SSRIs, and consider monitoring their bone density. Although individuals needing or taking antidepressants for valid reasons should be advised not to refuse a trial of SSRIs or to discontinue antidepressant use if effective, such patients should be alerted to the potential increased risk for osteoporosis. ●

#### References

- Ostbye T, Kristjansson B, Hill G et al. *Chronic Dis Can* 2005; 26(4):93-9.
- Michelson D, Stratakis C, Hill L *NEJM* 1996;335(16):1176-81.
- Schweiger U, Weber B, Deuschle M, Heuser I. *Am J Psychiatry* 2000;157(1):118-20.
- Robbins J, Hirsch C, Whitmer R et al. *J Am Geriatr Soc* 2001; 49(6):732-6.
- Whooley MA, Kip KE, Cauley JA et al. *Arch Intern Med* 1999; 159(5):484-90.
- Furlan PM, Ten Have T, Cary M et al. *Biol Psychiatry* 2005;57(8): 911-7.
- Kahl KG, Rudolf S, Stoeckelhuber BM et al. *Am J Psychiatry* 2005; 162(1):168-74.
- Laudisio A, Marzetti E, Cocchi A et al. *Int J Geriatr Psychiatry* 2008; 23(11):1119-26.
- Eskandari F, Martinez PE, Torvik S et al. *Arch Intern Med* 2007; 167(21):2329-36.
- Ray WA, Griffin MR, Malcolm E. *Arch Intern Med*. 1991 Apr; 151(4):754-6.
- Liu B, Anderson G, Mittmann N et al. *Lancet* 1998;351(9112): 1303-7.
- Hubbard R, Farrington P, Smith C et al. *Am J Epidemiol* 2003; 158(1):77-84.
- Schneeweiss S, Wang PS. *J Clin Psychopharmacol* 2004;24(6):632-8.
- Richards JB, Papaioannou A, Adachi JD et al. *Arch Intern Med* 2007; 167(2):188-94.
- Diem SJ, Blackwell TL, Stone KL et al. *Arch Intern Med* 2007; 167(12):1240-5.
- Haney EM, Chan BK, Diem SJ et al. *Arch Intern Med*. 2007 Jun 25; 167(12):1246-51.
- Mezuk B, Eaton WW, Golden SH. *Osteoporos Int* 2008;19(1):1-12.
- Gustafsson BI, Thommesen L, Stunes AK et al. *J Cell Biochem*. 2006 May 1;98(1):139-51.
- Bliziotes MM, Eshleman AJ, Zhang XW, Wires KM. *Bone* 2001; 29:477-486.
- Brown JP, Josse RG; Scientific Advisory Council of the Osteoporosis Society of Canada. *CMAJ*. 2002 Nov 12; 167(10 Suppl):S1-34.
- World Health Organization Collaborating Centre for Metabolic Bone Diseases, University of Sheffield, UK. Information and calculation tools available at [www.shef.ac.uk/FRAX](http://www.shef.ac.uk/FRAX).

Continued from page 3

## CASE 2: 16-month-old girl with juvenile idiopathic arthritis

Glucocorticoid-induced osteoporosis can also occur very early in life. A 16-month-old girl diagnosed with systemic juvenile idiopathic arthritis at 6 months of age was treated with prednisone for 9 months. Her nutritional status, including calcium and vitamin D intake, was excellent. She was Cushingoid and showed marked deceleration in growth velocity. Her bone age was delayed at 9 to 12 months, and she was found to have moderate vertebral fractures at T12 and L1. Given her young age, apparent lack of symptoms and the fact that she was undergoing a reduction in her glucocorticoid dose, bisphosphonate therapy was not administered. However, she continues to be carefully monitored for signs of deterioration and impact on quality of life.

### Diagnosis and management

These cases illustrate that children at different ages who are receiving glucocorticoids can develop osteoporosis. In the pediatric population, osteoporosis is not defined according to BMD testing alone; low BMD combined with vertebral or low-trauma extremity fractures must be present for children to be diagnosed with the condition. For BMD testing, the Z-score is used rather than the T-score, as the former refers to the number of standard deviations above or below the mean for the patient's chronological age and gender. Vertebral fractures can

occur in the first 12 months of glucocorticoid therapy in children, despite normal intake of calcium and vitamin D. They may be, but are not always, associated with back pain. There is a predilection for an adverse effect of glucocorticoids on the spine; however, low-trauma extremity fractures may also occur in children receiving glucocorticoid therapy.

Bisphosphonates can be used to treat osteoporosis in children. Intravenous (IV) therapy appears to be more effective in children than oral bisphosphonate treatment. Potential side effects resulting from the first IV infusion include low-grade fever, chills, hypocalcemia and malaise. To date, there have been no serious side effects noted in children who have received bisphosphonates at standard, published doses, but information on their long-term use remains limited. Experts therefore recommend that bisphosphonates be administered only to children with reduced bone mass plus symptomatic vertebral collapse and/or recurrent low-trauma extremity fractures, particularly when these occur in the face of persistent risk factors.

Currently, there is inadequate evidence to support treatment of reduced BMD alone with bisphosphonates in children. Minimization of glucocorticoid use (if possible), treatment of the underlying disease, encouragement of physical activity, and optimization of calcium and vitamin D intake are reasonable first steps in the care of children with risk factors for osteoporosis. ●

q.

**My patient has been taking osteoporosis medication for 7 years, with slight improvement of her bone density. When should I consider recommending that she discontinue therapy, or are osteoporosis medications meant to be taken for life? What about long-term risks?**

**Dr. Heather McDonald responds:** Chronic diseases usually require long-term, often indefinite, therapy. However, many patients ask when they can or should discontinue their antiresorptive medication, prompted by concerns about possible side effects with long-term use of these medications, especially bisphosphonates. The answer is always, “It depends on the patient,” and it must take into account the likely benefits along with the potential risks.

There have been some data in the experimental models of bone suggesting that long-term antiresorptive treatment can cause inferior bone quality over time and thus lead to increased risk of fracture. In the patient population, however, treatment for up to 10 years as part of the initial clinical trials does not support this concern. Available long-term data for alendronate and risedronate (both aminobisphosphonates) indicate that their antifracture benefit continues over moderately long periods of time (Bone HG et al. *N Eng J Med* 2004; 350[12]:1189-99; Mellström DD et al. *Calcif Tissue Int* 2004;75[6]:462-8). When the medications are discontinued, there is a measurable loss of bone over time. The rapidity of this loss seems to differ with the specific drug used: raloxifene (a selective estrogen receptor modulator [SERM]) appears to have the shortest, and alendronate the longest, impact post discontinuation (Neele SJ et al.

**Monitoring renal function, vitamin D intake (and 25[OH] vitamin D levels) and ability to adhere to proper dosing instructions can all help ensure that our patients get the most from their osteoporosis therapy**

**Heather McDonald-Blumer, MD, MSc, FRCPC**, is Program Director for Postgraduate Rheumatology at the University of Toronto and Associate Director of the Osteoporosis Program at the University Health Network, in Toronto.

**Susan J. Whiting, PhD**, is Professor at the College of Pharmacy & Nutrition, University of Saskatchewan.

**Angela Cheung, MD, PhD, FRCPC**, is Director of the Osteoporosis Program at University Health Network (UHN) and Mount Sinai Hospital, Associate Director of Women’s Health Program at UHN and Associate Professor at the University of Toronto.

*Bone* 2002;30[4]:599-603; Black DM et al. *JAMA* 2006; 296[24]:2927-38.) Interestingly, at least with alendronate, the fracture-protective effect seems to continue for up to 5 years after the medication is stopped.

It is generally agreed that stopping bisphosphonate therapy for a year or two may be reasonable if a patient:

- has been on it for 5 to 7 years
- has responded well, with no fractures and stable/improved bone mineral density (BMD)
- is not felt to be at extreme risk of fracture

It is important to ensure that the patient continues to take adequate calcium and vitamin D, minimizes all other risk factors and returns for a follow-up clinical and bone density assessment in 1 to 2 years.

For individuals considered to be at high risk for fracture — i.e. who have extremely low bone density, previous low-trauma fractures, ongoing risk factors such as chronic corticosteroid intake and/or increased risk for falls — continued antiresorptive therapy is generally advised, even if this takes them past 5 or 7 years of use.

A final consideration: When deciding whether or not to continue pharmacologic therapy for osteoporosis, it is important to be mindful of changes in general health that may preclude safe use of medication. Monitoring renal function, vitamin D intake (and 25[OH] vitamin D levels), ability to adhere to proper dosing instructions, etc. can all help ensure that our patients get the most from their osteoporosis therapy.

q.

**How does vitamin C affect bones and bone loss? What are the current recommended amounts to maintain bone health in adults?**

**Dr. Susan Whiting answers:** Vitamin C (ascorbic acid) plays 2 roles in bone health. It is essential for the synthesis of collagen, the major protein component of bone. Scorbutic animals show bone loss, and infants with scurvy present with rickets with deformation of the rib cage. Second, vitamin C is an antioxidant, able to scavenge free radicals. In the process of bone resorption, free radicals are formed that, if unchecked, can decrease bone formation and lead to loss of BMD (Basu et al. *Biochem Biophys Res Commun* 2001;288:275-9).

Current Recommended Dietary Allowance (RDA) values for vitamin C for adults — 90 mg for men and 75 mg for women — were set to provide antioxidant protection and are higher than amounts needed to prevent scurvy. The typical Canadian diet meets these requirements, provided sufficient fruits and vegetables are consumed. On average, Canadian men and women obtain 118 mg and 102 mg, respectively, from food sources alone (Health Canada. Canadian Community

## A recent study concluded that a daily high dose of vitamin K provides no protection against the age-related decline in BMD in postmenopausal women, but may protect against fractures and cancers in postmenopausal women with osteopenia



Health Survey Cycle 2.2, Nutrition (2004), Nutrient Intakes From Food, Provincial, Regional and National Summary Data Tables, Vol. 1. [www.hc-sc.gc.ca/fn-an/pubs/cchs-nutri-escce](http://www.hc-sc.gc.ca/fn-an/pubs/cchs-nutri-escce). Intake of vitamin C supplements is common, and can range from 50 mg to 1000 mg. An Upper Level of 2000 mg was set, as higher intakes can cause osmotic diarrhea (Health Canada. [www.hc-sc.gc.ca/fn-an/nutrition/reference/table](http://www.hc-sc.gc.ca/fn-an/nutrition/reference/table)).

A recent article examined the effect of vitamin C on BMD, as well as BMD loss over 4 years, in a group of older adults with mean age of 75 (Sahni et al. *J Nutr* 2008; 138:1931-8). From the longitudinal analyses, only men showed a significantly decreased rate of BMD loss in response to dietary (i.e. food-based) vitamin C intake. This effect was seen for total vitamin C intake (food and supplements) only in men who had either low vitamin E or low calcium intake, and disappeared when fruit and vegetable intake was controlled for. This finding suggests that it is not the vitamin C per se but the inclusion of fruits and vegetables in the diet that was protective, an effect seen in some studies (Prynne et al. *Am J Clin Nutr* 2006;83:1420-8) but not all (Macdonald et al. *Am J Clin Nutr* 2008;88:465-74). This is not surprising, as these foods contain other nutrients associated with bone health, e.g. lycopene (Rao et al. *Osteoporos Int* 2007; 18:109-15), vitamin K and alkaline potassium (Lanham-New. *J Nutr* 2008;138:172S-177S).

The bottom line? Following Canada's Food Guide (see [www.hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php](http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php)) and ensuring adequate calcium and vitamin D is the best advice.

q.

**Is there any conclusive evidence that vitamin K protects against loss of BMD? What do we know about its other risks and benefits?**

**Dr. Angela Cheung explains:** Vitamin K has been widely promoted as a supplement for decreasing bone loss in postmenopausal women, but we do not yet know

its long-term benefits and potential harms. A recent study published in October 2008 (*PLoS Med* 5[10]: e196. doi:10.1371/journal.pmed.0050196) has shown that vitamin K does not protect against decreased BMD related to aging, but may protect against fractures (as well as some cancers) in postmenopausal women.

The two-year randomized, placebo-controlled, double-blind trial was conducted to determine whether daily high-dose vitamin K1 supplementation safely reduces bone loss, bone turnover and fractures in postmenopausal women with osteopenia. The study randomized 440 postmenopausal women with osteopenia to receive either 5 mg of vitamin K1 or placebo daily for 2 years, and was extended for up to 4 years for earlier participants (261 women). All participants were supplemented with calcium (1200–1500 mg) and vitamin D (800–1000 IU) daily. Primary endpoints were BMD changes at the lumbar spine and total hip at 2 years. Secondary outcomes included BMD changes at other sites, bone turnover markers, height, fractures, side effects and health-related quality of life. Women in the study had adequate vitamin D levels, with a mean serum 25-hydroxyvitamin D level of 77 nmol/l at baseline.

Bone density scans after 2 and 4 years revealed no differences in BMD loss between the 2 groups of women. BMD decreased by -1.28% and -1.22% ( $p = 0.84$ ; 95% confidence interval [CI] -0.67% to 0.54%) at the lumbar spine and -0.69% and -0.88% ( $p = 0.51$ ; 95% CI -0.37% to 0.75%) at the total hip in the vitamin K and placebo groups, respectively. Daily vitamin K1 supplementation increased serum vitamin K1 levels by 10-fold, and decreased the percentage of undercarboxylated osteocalcin and total osteocalcin levels (bone formation marker). However, C-telopeptide levels (bone resorption marker) were not significantly different between the groups. Fewer women in the vitamin K group had clinical fractures (9 vs 20,  $p = 0.04$ ) and fewer had cancers (3 vs 12,  $p = 0.02$ ). Vitamin K supplements were well tolerated and there were no significant differences in adverse effects or health-related quality of life between the groups. The study concluded that a daily high dose of vitamin K provides no protection against the age-related decline in BMD in postmenopausal women, but may protect against fractures and cancers in postmenopausal women with osteopenia.

While these observations are intriguing, they are based on small numbers and the study was not powered to examine fractures or cancers. Until larger studies are done to confirm the findings, it is too early to recommend vitamin K1 supplementation to reduce the risk of osteoporosis. Meanwhile, women should continue to take adequate calcium and vitamin D, exercise, and eat a healthy balanced diet. ●

# OC–CIHR New Investigator Award

Osteoporosis Canada is pleased to announce the three recipients of the New Investigator Award in the Area of Osteoporosis under the Small Health Organizations Partnership Program (SHOPP), made possible by the partnership between Osteoporosis Canada and the Canadian Institutes of Health Research (CIHR). CIHR is Canada’s major federal funding agency for health research. The goal of the program is to “foster collaboration opportunities with small health charities and not-for-profit organizations with modest health research funding capacity by co-funding training and salary awards.”

Each of the following recipients will receive research funding for 5 years in their area of interest:

- Dr. Laura Targownik, University of Manitoba. *The delineation of the relationship between proton pump inhibitor (PPI) use and the development of osteoporosis and osteoporosis-related fractures*
- Dr. Suzanne Cadarette, University of Toronto. *Improving medication use, health care and quality of life through innovative health outcomes research*
- Dr. Brent Richards, McGill University. *The genetic epidemiology of osteoporotic fractures, from susceptibility genes to susceptible populations*

## Eli Lilly Canada Chair in Osteoporosis

Osteoporosis Canada is proud to report that Dr. Alexandra Papaioannou, geriatrician and Chair of the OC Scientific Advisory Council (SAC) has been named the inaugural holder of the endowed Eli Lilly Canada Chair in Osteoporosis at McMaster University. The endowment includes \$1 million from Eli Lilly Canada Inc., with matching research funds from the Division of Rheumatology at McMaster University’s Michael G. DeGroote School of Medicine. Dr. Papaioannou will investigate the best strategy for osteoporosis care, particularly with respect to fall and fracture prevention, and will train the next generation of physician scientists to look for a cure.

Also announced, Dr. Papaioannou holds a five-year

career award, the CIHR/Eli Lilly Canada Research Chair in Osteoporosis, Falls and Fracture Prevention, sponsored by the CIHR/Canada’s Research-Based Pharmaceutical Companies (Rx&D) research chair program. This position will enhance the work of the endowed chair. CIHR is the federal agency sponsoring peer-reviewed health research in Canada; Rx&D is the national association of Canada’s research-based pharmaceutical companies. The CIHR/Rx&D career award is valued at \$400,000 over five years.

Please join Osteoporosis Canada and the SAC in congratulating Dr. Papaioannou on this fitting tribute to her outstanding competence, commitment, leadership and mentorship of young scientists.



## Resources for your patients

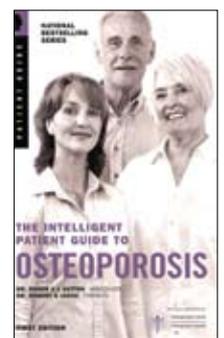
The Canadian Osteoporosis Patient Network (COPN) is a virtual network that works with Osteoporosis Canada to increase public and political awareness of osteoporosis by advocating for better access to effective diagnosis and treatment nationwide, providing osteoporosis patient perspectives to decision makers and researchers, and sharing their experiences and knowledge with the public.

Patients can access COPN through the OC website ([www.osteoporosis.ca](http://www.osteoporosis.ca)). COPN provides online tools and resources, including evidence-based facts about osteoporosis, information on clinical trials, advice on living well with osteoporosis, and updates on local initiatives. With the creation of COPN, OC hopes to recruit more patient volunteers from across the country to learn about the issues affecting them.

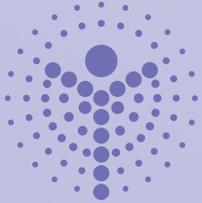
Urge your patients to get involved!

Osteoporosis Canada is pleased to officially endorse a new book, *The Intelligent Patient Guide to Osteoporosis*, which provides reliable, evidence-based information to help patients learn more about the causes, diagnosis and treatment of osteoporosis. Understanding more about their condition empowers patients to know the appropriate questions to ask their physicians and to take an active part in decision-making concerning their health. Research has shown that informed patients have better outcomes, both physically and psychologically.

Roger AL Sutton, DM, FRCPC, is a Professor Emeritus of Medicine and Urological Sciences at the University of British Columbia. Robert G Josse, MB BS, FRCPC, is a Professor of Medicine and Nutritional Sciences at the University of Toronto. He is the former Chair of the SAC, and is Director of the Osteoporosis Centre at St. Michael’s Hospital in Toronto. ●



***The Intelligent Patient Guide to Osteoporosis***, by Dr. Roger AL Sutton and Dr. Robert G Josse, Vancouver: Intelligent Patient Guide Ltd., First edition, 2009.



Osteoporosis Canada

Ostéoporose Canada



## about Osteoporosis Canada

Osteoporosis Canada is a national, not-for-profit organization dedicated to educating, empowering and supporting individuals and communities in the risk reduction and treatment of osteoporosis.

The organization, guided by its Scientific Advisory Council (SAC) made up of osteoporosis experts from across the country, works with healthcare professionals to make the latest prevention, diagnostic and treatment options available to Canadians.

[www.osteoporosis.ca](http://www.osteoporosis.ca)

## ASBMR 31<sup>ST</sup> ANNUAL MEETING

September 11–15, 2009

Colorado Convention Center  
Denver, Colorado

The American Society for Bone and Mineral Research (ASBMR) brings together clinical and experimental scientists involved in the study of bone and mineral metabolism. The ASBMR Annual Meeting is the premier international scientific meeting in the bone and mineral field. Attendees experience the highest level of scientific exchange, the best in professional development and tremendous networking opportunities. Rigorous basic, clinical and translational scientific programs offer a diverse array of educational forums: plenary lectures, symposia, state-of-the-art lectures, oral and poster sessions, workshops and meet-the-professor sessions.

For information, please visit [www.asbmr.org/meeting/index.cfm](http://www.asbmr.org/meeting/index.cfm)

## 6<sup>TH</sup> INTERNATIONAL CONGRESS ON GLUCOCORTICOID INDUCED OSTEOPOROSIS (GIO)

October 8 - 10, 2009

Siena, Italy

GIO 2009 continues the discussion of the latest science in skeletal biology and pharmacology, focusing on glucocorticoid therapy in diverse clinical settings. The meeting convenes top-level researchers and experienced clinicians, and aims to provide practical answers for healthcare professionals.

Held under the auspices of the International Osteoporosis Foundation (IOF), GIO 2009 will blend a quality scientific programme with pleasant social and cultural opportunities.

For more information: [www.symposium.it/gio2009/indexgio09.html](http://www.symposium.it/gio2009/indexgio09.html)

## ISCD BONE DENSITOMETRY COURSES

The ISCD offers courses for clinicians, technologists, scientists, researchers and healthcare providers.

For information and locations around the world, contact Anabela Gomes:  
Tel: 860-586-7563 ext 583  
Email: [agomes@iscd.org](mailto:agomes@iscd.org); [www.ISCD.org](http://www.ISCD.org)