What is adequate?

I read with interest the article “Premenopausal women and low bone density” by Aliya Khan.1 Many of us believe that management of low bone density in adults begins by maximizing bone accretion during childhood and adolescence. With current inadequate intakes of calcium and vitamin D in Canada and the poor exercise habits of many of our youth, this is an uphill battle!

There were 2 statements in Dr Khan’s article that could be adjusted. The first relates to screening for celiac disease. The author refers to a “celiac panel.” This might be a local laboratory test, but it is not uniform across the country. The antigliadin antibody test has, in general, gone out of use, as it has very poor specificity. The antitransglutaminase antibody test is far more specific. A recent review in the Canadian Journal of Gastroenterology2 notes, from the National Institutes of Health Consensus Conference on Celiac Disease, that “all diagnostic tests need to be performed while the patient is on a gluten-containing diet” and that antitransglutaminase and antiendomysial antibody tests are equally effective. It goes on to note that “small-bowel biopsy [is] indicated in any individual with a positive celiac disease antibody test.” In summary, make sure the patient is eating gluten daily; do an antitransglutaminase test; if test results are positive, arrange for a small-bowel biopsy.

My second point relates to the sentence, “It is important to ensure adequate calcium and vitamin D intake.” “Adequate” is one of those wonderfully stretchy words. What is adequate vitamin D intake? Health Canada still proposes 200 IU daily for everyone from extreme youth to older middle age. Our studies in children (3 to 16 years of age) in Edmonton, Alta, show that 200 IU daily is not even adequate for maintaining levels now considered mildly to moderately deficient (40 nmol/L), let alone optimum (<80 nmol/L).3 Rucker et al in Calgary4 and Vieth et al in Toronto5 have identified substantial deficiency in populations of healthy adults in Canada. From these and other studies across Canada we can extrapolate that Canadians in general have moderate to severe vitamin D deficiency. This deficiency will be exacerbated in those who do not drink fluid milk; do not take daily vitamin supplements; and do not get sun exposure on bare skin without sunscreen for at least 10 minutes during the middle of the day (about 11am to 4pm) at least twice weekly.

Adequate vitamin D intake is that which will ensure a circulating blood level of 25-hydroxycholecalciferol (25[OH]D3) of 35 to 50 ng/mL or 80 to 200 nmol/L. In general, this intake will be at least 1000 IU daily, plus normal dietary vitamin D, but might be as much as 4000 IU daily.

An excellent review can be found in “Benefits and requirements of vitamin D for optimal health.”6 Bone density for any individual relates to many factors, such as genetics, health issues, prior bone accretion in childhood and adolescence, and sex. It can, however, be improved for every individual through weight-bearing exercise and “adequate calcium and vitamin D intake.”

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References

Response

I thank Adrian Jones for his comments on the article “Premenopausal women and low bone density.”1 The objectives of this article were to provide direction for appropriate use of bone mineral density (BMD) testing and to provide an approach to management of low BMD in premenopausal women. The limited scope of the paper did not allow for more detailed description of each of the specific causes of low BMD in premenopausal women. For a more detailed review of each of the secondary causes of low BMD, I refer readers to our recently published Canadian standards document addressing skeletal health assessment in those with secondary causes of low BMD, including vitamin D deficiency.2 In this national standards document, we recommend that vitamin D deficiency, if present, should be corrected, aiming for 25-hydroxycholecalciferol levels of at least 75 nmol/L, and we recommend repeating BMD testing 1 year later. It is expected that BMD will increase or stabilize with correction of vitamin D deficiency and when parathyroid hormone levels return to normal.

I also agree that one of the most reliable tests for celiac disease is the measurement of serum immunoglobulin A antibodies to tissue transglutaminase. Antibodies directed against gliadin, endomysium, and tissue transglutaminase have shown good correlation.
with patients’ clinical condition, and measurements are best completed while patients are on gluten-containing diets.

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References

Chest pain, dyspnea, and cough

How benign is benign use of nitrofurantoin for prophylaxis of urinary tract infections (UTIs)? I have read with great interest an article by L. Nicolle and colleagues, “Uncomplicated urinary tract infection in women. Current practice and the effect of antibiotic resistance on empiric treatment.”1 The authors refer to the efficacy and safety profile of nitrofurantoin for short-term treatment of uncomplicated urinary tract infection. It is important to mention, however, that long-term treatment with nitrofurantoin can have dangerous complications.

Recently, I have seen several elderly women in the emergency department who were receiving prophylactic nitrofurantoin for recurrent UTIs. These patients have been prescribed nitrofurantoin for years, despite known warnings and adverse side effects that are well described in the nitrofurantoin monograph in the Compendium of Pharmaceuticals and Specialties.

Use of nitrofurantoin for longer than 6 months can lead to subacute, acute, or chronic pulmonary hypersensitivity reaction, the 2 most common forms of which are interstitial pneumonitis and pulmonary fibrosis. Patients might present with dyspnea on exertion, cough, chest pain, and malaise. Risk of lung toxicity varies among patients receiving prophylactic nitrofurantoin. A 10-year retrospective Swedish study of long-term nitrofurantoin use has demonstrated that older women are more prone to developing lung toxicity than their male counterparts or younger women.2

The potential irreversible side effects that are well described in the literature are not commonly considered when assessing patients in the emergency department who are receiving nitrofurantoin prophylaxis. A recent small study looked at the radiologic changes in elderly women receiving nitrofurantoin prophylaxis who presented with dyspnea, cough, and chest pain. Authors of the study concluded that the radiologic findings are relatively nonspecific on chest film and usually include bilateral areas of ground-glass opacities on computed tomography of the chest.3

There are several medications, chemicals, and bacteria—such as bleomycin, methotrexate, cyclophosphamide, amiodarone, procainamide, penicillamine, gold, asbestos, silica, mycobacteria, and fungi—that are well known to the medical community for their potential to induce pulmonary toxicity. However, health care providers, and especially trainees, are not well educated about potential risks related to nitrofurantoin-induced lung toxicity.

In the last decade, many immunologic mediators were shown to play a role in drug-induced lung fibrosis, such as interleukin-1, interleukin-13, tumour necrosis factor-alpha, and interferon gamma in bleomycin-induced pulmonary fibrosis.4 Nitrofurantoin induces pulmonary hypersensitivity reactions, likely via redox cycling of the nitro group and its radical anion; this process is also known as oxidative stress.5 Several medications have been shown to ameliorate drug-induced lung toxicity in animal models.6 No antidote has been found in human beings, however.5

No randomized controlled trials have examined potential treatment strategies for nitrofurantoin-induced pulmonary inflammatory reactions. The standard clinical approach is to discontinue an offending agent and determine whether the patient requires in-hospital monitoring and supportive care. Some reports refer to steroid therapy in acute and chronic cases as being beneficial for resolution of symptoms. Fortunately, most nitrofurantoin-induced lung toxicity is reversible when the medication is discontinued.

It is very important to consider these side effects when prescribing nitrofurantoin for prophylaxis and when assessing patients who have dyspnea, chest pain, and cough and who are receiving long-term therapy with nitrofurantoin.

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References

Clarifying omega-3 fatty acid recommendations

I applaud Dr Schwalfenberg’s review of omega-3 fatty acids, published in the June 2006 issue of Canadian...