

with patients' clinical condition, and measurements are best completed while patients are on gluten-containing diets.

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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.⁴ 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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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*