

# The Medical Letter®

## On Drugs and Therapeutics

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### ADDENDUM

#### Warfarin-Acetaminophen Interaction

A reader expressed disappointment that our recent listing of "Some Warfarin Drug Interactions"<sup>1</sup> did not include acetaminophen. Perhaps it should have. Acetaminophen can increase the anticoagulant effect of warfarin, particularly with continued use, but it does so inconsistently. The mechanism of this interaction has not been established, but may be related to an acetaminophen metabolite inhibiting vitamin K-epoxide reductase, the target for warfarin's anticoagulant effect.<sup>2</sup>

Patient susceptibility varies, possibly on a genetic basis; occasional use of acetaminophen generally has little or no effect on the international normalized ratio (INR) in patients on chronic warfarin therapy, but in some, even a few grams of the drug may cause a dramatic increase in INR. One study in healthy subjects found no effect of acetaminophen 4 g per day for 2 weeks, while another study in patients with the same acetaminophen dose for the same period of time found a moderate increase in INR.<sup>3,4</sup> It might be prudent to monitor INR in patients on chronic warfarin therapy more closely than usual when they take more than 2 g per day of acetaminophen for more than a few days.

1. Pharmacogenetic-based dosing of warfarin. *Med Lett Drugs Ther* 2008; 50:39.
2. HH Thijssen et al. Paracetamol (acetaminophen) warfarin interaction: NAPQI, the toxic metabolite of paracetamol, is an inhibitor of enzymes in the vitamin K cycle. *Thromb Haemost* 2004; 92:797.
3. D Kwan et al. The effects of acetaminophen on pharmacokinetics and pharmacodynamics of warfarin. *J Clin Pharmacol* 1999; 39:68.
4. I Mahe et al. Paracetamol: A haemorrhagic risk factor in patients on warfarin. *Br J Clin Pharmacol* 2005; 59:371.

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