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Antiepileptic drugs and warfarin

In a recent CMAJ commentary on drug interactions with warfarin,1 David Juurlink overlooked a very important category of drugs that interact with warfarin: antiepileptic drugs. Phenytoin, carbamazepine and phenobarbital are potent inducers of the cytochrome P450 system, and their interactions with warfarin have been known for decades.2-5 These drugs can substantially increase the rate at which warfarin is metabolized and thus reduce the effect of a previously adjusted dose. Likewise, sudden withdrawal of any of these drugs may decrease the rate at which warfarin is metabolized and put a patient taking a combination of these drugs at an increased risk of bleeding. Antiepileptic drugs are not only prescribed for epilepsy, which is estimated to affect 200 000 Canadians; they are also used to treat psychiatric disorders in a large population of patients. I suggest that Juurlink should add antiepileptic drugs as a ninth category to Table 1.1

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[The author responds:]

I thank Nizam Ahmed for his suggestion. Although the goal of Table 1 in my article¹ was not comprehensiveness, anticonvulsants can indeed alter the pharmacokinetics of warfarin, and their inclusion on the clinician's short list of drugs that may influence control of anticoagulation is worthwhile. Although carbamazepine and the barbiturates induce various isoforms of the cytochrome P450 enzyme system and thereby enhance the metabolism of warfarin, the interaction between phenytoin and warfarin is considerably more complex, resulting in an enhanced, reduced or even biphasic effect on the pharmacokinetics of warfarin.2 The consequences of phenytoin therapy in patients taking warfarin are therefore unpredictable, and close monitoring is advisable after treatment with phenytoin is begun or the dose is changed.

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Pharmacist prescribing

I was interested in the discussion about pharmacist prescribing at the Canadian Medical Association's most recent annual meeting. Every day, pharmacists help patients deal with drug-related problems, such as drug prescriptions with no clear indications, medical con-

ditions for which the patient needs a prescription drug but has not yet received it, drug side effects, drug-drug or drug-food interactions, suboptimal dosing and poor drug selection. Once the problems have been assessed, the pharmacist formulates a plan to resolve them, usually by initiating, stopping or changing the drug therapy or changing the dosing.

In most settings, we need to contact the patient's physician to complete this aspect of patient care. Canadian community pharmacists can alter drug therapy independently for nonprescription drugs (called counter prescribing in Britain), but in hospitals we cannot even start a patient on acetylsalicylic acid for a headache without going through his or her physician. How can this be good for patient care?

British pharmacists have been prescribing since 2003; they complete an accredited training program that includes a physician-supervised practicum. Concerns that pharmacists would prescribe drugs inappropriately have proven to be unfounded. Although British pharmacists can legally prescribe most drugs, in practice they only prescribe drugs within their area of expertise and according to their level of competence, just like physicians. The top 5 drugs prescribed by pharmacists in Britain are ramipril, bendroflumethiazide, simvastatin, amlodipine and acetylsalicylic acid (for antiplatelet therapy).2 Let us go beyond the fear of the unknown and seize this opportunity to optimize our use of health care resources for the benefit of patients.

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