Don't be so quick to ban medications

Although evidence-based medicine has caught on among physicians, it seems that regulatory agencies persist in generating hysteria-based blanket recommendations.

Donald Farquhar[1] wrote a clinical update for *CMAJ* on a case–control study showing that, mainly when it is used repeatedly for appetite suppresion, phenylpropanolamine is associated with increased risk of hemorrhagic stroke primarily in women who smoke cigarettes and are black, hypertensive and less well educated.[2] This population also seems to be at some risk even at first use of phenylpropanolamine-containing cough or cold remedies. On this basis the US Food and Drug Administration and Health Canada announced they were taking steps to remove phenylpropanolamine from all drug products and requested that all drug companies stop marketing products containing phenylpropanolamine.

Why? How many millions of patients find relief from using these medications each year, and what is their risk of stroke? The risk is not distributed evenly, because among men there was no increased risk of hemorrhagic stroke with use of phenylpropanolamine-containing products.[2]

What is the number needed to harm? Since 1969, only 60 cases of hemorrhagic stroke associated with the use of products containing phenylpropanolamine have been reported to the US Food and Drug Administration, or about 2 reported strokes per year.[2]

This isn't the first time good medicines have been killed because regulatory agencies have overreacted. Cisapride was removed from the market after the deaths of fewer than a dozen people with identifiable risk factors. However, these agencies are somewhat inconsistent: dozens of men have accepted the well-publicized risk of death associated with use of sildenafil and died, yet this drug remains on the market.

We place appropriate warning signs concerning the risk of stroke on cigarette packages. Why not do the same with medications? When risk factors for serious harm become known they should be placed in bold type on the drug packaging and made well known to health care workers. Products containing phenylpropanolamine should probably be placed behind the counter so pharmacists can advise those patients identifiably at increased risk to use other products; they shouldn't be banned from the marketplace.

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References

1. Farquhar D. Phenylpropanolamine and hemorrhagic stroke in women. *CMAJ* 2000;164(5):684.
2. Kernan WN, Viscoli CM, Brass LM, Broderick JP, Brott T, Feldmann E, et al. Phenylpropanolamine and the risk of hemorrhagic stroke. *N Engl J Med* 2000;343(25):1826-32.

Troponin assays for coronary syndrome diagnosis

I read with interest the article by David Fitchett and colleagues in *CMAJ*'s series on the management of acute coronary syndromes.[1] From a laboratory point of view, the reader should bear in mind several points, especially as troponins are now the arbiter par excellence of coronary syndrome diagnosis.[2] The first is that a low-sensitivity test (CK MB [creatine kinase – MB isoenzyme activity or mass] level) should not be used to clarify the results of a high-sensitivity test (troponin).[3,4] Laboratories are often asked for a CK MB level when a patient has an elevated troponin level in an unclear clinical situation; the results of the test for the CK MB level may be falsely negative. Secondly, the troponin I value considered "normal" is assay dependent and can differ among manufacturers. The clinician should be aware of the reference limits and the coefficient of variation at the lower limits of the troponin assay used at his or her institution. Both troponin and CK MB levels are proportional to myocardial damage, but the relationship between troponin and CK MB levels is more complex; one has to gain experience with each to know what to expect with, for example, a massive myocardial infarction. Lastly, risk stratification may become more complex and, one would hope, more exact with the use of additional markers such as C-reactive protein and homocysteine.

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References

1. Fitchett D, Goodman S, Langer A. New advances in the management of acute coronary syndromes: 1. Matching treatment to risk. *CMAJ* 2001;164(9):1309-16.
2. Myocardial infarction redefined: a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36(3):959-69.
3. Check W. Troponin triple crown: diagnosis, risk, Rx. *CAP Today* 2001;15(7):1-62.
4. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: executive summary and recommendations. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (committee on the management of patients with unstable angina). *Circulation* 2000;102(10):1193-209.

[The authors respond:]

Cardiac troponin I and T assays are indeed highly sensitive for the detection of myocardial injury. Approximately 30% of patients previously diagnosed with unstable angina with no increase in creatine kinase (CK) or its MB isoenzyme (CK MB) are found to have elevated levels of circulating cardiac troponin.[1] Today these patients are considered to have minor degrees of myocardial injury; by American College