

ADDERALL RESPONSE – Pharmacy and Therapeutics Committee

March 9, 2005

You may have heard that on February 10, 2005, Health Canada suspended sales of Adderall® from the Canadian market, based on US reports of 20 deaths, including 14 deaths in adolescents and children. Six of those patients had underlying heart disease that put them at risk of sudden death including hypertrophic cardiomyopathy and ventricular tachycardia. In the remaining patients the deaths may have had causes completely unrelated to Adderall® use. US FDA responded by noting there is insufficient data to reach a causative conclusion and is not removing Adderall® from the market, but is continuing to evaluate the available data. This widely reported decision has triggered some concern among patients and providers. An ad-hoc committee of the Pharmacy and Therapeutics Committee at Children's Hospital Boston, has carefully reviewed available data and feels that there is not cause for concern and advises prudence in prescribing this medication to certain high-risk patients.

Adderall XR® is the trade name for an extended-release, once-daily formulation of Adderall®. Adderall® combines d and l-amphetamine salts into a single product. Dexedrine® and Dextrostat® are trade names for dextroamphetamine products. Along with methylphenidate (Ritalin®, Concerta®, Focalin® and Metadate®), these stimulants are the primary choice when drug therapy is used for attention deficit hyperactivity disorder (ADHD). While modest cardiovascular effects of increased heart rate and blood pressure are common with all of these medications, they have generally been felt to be safe and effective. With an estimated 20 million prescriptions annually, at least 1.5 to 2 million patients are regularly receiving these medications.

The FDA analysis and our review of the available data finds that the number of deaths reported in children on Adderall® is comparable to that expected in a healthy population of adolescents. Assuming 2 years of therapy the risks of cardiac death on the drug were 0.001%/year, the same as the population risk. The same holds for patients on Ritalin®, Concerta®, Focalin® and Metadate®. There is insufficient data available to us at this point to conclude that Adderall®, the other dextroamphetamine products, or methylphenidate are dangerous, or that any one of these products is safer than the others. However, there continues to be valid reasons to be prudent about the use of any of these agents in patients with significant heart disease.

There are specific features of each of the agents on the market that may make one more or less effective for individual patients. Specific guidelines may be coming from the FDA over the coming months. In the interim our recommendations are:

For patients without known heart disease:

These patients deserve the level of screening given for pre-participation sports physicals in evaluating for potential familial heart disease (like hypertrophic cardiomyopathy or long QT) or other occult disease. We believe that a history examining for cardiac symptoms, a family history, and a physical examination represents the most effective *screening test*. During the discussion with patient and family, the following questions must be included in the assessment.

Does the patient have;

1. A past or current personal history of syncope, fainting or palpitations?
2. A past or current personal history of significant heart disease?
3. A family history of either cardiomyopathy or sudden death < age 40?

Patients and/or family who answer yes to any of those questions or whose examination suggests significant heart disease should be referred to cardiology.



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For patients with known heart disease.

There continue to be valid reasons to be prudent about the use of any of these agents in patients with significant heart disease. The current labeling of both the amphetamine based agents (Adderall[®], Dexedrine[®]) and the methylphenidate based agents (Ritalin[®], Concerta[®], Focalin[®], and Metadate[®]) cautions about the use of both agents in patients with high blood pressure, heart failure or those diseases where increasing blood pressure could be dangerous. Both classes of drugs are not recommended in patients with Long QT. Similar precautions are made for atomoxetine (Strattera[®])

Some patients with significant heart disease, particularly those who have had heart surgery as infants, may have an increased need for ADHD therapy.

Many forms of heart disease have no increased risk of arrhythmias or early mortality. Examples include most atrial septal defects, minimal aortic stenosis, isolated pulmonary stenosis, and closed or tiny ventricular septal defects.

Decisions regarding individual patients with heart disease should entail a standard risk/benefit discussion that is best managed among the family and the responsible providers.

No role for routine ECG screening.

While there have been suggestions that routine ECG screening is warranted in patients on stimulant therapy that is not our recommendation. This topic was reviewed by a select committee for the American Heart Association and the American Academy of Pediatrics in 1998 with no specific monitoring recommended at that time. The ECG, while relatively inexpensive, is a problematic screening test because a large number of normal children test positively for left ventricular hypertrophy or borderline QT intervals in the absence of any disease. On the other hand, some patients with serious diseases, like anomalous coronary artery, have completely normal ECGs. Hence, for the cardiovascularly asymptomatic patient with a reassuring family history and normal physical examination, routine ECG screening is likely to increase anxiety without significant benefit. For the patient with known or potential heart disease, the ECG is a routine part of the evaluation. There may be a limited number of situations when the ECG helps the primary care provider determine the importance of a cardiology referral.

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Specific links of interest include:

[Canadian Advisory on Adderall](#)

[FDA Public Health Advisory, Patient Information, Health Professional Information, Adderall Labeling](#)

Cardiovascular Monitoring of Children and Adolescents Receiving Psychotropic Drugs

<http://www.americanheart.org/presenter.jhtml?identifier=1773>



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