

start, but the entire area of native health care and well-being requires long-term cooperation.

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Accutane-induced teratogenesis

Drs. Robertson and MacLeod state that "Accutane [isotretinoin] is clearly a potent teratogen" (*Can Med Assoc J* 1985; 133: 1147-1148). I will not challenge this statement since I don't know whether it is true; however, the figures they supply appear to be nothing more than anecdotal. I am surprised that *CMAJ's* editors allowed such a strong statement without statistically significant representation of the problem.

What is presented appears to be a presumptive association. If the authors are aware of "hard" data, could they not have given us the benefit? Their figures for Canada show that of the 16 women who took the drug during pregnancy 1 gave birth to a child with abnormalities. This would be suspicious, but one also needs to know how many normal births occurred in all the women who took this drug before a sensible conclusion can be reached. Never mind a comparison with abortion and abnormality rates in comparable groups of women who did not take Accutane.

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[Drs. Robertson and MacLeod reply:]

We agree with Dr. Muckle that from a purely statistical standpoint our statement regarding the teratogenicity of Accutane cannot be proven. However, we are not surprised that *CMAJ's* editors allowed the statement to be published, in light of the very strong

evidence of an association between Accutane exposure and a select group of major malformations, evidence cited in references 1* and 5 of our article. This association is of such a magnitude that of the 16 Canadian women who took this drug during pregnancy 12 went on to have an elective termination of the pregnancy.

Shortly after we submitted our article Lammer and colleagues¹ published an extensive analysis of 154 human pregnancies with fetal exposure to isotretinoin, noting a relative risk of 25.6 for the major malformations cited. They believe that the evidence is "very strong" that isotretinoin is teratogenic for humans and speculate that although further study is required to prove the association, such research may not be done if recommendations for the avoidance of exposure during pregnancy are followed.

In short, despite the lack of formal statistical proof, isotretinoin must be regarded as teratogenic for humans. We feel that this is one instance in which rigorous statistical proof must give way to common sense.

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Reference

1. Lammer EJ, Chen DT, Hoar RM et al: Retinoic acid embryopathy. *N Engl J Med* 1985; 313: 837-841

It is a trifle embarrassing to have a report of Accutane-induced teratogenesis from a small centre

*As stated in a correction notice published in the Feb. 1, 1986 issue of *CMAJ* (134: 216), this reference should have been "Update on birth defects with isotretinoin. *FDA Drug Bull* 1984; 14: 15-16", a more recent article.

such as Kingston, Ont., where only three dermatologists practise. None of us prescribed for the patient in that case, but we feel a little bit under a cloud even though the physician was misled and a pregnancy test was performed.

We have a written protocol for the use of Accutane in female patients who have not been surgically sterilized and would be pleased to provide it to interested physicians.

We feel that Accutane should be administered only by dermatologists, but we appreciate that some more adventurous family physicians are also using the drug.

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Injuries in children wearing seat belts

Although injuries attributed to seat belts have been reported sporadically¹ there has been no clear documentation of their frequency.

I reviewed all 259 charts of children (neonatal to 15 years of age) who had been admitted over 5 years to five Calgary hospitals because of injuries suffered in automobile accidents. Of the 146 children (56%) for which there was information on the use of restraining devices, only 15 (10%) had been wearing restraints; 9 of them suffered head injuries (none fatal), 3 skeletal injuries that may not have been related to seat-belt use (fracture of the humerus in an infant strapped in a car seat, a minor lumbar spine compression fracture in a 10-year-old wearing a lap belt, and bilateral os calcis fractures in a 10-year-old wearing a lap and shoulder harness), 2 abdominal injuries (small bowel perforation and abdominal tenderness due to either mild pancreatitis or a mesenteric injury) and 1 a lumbar vertebral pedicle

injury. Only the injuries of the last three children, brothers aged 5, 7 and 8 years, each wearing a back-seat lap belt, fit the description of a "seat-belt syndrome". Nine of the children who had not been wearing restraints died in hospital, usually from head injuries.

Physicians should continue to wholeheartedly support the compulsory use of restraints for children in cars. Since injuries clearly related to these devices appear to be rare in children, we should de-emphasize them.

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Reference

1. Kuchtaruk A: Lap belt injuries [C]. *Can Med Assoc J* 1984; 130: 349-350

Swallow syncope: a form of glossopharyngeal neuralgia?

Drs. Armstrong, McMillan and Simon (*Can Med Assoc J* 1985; 132: 1281-1284) have correctly observed that the lack of response to carotid sinus massage in three of their five patients suggests that swallow syncope is distinct from carotid sinus syndrome. Another condition in which bradycardia has been reported in association with syncope is glossopharyngeal neuralgia. As of 1982, 30 cases had been described; in most, syncope resulted, and in only 4 were the symptoms reported to be reproduced with carotid sinus massage.¹

Patient 3 in Armstrong and colleagues' report had asystole for 4.5 seconds while drinking hot water. A patient with glossopharyngeal neuralgia associated with syncope and seizures described in 1982¹ had asystole of identical duration immediately after an episode of left-sided throat pain. His pain was usually

precipitated by swallowing or coughing. The typical paroxysms of pain in glossopharyngeal neuralgia are usually brought on by swallowing, especially of cold liquids, regardless of whether cardiovascular signs and symptoms have also been observed.^{1,2}

The similarity of these groups of patients suggests that swallow syncope is due to the same underlying factors as glossopharyngeal neuralgia and is a partial expression of the condition of glossopharyngeal neuralgia associated with bradycardia and syncope. The gross pathological abnormality in glossopharyngeal neuralgia is compression of the vagus and glossopharyngeal nerves by tortuous branches of the vertebralbasilar system. The resultant demyelination² would allow so-called false synapses (ephapses) to exist; thus, impulses from the nerve fibres carrying somatic sensory impulses from the pharynx could spread to the sinus nerve of Hering, a branch of the glossopharyngeal nerve.¹ The final result would be bradycardia, hypotension and syncope.

In view of these observations a trial of therapy with phenytoin or carbamazepine should be considered for patients with swallow syncope. If this is not successful, I propose that microvascular decompression³ of the vagus or the glossopharyngeal nerve, or both, be considered, although Armstrong and colleagues have documented favourable results after insertion of a transvenous pacemaker.

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References

1. St John JN: Glossopharyngeal neuralgia associated with syncope and seizures. *Neurosurgery* 1982; 10: 380-383
2. Bruyn GW: Glossopharyngeal neuralgia. *Cephalalgia* 1983; 3: 143-157
3. Tsuboi M, Suzuki K, Nishimoto A: Glossopharyngeal neuralgia with cardiac syncope. A case successfully treated by microvascular decompression. *Surg Neurol* 1985; 24: 279-283

LANOXIN*

(digoxin)

INDICATIONS:

1. Congestive heart failure. Congestive failure of all degrees is the primary indication. 2. Atrial fibrillation with rapid ventricular response. 3. Atrial flutter. 4. Paroxysmal atrial tachycardia. Digitalis is not indicated in sinus tachycardia in the absence of heart failure. 5. Cardiogenic shock.

CONTRAINDICATIONS:

The presence of toxic effects induced by any digitalis preparation is a contraindication to all of the cardiac glycosides. Allergy, though rare, does occur. It may not extend to all preparations and another may be tried. Ventricular fibrillation.

WARNINGS:

Dosage must be carefully titrated. Many of the arrhythmias for which digitalis is advised are identical with those reflecting digitalis intoxication. If the possibility of digitalis intoxication cannot be excluded, cardiac glycosides should be temporarily withheld if permitted by the clinical situation. Patients with renal insufficiency are apt to be unusually sensitive to digoxin.

PRECAUTIONS:

Atrial arrhythmias associated with hypermetabolic and febrile states are particularly resistant to digitalis treatment. Care must be taken to avoid digitalis toxicity if digoxin is used to help control the arrhythmia. Potassium depletion sensitizes the myocardium to digitalis and toxicity is apt to develop even with usual dosage. Acute myocardial infarction, severe pulmonary disease, or far advanced heart failure often is accompanied by a greater sensitivity to digitalis and its disturbances of rhythm. Renal insufficiency delays the excretion of digitalis and dosage must be adjusted accordingly in patients with renal disease.

ADVERSE REACTIONS:

Allergic reactions. Gynecomastia. 1. Anorexia, nausea, vomiting, and diarrhea are the most common early symptoms of overdose in the adult, but are rarely conspicuous in infants and children. Uncontrolled heart failure may also produce such symptoms. 2. Central Nervous System. Headache, weakness, apathy, and visual disturbances (blurred vision, yellow vision) are often signs of digitalis toxicity in adults. 3. Cardiac Disturbances or Arrhythmias. Ventricular premature ectopic activity is the most common arrhythmia, except in infants and young children where nodal and atrial arrhythmias are more common. 4. Conduction Disturbances. Excessive slowing of the pulse is a clinical sign of digitalis overdose. Atrioventricular block of increasing degree may proceed to complete heart block.

CAUTION:

Potassium should not be used and may be dangerous for severe or complete heart block due to digitalis and not related to any tachycardia.

DOSAGE AND ADMINISTRATION:

Adults: Digitalis is administered slowly or rapidly as required until the desired therapeutic effect is obtained without symptoms of overdose. Recommended doses are practical average figures which may require considerable modification as dictated by individual sensitivity or associated conditions. Diminished renal function is the most important factor which requires modification of recommended or average doses. The following recommended doses can merely serve as guidelines and should be adjusted according to the circumstances. The average digitalizing dose (i.e., amount accumulated) with oral digoxin is 1.0 to 1.5 mg. A loading dose of 0.5 to 0.75 mg orally usually produces a detectable effect in one to two hours which becomes maximal in six to eight hours. Additional doses of 0.25 to 0.50 mg may be given cautiously at six to eight hour intervals to full digitalization. The usual daily oral maintenance dose is 0.125 to 0.50 mg (usually 0.25 mg). In elderly patients, 0.125 to 0.25 mg should be considered the average maintenance dose. It cannot be overemphasized that the values given are averages and substantial individual variation can be expected.

HOW SUPPLIED:

LANOXIN Digoxin Tablets, each yellow tablet contains 0.125 mg digoxin, and coded LANOXIN Y3B. Bottles of 100 and 1000. LANOXIN Digoxin Tablets, each white tablet contains 0.25 mg digoxin and coded LANOXIN X3A. Bottles of 100 and 1000. LANOXIN Digoxin Injection 0.25 mg per mL—2 mL ampoules. LANOXIN Pediatric Digoxin Injection, 0.05 mg per mL—1 mL ampoules. LANOXIN Digoxin Elixir, Pediatric. Bottles of 100 mL.

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