Correspondance

Cardiac markers for acute myocardial infarction: When should we test?

I read with keen interest the article by Eugene Dagnone and colleagues.[1] As the director of a typically overcrowded Canadian emergency department I am constantly searching for clinical tools to avoid admitting patients to hospital and facilitate their safe and expeditious discharge. Patients presenting with chest pain represent a large group who require cautious and time-sensitive evaluation before discharge.

I was disappointed by the methodology used in this study, specifically with regard to the use of the cardiac troponin I (cTnI) enzyme test. The authors stated that "the time profile of cTnI parallels that of the CK MB [creatine kinase and its MB isoenzyme] fraction." From Table 1 in the article it is evident that 73% of patients enrolled in the intervention group had cTnI evaluated at less than 6 hours after onset of chest pain and 88% at less than 12 hours. It is likely that clinical decision-making would not have been enhanced by results obtained at a time when the sensitivity of the cTnI assay was less than optimal.

Had the study mandated cTnI evaluation at no less than 10 hours after the onset of chest pain, the emergency physician would more reliably have been able to incorporate this test into his or her decision process for admission. I suggest that this modification would very possibly have significantly altered the outcome of the study.

I would encourage the authors or others to undertake further studies utilizing cardiac markers in a time-sensitive manner to evaluate their utility in safely avoiding admissions of patients presenting with chest pain.

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Reference

1. Dagnone E, Collier C, Pickett W, Ali N, Miller M, Tod D, et al. Chest pain with nondiagnostic electrocardiogram in the emergency department: a randomized controlled trial of two cardiac marker regimens. *CMAJ* 2000;162(11):1561-6.

[Two of the authors respond:]

A firmly held tenet of cardiac investigations is that serial testing is imperative.[1] Serial testing is especially relevant for patients with nondiagnostic or negative electrocardiograms.[2]

Stylized time profile graphs are often used to depict the benefit of early markers. Earlier peaks and apparently faster rises in the first couple of hours in a time profile that often extends over 72 hours are purported to indicate the superiority of early markers. Histological and electron microscopic studies have demonstrated that irreversible damage occurs after only 20 minutes of occlusion. When most patients present, on average 3 or more hours later, the distinction between small and slightly larger molecules (17 000 v. 86 000 daltons) is probably a moot point. We postulate that when ischemic damage is severe and prolonged, cellular location and concentration and intravascular metabolism are more important in determining release kinetics from the myocardium than molecular size.

Howard Dyan observed that 25–30% of our patients presented within 2 hours of the onset of chest pain whereas 30–40% presented within 2–6 hours. As a result, serial cardiac marker testing occurred at 2–4 hours for the early presenters and 2–8 hours for the latter group. Although not directly reported in our article owing to space limitations, discharged patients were also sampled at 24–48 hours for cTnI and CK MB whereas admitted patients were sampled at 8 hours for CK MB and at 16 hours for CK MB and cTnI. More than 80% of our patients with acute myocardial infarction had a positive cTnI test at 16 hours after admission.

This first report on the study focused only on the data that were available to physicians in the emergency department, as this is where the main triage decision on admission or discharge is made. The decision to test early rather than at an optimal theoretical point was a deliberate strategy to attempt to test the value of troponin measurements under real-life emergency department conditions. Positive cTnI results at 16 hours had no influence on our admission decision.

Our current emergency department investigation thus recommends serial sampling of CK at 0 and 3 hours, with a subsequent sample at 6 hours if the results and the patient's condition are inconclusive. Emergency physicians order either a CK MB or a cTnI test on one of these samples (usually the first sample). If the CK level does not change or decreases on subsequent sampling, then the CK MB – cTnI results on the first sample are valid. If the CK increases over time and the initial CK MB or

cTnI test was negative, then repeat testing may be requested.

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2. Young GP, Gibler WB, Hedges JR, Hoekstar JW, Slovis C, Aghababian R, et al. Serial creatine kinase–MB results are a sensitive indicator of acute myocardial infarction in chest pain patients with non-diagnostic electrocardiograms: the second Emergency Medicine Cardiac Research Group. *Acad Emerg Med* 1997;4:869-77.

Folic acid supplementation: more work is needed

James House and colleagues recently reported that 25% of Newfoundland women had low or indeterminate red blood cell folate levels (< 420 nmol/L) at their first prenatal visit.[1] Booth and colleagues reported that the reference values in use today were defined on the basis of absence of biochemical signs of folate deficiency.[2] These values do not reflect recommendations for folic acid intake to prevent neural tube defects.[3] Booth and colleagues found that for women of childbearing age attempting to reach a folate intake of 400 μg/day, deficiency is best defined as a serum homocysteine value above 10 μmol/L or a red blood cell folate value below 615 nmol/L.[2]

We recently completed a case–control study of 28 women with a previous pregnancy resulting in a neural tube defect and 38 matched controls with a normal pregnancy outcome. All mothers were ascertained to be screen positive by an elevated maternal serum α-fetoprotein level between 1983 and 1999. We used a semiquantitative food frequency survey to measure dietary and supplemental intake of folate and vitamins B_{12} and B_6. The dietary survey was later validated using biochemical results from 25 and 32 of the case and control mothers respectively. Linear regression analysis showed significant correlation between reported intake of folate and serum folate (p = 0.018) and red blood cell folate levels (p = 0.002), but an inverse correlation with serum homocysteine levels (p = 0.029). Analysis indicated consistent underreporting of actual vitamin intake (common in food frequency surveys). We found no difference between case and control subjects in terms of intake or eating patterns.

Even after correcting for underreporting, we found that in our case and control groups combined, 58% of women were not consuming enough folate, 46% were not consuming enough vitamin B_6 and 28% were not consuming enough vitamin B_{12}. Only 12% reported preconceptional supplementation whereas 82% reported supplementing after they became pregnant. There was no difference in preconceptional supplementation patterns after 1994, when preconceptional supplementation with folic acid was recommended.[4]

Although none of our mothers were folate deficient according to current reference values, 34% had serum homocysteine values in excess of 10 μmol/L and 10% had levels higher than 13 μmol/L, the current reference value. Our results, albeit in a much smaller and differently selected group, support the results of the Newfoundland study and indicate that vitamin B_6 intake may also be suboptimal in many women of child-bearing age.

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1. House JD, March SB, Ratnam S, Ives E, Brosnan JT, Friel JK. Folate and vitamin B_{12} status of women in Newfoundland at their first prenatal visit. *CMAJ* 2000;162(11):1557-9.
2. Booth CK, Clark T, Fenn A. Folic acid, riboflavin, thiamine, and vitamin B-6 status in a group of first time blood donors. *Am J Clin Nutr* 1998;68(5):1075-80.
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[One of the authors responds:]

We are pleased that data presented by the group led by Natalie Björklund, Jane Evans and Cheryl Greenberg support our results showing a high risk for neural tube defects in Newfoundland.[1] If we had applied the less conservative interpretation suggested by Booth and colleagues[2] to our data, our results would have indicated that even more Newfoundland women were at risk.

It is clear from the work of Björklund and colleagues and from our own experience that public education in this area has been truly neglected, to the detriment of all Canadian women. Canadian women are simply not going to get the 400 μg/day of folate needed to prevent neural tube defects from a normal diet. Folate fortification at current levels is not sufficient to meet dietary goals, let alone reduce the incidence of neural tube defects. Furthermore, there is no evidence that public health attempts to raise the awareness of women of childbearing age about the necessity of taking a dietary folate supplement to prevent neural tube defects have been successful.

Data from a Chinese study confirm unequivocally that just 400 μg/day will nearly eliminate this disease.[3] As health professionals we are morally obligated to push forward these findings to our policy-makers and to our patients.

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1. House JD, March SB, Ratnam S, Ives E, Bros-

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Driving and our aging population

The Canadian Medical Association has prepared and published a handbook to help physicians determine whether their patients are medically fit to drive.[1,2] By 2024, it is expected that 1 in 4 Canadians will be older than 65. With the growing number of elderly people who drive, physicians are increasingly being called upon to assess the driving skills of their older patients, some of whom have cognitive deficits.

In the section on identifying patients with progressive dementia, the guide indicates that "individuals showing a score of less than 24 on this test [the Mini-Mental State Examination] are ineligible to hold a driver licence of any class pending complete neurological assessment."

Use of a specific score as a cut-off for this examination has never been validated because it is only a screening instrument with a specificity and sensitivity in the range of 85%. As the authors of the guide state, the test can be affected by language difficulties, lack of education and an age of more than 85 years.

In the current format, with the above explicit statements, are physicians liable legally if their patients with a score of 23 are responsible for an accident? The guide is also not clear on what is meant by a complete neurological assessment. Does it mean that all patients with a score of less than 24 need to be referred to a neurologist? This guideline seems not only scientifically unsupported but also legally charged.

With the greying of Canada, we urgently need a scientifically sound and well-validated assessment tool to evaluate fairly the increasing number of Canadians with cognitive deficits who may be at risk, and may be putting others at risk, while driving.

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References

1. Canadian Medical Association. *Determining medical fitness to drive: a guide for physicians*. Ottawa: The Association; 2000.
2. Sibbald B. Revised fitness-to-drive guide now available. *CMAJ* 2000;163(2):198.

[The Chair of the Project Advisory Group responds:]

Anna Byszewski and William Dalziel call for a scientifically sound and well-validated assessment tool to screen drivers for dangerous cognitive deficits. We echo that call. We acknowledge that the Mini-Mental State Examination has been criticized as a tool to effectively identify individuals who perform poorly on a road test[1] and that widespread consensus is lacking regarding the use of cut-off scores on this examination.[2]

However, it is impractical to suggest to physicians that all patients with suspected cognitive difficulty be referred for a standardized on-road, or even simulated, evaluation. Doctors in clinical practice need a screening tool to assist decision-making. Despite the above-mentioned concerns, the Mini-Mental State Examination has been shown to correlate with on-road driving test results,[3] and poor performance on parts of the Mini-Mental State Examination correlates with the risk of adverse driving events.[4] Decisions concerning driving aptitude must often be made on uncertain grounds. It should be noted that the statement referenced by Byszewski and Dalziel is a direct quotation from the standards found in the National Safety Code[5] developed by the medical consultants for the provincial and territorial driver licensing authorities. Extracted from the context of the National Safety Code quotation, the statement quoted by Byszewski and Dalziel on the Mini-Mental State Examination test scores reads as a hard-and-fast rule; the CMA guide[6] specifically mentions that physicians should consider the impact of education and language on test results.

As noted in the CMA guide,[6] liability can result when physicians fail to report potentially medically unfit patients if these patients subsequently have an accident and cause harm to others. The Mini-Mental State Examination is one tool for identifying potential unfitness to drive. Physicians, *especially where there is a mandatory reporting system*, should err on the side of caution and report potentially medically unfit drivers.[6] A physician could deem a patient potentially unfit even without the administration of the Mini-Mental State Examination. It is only one tool to assist physicians in determining medical fitness to drive.

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1. Dobbs AR. Evaluating the driving competence of dementia patients. *Alzheimer Dis Assoc Disord* 1997;11(Suppl 1):8-12.
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6. Canadian Medical Association. *Determining medical fitness to drive: a guide for physicians*. Ottawa: The Association; 2000.

Dancing through time

The excellent article by Erica Weir on dance raves[1] was devoid of any mention of their historical counterparts — the medieval dancing manias. There are numerous parallels. Participants in both activities engaged in prolonged dancing to music and in behaviour deemed as nonconformist or bizarre (but not necessarily pathological) by those outside the subculture. Dancing mania participants typically ingested wine while dancing to achieve ecstatic states; their modern counterparts often take hallucinogenic or mood-altering substances, including the drug ecstasy.

Sigerist contends that St. Vitus' dance was similar to ancient Greek orgiastic rites that had been outlawed by Christian authorities but were secretly practised. (It should be noted that although St. Vitus' dance has entered the medical lexicon as an alternative term for Sydenham's chorea, few modern-day researchers claim that participants in dancing manias were literally suffering from chorea.) Eventually the dancing manias grew more open when authorities realized they could not suppress them.[2] Modern raves began as clandestine gatherings at secret venues with the location revealed just hours before the event to deter law enforcement surveillance. Six hundred and fifty years ago German magistrates paid musicians to perform for participants and to serve as dancing companions. This was designed to reduce injuries and mischief during their procession to the nearby St. Vitus' chapel.[3] Today, volunteer groups attend raves to offer safety advice; some government agencies, including those in Canada, sanction supervised raves. These measures are intended to prevent these gatherings from spiralling out of control and to reduce harm to participants.

Contrary to popular psychiatric portrayals of medieval dancing manias, women were not overrepresented among participants and episodes were not spontaneous but highly structured, and they involved sects engaging in strange or unfamiliar customs.[4,5] Modern ravers are male and female adolescents and young adults who espouse counterculture values.

Participants in medieval dancing manias and tarantism worshipped in a discernible pattern. They would typically begin dancing at sunrise, stop at midday to sleep, sweat and bathe and then dance until evening when they would sleep and sweat, eat a light meal and then sleep until sunrise. This ritual was typically repeated over 4 or 5 days, and sometimes over weeks.[6] Today, a prominent harm-reduction strategy at supervised raves includes taking breaks from dancing and drinking plenty of fluids.

Modern-day raves resemble the dancing manias within a different historical and cultural context, fulfilling similar social and psychological needs.

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Corrections

A recent Heart & Soul article stated incorrectly that Captain James Cook spent the 4 summers following 1767 surveying the coast of Newfoundland.[1] In fact, Cook spent the 4 summers before 1767 conducting his survey.

Reference

1. Ryan B. MD explores hidden history of Captain Cook's journey to Newfoundland. *CMAJ* 2000; 163(5):684.

The health status data were presented incorrectly in Fig. 2 of a recent article by Kue Young and colleagues[1] owing to an editing error. The correct figure appears below.

Reference

1. Young TK, Reading J, Elias B, O'Neil JD. Type 2 diabetes mellitus in Canada's First Nations: status of an epidemic in progress. *CMAJ* 2000; 163(5):561-6.