Letters

Human study participants

We read with interest Fletcher’s editorial on ethics approval for all studies involving human participants as a condition of publication, and the importance of having this done by ethics review boards as knowledgeable and unbiased third parties.1 As noted, although this approach is now standard for experimental studies, the practice for observational studies is inconsistent, and there are calls for exemption from ethics review for quality improvement, practice audits and similar endeavours.

Fletcher points to streamlined ethics review processes introduced in New Zealand and the United Kingdom. There is also a Canadian solution. Public Health Ontario has developed a process wherein all studies involving human participants receive an initial risk screening to determine the required level of ethical scrutiny.2 Similar to the New Zealand protocol with 24 questions,3 the Public Health Ontario process involves a 20-item risk-screening tool, which sorts projects into one of four review levels: full ethics board review, a conventional delegated review process, an expedited delegated review process or no further review with periodic audit (manuscript currently under review).

This approach supports CMAJ’s desire for an expanded yet balanced scope of ethics review and is broadly applicable in other settings where quality improvement and other observational studies are conducted.

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The Lyme law

I recently read CMAJ’s interview4 with Dr. David Patrick, who used words like “junk science” and “pseudoscience” regarding the diagnosis and treatment of Lyme disease. I worked as a consultant physician at the University of British Columbia’s Complex Chronic Diseases Program from 2013 to 2014, a clinic formed to improve testing and treatment for patients with Lyme disease, fibromyalgia and chronic fatigue syndrome/myalgic encephalomyelitis.

The issue in Lyme disease treatment is that there is inadequate research to lend evidence-based support to any guidelines. Certainly there is evidence that Borrelia burgdorferi persists in dogs, rats, monkeys, people and even in the test tube after antibiotic treatments.2-5

The National Institute of Allergy and Infectious Diseases (NIAID) states on its website that “additional research is needed and continues to be supported by NIAID to learn more about persistent infection in animal models and its potential implication for human disease.”6 In the absence of good evidence-based guidelines, patients are floundering and physicians are afraid to treat.

A review of the evidence7, using the GRADE system, shows all the evidence that exists (and all that is lacking) at each stage of tick bite, erythema migrans rash and chronic Lyme disease. What I appreciate about this review is that it explores the role of patient preference at each stage of Lyme disease, where clear evidence is lacking as to treatment duration.

Physicians have a duty to explore concerns about risks of long-term use of an antibiotic. In each case, we must look at the risk–benefit ratio. This is not new to the treatment of Lyme disease. In Lyme disease, we must analyze, upon tick-bite exposure, the risk of a tick carrying the disease, and of not treating a documented erythema migrans rash long enough. We must consider whether a patient is more concerned about Lyme disease prevention or about the risks of unnecessary antibiotics and adverse reactions.

It is messy work, and the research needs to be done. In the meantime, physicians are in the trenches and patients are sick. The US Centers for Disease Control and Prevention estimate 300 000 US cases per year of Lyme disease, and we cannot be so naive as to think this disease stops at the US border. In 2007, only 13 cases were officially reported in British Columbia. However, a survey by the BC Centre for Disease Control in 2007 showed that 148 physician respondents (8.8% of their sample) had diagnosed a total of 221 cases of Lyme disease in the preceding year.8 If 221 cases were diagnosed by such a small sample of physicians, why were only 13 cases officially reported?

We are dramatically underestimating the number of cases of Lyme disease, and I am glad to see that Bill C-442 is proceeding so that we can improve research into testing and treatment of this disease. We are at a stage with chronic Lyme disease similar to where we were with HIV in the 1990s, when clinicians had to use clinical judgment to treat those who were sick while awaiting quality evidence to be published. I am hoping that Bill C-442, which has the support of the Canadian Medical Association, will allow this to happen nationally.

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Syncope confusion

Soong and colleagues’ intent was to highlight the overuse of investigations, particularly neuroimaging, among patients with syncope.1 Although Soong and colleagues cited the 2009 European Society of Cardiology guideline,2 they failed to differentiate syncope from other causes of transient loss of consciousness. Syncope is caused by global cerebral hypoperfusion, and none of the listed neurologic diagnoses cause syncope.

This confusion has led to great research efforts, consensus conferences, guidelines and statements developed by the European Society of Cardiology, the Gargnano multidisciplinary consensus conference (led by internists), and the Canadian Cardiovascular Society, all of which uniformly exclude neurologic conditions causing transient loss of consciousness from syncope.

Based on current evidence, syncope is defined as a transient loss of consciousness due to global cerebral hypoperfusion characterized by rapid onset, short duration, and spontaneous complete recovery. Sadly, this article1 worsens the confusion by clearly stating that neurologic causes of syncope exist. This could cause practising physicians to include neurologic causes in the differential diagnosis for true syncope, and to not differentiate syncope from other causes of transient loss of consciousness. This is important, as the literature evidence regarding the risk of “cardiac syncope,” and use of neuroimaging exist only for true syncope patients and cannot be applied to all patients with transient loss of consciousness. The authors could also have cited new evidence for high-risk features for “cardiac syncope” that have been summarized, based on evidence.6,7

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The authors respond
We thank Thiruganasambandamoorthy and Sheldon for clarifying the definition of syncope as a transient loss of consciousness due to global cerebral hypoperfusion characterized by rapid onset, short duration and spontaneous complete recovery.1 However, experts acknowledge that this approach has pragmatic limitations, particularly when applied to undifferentiated patient presentations in the emergency department. To guide clinicians in the emergency department, our approach focuses on all potential causes of transient loss of consciousness, including syncope “mimickers.” We agree that stroke, transient loss of consciousness, seizure and metabolic disturbances do not represent true syncope.

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Group A streptococcus

It was gratifying to read that the authors of this commentary1 on group A streptococcus mention the significant rate of colonization versus infection. Surprisingly, this was not mentioned in the related research article.2 This continuing uncertainty, so appropriate in science, highlights the need for the art of medicine — the art in which clinicians dance with the complexity of uncertainty, balance their sense of whether the child is quite ill (“toxic”) or otherwise medically fragile, converse with parents to assess their resourcefulness and preferences, and balance all of this with the public health issues. I would appreciate a review of the implications of the treatment of carrier states, with respect to group A streptococcus in particular.

Another CMAJ paper,3 examining the potential harms of the use of amoxicillin and amoxicillin–clavulanic acid, also surprised me by treating the two drugs as if they were similar. I understand that the latter is one of the broadest spectrum agents, and one I reserve for very specific situations. I am of the old school, and I still do not even use amoxicillin for group A streptococcus, preferring penicillin V (which is often not even available in the suspension form).

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