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[John Lowman responds:]

Contrary to Ian Mitchell's defence of john school, direct observation of the curriculum tells a different story. When Tom Barrett, a journalist, attended john school 4 years ago, one of the pupils asked, "Why doesn't Canada have government-regulated whorehouses?" One of the police officers present replied, "Because people view it as an immoral activity."[1] Another officer told the audience that prostitution is "slavery. They are forced to be there." Canadian research does not substantiate these sweeping claims (see, for example, Benoit and Millar[2]).

Furthermore, there is no evidence that the curriculum has changed in the intervening period. Earlier this year, as part of his honour's degree research, one of my students attended Mitchell's john school and concluded that "the way that sex work is projected is selective and inherently political."[3]

Although the nuisance aspect is on the agenda, the very moniker "john school" gives the game away. The target is the purchase of sex, not the nuisance component. If john school really does let johns decide for themselves, I anticipate that Mitchell will accept my offer to make a regular john school presentation on Canadian prostitution research.

As for Dawn Hodgins' call to help women leave prostitution, such a stance is no reason to abandon the women (and men) who continue to sell sex. One legitimate concern is that decriminalization might trap women in prostitution, with welfare payments being denied to those who want to leave the trade. However, New Zealand's legislation makes it illegal to cut a person off welfare if they refuse to prostitute. At the same time, prostitutes can work in situations where they are not vulnerable to serial killers. In contrast, by ruling out harm reduction strategies, the Swedish approach exposes prostitutes to harm.[4]

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Risks and benefits of β-blockade

P.J. Devereaux and associates[1] state that the current situation with respect to evidence for β-blocker therapy before surgery is similar to the situation that existed 12 years ago when estrogen replacement was widely recommended. I disagree. Estrogen has been implicated in the genesis of many fatal diseases, including breast cancer and thromboembolic diseases.[2,3] The same material risks do not exist for β-blockers. Furthermore, the authors do not disclose or discuss the theoretical or empirical life-threatening risks of β-blockade.

Devereaux and associates[1] also argue that the benefits of preoperative β-blockade in small studies completed to date are "too good to be true." They base this assessment upon the long-term benefits of β-blockade in coronary artery disease and congestive heart failure. However, for these conditions the drugs are administered over long periods, and in combination with many other drugs, to modify the long-term outcome of progressive and often fatal diseases. A more analagous situation is the relative risk of a myocardial infarction induced by another acute stressor, strenuous exercise. One study found that the relative risk of myocardial infarction during or immediately after vigorous exercise was increased 100-fold for habitually sedentary individuals.[4] Most of the patients whom I am asked to see preoperatively are sedentary and thus very likely to benefit from preoperative β-blockade.

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[The authors respond:]

Contrary to Stephen Workman's experience in treating patients perioperatively, our review[1] suggested that the true effects of β-blocker therapy in patients undergoing noncardiac surgery remain uncertain because of a lack of adequately powered, blinded randomized controlled trials (RCTs).

Members of our group recently reported results from a new RCT of perioperative β-blocker therapy.[2] The Metoprololol after Vascular Surgery (MaVS) trial randomly assigned 496 patients undergoing elective vascular surgery to receive metoprolol or placebo starting 2 hours before surgery and continuing for 5 days. This blinded trial is the largest perioperative β-blocker trial reported to date, with more than 4 times as many patients as an unblinded RCT by Poldermans and colleagues[3] of β-blocker therapy for vascular surgery. Those authors reported a statistically significant 90% relative risk reduction with β-

blocker therapy for the composite outcome of cardiovascular death or nonfatal myocardial infarction, despite the occurrence of only 20 events (2 in the β-blocker group and 18 in the group receiving standard care). In contrast, the MaVS trial did not demonstrate a statistically significant effect with β-blocker therapy for the same composite outcome, even though there were 41 events (19 in the β-blocker group and 22 in the placebo group).

The MaVS trial also informs the issue of risk that Workman raises. In the MaVS trial more of the patients who received metoprolol had intraoperative bradycardia requiring treatment (53/247 v. 19/250, $p < 0.01$) and intraoperative hypotension requiring treatment (84/247 v. 26/250, $p < 0.01$).

Workman contends that because of duration of therapy and a multitude of concurrent medications, the effect sizes demonstrated in long-term β-blocker trials of patients with coronary artery disease and congestive heart failure do not inform the plausible magnitude of effect of β-blocker therapy in patients undergoing noncardiac surgery. Workman's contention is refuted, however, by the trials of β-blocker therapy in acute myocardial infarction, which have demonstrated relative risk reductions of 15% to 25% at 30-day follow-up,[4] and by current perioperative care, which often includes multiple medications and regional anesthesia. Finally, relative risk reductions beyond 35% are now extremely uncommon; hence our description of such results as "too good to be true."[5]

The results of the MaVS trial[2] reinforce the message that perioperative β-blockers have risks and as-yet-unproven benefits. Fortunately, a large, adequately powered trial that is now in progress, the PeriOperative Ischemic Evaluation (POISE) trial, should definitively establish the effect of perioperative β-blocker therapy in patients undergoing noncardiac surgery.

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Competing interests: P.J. Devereaux and Homer Yang are the principal investigators of the POISE Trial, Salim Yusuf is the chair of the POISE Steering Committee, Peter Choi is a member of the POISE Steering Committee, and Gordon Guyatt is a member of the POISE Steering Committee and the chair of the Adjudication Committee.

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Patient–physician–regulator triad

We feel that the commentary by Gideon Koren and associates[1] regarding safety concerns related to isotretinoin has the potential to serve as a catalyst for safer use of this drug.

We concur that proper measures to prevent pregnancy in patients taking isotretinoin must be in place and that such measures must be user-friendly for both the health care provider and the patient. Implementation of safety measures should be consistent and universal, regardless of whether (or how many) generic forms of the drug have been authorized on the Canadian market. Currently, no approved generic isotretinoin products are available on the Canadian market, but approval of such generics would require a patient information program equivalent to the program now in effect for Accutane.

Health Canada attended the US Food and Drug Administration (FDA) advisory committee meeting on this subject in February 2004 and is aware of the FDA's proposal for tighter control of prescription of these drugs. Although the FDA had access to information suggesting a significant rate of pregnancy among women taking isotretinoin in the United States,[2,3] Health Canada's pharmacovigilance program, which includes but is not restricted to spontaneous reporting of adverse drug reactions and review of periodic safety update reports by the manufacturer, has shown no evidence of a comparable situation in Canada.

Part of Health Canada's mandate is to convey information that will minimize the risks and maximize the benefits of pharmaceutical products on the Canadian market. However, it will take more than regulatory due diligence to solve safety problems related to isotretinoin: endorsement of existing recommendations through physicians' daily practice remains an essential ingredient. Patients must also play an active role: once informed of a potential risk, their behaviour and compliance with the contraceptive methods become part of the equation, and closer follow-up must be planned if there is suspicion of noncompliance. The patient–physician–regulator triad is pivotal in optimizing the safe use of isotretinoin, as for any pharmaceutical product.

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