Use of antiretrovirals in newborns

The recommendation from the US Centers for Disease Control and Prevention (CDC) for a health care worker with exposure of non-intact skin to a small volume of secretions from an HIV-infected person with an undetectable viral load is that he or she should receive 2 antiretroviral drugs for 4 weeks.[1] If the viral load of the HIV-infected person is more than 1500 RNA copies/mL and the volume of secretions is large, the health care worker should receive 3 antiretroviral drugs.[1]

In contrast, the Canadian consensus guidelines for the management of pregnancy, labour and delivery and for postpartum care of HIV-positive women and their offspring[2] recommend that infants born to women who received suboptimal or no antiretroviral therapy during pregnancy should be given only the usual 6 weeks of oral zidovudine plus a single dose of nevirapine. There is an understandable reluctance to prescribe drugs to neonates when there is limited information on efficacy, correct dose and adverse effects in this age group. However, in the section on preconception counselling, the guidelines[2] advocate the use of a wide variety of antiretrovirals during the second and third trimester of pregnancy. They also state, "In women who would benefit from antiretroviral intervention before becoming pregnant, the objective is to achieve stable, maximal suppression of the viral load before conception." Presumably, the antiretrovirals administered for this purpose would be continued throughout the first trimester. I am therefore surprised that the authors are reluctant to recommend at least a 2-week course of combination antiretrovirals for an infant with a significant risk of acquiring HIV. Surely it is worth exposing an infant to a combination of drugs that appears safe but for which we have only limited data if there is any reasonable possibility that the regimen will prevent HIV infection.

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[Five of the authors respond:]

Joan Robinson is correct in pointing out the discrepancy between the Canadian consensus guidelines for the management of pregnancy, labour and delivery and for postpartum care in HIV-positive women and their offspring[1] and the CDC guidelines for prophylaxis after needle-stick exposure.[2] However, the issue of how best to manage infants born to HIV-positive women who probably have incompletely suppressed plasma viral load at term requires further study. We attempted to develop evidence-based guidelines, and currently there are good data supporting the use of zidovudine and nevirapine in the infant; hence our recommendation. Other approaches, such as the use of more extensive combination therapies in the infant, may eventually prove helpful in specific high-risk situations, but at present, in our opinion, there is insufficient safety or efficacy data to warrant such a recommendation.

It is noteworthy that the CDC guidelines for the management of occupational exposure[2] are based largely on expert opinion, with very limited supporting data. It is also noteworthy that, with respect to this issue, the US Public Health Service Task Force guidelines for prevention of perinatal HIV transmission[3] are identical with the Canadian consensus guidelines.[1] With the currently recommended approach, vertical transmission of HIV has been reduced from about 25% to less than 1%.[4] Although it would clearly be desirable to improve further on these results, we believe that an evidence-based approach is imperative in any such efforts, especially given the increasing concerns about the safety of these medications.

More research is needed into the precise role of and optimal approach to the infant component of perinatal prophylaxis for HIV infection. However, until more data become available, we remain comfortable with the current recommendations.

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Opioids and chronic pain

Jacqueline Gardner-Nix[1] advocates the use of opioids for chronic noncancer pain, but this issue is more controversial than her article indicates.[2,3] Both the Ontario Workplace Safety and Insurance Board (WSIB)[4] and the College of Physicians and Surgeons of Ontario (CPSO)[5] have prepared evidence-based guidelines for the management of chronic noncancer pain. The WSIB[4] found only 2 studies of sufficient quality for use in making recommendations for opioids, and the WSIB noted that these drugs were of limited use for up to 6 months. The CPSO[5] concluded that there was some evidence of benefit of short-term (up to 9 weeks) opioid use but noted that "long term opioid therapy may or may not improve functional status and there is some evidence that a treatment program that focuses on analgesics can reinforce pain-related behaviour at the expense of functional restoration."

The single randomized trial[6] that both the WSIB[4] and the CPSO[5] felt was of highest quality reported only modestly lower pain intensity with morphine relative to placebo; in addition, vomiting (39% in the morphine group), dizziness (37%), constipation (41%), poor appetite or nausea (39%) and abdominal pain (22%) were significantly more frequent with morphine use. The study had a 25% drop-out rate (15 of 61) and did not demonstrate any significant improvement in psychological or functional outcome, nor did it find a significant overall patient preference for morphine over placebo.

The role of opioid analgesics in the management of chronic noncancer pain has not been well established. Further research is needed to determine if the benefits exceed the costs.

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Jacqueline Gardner-Nix[1] claims that "It is now acknowledged that opioids may be appropriate in a subset of the population with a variety of conditions that cause chronic pain, including those that are impossible to diagnose exactly." Chronic nonmalignant pain occurs in a wide range of situations. As rheumatologists, we agree that narcotics are appropriate in some cases, for example, an older patient with serious, painful osteoarthritis of the hip who also has contraindications to surgery. Similarly, where palliative care is the goal, then surely it's appropriate to make the patient's terminal years as comfortable as possible. And for short-term problems, such as post-herpetic neuralgia, narcotics may well allow a patient to enjoy life with adequate function.

Conversely, we see a large number of patients — constituting perhaps the largest single diagnostic group in our practice — who have chronic musculoskeletal pain with no clear-cut structural basis. These medically unexplained symptoms include myofascial pain, fibromyalgia and sometimes chronic low back pain. The introduction of narcotics may provide transient pain relief, but no convincing evidence has been published to indicate that they will restore function, get patients back to work or indeed have any long-term benefit whatsoever.[2,3] The patients themselves typically describe opioids as merely "taking the edge off the pain."

In treating such patients, the physician must cope not only with underlying pain-avoidance behaviours and fear of a serious structural diagnosis, but also the potential for increasing use of narcotics. In addition, there is the unspoken belief that if narcotics are being used, then the problem must be "really bad," which may further aggravate the patient's illness behaviour.

Therefore, to Box 1 in Gardner-Nix's article,[1] which lists barriers to prescribing opioids, we would add the lack of evidence of any long-term beneficial impact, in particular improvement of function or restoration of a more normal lifestyle. In the absence of such evidence, we think a sharp distinction should be drawn between situations where it is appropriate to use narcotics for palliation and situations in which these drugs would not be used under any but extraordinary circumstances.

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