Using antidepressants during preganancy

In a recent *CMAJ* article, Gideon Koren and associates discuss maternal use of selective serotonin reuptake inhibitors (SSRIs) in the third trimester of pregnancy.[1] Clinicians often speculate that a particular person with depressed mood has an abnormality of serotonin metabolism; however, life events, ingestion of toxins, abnormal biology and even poor diet or lack of exercise may be responsible for the depression instead. SSRIs and other antidepressant medications are often prescribed even though a specific test has not been done to confirm that the patient has abnormalities of serotonin levels or serotonin metabolism.

There is a dearth of strong evidence showing that antidepressant medications are substantially more effective than placebo or that the benefits of antidepressant medication outweigh the harms.[2-4] We have not found any well-controlled studies showing that antidepressants reduce the risk of suicide in pregnancy, nor strong evidence that antidepressant medications are substantially more effective than placebo in reducing the pain of depression in pregnant women.

Koren is reported to have said, elsewhere, "What we found was that [among] pregnant women who use Paxil through pregnancy until birth, their offspring are more likely to have several stormy weeks at infancy."[5] In the absence of strong evidence that antidepressant medications are helpful, it seems reasonable to conclude that pregnant women and women of childbearing age, at least, should avoid taking antidepressants.

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We thank David Zitner and Angela Bischoff for their interest in our commentary.[1] Unfortunately, they do not consider an increasing body of evidence on the serious risks of untreated depression in pregnancy, including the risks of suicidal ideation, suicide attempts and perinatal complications. In addition, gestational depression is the strongest predictor of postpartum depression.[2] The results of our risk–benefit analysis have been confirmed by similar expert reviews.[3,4]

We agree that the cause of depression is often multifactorial and that an abnormality of serotonin levels or serotonin metabolism is often not demonstrated. However, it is not practical to use a specific test to confirm such an abnormality in the clinical setting.

The suggestion by Zitner and Bischoff that pregnant women and women of childbearing age should avoid taking antidepressants because of a lack of well-controlled studies show-

ing a benefit over placebo is analogous to not treating meningitis in pregnancy because there are no randomized trials to demonstrate that penicillin is better than placebo in pregnancy.

Zitner and Bischoff quote one of us as having said, elsewhere, that "What we found was that [among] pregnant women who use Paxil through pregnancy until birth, their offspring are more likely to have several stormy weeks at infancy." This was taken out of context, as they omitted the accompanying statement that "Many of these babies have to stay in the hospital for two to three weeks after they're born, but they suffer no long-term health effects."[5]

Although it may be possible for some women to avoid taking antidepressants as Zitner and Bischoff suggest, they do not offer an alternative approach for the substantial number of women who have major depressive symptoms during pregnancy. Antidepressants continue to be prescribed and it is important that pregnant women and their health care providers have accurate information upon which to base an informed decision regarding therapy.

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A positive prognosis

We read with interest the recent report by Krishna Sharma[1] of a case of malignant fibrous histiocytoma, metastatic to the lung, with spontaneous expectoration of large tumour fragments. We felt it would be illustrative to present a similar case with a much more favourable outcome.

This patient presented in 1975 at the age of 42 years with a slowly enlarging mass, involving the right patellar tendon. A biopsy revealed it to be a malignant sarcoma, and a subsequent wide local excision was accomplished with clear margins. Pathology review confirmed the diagnosis of malignant fibrous histiocytoma. No adjuvant treatment was administered.

Five years after primary resection, the patient developed pulmonary nodules, one adjacent to each hilum, visible on both routine posteroanterior chest radiographs and lung tomograms. He was asymptomatic, and no further treatment was recommended. Over the next 8 months, he developed mild but progressive wheezing. This culminated in the spontaneous expectoration of a tumour nodule described as a plug of tissue measuring 2.5 ∞ 1 cm and found to be histologically identical to his primary cancer. The wheezing completely resolved at this point but because of the enlargement of his remaining disease site, with the largest nodule measuring 5 cm in diameter, a course of radiation therapy was recommended. He received 30 Gy in 15 fractions, encompassing both hila and the carina, using cobalt 60. This was well tolerated aside from transient fatigue. The patient's tumour masses began to shrink promptly, and he was eventually left with a small amount of residual scarring near his left hilum.

When last seen in follow-up in 2003, some 22 years after the spontaneous expectoration of one of his lung nodules and subsequent "palliative" radiation treatment of his residual disease, the patient remained alive and well, without disease recurrence.

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Predicting cardiac outcomes

Despite substantial advances in the diagnosis of suspected acute coronary syndromes, significant challenges persist.[1] Andrew Worster and colleagues recently reported in *CMAJ* that ischemia-modified albumin (IMA) was a poor predictor of cardiac outcomes in patients with potential cardiac ischemia symptoms.[2] The authors tested 2 thresholds for IMA: 85 μ/mL, as suggested by the manufacturer, and 80 μ/mL. It is important to point out, however, that IMA levels vary considerably, even among healthy individuals. Taking these variations into account may improve the predictive characteristics of IMA.

We examined 35 healthy men (age range 25–54 years) recruited from the general public who had not had a myocardial infarction. Using standard laboratory techniques we found that the average resting IMA concentration was 94 μ/mL (97.5% confidence interval 84–104 μ/mL). IMA concentration was significantly and inversely correlated with serum albumin but not with creatinine concentration. Serum IMA concentration was also significantly associated with serum lactate concentration.[3] Taking these and other known factors into