Depression during pregnancy

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Depression is common, disabling, and treatable. As many international studies have shown, depression is a leading cause of disability among women aged 18 to 44.[1] The 12-month prevalence rate of depression in the Canadian Community Health Survey is approximately 4.5% among all Canadians older than 12 years.[2] This rate is much higher among women during their reproductive years.[3] One of the curious, but consistently documented, findings of epidemiologic studies is that rates of depression in boys and girls are roughly equal until puberty, when adolescent girls' rates suddenly increase to twice those of boys. These doubled rates of depression among women remain constant until menopause; then they gradually decline until death.[4]

Reasons for this sex differential are controversial but are likely multifactorial, comprising biologic, psychologic, and sociocultural factors. Recent studies show that adverse events in childhood, such as abuse and neglect, loom large among later risks for depression, especially for women already at increased genetic risk.[5]

Given that rates of depression are highest among women aged 18 to 44, it is unsurprising that depression is frequently seen in pregnant and recently pregnant women. Whether prevalence of depression is increased by pregnancy, however, is debatable; if it is increased, rates are probably only slightly higher than among non-pregnant women of comparable age and socioeconomic status.[6] What makes depression during and after pregnancy special is the context in which it occurs and the effects it can have on women, fetuses, infants, and families.[7] Depressed pregnant women are less likely to eat and sleep well and more likely to neglect personal hygiene and to smoke and drink alcohol. They are less likely to seek prenatal care or to adhere to medical recommendations. In addition to personal suffering and disability, these women might be at risk of harming themselves or even committing suicide. The biologic correlates of depression, including high cortisol levels and perturbed hypothalamic-pituitary-adrenal axis and beta endorphins, can result in harmful effects on a developing fetus, including prematurity, lower birth weight, and slower fetal activity and development. Infants of depressed mothers sometimes receive suboptimal physical and psychological care. Older children and spouses can also suffer from the secondary effects of maternal depression.[8]

Symptoms of depression during pregnancy and the postpartum period are similar to those at other times of life, but can be more difficult to disentangle from physical symptoms related to pregnancy or infant care, such as poor sleep, low energy, and weight changes. Not surprisingly, depressive thoughts often focus on pregnancy, labour, infant feeding, bathing, health, and safety. The one exception is postpartum psychosis, which is rare, sudden, and severe, with thoughts that are out of touch with reality.

Depression and anxiety often go hand in hand, and this is true during pregnancy as well. A recent community study of 8323 pregnant women in England found 11% had anxiety and 13% had depression during pregnancy, and 13% had anxiety and 13% had depression postpartum. Most postpartum depression and anxiety was preceded by antenatal depression and anxiety. Antenatal anxiety also predicted postpartum depression, even after controlling for antenatal depression.[9] In most studies, depression during pregnancy is the strongest predictor of postpartum depression.[10]

Identifying and treating depression

As depression during pregnancy is a major threat to maternal health, and increasing evidence

indicates it also harms fetuses and infants, how can we best identify and treat it in busy clinical practices? A brief, valid, reliable instrument with good sensitivity and a low false-positive rate is needed. The Edinburgh Postnatal Depression Scale[11] has been used in prenatal care, as have the Antenatal Psychosocial Health Assessment form (ALPHA)[12] and instruments developed by Austin[13] and Matthey et al.[14] All of these questionnaires, however, might be too long for many prenatal environments. More recently, one to five probe questions from the Mental Health Inventory,[15] Patient Health Questionnaire,[16] or ALPHA have been introduced, sometimes without rigorous evaluations. For example, the Ontario Antenatal Record has incorporated five topics from ALPHA for discussion during prenatal care, and although the full ALPHA performs well in practice, evaluation of this abbreviated version is still needed. Most promising are two probe questions recommended by the United States and Canadian task forces on preventive health care and common to many of the above instruments: "Over the past 2 weeks have you felt down, depressed, or hopeless?" and "Over the past 2 weeks have you felt little interest or pleasure in doing things?" These two questions are almost as effective as longer instruments.[17-19]

Once depression is diagnosed in pregnant women, how should it be managed? Women, their families, and health care providers are understandably wary of antidepressants—especially in the current context of black-box warnings; unsuspected adverse events; drug recalls; and increasing revelations of the effects of pharmaceutical company funding on published clinical trials, prescriptions written, and opinions of experts. Clearly partner, social, and environmental support and cognitive and interpersonal psychotherapy are first-line approaches, but they do not work for everyone, especially if depression is severe. Before psychotropic drugs are prescribed, an individual risk-benefit decision must be made in collaboration with the woman and, if appropriate, her family.[20,21]

But how do clinicians evaluate the benefits and harms of antidepressant drugs for pregnant women? The article in this issue of *Canadian Family Physician* by Ryan et al (**page 1087**) attempts to do this, but appears to conclude that antidepressants are safe and neonates do not show short-term or long-term adverse effects. Both of these assurances need caveats, as there is much we do not know.

The Canadian Task Force on Preventive Health Care[19] grades recommendations based on the quality of published evidence and places greatest weight on study design and analysis. The strongest evidence comes from well designed studies with appropriate follow up, such as randomized controlled trials. An underpowered or poorly designed randomized controlled trial, however, might be of less value than a well designed large cohort study. Consequently, the Canadian Task Force on Preventive Health Care has suggested that an internal validity rating of "good," "fair," or "poor" also be assigned to inform ranking for grade A recommendations (good evidence to support) to grade E recommendations (good evidence to exclude) the intervention. Unfortunately, most studies of antidepressant use in pregnancy have serious flaws in power, design, and follow up; many medical interventions share the same leaky boat, and the Canadian Task Force on Preventive Health Care has recently added another classification—grade I—for interventions for which there is "insufficient evidence (in quality and quantity) to make a recommendation; however, other factors may influence decision making."[19] Grade I is clearly where antidepressant use during pregnancy belongs. There are no sufficiently powered, double-blind, randomized controlled trials with sufficient follow up on these drugs, and recently there have been some worrying withdrawal and toxicity findings in pediatric neurophysiologic studies.[23,24]

The bottom line is that we do not know the effects of antidepressants (all of which affect the neurotransmitter system) on immature and rapidly developing fetal and neonatal brains. Might they lead to later perturbations in mood or cognition? A more cautious and honest approach is to admit to ourselves and our patients that definitive answers on the safety of antidepressants during pregnancy are not yet available, but untreated depression also poses some risks to mothers, fetuses, and infants.[24] While the advantages of antidepressants are clear

for severely depressed pregnant women, the risk-benefit decisions are much less obvious for mildly depressed and anxious women, for whom nonpharmacologic treatments should be first line.

I often prescribe or continue antidepressants for severely depressed women after discussing the risks of untreated depression compared with the known risks of antidepressants. Family physicians who are familiar with these drugs and aware of the evolving literature should feel comfortable doing likewise. In light of current data, the risk of serious complications due to use of selective serotonin reuptake inhibitors during pregnancy appears small. An excellent authoritative article states that the exception might be in late pregnancy, during which treatment should be kept to the minimum effective dose, due to the possibility of premature birth and adverse drug effects on newborns.[24]

Moving forward

Where do we go from here? We need better public information about depression, its symptoms, and treatments. People in general, and women in particular, need to know that depression is real and not a character flaw. Stigma is still a powerful deterrent to seeking and accepting treatment. Pregnancy is a unique period during which most women are in frequent contact with health care providers. It offers an unparalleled opportunity for education about depression and for identifying and treating it. We need broader use of screening tools to identify depression in antenatal care, but identification is useless without timely, easily accessible, women-friendly treatment facilities. We also need to ensure that, as clinicians, we are aware of best practices (both nonpharmacologic and pharmacologic) in the management of depression, including depression during pregnancy. And finally, we need to continue to advocate for better research and evidence so we can be more confident in our future advice to pregnant women.

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References

1. Murray CJL, Lopez AD. Alternative visions of the future: projecting mortality and disability, 1990-2020. In: Murray CJL, Lopez AD, editors. *The alobal burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020.* Boston, Mass: Harvard University Press; 1996. p. 325-95.
2. Statistics Canada. *Canadian Community Health Survey: mental health and well-being.* Ottawa, Ont: Statistics Canada; 2003. Available at: **www.statcan.ca/english/freepub/82-617-XIE/index.htm**. Accessed 2005 May 12.
3. Kessler RC. Epidemiology of women and depression. *J Affect Disord* 2003;74(1):5-13.
4. Stewart DE, Gucciardi E, Grace SL. Depression. In: DesMeules M, Stewart DE, editors. *Women's health surveillance report: a multidimensional look at the health of Canadian women.* Ottawa, Ont: Canadian Institutes for Health Information; 2003. p. 39-40.
5. Kendler KS, Khun JW, Prescott CA. Childhood sexual abuse, stressful life events and risk for major depression in women. *Psychol Med* 2004;34(8):1475-82.
6. O'Hara MW. Social support, life events, and depression during pregnancy and the puerperium. *Arch Gen Psychiatry* 1986;43(6):569-73.
7. Miller LJ. Psychiatric disorders during pregnancy. In: Stotland NL, Stewart DE, editors. *Psychological aspects of women's health care: the interface between psychiatry and obstetrics and gynecology.* 2nd ed. Washington, DC: American Psychiatric Press, Inc; 2001. p. 51-66.
8. Robinson GE, Stewart DE. Postpartum disorders. In: Stotland NL, Stewart DE, editors. *Psychological aspects of women's health care: the interface between psychiatry and obstetrics and gynecology.* 2nd ed. Washington, DC: American Psychiatric Press, Inc; 2001. p. 117-40.
9. Heron J, O'Connor TG, Evans J, Golding J, Glover V, The ALSPAC Study Team. The course of anxiety and depression through pregnancy and the postpartum in a community sample. *J Affect Disord* 2004;80(1):65-73.
10. Stewart DE, Robertson E, Dennis CL, Grace SL, Wallington TA. *Postpartum depression: literature review of risk factors and interventions.* Toronto, Ont: University Health Network Women's Health Program and Toronto Public Health; 2003. Available at: **www.city.toronto.on.ca/health/pp_depression.htm**. Accessed 2005 May 27.
11. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1987;150(6):782-6.
12. Reid AJ, Biringer A, Carroll JD, Midmer D, Wilson LM, Chalmers B, et al. Using the ALPHA form in practice to assess antenatal psychosocial health. *CMAJ* 1998;159(6):677-84.
13. Austin MP. Antenatal screening and early intervention for "perinatal" distress, depression and anxiety: where to from here? *Arch Women Ment Health* 2004;7(1):1-6.
14. Matthey S, White T, Panasetis P, Hopper U, Larkin M, Glossop T, et al. *Evaluation of the routine psychosocial assessment at Liverpool Hospital antenatal clinic. June 2002.* Sydney, Australia: Infant, Child and Adolescent Mental Health Service, South Western Sydney Area Health Service; 2002.
15. Veit CT, Ware JE. The structure of psychological distress and well-being in general populations. *J Consult Clin Psychol* 1983;51(5):730-42.
16. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. *JAMA* 1999;282(18):1737-44.
17. US Preventive Services Task Force. Screening for depression: recommendations and rationale. *Ann Intern Med* 2002;136(10):760-4.
18. Whooley MA, Avins AL, Miranda J, Browner WS. Case-finding instruments for depression. Two questions are as good as many. *J Gen Intern Med* 1997;12(7):439-45.
19. Canadian Task Force on Preventive Health Care. New grades for recommendations from the Canadian Task Force on Preventive Health Care. *CMAJ* 2003;169(3):207-8.
20. Wisner KL, Zarin DA, Holmboe ES, Appelbaum PS, Gelenberg AJ, Leonard HL, et al. Risk-benefit decision making for treatment of depression during pregnancy. *Am J Psychiatry* 2000;157(12):1933-40.
21. Ross LE, Dennis CL, Robertson E, Stewart DE. Postpartum depression: a guide for frontline health and social service providers. Toronto, Ont: Centre for Addiction and Mental Health; 2005.
22. Laine K, Heikkinen T, Ekblad U, Kero P. Effects of exposure to selective serotonin reuptake inhibitors during pregnancy on serotonergic symptoms in newborns and cord blood monoamine and prolactin concentrations. *Arch Gen Psychiatry* 2003;60(7):720-6.
23. Zeskind PS, Stephens LE. Maternal selective serotonin reuptake inhibitor use during pregnancy and newborn neurobehaviour. *Pediatrics* 2004;113(2):368-75.
24. Hallberg P, Sjoblom V. The use of selective serotonin reuptake inhibitors during pregnancy and breast-feeding: a review and clinical aspects. *J Clin Psychopharmacol* 2005;25(1):59-73.