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# Letters ❖ Correspondance

## Metronidazole and pregnancy

I would like to comment on the Critical Appraisal article[1] in the May issue. There is a big flaw with your question right at the start: a vaginal swab for *Gardnerella vaginalis* is never recommended. See The Canadian guidelines for sexually transmitted diseases,[2] page 91 of the 1998 edition, not those of 1992!

In the same guidelines, we recommend oral treatment for prevention of complications because topical treatment with clindamycin was associated with more complications of pregnancy than the oral form. Topical treatment with metronidazole was never tested in the context of pregnancy.

To comment on the Motherisk article[3] in the same issue, clindamycin is not contraindicated during pregnancy. But because of the pseudomembranous colitis, it should be reserved for the few women who have contraindications to metronidazole. The 1998 sexually transmitted diseases guidelines do warn us against metronidazole treatment during pregnancy, which caused a big debate (among experts and editors). The editors of the 1998 edition were not keen to publish without the warning even with the Motherisk report stating there was no more risk with use of metronidazole. The warning will be taken out in future editions, but topical metronidazole (either gel or cream) should not be used because we have no data on safety, and there is good evidence that oral metronidazole is relatively safe to use during pregnancy.

*—Marc Steben, MD*
*Member of the Sexually Transmitted Diseases Guidelines Expert Group*
*Montreal, Que*
*by e-mail*

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## *Response*

We thank Dr Steben for his thoughtful comments. There is increasing evidence of the safety of metronidazole, and, as Dr Steben points out, women should be treated effectively. Motherisk continues to review systematically safety data on drugs given to women. We are gratified by our daily dialogue with family physicians from coast to coast.

*—Gideon Koren, MD*

## *Response*

I agree with Dr Steben's statement that "a vaginal swab for *Gardnerella vaginalis* is never recommended." There are, however, several instances where physicians have done a vaginal swab during routine antenatal checkups looking for chlamydia and gonorrhea, and the swab result comes back positive for *G vaginalis*.

Given the controversy surrounding the articles cited in the past that found a potential link between preterm births and bacterial vaginosis, family physicians were often confused as to whether to treat these patients.

The article that I appraised simply puts good evidence behind the management plan to treat only those women who are symptomatic and to not treat women who are asymptomatic.[1] Special consideration could be given to those who have had previous preterm births, but as this article and a meta-analysis in 2001 outlines, no increased risk of prematurity is associated with asymptomatic bacterial vaginosis.[1,2]

*—Rich Trenholm, MD, MSC*

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2. Guise JM, Mahon SM, Aickin M, Helfand M, Peipert JF, Westhoff C. Screening for bacterial vaginosis in pregnancy. *Am J Prev Med* 2001;20(Suppl 3):62-72.

# St John's wort as treatment for depression

I read with interest the paper[1] by van Gurp et al on use of St John's wort (SJW) for depression. This paper exhibits some elements that merit comment.

A general problem with psychotherapeutic trials is that the very act of being in a study and receiving attention has salutary effects. The challenge is to demonstrate that the putative therapy is superior to placebo. It has been recognized for some time that mild forms of depression tend to improve just as much with placebo as with antidepressants.[2] This phenomenon certainly is consistent with many of the European trials of antidepressants, which found no difference between placebo and active therapy.[3,4]

The reduction in scores on the Hamilton Rating Scale for Depression (Ham-D) noted in this paper for both groups is in keeping with those seen for placebo in other trials.[2] A recent compelling review of 45 Food and Drug Administration phase 2 and 3 clinical antidepressant trials reveals that, for patients with Ham-D scores lower than 24, the effect of antidepressants added little over placebo, but that for patients with scores higher than 28 the superiority of antidepressants was very clear.[5] Therein lies what is perhaps the greatest weakness of this trial. Mean Ham-D score on entry was 19.3, well within the range where placebos would be expected to give results similar to antidepressants.

In this light, these results are not surprising. One might argue, however, if the sertraline patients had been as compliant as the SJW patients, they would likely have improved more.

The authors' conclusion that SJW has a role as a first treatment option for mild-to-moderate depression is not supported by this study. The best that can be said is that two agents that would be expected to act as placebos did precisely that. In these circumstances, favouring one agent because of a lower side effect profile would seem to lend more support to simply giving a sugar pill rather than a herbal compound with its attendant risks.

*—Lloyd Oppel, MD, CCFP(EM)*
*Vancouver, BC*
*by e-mail*

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## *Response*

We thank Dr Oppel for his interest and his observations. Our aim was to conduct a trial on primary care patients treated by family physicians. We deliberately selected a lower Ham-D inclusion criterion in order to accurately reflect the less severe forms of major depression in this population. As Dr Oppel notes, recent evidence suggests that milder forms of major depression might improve as much with placebo as with antidepressants. At the time of study design, standard therapy for even less severe forms of major depression included prescription of an antidepressant agent. The idea was to compare standard treatment with an alternative herbal treatment: St John's wort (SJW).

Dr Oppel's comments are based mainly on a review of a Food and Drug Administration database of 45 antidepressant clinical trials.[1] The authors of the review concluded that, in studies where mean pretreatment Ham-D scores were 24 or less, antidepressants performed no better than placebo.

To explore this issue, we examined treatment response in patients with pretreatment Ham-D scores 24 or higher (n = 11) and in patients with scores lower than 24 (n = 76). There was no interaction between pretreatment Ham-D scores and study outcomes. In both study groups, the mean decline in Ham-D score from baseline to 12 weeks was similar among those with higher and lower baseline Ham-D scores.

Dr Oppel also refers to a difference in compliance between the two treatment groups. In fact, compliance was similar. What was different was that the sertraline patients reported adverse effects roughly twice as frequently as the SJW patients.

We doubt that, on the strength of evidence currently available, family physicians would be comfortable withholding antidepressant therapy from all but the most severely depressed patients. Until future research supports such a departure from current practice, our data suggest that SJW is a reasonable first treatment option in this population given its apparently similar effectiveness and more favourable side effect profile when compared with selective serotonin reuptake inhibitors. Physicians should be aware of potential interactions with anticonvulsants, warfarin, oral contraceptives, digoxin, and antiretroviral agents.

*—Gerald van Gurp, MD*
*—Greg Meterissian, MD, FRCPC*
*—Laura Haiek, MD, MSC*
*—Jane McCusker, MD, DRPH*
*—François Bellavance, PHD*

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1. Khan A, Leventhal RM, Khan SR, Brown WA. Severity of depression and response to antidepressants and placebo: an analysis of the Food and Drug Administration database. *J Clin Psychopharmacol* 2002;22(1):40-5.