## Menstrual manipulation

(JULY 2010)

TO THE EDITOR: In the article, "Menstrual manipulation: Options for suppressing the cycle," the authors described advantages and disadvantages of various hormone-based methods of menstrual manipulation, including prolonged use of oral contraceptives. We believe the authors underemphasized the risks associated with oral contraceptives. Blood clots, stroke, and death are often included in print and television ads by law firms recruiting patients harmed by these drugs. In addition, the authors failed to mention the risk of premenopausal breast cancer due to oral contraceptives, which are now classified as group 1 carcinogens by the World Health Organization.<sup>2</sup>

In October 2006, we published the most current meta-analysis to date regarding oral contraceptive use and the risk of premenopausal breast cancer.<sup>3</sup> We found that 21 out of 23 studies showed a positive trend or positive risk for premenopausal breast cancer with oral contraceptive use prior to first-term pregnancy. This resulted in a highly statistically significant cumulative risk of 44% (ie, odds ratio 1.44, 95% confidence interval 1.24–1.68). Our meta-analysis remains the most recent study in this area and updates the Oxford pooled analysis,<sup>4</sup> which relied on older studies with older women (two-thirds of whom were over age 45).

A more recent collaborative study coauthored by investigators from the National Cancer Institute, the Hutchinson Cancer Research Center, and the University of Washington includes oral contraceptives in the list of risk factors for breast cancer in younger women.<sup>5</sup> We ask your readers to consider that patients are entitled to know about this important risk factor before making a decision regarding hormonal menstrual manipulation.

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## REFERENCES

- Hicks CW, Rome ES. Menstrual manipulation: options for suppressing the cycle. Clev Clin J Med 2010; 77:445–453.
- Cogliano V, Grosse Y, Baan R, et al, WHO International Agency for Research on Cancer. Carcinogenicity of combined oestrogen-progestagen contraceptives and menopausal treatment. Lancet Oncol 2005; 6:552–553.
- Kahlenborn C, Modugno F, Potter DM, Severs WB. Oral contraceptive use as a risk factor for premenopausal breast cancer: a meta-analysis. Mayo Clin Proc 2006; 81:1290–1302.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: further results. Contraception 1996; 54(3 suppl):15–106S.
- Dolle JM, Daling JR, White E, et al. Risk factors of triple-negative breast cancer in women under the age of 45 years. Cancer Epidemiol Biomarkers Prev 2009; 18:1157–1166.

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**IN REPLY:** Thank you for reading our article. Although the focus was geared more toward a comparison of different means of menstrual manipulation, we appreciate your comments on oral contraceptives and the link to premenopausal breast cancer.

As you noted, oral contraceptives have been linked to an increased risk of breast cancer, both in your meta-analysis1 and again more recently in a prospective study of 116,608 female nurses from 25 to 42 years of age. Interestingly, data from the latter study suggested that different formulations of oral contraceptives may pose different risks, and specifically that the use of triphasic preparations with levonorgestrel as the progestin had the highest risk. However, there is otherwise a paucity of data regarding the risk of specific formulations. There is currently no evidence of an association between oral contraceptive use and death from breast cancer, nor is there evidence that longer use of an oral contraceptive increases one's risk of death from breast cancer.3

Oral contraceptives have also been associated with a reduced risk of ovarian cancer,<sup>4</sup> and they appear to protect against death from ovarian cancer and uterine cancer.<sup>3</sup>

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Therefore, the clinician must consider the individual patient before making treatment recommendations, taking into account personal risk factors and other health concerns. (For a full list of contraindications to oral contraceptives, please refer to TABLE 2 in our original article.) Further guidelines may also be obtained from the "US Medical Eligibility Criteria for Contraceptive Use 2010," issued by the US Centers for Disease Control and Prevention in May 2010,<sup>5</sup> which delineates the eligibility criteria for initiating and continuing specific contraceptive methods, including oral contraceptives.

Thank you again for sharing your concerns. We appreciate the opportunity to clarify this important point.

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## REFERENCES

- Kahlenborn C, Modugno F, Potter DM, et al. Oral contraceptive use as a risk factor for premenopausal breast cancer: a meta-analysis. Mayo Clin Proc 2006; 81:1290– 1302
- Hunter DJ, Colditz GA, Hankinson SE, et al. Oral contraceptive use and breast cancer: a prospective study of young women. Cancer Epidemiol Biomarkers Prev 2010; 19:2496–2502.
- Vessey M, Yeates D, Flynn S. Factors affecting mortality in a large cohort study with special reference to oral contraceptive use. Contraception 2010; 82:221–229.
- Lurie G, Thompson P, McDuffie KE, et al. Association of estrogen and progestin potency of oral contraceptives with ovarian carcinoma risk. Obstet Gynecol 2007; 109: 597–607.
- Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, US Centers for Disease Control and Prevention (CDC), Farr S, et al. US medical eligibility criteria for contraceptive use, 2010: adapted from the World Health Organization medical eligibility criteria for contraceptive use, 4th edition. MMWR Recomm Rep 2010; 59:1–86.

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