

### What is already known on this topic

The premenstrual syndrome affects about 1.5 million women in the United Kingdom

There are numerous treatment options, progesterone being one of the most strongly advocated

Progesterone and progestogens are among the most widely prescribed treatments for premenstrual syndrome in the United Kingdom and the United States

### What this study adds

There is no evidence to support the claimed efficacy of progesterone in the management of premenstrual syndrome

There is insufficient evidence to make a definitive statement about progestogens, but current evidence suggests that they are not likely to be effective

meant that a comparative analysis of individual progestogens could not be undertaken.

While the role of endogenous progesterone and its metabolites in the aetiology of premenstrual syndrome remains unclear, it is evident from this meta-analysis that exogenous administration of either progestogens or progesterone does not improve symptoms. This is not surprising as there are reliable data to refute the theory that premenstrual syndrome is caused by a progesterone deficiency. With this review, there is now no convincing evidence to support the continued prescription of progesterone or progestogens for the management of premenstrual syndrome.

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- 1 Hylan TR, Sundell K, Judge R. The impact of premenstrual symptomatology on functioning and treatment-seeking behavior: experience from the United States, United Kingdom, and France. *J Womens Health Genet Based Med* 1999;8:1043-52.
- 2 Dalton K. *The premenstrual syndrome and progesterone therapy*. 2nd ed. Chicago, IL: Year Book Medical Publisher, 1984.
- 3 Rapkin AJ, Morgan M, Goldman L, Brann DW, Simone D, Mahesh VB. Progesterone metabolite allopregnanolone in women with premenstrual syndrome. *Obstet Gynecol* 1997;90:709-14.
- 4 Redei E, Freeman EW. Daily plasma estradiol and progesterone levels over the menstrual cycle and their relation to premenstrual symptoms. *Psychoneuroendocrinology* 1995;20:259-67.
- 5 Hammarback S, Backstrom T, Holst J, von Schoultz B, Lyrenas S. Cyclical mood changes as in the premenstrual tension syndrome during sequential estrogen-progesterone postmenopausal replacement therapy. *Acta Obstet Gynecol Scand* 1985;64:393-7.
- 6 Stewart A. *A rational approach to treating the premenstrual syndrome*. Seal, Kent: National Association of Premenstrual Syndrome, 1989.
- 7 Lyon KE, Lyon MA. The premenstrual syndrome. *J Reprod Med* 1984;29:705-11.
- 8 Jadad A, Moore M, Carrol D, Jenkinson C, Reynolds DJ, Gavaghan DJ. Assessing the quality of reports of randomised clinical trials; is blinding necessary? *Control Clin Trials* 1996;17:1-12.
- 9 Cohen J. *Statistical power analysis for the behavioural sciences*. Mahwah, NJ: Lawrence Erlbaum, 1988.
- 10 Hasselblad V, Hedges LV. Meta-analysis of screening and diagnostic tests. *Psychol Bull* 1995;117:167-78.
- 11 Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629-34.

- 12 Vanselow W, Dennerstein L, Greenwood KM, de Lignieres B. Effect of progesterone and its 5 alpha and 5 beta metabolites on symptoms of premenstrual syndrome according to route of administration. *J Psychosom Obstet Gynaecol* 1996;17:29-38.
- 13 Freeman EW, Rickels K, Sondheimer SJ, Polansky M. A double-blind trial of oral progesterone, alprazolam, and placebo in treatment of severe premenstrual syndrome. *JAMA* 1995;274:51-7.
- 14 Magill PJ. Investigation of the efficacy of progesterone pessaries in the relief of symptoms of premenstrual syndrome. Progesterone study group. *Br J Gen Pract* 1995;45:589-93.
- 15 Freeman E, Rickels K, Sondheimer SJ, Polansky M. Ineffectiveness of progesterone suppository treatment for premenstrual syndrome. *JAMA* 1990;264:349-53.
- 16 Corney RH, Stanton R, Newell R. Comparison of progesterone, placebo and behavioural psychotherapy in the treatment of premenstrual syndrome. *J Psychosom Obstet Gynaecol* 1990;11:211-20.
- 17 Maddocks S, Hahn P, Moller F, Reid RL. A double-blind placebo-controlled trial of progesterone vaginal suppositories in the treatment of premenstrual syndrome. *Am J Obstet Gynecol* 1986;154:573-81.
- 18 Andersch B, Hahn L. Progesterone treatment of premenstrual tension—a double blind study. *J Psychosom Res* 1985;29:489-93.
- 19 Dennerstein L, Spencer-Gardner C, Gotts G, Brown JB, Smith MA, Burrows GD. Progesterone and the premenstrual syndrome: a double blind crossover trial. *BMJ* 1985;290:1617-21.
- 20 Van der Meer YG, Benedek-Jaszmann LJ, Van Loenen AC. Effect of high-dose progesterone on the pre-menstrual syndrome; a double blind crossover trial. *J Psychosom Obstet Gynaecol* 1983;2:220-2.
- 21 Rapkin AJ, Chang LH, Reading AE. Premenstrual syndrome; a double blind placebo controlled study of treatment with progesterone vaginal suppositories. *J Obstet Gynecol* 1987;7:217-20.
- 22 West CP. Inhibition of ovulation with oral progestins—effectiveness in premenstrual syndrome. *Eur J Obstet Gynecol Reprod Biol* 1990;34:119-28.
- 23 Williams JGC, Martin AJ, Hulkenberg-Tromp A. Premenstrual syndrome in four European countries. Part 2. A double blind controlled study of dydrogesterone. *Br J Sexual Med* 1983;10:8-18.
- 24 Dennerstein L, Morse C, Gotts G, Brown J, Smith M, Oats J. Treatment of premenstrual syndrome. A double-blind trial of dydrogesterone. *J Affect Disord* 1986;11:199-205.
- 25 Strecker JR. Treatment of premenstrual syndrome with retroprogesterone (Duphaston). *Fortschr Med* 1980;98:145-7.
- 26 Lee JR. *Natural progesterone. The multiple roles of a remarkable hormone*. Sebastopol, CA: BLL Publishing, 1995.
- 27 Maxson WS. The use of progesterone in the treatment of premenstrual syndrome. *Clin Obstet Gynecol* 1987;30:465-77.
- 28 Dimmock PW, Wyatt KM, Jones PW, O'Brien PMS. Efficacy of selective serotonin re-uptake inhibitors in premenstrual syndrome: a systematic review. *Lancet* 2000;356:1131-6.

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### Corrections and clarifications

#### *Tobacco litigation worldwide*

A reader queried the absence of a competing interests statement in this Education and Debate article by R A Daynard, C Bates, and N Francey (2000;320:111-3). Professor Daynard would like to declare that he has been involved as counsel in suing tobacco companies and has received grants for research into the use of litigation to control tobacco use.

#### *Joint British recommendations on prevention of coronary heart disease in clinical practice: summary*

The authors would like to clarify one point in these summary recommendations from the British Cardiac Society, the British Hyperlipidaemia Association, the British Hypertension Society, and the British Diabetic Association (2000;320:705-8). In the guidance on "Using the coronary risk prediction chart for primary prevention" the first sentence states that the charts are for estimating the risk of coronary heart disease and defines that as "non-fatal myocardial infarction and death from coronary heart disease." In fact the end points should have been described as "non-fatal myocardial infarction, coronary death, and new angina pectoris." The *British National Formulary* will include the correct definitions of the end points from March 2002. The recommendations of the joint British Societies and of the NHS Framework are unaffected, and the end point for coronary heart disease including new angina pectoris is the same as for all Framingham based methods of coronary risk prediction.