

Thrombophilia screening and adverse pregnancy outcomes associated with uteroplacental insufficiency

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TO THE EDITOR: The recent article by the Obstetric Medicine Group of Australasia alluded to the increasing relevance and importance of thrombophilia screening following adverse pregnancy outcomes, namely recurrent miscarriage, stillbirth, retarded intrauterine growth and pre-eclampsia.¹ Formerly, these outcomes were generally attributed to "placental insufficiency", where a cause was not readily identified.

Screening for disorders in the uteroplacental circulation after such adverse pregnancy outcomes was formerly confined to investigations for an autoimmune basis, such as antinuclear antibodies, anticentromere antibodies, anti-DNA antibodies and the lupus inhibitor. However, in recent years, it has become more apparent that inherited or acquired thrombophilias may play a significant role in certain adverse pregnancy outcomes.²⁻⁵ Reports from Israel^{2,3} and elsewhere have suggested that thrombophilias can be found in up to 65% of women with recurrent pregnancy loss of unknown cause, as well as in cases of intrauterine growth retardation, stillbirth, placental abruption and pre-eclampsia. It is also known that certain thrombophilic factors are more likely to produce thrombogenic changes and hence are possible deficiencies in the uteroplacental circulation.

Preliminary work has shown that treating women who have had recurrent pregnancy loss complicated by thrombophilia with antithrombotic agents (low molecular weight heparins) is beneficial, with improved pregnancy outcomes in a significant number of these cases.³

With the growing understanding of the role of thrombophilias in pregnancy, it seems that thrombophilia screening will assume a more prominent role in investigating patients after recurrent miscarriage, stillbirth, intrauterine growth retardation and pre-eclampsia.

1. Hague WM, North RA, Gallus AS, et al. Anticoagulation in pregnancy and the puerperium. *Med J Aust* 2001; 175: 258-263.
2. Brenner B. Inherited thrombophilia and pregnancy loss. *Thromb Haemost* 1999; 82: 634-640.
3. Brenner B, Hoffman R, Blumenfeld Z, et al. Gestational outcome in thrombophilic women with recurrent pregnancy loss treated by Enoxaparin. *Thromb Haemost* 2000; 83: 693-697.
4. Preston FE, Rosendaal FR, Walker ID, et al. Increased fetal loss in women with heritable thrombophilia. *Lancet* 1996; 348: 913-916.
5. Rai R, Regun L, Hadley E, et al. Second trimester pregnancy loss is associated with activated protein C resistance. *Br J Haematol* 1996; 92: 489-490. □

Safety of hormone replacement therapy after mastectomy

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TO THE EDITOR: I agree with the assessment by Del Mar and colleagues of available data according to evidence-based guidelines on hormone replacement therapy (HRT) after mastectomy.¹ As they note, these data are not definitive. Standard practice has been to avoid oestrogen use in women with a history of breast cancer.

Ours is an increasingly litigious society and courts make decisions according to different criteria than do scientists. In particular, precedent is very important to the law of tort, even if the scientific basis for the precedent is unproven.

For some years now, I have seen 100 or more new patients per year with recently diagnosed early breast carcinoma. By the time I see them, every single one already knows that:

- anti-oestrogens are used in treatment of breast cancer; and

- women are at least 30% more likely to develop breast cancer after five years of HRT.

Further, these women fear recurrence of breast cancer more than any other health problem.

Hence, I am concerned that the sound evidence-based conclusions reached by Del Mar and colleagues could be successfully challenged in court by a woman who developed recurrence of breast cancer while receiving HRT.

In addition to the costs and stress for the individual practitioner involved and other members of his medical indemnity organisation, such action would set back scientific enquiry into this important subject, possibly forever.

There is a wealth of well conducted research into non-oestrogenic management for menopausal symptoms. Lifestyle measures (clothing and activity) and dietary modifications (avoiding spicy foods, alcohol) have a role in well-being. Oral progestogens, clonidine, venlafaxine, black cohosh, and probably tibolone, all produce better outcomes than placebo.² Evening primrose oil, pyridoxine, dong quai, Chinese herbs, progestogen and yam creams, and phytoestrogens do not work better than placebo.³ The last may actually be harmful. Advisory statements for general practitioners about oestrogen replacement therapy for managing menopausal symptoms after breast cancer should be prefaced with this information, as should any discussion with patients. I do prescribe oestrogens for distressing menopausal symptoms after breast cancer treatment, but only after several consultations to allow time for women to appreciate the uncertainties involved.

1. Del Mar CB, Glasziou PP, Spinks AB. Safety of hormone replacement therapy after mastectomy. *Med J Aust* 2002; 176: 285.
2. Davis SR. Menopausal symptoms after breast cancer. *Australian Doctor* 2002, 1 February.
3. Eden J. Managing menopause after breast cancer. Proceedings of Annual Hormone Update and Education Day, Sydney: Sydney Menopause Centre, 16 February 2002. □

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TO THE EDITOR: I was pleased to see the issue of hormone replacement therapy (HRT) after breast cancer raised by Del Mar and colleagues in a recent issue of the Journal.¹ However, I was a little disappointed to see that Australian research in this area had been "missed" by their search.^{2,3} There are a number of other

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