

Clinical Algorithms

Premenstrual syndrome

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A woman who complains of regularly recurring psychological or somatic symptoms, or both, which occur specifically during the luteal phase of the cycle is suffering from premenstrual syndrome. The symptoms are relieved by menstruation, so that there is at least one symptom free week after menstruation. Nearly all women experience some premenstrual changes, while 30-40% report considerable disruption of their lives. For a few women the effects may be devastating. Hence some workers have added that for a diagnosis of premenstrual syndrome the changes should be of sufficient severity to interfere with normal relationships or normal activity, or both. Despite much research (of variable quality) the aetiology¹ and treatment² of premenstrual syndrome remain uncertain, although there have been many claims to the contrary.

Symptoms and diagnosis

Many symptoms have been attributed to premenstrual syndrome, some of which appear typical such as irritability, aggression, depression, anxiety, and changes in libido (the psychological symptoms). In addition, somatic symptoms have been described such as lethargy, breast tenderness, pelvic pain, headache, bloatedness, and weight increase (or more often a sensation of weight increase), but only rarely oedema. The last three symptoms have been attributed to water retention, though in many women both bloatedness and a feeling of weight increase occur in the absence of actual weight gain, making water retention an occasional, but not an essential, feature of premenstrual syndrome. A wide range of behavioural problems have also been attributed to premenstrual syndrome; these include intrafamilial discord, poor concentration, incoordination, and clumsiness. The symptoms are so variable that the diagnosis is made not so much on their character but on their timing. Thus the fact that symptoms appear before menstruation and disappear with menstruation is probably the most important factor distinguishing premenstrual syndrome from a host of other conditions with which it may be confused.

Differential diagnosis

Premenstrual syndrome has been confused with psychiatric,³ gynaecological, medical, and surgical disorders. Table I shows the differential diagnosis. Many women use premenstrual syndrome as a label to legitimise their underlying psychological problems. Psychiatric disorders such as manic depression or neurosis may be attributed to premenstrual syndrome, especially by the patient.

TABLE I—*Differential diagnosis of premenstrual syndrome*

Neurological disorders	Obesity
Psychiatric disorders	Ideopathic oedema
"Label"	Diuretic abuse
Migraine	Anaemia
Menopause	Thyroid disease
Endometriosis	
Pelvic inflammatory disease	Fibroadenosis
Dysmenorrhoea	Breast cancer
Ovarian cysts	Non-cyclical mastalgia
Ascites	Tietze's syndrome

Previous knowledge of the woman's personality is obviously helpful. Symptoms such as migraine, headache, and incoordination may rarely be due to neurological disease rather than to the premenstrual syndrome.

Symptoms in the early stage of the menopause are often confused with those of premenstrual syndrome. The age of the patient, her history, and the presence of flushes will favour a diagnosis of the menopause, however, and this can be confirmed by measuring gonadotrophin (follicle stimulating hormone and luteinising hormone) concentrations. Many patients (and doctors) fail to distinguish between premenstrual syndrome, the menopause, and dysmenorrhoea. The premenstrual dysmenorrhoea of endometriosis may easily be confused, and if there is any doubt a referral to a gynaecologist may be necessary with a view to laparoscopy. Occasionally, progressive bloatedness may be attributed to premenstrual syndrome when the problem is one of progressive obesity (commonly) or ascites or ovarian cysts (rarely). Bloatedness in premenstrual syndrome is, however, a common symptom, which may be related to premenstrual constipation, colonic distention, and only rarely true water retention. To distinguish between these various causes of swelling and bloatedness it is important to ascertain (a) whether there is a measurable weight increase; (b) if so, whether this weight increase is truly related to the menstrual cycle; and (c) whether there is a history of inappropriate diuretic treatment or abuse.

Anaemia, hypothyroidism, and other general diseases sometimes present as lethargy; patients occasionally attribute this to premenstrual syndrome. Similarly, irritability and anxiety due to thyrotoxicosis may be attributed to premenstrual syndrome.

There are many causes of breast swelling and pain—for example, fibroadenosis, non-cyclical mastalgia, and Tietze's syndrome. Of course, it is particularly important to exclude breast cancer both from the point of view of diagnosis and to reassure the patient.

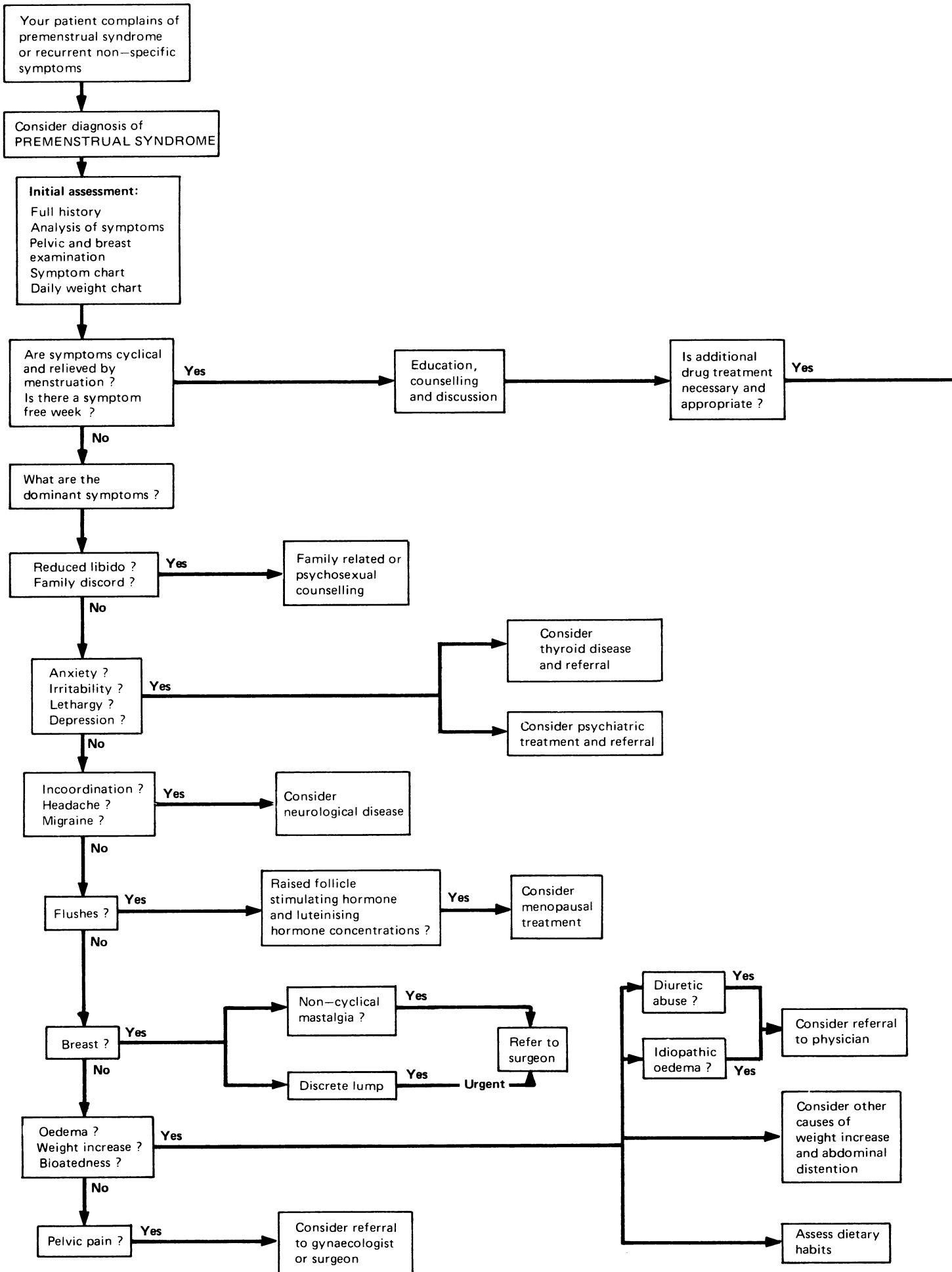
Management

The diagnosis of premenstrual syndrome can usually be made from the history in conjunction with a chart on which menstruation and symptoms are recorded on a daily basis. This shows the important fact that symptoms are relieved by the onset of menstruation. Daily weight measurements determine whether or not

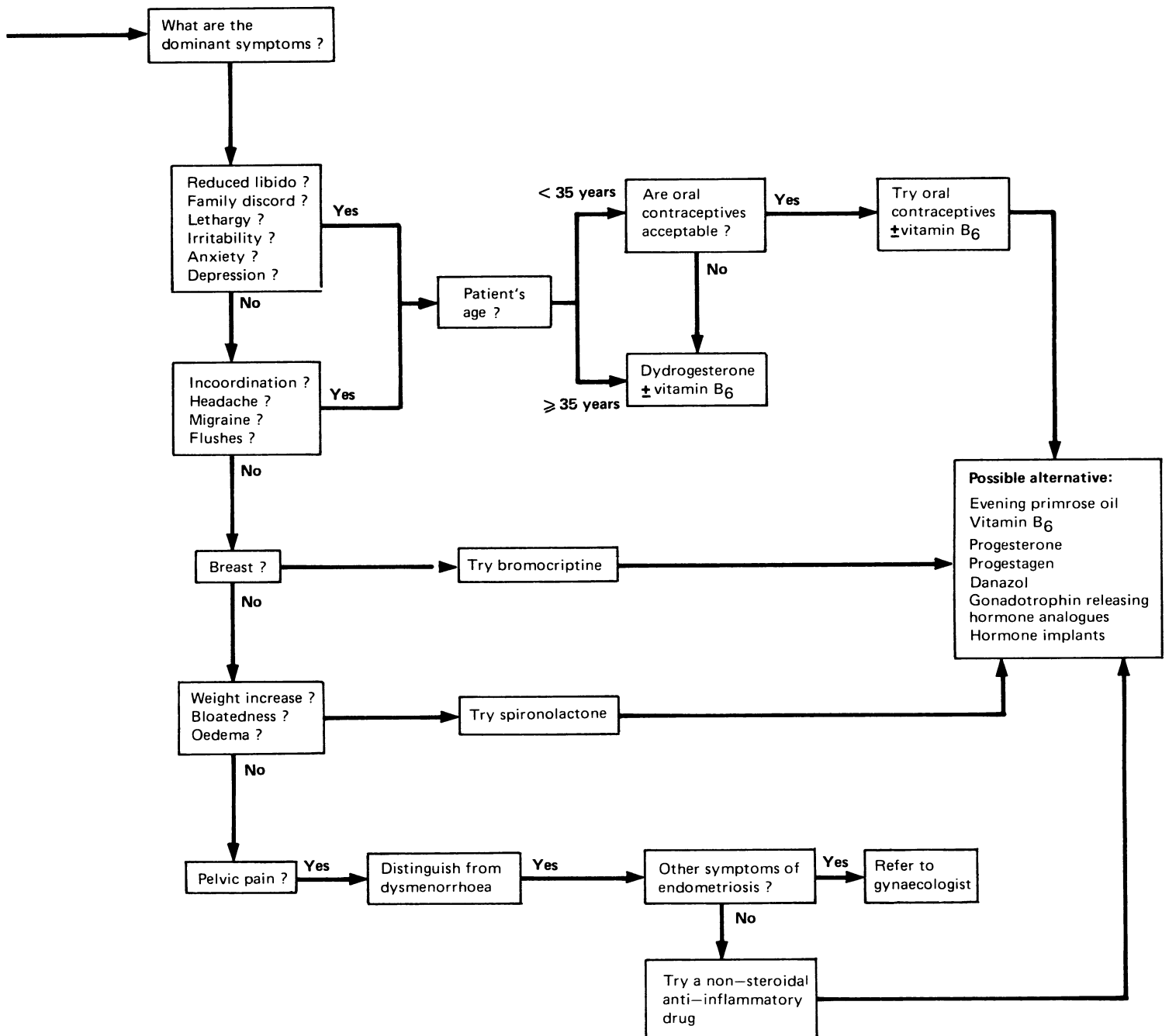
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there is associated water retention. There are no specific blood tests to help confirm the diagnosis of premenstrual syndrome. Problems such as the menopause or thyroid disease should, of course, be excluded.

Most patients will benefit from counselling, reassurance, discussion, and explanation. For many women this will be the first opportunity to discuss their premenstrual symptoms. Time is required, and it is therefore quite inappropriate to try to deal with this problem in a busy general practitioner's surgery or the outpatients clinic of a gynaecology department. In cases where there are intrafamilial problems it is probably of further benefit if the patient's partner is present, since fuller understanding by the partner may help to reduce escalating misunderstandings and tensions.

Several simple dietary measures have been suggested; these include preventing hypoglycaemia (which may result in mood swings and lethargy) by having small regular meals of nutritional value. Supplementation with multivitamins or vitamin B₆, or both, together with the administration of polyunsaturated fatty acids (evening primrose oil) have all been tried, but none of these has yet been adequately evaluated. Other self help measures include an increase in exercise and relaxation, together with general awareness of ways of reducing stress. Counselling and dietary manipulation may be the only acceptable approach for many women, particularly those with only moderate symptoms, who have a bias against hormone treatment.

Some consideration must be given before embarking on hormone or other drug treatment: the severity of the symptoms must be weighed against the potential side effects of treatment.

Drug treatment

Claims have been made for a multitude of treatments, none of which has been shown to be fully effective (table II). The results show high placebo responses, often more than 50%, resulting in optimistic claims for unproved regimens. Treatment is essentially empirical, and unfortunately no two patients seem to respond in the same way.

TABLE II—Current approaches to treatment

Psychotherapy or counselling	Oral contraception
Dietary manipulation	Dydrogesterone
Evening primrose oil	Norethisterone
Vitamin B ₆	Pure progesterone
Diuretics	Hormone implant
Non-steroidal anti-inflammatory drugs	Bromocriptine
	Danazol
	Gonadotrophin releasing hormone analogues

A simple approach would be to use oral contraception for younger women who do not want to become pregnant and a progestagen, such as dydrogesterone, for women unsuitable for oral contraception. Both of these regimens may be combined with vitamin B₆.

This approach and other treatments can be prescribed as follows.

Vitamin B₆ (pyridoxine) 100 mg daily is effective for psychological symptoms, although it may act only as a placebo. A small number of reversible neurological complications have been reported with higher, prolonged dosages—that is, more than 500 mg daily.

Oil of evening primrose, four to eight capsules daily, appears to be valuable for breast symptoms, but more evidence is required for other premenstrual symptoms. This so called natural preparation is not available on prescription and is expensive.

Dydrogesterone 10 mg twice daily from day 12 to day 26 of the menstrual cycle; there has been limited evaluation suggesting benefit when symptoms are multiple.

Pure progesterone 400 mg daily from day 14 to day 26 of the menstrual cycle, given as pessaries or suppositories, may be used when patients request this as "natural" hormone treatment, but results of trials have been inconclusive.

Combined oral contraceptive pills improve symptoms in many women, although some are made worse. Suppression of the cycle with continuous treatment may be more successful.

Oestradiol implants 100 mg subcutaneously, have been used, particularly for severe cases near the menopause. This must always be combined with cyclical progestagen—for example, dydrogesterone as above.

Bromocriptine 5 mg nightly from day 10 to day 26 of the menstrual cycle appears to be particularly effective for severe breast symptoms. Side effects can be partially avoided by taking the drug at night.

Danazol 200-400 mg daily seems to be effective when given continuously. This is expensive with potential side effects. It is rarely given as first line treatment but is useful in patients resistant to other treatments.

Diuretics given in the absence of water retention may produce secondary aldosteronism and cyclical oedema. Spironolactone 100 mg daily taken three days before the expected onset of symptoms therefore has at least theoretical advantages; potassium supplements should not be given.

Non-steroidal anti-inflammatory drugs are probably of value where symptoms of pain predominate. Some are available without prescription.

Gonadotrophin releasing hormone analogues may be useful short term drugs in the future, but their use will be limited because a "medical menopause" will be produced, causing hot flushes and, theoretically, osteoporosis.

Conclusion

In the treatment of premenstrual syndrome it is important to obtain an exact diagnosis. This is based on the timing of symptoms. Treatment should be preceded by an evaluation of symptoms using a daily record chart for at least one month. Initial treatment should be aimed at counselling, self help, and simple therapeutic measures. The wide range of treatments indicates that no single approach is adequate, and it is difficult to predict which specific treatment will be effective in a particular patient. The algorithm should be used as a guide to diagnosis and as an approach to treatment until more is known of the aetiology, which should lead to a more definitive treatment regimen for the syndrome.

References

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A 15 year old girl was given BCG immunisation as she had missed her routine immunisation. It was discovered later that she was eight weeks pregnant. Obviously there was some concern as BCG vaccine is live. Could the vaccine have harmful effects on the fetus?

I know of no evidence of a harmful effect on the fetus, especially in producing an active tuberculous infection, by immunising with BCG vaccine, which is an attenuated strain of *Mycobacterium bovis*. Experimentally, at a time when this vaccination, newly introduced, was under particularly close scrutiny for side effects and possible reversal to virulence, Irvine,¹ an authority on the clinical aspects, quoted tests on guinea pigs by Nélis and Picard, who found no sign of congenital tuberculosis in newborn offspring of pregnant animals given massive doses of BCG.² A safe conclusion is that, provided general immunological deficiency is absent, BCG does not constitute a danger to the fetus if given during pregnancy. It is quite usual to vaccinate newborn infants of a tuberculous parent, and in mass vaccination campaigns.—PHILIP HART, National Institute for Medical Research, London.

1 Irvine KN. *The BCG vaccine*. Oxford: Oxford Medical Publications, 1934.

2 Nélis P, Picard E. Sur l'innocuité du BCG. *Comp Rend Soc Biol* 1930;105:185-7.