

suggestions. Why, then, do we not capitalize on this good reputation? Why have the College's extending overseas contacts (see our reports on Council meetings, *passim*) been largely confined to the oil-rich countries of the Middle East? Is there no sort of advance that we could make to Tanzania, say, or Honduras, where the prospect of any kind of return to the College would have to be measured for the foreseeable future in terms of goodwill only?

There is a saying that people are what they do. We are doing very little. Don't we care?

S. L. BARLEY  
Editor

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## Notes

1. *World Health Forum: An International Journal of Health Development* is a quarterly journal with a subscription of Sw Fr 40-. WHO publications may be obtained, direct or through booksellers, from HMSO bookshops in London, Edinburgh, Cardiff, Belfast, Manchester, Birmingham and Bristol.
2. The address of Voluntary Service Overseas is 9 Belgrave Square, London SW1X 8PW (tel: 01-325 5191).
3. The address of the Bureau for Overseas Medical Service is London School of Hygiene and Tropical Medical, Keppel Street, London WC1 (tel: 01-636 8638 or, evenings and weekends, Ansaphone service 01-455 6332).

# What is this PMS?

IN 1980 the Sixth International Congress of Psychosomatic Obstetrics and Gynaecology concluded that "premenstrual syndrome (PMS) must be regarded as an endocrinopathy . . . deserving of a place in the future, not only at psychosomatic meetings but also at scientific conventions" (Van Keep and Utian, 1981), thus recognizing the hormonal element in PMS. Nevertheless it is only general practitioners, observing patients in health and sickness, who are the most likely doctors to recognize the changes in mood during the menstrual cycle, so characteristic of PMS; only they know the impact it has on the patient's family, neighbours and workmates. The general practitioner also has the clinical competence to make the diagnosis and supervise treatment. PMS is thus the specialty of general practice.

Frank first described premenstrual tension in 1931 as "a feeling of incredible tension from 10 to 7 days preceding menstruation, which in most instances continues until the time the menstrual flow occurs". Later it was appreciated that many other symptoms may be involved, such as headaches, nausea, vertigo, joint pains, skin and mucosal lesions, rhinorrhoea, asthma, epilepsy and mastalgia. In 1953 the term 'premenstrual syndrome' was introduced "to prevent missing the diagnosis when tension was absent or overshadowed by a more serious complaint" (Greene and Dalton, 1953). PMS was defined as "the presence of recurrent symptoms in the premenstruum or early menstruation with complete absence in the postmenstruum". It must be

emphasized that Frank's definition and this one are the same, and depend on the timing of symptoms, not on their type. They are themselves commonplace, and also occur with great frequency in men, children and postmenopausal women. Greene and Dalton insisted on the minimum time of recurrences of symptoms as three menstrual cycles, with an absence in each postmenstruum. Today some investigators consider that self-rating questionnaires used by women in only one premenstrual week are sufficient for a diagnosis (Clare, 1977). This is not good enough.

PMS covers a wide spectrum from normality to gross abnormality. It has been studied by sociologists, psychologists, psychiatrists, gynaecologists, endocrinologists and physicians, and is a popular subject in the medical and lay press, but too often definitions are absent or incorrect so that comparisons cannot be made. A recent review of PMS by Reid and Yen (1981) describes it on the basis of symptoms: "The patient with severe PMS develops breast swelling and tenderness, abdominal bloating and a variable degree of oedema in the extremities in the luteal phase", but fails to define PMS. This again is not enough; there must be evidence of timing of symptoms, and a symptom-free phase in the postmenstruum or pre-ovulatory phase.

Earlier doctors limited 'symptoms' to those complaints severe enough to require medical attention. Today's psychologists administer self-rating questionnaires to identify premenstrual complainers in a healthy

population and, having divided them into psychiatrically healthy and ill premenstrual complainers, draw conclusions on the degree of neuroticism and personality traits of PMS sufferers (Clare, 1982). Surveys of this type are as irrelevant to the elucidation of the aetiology and treatment of PMS as a similar general population study of diarrhoea sufferers would be in investigating the aetiology and therapeutic factors involved in ulcerative colitis or Crohn's disease.

Women presenting with premenstrual symptoms need a full clinical examination, for it is not uncommon to find evidence of hypertension, hypothyroidism, galactorrhoea, ovarian cysts, salpingitis or endometriosis, all conditions which require specific treatment. Women in whom no physical abnormalities are discovered should be given a menstrual chart on which to record, with any chosen symbol, the three worst symptoms on the days they occur and also the dates of menstruation (Dalton, 1977). Positive charts are those showing symptoms occurring at the same time in the luteal phase of each cycle, and at least seven consecutive days free from symptoms at the same time in each postmenstruum. This recording does not entail a great intellectual demand and can be used equally well by those with a poor understanding of English. In a few cases it may be possible to obtain retrospective information from prison or police documents (Dalton, 1980), medical records or worksheets, from which it may be possible to make a positive diagnosis and institute immediate treatment.

Many studies have relied on the Moos Menstrual Distress Questionnaire (MMDQ), which as its name suggests was designed to identify sufferers of menstrual distress (Moos, 1968). In such a questionnaire a woman is asked to rate some 47 symptoms on a six-point scale. The success of the self-assessment questionnaire depends on the diligence of the woman completing it each night for a minimum of three months, including high days and holidays. The findings are relevant only in the highly motivated or the obsessional woman, and there is the ever-present danger that she will forget to complete it one night and fill it in some days later giving a false answer. Even using the shortened Form T with Sampson and Jenner's (1977) sine wave modification, it is of no value in the diagnosis of PMS. No questions are asked regarding the absence of symptoms in the postmenstruums or the recurrence of symptoms in successive premenstruums. Such criteria cannot produce the necessary evidence so essential to the diagnosis of PMS. Sampson's 1979 paper on "PMS—a double blind controlled trial of progesterone and placebo" relied on such evidence from the MMDQ and even showed in Figure 1 the results of the questionnaire demonstrating the presence of symptoms in the postmenstruum in both the cycle under observation and the cycle before treatment commenced. Such trials merely demonstrate that progesterone has no value in menstrual distress, a term covering dysmenorrhoea, endometriosis and menstrual

exacerbation of symptoms present throughout the cycle. It is recognized that progesterone is specific to PMS and is of no value in dysmenorrhoea or endometriosis, so it was not unexpected that the value of progesterone in the trials of menstrual distress was no better than placebo.

PMS occurs in both ovular and anovular cycles, so that basal temperature charts are of no diagnostic value (Reid and Yen, 1981). Similarly, as weight swings are normal physiological happenings, a daily weight chart alone is not diagnostic. At present the only biochemical test of diagnostic value in PMS is the sex hormone binding globulin (SHBG) estimation, which in 50 women with well-diagnosed severe premenstrual syndrome was found to be below the normal level of 50–80 nmol/DHT/l, whereas 50 control women, who denied having any premenstrual symptoms all had values in the normal range (Dalton, 1981). However, the use of SHBG is limited to those who are free from medication, and who are not obese or hirsute, so that the ethnically hirsute races cannot be included. Furthermore, at present SHBG estimations are available only at a few specialized laboratories.

Noting the following points when taking a history can alert the clinician to a positive diagnosis of PMS. PMS starts and also increases in severity at times of hormonal upheaval, such as puberty, after a pregnancy, during or after taking oral contraceptives, after a spell of amenorrhoea or after sterilization. PMS sufferers are usually symptom-free during pregnancy (Greene and Dalton, 1953) and are unable to tolerate the Pill due to side-effects. Women who have suffered from pre-eclampsia show an 87 per cent incidence of PMS afterwards (Dalton, 1954) and a 90 per cent incidence after postnatal depression (Dalton, 1977). Women with PMS also tend to have food cravings and are unable to tolerate long intervals without food (Okey and Robb, 1925; Harris, 1944; Billig, 1947; Dalton, 1977). Their tolerance to alcohol also varies over the cycle, being worse premenstrually. Their libido is often highest in the premenstruum (Israel, 1938; Gray, 1941), in contrast to sufferers of depression, who have a loss of libido throughout the month.

The many difficulties encountered in studies of PMS include the individual variations in the length of cycle in the same woman and between women. There are variations in the duration of the menstrual flow, the effects of stress (Dalton, 1968), age and parity (Dalton, 1954), a past history of pre-eclampsia (Greene and Dalton, 1953) or postnatal depression (Dalton, 1977), variations in hormonal states due to oral contraceptives, the woman's attitude to a possible pregnancy and the selection of suitable controls. The literature on PMS includes many examples of biased selection of subjects or controls, for example the use of women attending an infertility clinic (Benedek-Jaszmán and Hearn-Sturtevant, 1976), and the use of lithium in 19 hospitalized women, including five with schizophrenia, four neurotics and three psychotics (Singer *et al.*, 1974). A study

## Prescribing Information

# Zantac

RANITIDINE

## Uses

**Indications:** Zantac Tablets are indicated for the treatment of duodenal ulcer, benign gastric ulcer, post-operative ulcer, reflux oesophagitis and the Zollinger-Ellison syndrome.

**Mode of action:** Zantac is a highly effective, rapidly acting histamine H<sub>2</sub>-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume and the acid and pepsin content of the secretion. Zantac has a relatively long duration of action and so a single dose effectively suppresses gastric acid secretion for twelve hours.



## Dosage and administration

**Adults:** The usual dosage is one 150 mg tablet twice daily taken in the morning and before retiring. It is not necessary to time the dose in relation to meals. In most cases of duodenal ulcer, benign gastric ulcer and post-operative ulcer, healing occurs in four weeks. In the small number of patients whose ulcers have not fully healed, healing usually occurs after a further course of treatment. Maintenance treatment at a reduced dosage of one 150 mg tablet at bedtime is recommended for patients who have responded to short-term therapy, particularly those with a history of recurrent ulcer.

In the management of reflux oesophagitis, the recommended course of treatment is one 150 mg tablet twice daily for up to 8 weeks.

In patients with Zollinger-Ellison syndrome, the starting dose is 150 mg three times daily and this may be increased, as necessary, to 900 mg per day.

**Children:** Experience with Zantac Tablets in children is limited and such use has not been fully evaluated in clinical studies. It has, however, been used successfully in children aged 8-18 years in doses up to 150 mg twice daily without adverse effect.

## Contra-indications

There are no known contra-indications to the use of Zantac Tablets.

## Precautions

Treatment with a histamine H<sub>2</sub>-antagonist may mask symptoms associated with carcinoma of the stomach and may therefore delay diagnosis of the condition.

Accordingly, where gastric ulcer is suspected the possibility of malignancy should be excluded before therapy with Zantac Tablets is instituted.

Ranitidine is excreted via the kidney and so plasma levels of the drug are increased and prolonged in patients with severe renal failure. Accordingly, it is recommended that the therapeutic regimen for Zantac in such patients be 150 mg at night for 4 to 8 weeks. The same dose should be used for maintenance treatment should this be deemed necessary. If an ulcer has not healed after treatment for 4 to 8 weeks and the condition of the patient requires it, the standard dosage regimen of 150 mg twice daily should be instituted, followed, if need be, by maintenance treatment at 150 mg at night. Although the incidence of adverse reactions in clinical trials of one year's duration and longer has been very low and no serious side effects have been reported with Zantac treatment, care should be taken to carry out periodic examinations of patients on prolonged maintenance treatment with the drug as a safeguard against the occurrence of unforeseeable consequences of drug treatment.

Like other drugs, Zantac should be used during pregnancy and nursing only if strictly necessary. Zantac is secreted in breast milk in lactating mothers but the clinical significance of this has not been fully evaluated.

## Side effects

No serious adverse effects have been reported to date in patients treated with Zantac Tablets. There has been no clinically significant interference with endocrine, gonadal or liver function, nor has the drug adversely affected the central nervous system even in elderly patients.

## Further information

**Drug interactions:** Ranitidine does not inhibit the cytochrome P450-linked mixed function oxygenase enzyme system in the liver and therefore does not interfere with the effects of the many drugs which are metabolised by this enzyme system. For example, there is no interaction with warfarin or diazepam.

**Pharmacokinetics:** Absorption of ranitidine after oral administration is rapid and peak plasma concentrations are usually achieved within two hours of administration. Absorption is not impaired by food or antacids. The elimination half-life of ranitidine is approximately two hours. Ranitidine is excreted via the kidneys mainly as the free drug and in minor amounts as metabolites. Its major metabolite is an N-oxide and there are smaller quantities of S-oxide and desmethyl ranitidine. The 24-hour urinary recovery of free ranitidine and its metabolites is about 40% with orally administered drug.

**Use in renal transplants:** Zantac has been used without adverse effect in patients with renal transplants.

**Product licence number** 0004/0279

**Basic NHS cost** (exclusive of VAT) 60 tablets £27.43.

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into minor psychiatric and physical symptoms selected seven control women who had undergone a hysterectomy (Beaumont *et al.*, 1975). The absorption and metabolism of oral progesterone was studied in five postmenopausal women (Whitehead *et al.*, 1980), and another studied the effects of progesterone and four synthetic progestogens using 20 male medical students (Oelkers *et al.*, 1974). An appeal on commercial radio asked for volunteers for PMS trials: the authors stated that a telephone conversation had ensured that the volunteers all had premenstrual complaints, but after a month's charting of symptoms only three had premenstrual symptoms alone, and 34 women had premenstrual and menstrual symptoms (Wood and Jakubowicz, 1980). None of these trials is acceptable because of their biased selection.

Perhaps the greatest problem comes in the selection of subjects for double-blind controlled therapeutic trials; because it is ethically wrong to include those in danger to themselves or others, those at risk of epileptic fits, acute asthma attacks, suicide, homicide, baby batterers, criminal damage and alcoholic bouts are automatically excluded. Those with moderate symptoms, having completed a three-month chart, are usually at the end of their tether and demand treatment; they are no longer ready to accept the possibility of receiving a placebo. This difficulty can be partially overcome by treating the patients first and, when they are completely symptom-free on medication, allowing them one month's trial of another drug (Dalton, 1959 and 1976). The women then know their suffering can be relieved and have permission to return to effective treatment should they consider it necessary. On the other hand, women with only mild symptoms do not really need treatment.

In PMS there are two areas demanding further study which should not be confused: a fuller understanding of how the hormonal changes of menstruation affect normal women, and the prevention of suffering for those who are in distress during each premenstruum. PMS does exist and has only one definition: it is a syndrome needing treatment. It is the general practitioner's responsibility to diagnose and treat this common problem which has innumerable manifestations and, all too often, dire consequences.

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## Stopping thyroid medication

AT first sight it may seem that thyroid medication is not a subject of great priority in practice. Thyroxine is cheap, relatively harmless and has few side-effects; its dose and effectiveness are easily monitored clinically and biochemically. However, thyroid medication has often been started in the past for reasons which would nowadays be considered insufficient or inappropriate. Obesity, lymphoedema, depression, infertility, menstrual disorders, constipation and falling hair are among the symptoms for which a 'trial' of thyroid extract may have been undertaken. The placebo response and natural cure have been too readily taken as therapeutic response. A fear that prolonged medication may permanently suppress the thyroid/pituitary axis may act as a deterrent; the difficulty is to know if and when to stop medication. Thyroid therapy may also have been initiated at hospital after definitive treatment for thyrotoxicosis. It is now known that transient hypothyroidism may occur after surgery and radioactive iodine therapy. Sawers and colleagues (1980) recommend that if biochemical hypothyroidism should occur during the first six months after radioactive iodine, replacement therapy should be withheld for a further two months (unless the severity of symptoms demands it) to allow natural recovery of thyroid function to occur. In Hashimoto's thyroiditis, operative intervention is more likely to result in hypothyroidism, so that replacement therapy is often considered mandatory.

Clinically, thyroid disease may be suspected frequently but not so often confirmed biochemically. White and Walmsley (1978) found that the presence of only one or two symptoms rarely (only twice in 442 patients referred for thyroid function studies) indicated thyroid dysfunction. One patient out of 35 with three or four symptoms required treatment, while five or more symptoms indicated dysfunction in 18 out of 23 patients.

Hypothyroidism is a common diagnosis, with prevalence rates of up to 15 or even 20 per thousand adult women. Since treatment is life-long, the resources needed to continue treatment and monitor it assume significant proportions for the general practitioner, the laboratory, occasionally for hospital outpatients, and certainly in financial terms for the National Health Service. The patient must take tablets regularly, obtain prescriptions, attend the doctor, and have blood tests.

Stopping thyroxine in suspected hypothyroid patients is potentially dangerous because of the risk of hypothermia and the insidious onset of myxoedema; hypercholesterolaemia and the attendant cardiovascular threats have to be prevented. In excess, thyroxine can cause tachycardia, angina, nervousness, tremors, diarrhoea, insomnia, sweating, muscle cramps, muscle weakness and wasting, and weight loss, and has the risks of sympathetic overdrive in patients with cardiovascular disease.

The development of a test applicable in general practice, which will enable us to determine whether