# **Premenstrual Syndrome (PMS)**

#### Katharina Dalton

University College Hospital, London, U.K.

- I. Introduction
- II. Symptoms
- III. Signs
- IV. Characteristics
- V. Diagnosis
- VI. Diagnostic Pointer Checklist
- VII. Etiology
- VIII. Treatment

**Follicular Phase** Covers the days from menstruation until ovulation.

**Intermenstruum** Covers those days of the menstrual cycle that are not included in the paramenstruum.

**Luteal Phase** The days from ovulation until menstruation.

**Menstrual Cycle** Measured from the first day of menstruation until the day before the next menstruation.

**Paramenstruum** The four days immediately before menstruation and the first four days of menstruation. **Premenstruum** The days from ovulation until menstruation.

**PREMENSTRUAL SYNDROME** (PMS) is the recurrence of disabling physical or psychological symptoms occurring in the premenstruum with complete relief in the postmenstruum.

PMS has a precise definition requiring recurrence of the same symptoms at the same phase of the cycle for at least the last three menstrual cycles. The symptoms may last less than 1 day (e.g., epilepsy, migraine, confusion, or hallucinations), but may not last longer than 14 days, and there must be complete absence of all symptoms for at least 7 days before ovulation. The symptoms should be severely disabling and interfering with work capacity and/or social life, thus excluding the valuable warning symptoms marking the approach of menstruation. Occasionally only one symptom is present, but more frequently the women are polysymptomatic.

#### I. INTRODUCTION

Before normal bodily functions there are valuable, warning sensations. For instance, these sensations inform the individual when the bladder is full, or when the bowels need emptying. There is a nasal tickling before sneezing, and thirst when dehydrated. In the same way there are valuable, warning sensations before menstruation. These sensations should not be considered premenstrual symptoms, but this does account for the findings of some surveys of an incidence of PMS exceeding 90%. On the other hand there are women whose premenstrual symptoms are disabling, interfering with normal working and social life, they suffer from PMS and are deserving of consideration and treatment.

A normal menstrual cycle varies from 21 to 35 days, and is considered to be regular if variations, cycle to cycle, do not exceed 4 days. Normal menstruation may last from 2 to 8 days, with the bleeding being pink, bright red, or dark brown. The normal

age of menarche is from 12 to 14 years, but the age does vary with race, economic, and social factors. Early menarche is usual in the blind, deaf, and congenitally physically handicapped (hydrocephalus, spina bifida, dislocated hip). The normal age of menopause is between 45 and 55 years, therefore if menstruation stops before the age of 45 years, or if bleeding becomes heavy then gynecological examination is indicated. Cyclical symptoms may occur for up to 2 years before the menarche, and up to 2 years after the menopause. Following recovery from the trauma of hysterectomy or bilateral oophorectomy, cyclical symptoms return.

#### II. SYMPTOMS

There are no unique symptoms; all symptoms also recur in men, children, and postmenopausal women, and almost all organs are involved. The diagnosis depends entirely on the timing and severity of symptoms. Even women with diagnosed PMS may, under certain circumstances, suffer their typical premenstrual symptoms at other times of their menstrual cycle. During pregnancy, when menstruation is temporarily abolished, PMS disappears, and years later the patient will usually recall pregnancy as the time of exceptional good health. However, PMS often returns with increased severity after the pregnancy, especially if complicated by preeclampsia, postnatal depression, or puerperal psychosis. Cyclical symptoms disappear temporarily when ovulation is stopped with estrogen implants, Danazol, or GnHR agonists, but reappear if progestins are used to cause withdrawal bleeding. Cyclical monthly symptoms reappear after recovery from the trauma of hysterectomy or oophorectomy, which may take up to 3 years.

More than 150 symptoms have been described, of which 33% are psychological. These include tension (with the triad of depression, irritability and lethargy), mood swings, anxiety, crying, self-mutilation, as well as psychosis with delusions, hallucinations, and paranoia. Common behavioral symptoms include food cravings, decreased motivation, increased alcohol urges, social isolation, increased libido, insomnia or hypersomnia, clumsiness and forgetfulness. Among the common physical symptoms are headaches, breast tenderness, asthma, sinusitis, epilepsy, skin lesions, conjunctivitis, and joint and muscle pains.

Symptoms never exceed 14 days, but may only last a few hours, for example, panic attacks, psychosis, epilepsy, migraine. Symptoms always increase in severity as menstruation approaches; thus, symptoms that occur a week before the onset of menstruation and then disappear are unlikely to be repeated at the same phase of the cycle month after month. Occasionally, symptoms start during menstruation. This occurs in women who have a slight menstrual bleed for a few days before the full menstrual flow, when symptoms are occurring in the physiological "premenstruum," although recorded as chronological "menstruation." A single severe symptom (e.g., epilepsy, migraine, aggressive outburst, self-mutilation) may occur in the morning, with menstruation starting in the evening, in which case the premenstrual event is recorded as occurring on the first day of menstruation. This is the reason most sociological surveys (accidents, criminal offenses, examination results, hospitalization) compare incidents during the paramenstruum with the other days of the menstrual cycle.

Typically, patients are polysymptomatic, with six or more symptoms recurring during the premenstruum, and with symptoms tending to span more than one medical speciality. Neurologists, rheumatologists, dermatologists, otologists, chest physicians, urologists, and gastroenterologists are also frequently involved. Many workers prefer to limit the initial daily recording to the three priority symptoms, as when those are satisfactorily treated the other minor symptoms tend also to disappear.

Depression is a common PMS symptom, but differs from major depression in that the timing is predictable and shorter, never more than 14 days, and is followed by days of complete normality. It is characterized by weight increase with food cravings and binges, in contrast to the weight loss and diminished appetite of typical depression. Those with PMS have a yearning for sleep and would like to stay in bed all day, as opposed to the early morning waking and restlessness of other depressives, who get up, wander round the house, make tea or even do the housework. Marked irritability and mood swings accompany the depressive days but are absent in the follicular phase. Nulliparous women may have nymphomania during the premenstruum, which differs from the complete loss of libido in other depressions. [See Depression.]

With PMS irritability there may be loss of self-

control resulting in verbal abuse with shouting, yelling, and swearing, as well as violence with banging, slamming, throwing, and hitting. She may become impatient, irrational, illogical, hostile, and paranoidal. Her behavior may lead to criminal offenses for damage to property, grievous bodily harm, or attempted or actual murder.

A cry for help during the premenstruum may be an attempted suicide, hoax telephone calls, or arson. PMS-related crimes tend to be committed alone, to the surprise of those near to them at the time; they do not appear to be premeditated; they are without apparent motive; and there is usually no attempt to escape detection.

The headaches tend to be hemicranial or centered in, above, below, or behind one or both eyes, and they may describe the eye as being "stoney hard." Migrainologists recognize "tension headaches" as being occipital, with radiation of pain down the neck and across the shoulders, but this is not the most common type of PMS headache.

#### III. SIGNS

There are few signs of PMS, although a partner may recognize darkening under and puffiness of the eyes. He is unlikely to recognize excessive weight gain during the premenstruum, unless alerted by the patient, for healthy normal women may also experience weight swings of up to five pounds each cycle.

If one records daily blood pressure readings, there may be paramenstrual swings about 20 mm Hg in both the diastolic and systolic pressure compared with intermenstrual readings, but not reaching hypertensive levels. Those complaining of headaches centered on the eyes may, with daily recording, note an increase in intraocular tension of about 5 mm Hg during the paramenstruum compared with the intramenstruum, occurring both in those whose intraocular tension is normal and those with early or treated glaucoma. There may be proteinuria in catheter specimens of urine during the paramenstruum compared with the intramenstruum. The day-by-day changes in severity of a patient with asthma are easily shown by the peak flow meter. Investigation of these signs in individuals are not always necessary, although they are interesting findings for research.

#### IV. CHARACTERISTICS

These characteristics of PMS are helpful at the initial screening of women who have not yet started regular recording of symptoms. If present they are accepted in English law as sufficient reason to delay sentencing or court appearances until a positive diagnosis can be made.

PMS women are normal on gynecological examination. They have regular and painless menstruation, with normal loss, normal blood levels of estrogen, follicle stimulating hormone, luteinizing hormone, and prolactin, and do not have infertility problems. Cyclical symptoms may recur for 2 years before menarche, continue for about 2 years after the natural menopause, and also restart up to 3 years after recovery from the trauma of hysterectomy or oophorectomy.

Pain with menstruation is *not* a presenting PMS symptom and always requires further investigation. Common causes of premenstrual and menstrual pain include spasmodic dysmenorrhea, which only occurs in ovulatory cycles and so disappears with the contraceptive pill; endometriosis, which is accompanied by dyspareunia and pain on moving the uterus at vaginal examination; and pelvic inflammatory disease, which causes pain throughout the cycle that is worse in the premenstruum and is usually accompanied by a vaginal discharge.

PMS tends to start at times of hormonal up-heaval—32% at puberty and 33% after pregnancy—while others start on stopping the contraceptive pill, after amenorrhea (e.g., due to anorexia, head injury), after sterilization, and after unilateral oophorectomy. These are also the times when PMS may increase in severity. PMS follows recover from preeclampsia and postnatal depression in 80% of cases. Symptoms are increased at times of stress. One frequently hears a woman describe how she had a difficult time with PMS at puberty, but that it then eased for many years until after a pregnancy, or when she was under stress from an unsatisfactory relationship, a bereavement, redundancy, or a financial problem.

PMS women have difficulty in tolerating progestin medication, whether administered orally, transdermally, or as long-term injections, in contraceptive pills, or HRT, for progestins lower the blood progesterone level. They have difficulty in tolerating long intervals without food, and easily become shaky, tired,

anxious, or aggressive at such times. Symptoms tend to increase if there is sleep deficit, and they are poor jet-lag travelers. While they can tolerate normal alcohol intake during the intermenstruum, they may have uncontrollable alcohol urges premenstrually. Regardless of their poor premenstrual behavior, it is then that their libido is increased and may reach nymphomanic proportions. Monthly weight swings of up to five pounds occur in normal, healthy women, but during their adult years PMS women experience weight swings exceeding 28 pounds between their highest nonpregnant weight and their lowest weight since the age of 16 years.

In common with most hormonal diseases a positive family history is frequent, with three or four generations suffering. This genetic factor has been demonstrated in twin studies, where if one monozygous twin suffers from PMS the other will also be suffering, whereas in female dizygous twins the incidence is similar to that found in sisters. Similarly, adoption studies have shown a statistically significant difference between the low incidence of PMS in mothers of adopted daughters compared with the high incidence in mothers of biological daughters.

Finally, PMS can occur together with any chronic condition (e.g., schizophrenia, Down's syndrome, congenital mental handicap, rheumatoid arthritis, fibromyalgia, bronchitis, tuberculosis), in which case treatment of PMS will only improve premenstrual symptoms and not the underlying condition.

#### V. DIAGNOSIS

The diagnosis of PMS depends on prospective, daily recording by the patient or responsible person of the days of symptoms and days of menstruation for a minimum of 2 months. This is easier when recording a specific symptom with a marked onset and end (e.g., migraine, new acne papules, epilepsy, sore throat), but it is more difficult when considering symptoms present throughout the cycle and while trying to record an increase or decrease in severity (tiredness, clumsiness, forgetfulness). Ideally, no more than the three most severe symptoms should be recorded; otherwise it makes the patient unduly introspective, or recording is made without full consideration. Therapists, including males working with PMS, should try to record

their symptoms daily for at least 2 months, for only then will they appreciate the difficulties of recording after a late night party, on holiday, or during a stressful event, and they will then understand the need to keep the recording as simple as possible. A simple menstrual chart, which gives the diagnosis of PMS at a glance, is shown in Table I. The patient is advised to keep it by her bed and to mark it with a pen each night before retiring.

Many daily rating scales and visual analog scales have been developed; some demand daily body temperature and body weight, which may be helpful for clinical trials of mild to moderate cases, but will never be completed by desparate women demanding immediate help. Many daily symptom charts list some 30 different symptoms that patients may never have considered, but that they can easily manipulate. Questionnaires are of limited value, as the more often one is used, the less attention the patient pays in completing it. All too often patients completing certain questionnaires tend to confuse menstrual pain with PMS.

In severe cases the partner, or other responsible person, may be able to note the days when symptoms are present. Otherwise it may be necessary to gather particulars of precise dates of specific incidents from other sources such as hospital emergency rooms in cases of suicide attempts or the suturing of slashed wrists; from police in relation to domestic violence or alcohol abuse; from prison for indicipline, causing a disturbance, or aggressive attacks; from schools or community centers where records are kept of disturbances covering instances of bodily harm or arson attempts; and from college registers showing absences.

No blood tests are diagnostic of PMS. In particular progesterone blood level is of no importance, as progesterone level only rises in the luteal phase in ovular cycles, but PMS also occurs in anovular cycles. Progesterone is secreted in spurts, and is lower after meals. The sex hormone binding globulin (SHBG) level is frequently low in PMS, but the estimation must be done when the patient has been free of all medication (including analgesics, vitamins, minerals, laxatives) for at least 7 days and free of hormone medication (including the pill and HRT) for at least 1 month. Furthermore, it is not reliable in those with thyroid disorder, liver disease, obesity, or hirsuitism, and the blood must be kept frozen until analyzed.

A ferritin estimation is worthwhile and is often sur-

Table i Menstrual Charts

	Jan.	Feb.	Mar.			Oct.	Nov.	Dec.
1					1			
2					2			
3					3			
4					4			
5					5			
6					6			
7	X				7			
8	X				8			
9	X			1	9			
10	X				10			
11	X	Х			11			
12	X	X		1	12			Н
13	X	X		1	13			Н
14	X	X	X		14		Н	hM
15	MX	X	X		15		Н	М
16	MX	X	X		16		Н	M
17	M	X	X		17		МН	M
18	M	X	X		18		Mh	M
19		М	X		19	Н	M	M
20		M	X	1	20	Н	М	
21		M	Х	1	21	Н	М	
22		М	X	1	22	Н	М	
23			M	]	23	M	M	
24			М		24	M		
25			M		25	M		
26			M		26	М		
27			M		27	М		
28					28			
29					29			
30					30			
31					31			

X = tension hH = headache M = menstruation

prisingly low in PMS patients, who otherwise have a good hemoglobin level and normal hematology. It is a reflection of their iron store, and low levels are found in those who habitually allow their blood glucose lev-

els to drop. Restoring the patient's ferritin level to more than 30  $\mu$ g/l by giving an iron supplement or improving the diet, will improve their stamina and energy level.

Table II Diagnostic Checklist

Irrelevant/positive/negative

Hormonal time of onset.

Hormonal time of increased severity.

Painless menses (2 -ves if painful).

Increased libido in premenstruum.

Pre-eclampsia.

Postnatal depression.

Side effect with the pill.

Adult weight swing exceeding 12 kg.

Food craving in the premenstruum.

Alcohol urges in the premenstruum.

Family history of PMS.

Total

% Score = 
$$\frac{\text{positives} \times 100}{\text{positives} + \text{negatives}}$$

#### VI. DIAGNOSTIC POINTER CHECKLIST

When a 2-month menstrual record is not immediately available a diagnostic pointer checklist, compiled from the characteristics mentioned earlier, is helpful. Items are scored "positive," "negative," and "irrelevant," while those whose presenting symptom is pain with menstruation, or dysmenorrhea, score two negatives. The total positive scores are multiplied by 100, and divided by the sum of the positives and negatives. Women with a diagnostic pointer scores exceeding 66% are likely to produce a positive menstrual chart after charting for 2 months (Table II).

## **VII. ETIOLOGY**

The many hormonal and chemical interactions, which result in PMS, are not fully understood, although many etiological theories exist. An acceptable etiological theory must be able to explain at the molecular level the following facts known to occur in PMS:

- Psychological and physical symptoms present in the luteal phase with absence in the follicular phase.
- 2. Absence of symptoms and general well-being in pregnancy.
- 3. High incidence after pregnancy, and particularly after postnatal depression.

- 4. Inability to tolerate progestins, and their failure to relieve PMS.
- 5. Increased intensity of symptoms at times of stress.
- 6. Inability to tolerate long food gaps, and symptom relief from the "three hourly starch diet."
- 7. Relief from high-dose natural progesterone.
- 8. Symptoms occur in both ovular and anovular cycles.
- 9. Persistence of symptoms after recovery from the trauma of hysterectomy and oophorectomy.
- 10. Cyclical symptoms can occur two years before menarche and continue for two years after the natural menopause.

Critical to the diagnosis is the fact that PMS occurs in the luteal phase and not in the follicular phase. Estrogen, measured in picograms, is present in the blood in varying amounts throughout the menstrual cycle. Progesterone is only present in the luteal phase, and is absent in the follicular phase; it is measured in nanograms, which is 1000 times higher than picograms; thus, fluctuations of amplitude of estrogen relative to progesterone are minimal. During pregnancy, when there is a massive increase in progesterone from the placenta, PMS eases and there is a sense of well-being. At labor, when the placenta is also delivered, the progesterone blood level falls abruptly; postnatal blues and a high incidence of postnatal depression follow. The involvement of progesterone in the etiology of PMS is supported by facts 1, 2, and 3.

Molecular biologists in the last decade have further supported the hypothesis that progesterone is involved in PMS by their discovery of progesterone receptors. Progesterone receptors are compounds, found in the hundreds, in those cells that require progesterone. The task of progesterone receptors is to bind to progesterone molecules and to transport the progesterone molecules to the nucleus. Using new technology and animal studies researchers have been able to recognize some of the unique characteristics of progesterone receptors. For instance, after an initial dose of progesterone the receptors become hyposensitive and require a high dose of progesterone to stimulate them again. Progesterone receptors do not accept progestins in the same way as progesterone molecules in the presence of adrenalin, such as occurs at times of stress and at low blood glucose level, for then the progesterone receptors function as corticosterone receptors, correcting the adrenalin balance. Thus, unless current stress can be ameliorated and low blood glucose levels avoided, the administration of progesterone will not help PMS.

Progesterone receptors are widespread throughout the body, with the highest concentration in the limbic area, the center of emotion, which may explain the predominance of psychological symptoms in PMS. Other areas of high concentration of progesterone receptors are the meninges, the nasopharyngeal passages and lungs, eyes, bones, and skin, which would account for headaches, sinusitis, asthma, conjunctivitis, sties, joint and muscle pains, and skin lesions, respectively. It has recently been shown that progesterone receptors are controlled within the cells by a specific stress protein, hsp90. Thus, a fault in the functioning of progesterone receptors, or of the stress proteins controlling them, would explain facts 4, 5, 6, and 7. The function of progesterone receptors in the systemic cells, where PMS symptoms originate, occurs whether or not ovulation is occurring, thus explaining facts 8, 9, and 10.

PMS women do not have hypoglycemia, but a hyperefficient lower controlling mechanism that releases adrenalin whenever the blood glucose level nears the lower optimum level. This adrenalin release mobilizes glucose in cells, which passes into the blood, correcting the low blood glucose level. However, the empty cells soon fill with water, giving the bloatedness and weight gain so familiar to PMS subjects. Adrenalin is the hormone of fight, flight, and fright, which in turns is responsible for the tension and behavioral symptoms.

It is easy to negate the involvement of progesterone in the etiology by recalling that there is no evidence that progesterone blood levels are low in PMS. Recognition of the function of progesterone receptors explains why the blood progesterone level is irrelevant, and also why low-dose progesterone, as used in current double-blind placebo controlled trials is doomed to failure. It is going to be difficult to arrange double-blind controlled trials of high-dose progesterone, which also control for the avoidance of stress and of transient episodes of low blood glucose levels. Both stress and low blood glucose levels stimulate adrenalin and inhibit the action of progesterone receptors.

Progesterone is formed in the adrenals by both sexes and at all ages, and is then converted to estro-

gens, testosterones, and cortisones. The exact mechanism that controls the menstrual cycle remains unknown. It is though to be in the hypothalamus, at the base of the brain. Zuspan and his colleagues, using a culture of human placental cells, have demonstrated that progesterone has an inhibitory effect on monoamine oxidase activity; in short, progesterone is a natural MAOI antidepressant.

Others have unsuccessfully suggested etiological theories that do not explain the 10 facts enumerated above. These include deficiency of pyridoxine, magnesium, essential fatty acids, dietary irregularities, allergies, and thyroid dysfunction. Most of these studies have been done on LLPPD without consideration of the characteristics of PMS. Ashby and his coworkers noted low serotonin levels in LLPPD, and several reports have appeared of the beneficial effect of the selective serotonin reuptake inhibitors (SSRIs) in PMS. The action of SSRIs on the brain cells is similar to that of progesterone on brain cells, but in other parts of the body progesterone has other effects, such as building up bones, which are not shared by SSRIs.

#### **VIII. TREATMENT**

A disease with no universally accepted etiology is always subject to numerous suggested treatments, some that have never been clinically tested and others that rely on symptomatic relief of the common symptoms of PMS. If one accepts the part played by progesterone receptors then the relief of stress and the maintenance of a stable blood sugar level are two imperatives in treatment.

### A. Stress Relief

In the past there may have been family members or religious leaders with whom one could openly discuss the day-to-day problems that cause stress. Today, members of our nuclear societies are often unable to unburden themselves. Counsellors or therapists are needed to help PMS women understand themselves and their problems, while some may need full psychotherapy, either cognitive or behavioral. Abnormal behavior in the premenstruum may be followed by ex-

cessive guilt, which is best handled by a therapist. Many benefit from relaxation, stress-relieving, or assertiveness classes. Life-style changes may be needed, through stopping smoking, drugs, or excess alcohol, preventing sleep deficit, and avoiding night work. The woman may need to be advised to change from hormonal contraception, all of which contains progestins, which exacerbates symptoms. Recording of day-to-day symptoms on a menstrual chart should be continued throughout treatment to assess progress.

## **B. Dietary Advice**

Too often one finds women who ensure that their children and partners have regular food while neglecting their own. One English survey found that half of PMS women did not stop for breakfast; in fact, they unknowingly started the day with a blood glucose drop. The "three hourly starch diet" has been found to be the most effective tool in easing PMS in 68% of sufferers. Women are advised to divide their usual day's starch intake (flour, potatoes, rice, rye, oats, and corn) into six or seven portions, and have a starchy snack every 3 hours throughout the day, always within 1 hour of waking and 1 hour of retiring. The diet should be continued throughout the cycle, and other nutrients (especially proteins, fruit, and vegetables), which they normally eat, should be continued. It is worth reminding patients that when they exceed 3 hours on only one occasion it may take up to 7 days before the normal utilization of progesterone can occur. It is a simple multicultural diet, and patients soon get into the habit of always eating little and often. There should be no weight gain if the individual is eating the same amount of starch each day, but in seven portions instead of the more usual three meals. Those who are initially overweight find they lose weight as bloating is eliminated.

Taking a full dietary history is essential before teaching the patient the three hourly starch diet, so any other nutritional deficiencies can be corrected. It should not be necessary to add extra vitamins or minerals, which should be available in the normal diet. In particular, vitamin B6 (pyridoxine) should not be advised now that the possibility of causing pyridoxine overdose neuropathology is recognized.

## C. Symptomatic Treatment

If one premenstrual symptom predominates above all others, particularly in LLPPD where 30% of the symptom may be present throughout the cycle, then individual symptomatic treatment may be preferable. This applies to those likely to benefit from selected antidepressants, anxiolytics, tranquilizers, anticonvulsants, analgesics, or muscle relaxants. It applies even more with respect to physical symptoms, where headaches, asthma, skin lesions, conjunctivitis, and sinusitis are the only PMS symptom. Here, the most effective symptomatic treatment should be used in addition to training the patient on the three hourly starch diet and counseling her on avoiding hormonal contraception. Among the antidepressants most likely to be effective in PMS are the selective serotonin reuptake inhibitors (SSRIs) or the monoamine oxidase inhibitors (MAOIs).

# D. Progesterone Therapy

Only a few severe sufferers of PMS require progesterone therapy; the majority will benefit from treatments already suggested. Even if progesterone is needed, the three hourly starch diet is still required.

Progesterone treatment is essentially prophylactic and needs to be started before symptoms develop, so it is usually started 14 days before the next expected menstruation and it is continued until the onset of bleeding. Progesterone cannot be utilized if administered orally or transdermally. The minimal dose is 400 mg suppositories used vaginally or rectally twice daily, but this may be increased to 400 mg used 6 times daily, or progesterone intramuscularly into the buttock in doses of 50 mg or 100 mg daily. It is not possible to overdose with our present methods of administration, which cannot reach the blood progesterone levels found in mid or late pregnancy. There are no interactions with other medications. If vaginal candidiasis is present, symptoms may be exacerbated by progesterone, but today candidiasis can be treated with a single capsule of fluconazole 150 mg given to both the patient and her partner.

There is anecdotal evidence of the effectiveness of progesterone in PMS in the British National Health Service Tribunal on overspending in 1958, and in individual women charged in England with serious crimes, including murder and infanticide, but the only

successful double-blind placebo controlled trial was that by Magill in general practice using 400 mg twice daily. All other trials using a lower dose of progesterone have been unsuccessful.

Progesterone can also be used as a contraceptive in cases of severe PMS by starting with a small daily dose of progesterone 100 mg from day 8, raising to the patient's normal progesterone dose on day 14, and continuing until menstruation.

## **BIBLIOGRAPHY**

- Dalton, K., & Holton, D. (1994). PMS: The essential guide to Treatment Options. London & San Francisco: HarperCollins Publishers.
- Dalton, K. (1984). The Premenstrual Syndrome and Progesterone Therapy (2nd ed.). London: W. Heinemann Medical Books, Ltd., and Chicago: Year Book Medical Publishers, Inc.
- Smith, S., & Schiff, I. (1993). Modern management of premenstrual syndrome. New York and London: Norton Medical Books.