Premenstrual Syndrome: A Study of Change in Cyclicity, Severity and Sexuality

by

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From the department of Obstetrics and Gynecology and Physiology
University of Umeå, Sweden
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ABSTRACT

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82 women seeking help for the Premenstrual syndrome (PMS) were successively recruited into a research project on PMS. All of them performed daily self-ratings during one menstrual cycle and 54 of them during two cycles.

Including the patients with two rated cycles the change between cycles in cyclicity and preovulatory symptoms was studied. They were diagnosed and subgrouped as having "Pure PMS" with significant cyclicity and only premenstrual symptoms, "PM aggravation" with significant cyclicity but with additional preovulatory symptoms or "Non-PMS" without cyclicity. 78% showed the same cyclical pattern in both cycles and 65% were allocated to the same subgroup. The presence or absence of preovulatory symptoms was a more stable factor than the occurrence of cyclicity. The cycle more resembling an "ideal PMS pattern" better separated groups of patients regarding neurotic personality and psychiatric history.

When all 54 patients were investigated together there was no change in severity between the two cycles when the whole cycles were compared, and using the premenstrual phase only difference in one symptom. When divided into subgroups it was found that the "Pure PMS" group felt worse during the first rated cycle while the "PM aggravation" group felt better during the first cycle.

A method for estimating the severity of PMS was developed and tried. A severity-score was calculated and ± 1 SD was used to subdivide the patients into severity-groups giving 20% classified as having mild PMS, 61% as moderate and 19% as severe. The symptoms with the highest correlation to the severity-score were anxiety, tension and irritability.

The validity of the severity-score was studied by comparing it with other ways of estimating severity of PMS. There was very good agreement between the severity-score and the prospective rating of influence on family, work and social life, fairly good between the result of a Moos Menstrual Distress Questionaire (MDQ) and the severity-score and also between the retrospective rating of influence and the severity-score. There was good agreement when the severity-score from two rated cycles was compared.

Sexual parameters and the relationship to androgen levels and SHBG were studied. All sexual parameters showed cyclical change except the parameter "unpleasant sexual thoughts" in the group with high levels of androstenedione, testosterone and SHBG when using combined p-value. The patients with a low level of androstenedione had more days with maximum ratings of the parameters "sexual feelings" and "pleasant sexual thoughts". Patients with "Pure PMS" had a lower level of testosterone compared with the "PM aggravation" group.

Four different methods for diagnosis of PMS, a nonparametric test, effect size, run test and 30% change were compared. Results showed high agreement except for the method of using 30% of the scale as condition for cyclicity, which resulted in fewer patients with cyclicity than the other methods used.
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To the memory of
my mother Adele
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Including the patients with two rated cycles the change between cycles in cyclicity and preovulatory symptoms was studied. They were diagnosed and subgrouped as having "Pure PMS" with significant cyclicity and only premenstrual symptoms, "PM aggravation" with significant cyclicity but with additional preovulatory symptoms or "Non-PMS" without cyclicity. 78% showed the same cyclical pattern in both cycles and 65% were allocated to the same subgroup. The presence or absence of preovulatory symptoms was a more stable factor than the occurrence of cyclicity. The cycle more resembling an "ideal PMS pattern" better separated groups of patients regarding neurotic personality and psychiatric history.

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A method for estimating the severity of PMS was developed and tried. A severity-score was calculated and ± 1 SD was used to subdivide the patients into severity-groups giving 20% classified as having mild PMS, 61% as moderate and 19% as severe. The symptoms with the highest correlation to the severity-score were anxiety, tension and irritability.

The validity of the severity-score was studied by comparing it with other ways of estimating severity of PMS. There was very good agreement between the severity-score and the prospective rating of influence on family, work and social life, fairly good between the result of a Moos Menstrual Distress Questionnaire (MDQ) and the severity-score and also between the retrospective rating of influence and the severity-score. There was good agreement when the severity-score from two rated cycles was compared.

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Four different methods for diagnosis of PMS, a nonparametric test, effect size, run test and 30% change were compared. Results showed high agreement except for the method of using 30% of the scale as condition for cyclicity, which resulted in fewer patients with cyclicity than the other methods used.
This thesis is based on the following original papers which will be referred to in the text by their roman numerals:


III. Ekholm U-B, Ringqvist J, Bäckström T. Premenstrual syndrome: Description of a procedure to estimate severity based on prospective symptom ratings. (manuscript)


V. Ekholm U-B, Bäckström T, Grankvist K, Selstam G. Androgens and sexuality in women with cyclical mood changes and premenstrual syndrome. Psychoneuroendocrinol (accepted)

VI. Ekholm U-B, Ekholm N-O, Bäckström T. Premenstrual syndrome: Comparison between different methods to estimate cyclicity using daily symptom ratings. (manuscript)
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>APA</td>
<td>American Psychiatric Association</td>
</tr>
<tr>
<td>CPE</td>
<td>Calendar of Premenstrual Experiences</td>
</tr>
<tr>
<td>DRF</td>
<td>Daily Ratings Form</td>
</tr>
<tr>
<td>DSM-III-R</td>
<td>Diagnostic and Statistical Manual for Mental Disorders, Third Edition, Revised version</td>
</tr>
<tr>
<td>DSRS</td>
<td>Daily Symptom Rating Scale</td>
</tr>
<tr>
<td>EPI</td>
<td>Eysenck Personality Inventory</td>
</tr>
<tr>
<td>ES</td>
<td>Effect Size</td>
</tr>
<tr>
<td>FSH</td>
<td>Follicle Stimulating Hormone</td>
</tr>
<tr>
<td>IHS</td>
<td>International Headache Society</td>
</tr>
<tr>
<td>K</td>
<td>Kappa (statistic)</td>
</tr>
<tr>
<td>LH</td>
<td>Luteinizing Hormone</td>
</tr>
<tr>
<td>LLPDD</td>
<td>Late Luteal Phase Dysphoric Disorder</td>
</tr>
<tr>
<td>MDQ</td>
<td>Moos Menstrual Distress Questionnaire</td>
</tr>
<tr>
<td>PAF</td>
<td>Premenstrual Assessment Form</td>
</tr>
<tr>
<td>PM</td>
<td>Premenstrually</td>
</tr>
<tr>
<td>PMS</td>
<td>Premenstrual Syndrome</td>
</tr>
<tr>
<td>Rs</td>
<td>Spearman’s rank correlation coefficient</td>
</tr>
<tr>
<td>PO</td>
<td>Preovulatory</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SHBG</td>
<td>Sex Hormone Binding Globulin</td>
</tr>
<tr>
<td>VAS</td>
<td>Visual Analogue Scale</td>
</tr>
<tr>
<td>VRS</td>
<td>Verbal Rating Scale</td>
</tr>
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</table>
INTRODUCTION

The problem of PMS

Prevalence

That some women feel bad physically and/or mentally the days prior to menstruation is well known since ancient times. In two retrospective Swedish surveys each comprising over 1000 women of fertile age, the prevalence of cyclical mood and/or body change was found to be 73\% (Hallman 1986) and 92\% (Andersch 1986) respectively. One study from USA, showed 29\% of black women and 31\% of white women to have at least one premenstrual symptom (Stout 1986a), while another showed 95\% of women complaining of at least one negative premenstrual symptom (Stewart 1989). In a study comprising a self-selected sample of readers of a woman’s magazine 62\% considered themselves as suffering from PMS (Warner 1990).

Socio-economic consequences

The majority of women do however not consider their cyclical changes as a problem but more as a natural part of their lives. Keye suggests that fewer than 10\% suffer such severe symptoms that their lives and functional level are significantly affected (Keye 1988), and Reid suggests a figure of 3 to 5 percent (Reid 1991). In Andersch’s study, 10\% of the women were, because of PMS, absent from work on at least one occasion during six months and 3.2\% on more than two occasions during the same time. 14\% of the 1083 women experienced their premenstrual symptoms to such an extent that they wished some kind of treatment and 11\% wished to see a physician because of this (Andersch 1986). Hallman found that 3.9\% were absent from work once and 2.1\% more than twice during a six-month period and 7.5\% wished to see a physician (Hallman 1987).

From the figures above it’s easy to understand that a problem causing absence from work regularly in between 3 and 10\% of all fertile women is a great problem socially and economically not just for the women meeting with the discomfort but also for the society as a whole.

There have been conflicting reports about the relationship between accidents and PMS. Patel and co-workers found that women with symptoms of PMS differ in pattern of accidents from women not having PMS symptoms, the former being more liable to accidents during the immediate premenstrual phase while women without PMS peaks in accidents around midcycle (Patel 1985). In a danish study the opposite was shown, that there was no relationship between phase of the menstrual cycle and death in accidents (Helweg-Larsen 1985).

MacKinnon & MacKinnon performed a study and found clear evidence that the frequency of suicide, death in accidents and diseases was significantly higher during the luteal phase than during the follicular phase, and the peak was during the mid-luteal phase (MacKinnon 1959). Dalton has shown a relationship between suicide attempts and the paramenstruum and also between acute psychiatric admissions and the time around menstruation (Dalton 1959). In a retrospective study on women seeking help for PMS a higher life-time history of suicide attempts and substance abuse was found in patients compared with controls (Stout 1986b). Harrison and co-workers have later confirmed these findings in a prospective study, but also shown that among women seeking for PMS symptoms there is a group of
patients with current mental disorder and when they are excluded the women with PMS do not differ from controls in psychiatric case history (Harrison 1989a). Keye reports that approximately 75% of women evaluated for premenstrual symptoms had recurrent suicidal thoughts and 20% had made suicide attempts during the luteal phase of the cycle (Keye 1988).

There have also been reports about an increased frequency of child battering, violence, murder, marital breakdowns (Clare 1983, Keye 1988) alcohol abuse (Belfer 1971, Stout 1986b) during the premenstrual phase. An increase in crimes of violence during the paramenstruum has been shown but the offences were unrelated to symptoms of premenstrual tension (d'Orban 1980).

In this context it is however important to call attention to the fact that the rates for accidents, crimes and suicides are still lower than those for men.

Symptomatology

Over 150 different symptoms of both physical and mental nature have been listed as possible contributors to the premenstrual syndrome (Moos 1969, Coyne 1984, O'Brien 1987). Certain symptoms recur as part of the syndrome in most works in the field, for example, irritability, depression, anxiety, lethargy, lack of energy, swelling, breast tenderness and headache.

In Table 1, a list is shown with the ten most commonly reported symptoms of PMS based on reports from ten different workers in the PMS field.

Table 1. Shows the rank and the mean rank of the retrospectively most commonly reported symptoms of PMS. For each worker the five most commonly reported symptoms are listed and the mean rank is then calculated for all symptoms appearing on the top-five chart more than four times. For the symptoms below the line no ranking is made.

<table>
<thead>
<tr>
<th>Worker</th>
<th>BA</th>
<th>KD</th>
<th>UH</th>
<th>JH</th>
<th>RM</th>
<th>DS</th>
<th>NW</th>
<th>PW</th>
<th>EF</th>
<th>JT</th>
<th>Mean-Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritability</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Mood swings</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>2.6</td>
</tr>
<tr>
<td>Depression</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>2.8</td>
</tr>
<tr>
<td>Swelling,</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.9</td>
</tr>
<tr>
<td>bloatedness</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>3</td>
<td>-</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3.0</td>
</tr>
<tr>
<td>tenderness</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Abdominal</td>
<td>-</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>pain, cramps</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Tension</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>5</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Tiredness</td>
<td>-</td>
<td>3</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

**Mental symptoms**

The most frequent mental symptom retrospectively reported in most community studies is irritability (Coppen & Kessel 1963, Andersch 1986, Hallman 1986, Stout 1986a, Warner
1990) while depression (Dalton 1984, Freeman 1985) along with irritability (Steiner 1980) and fatigue (Sanders 1983, Mortola 1990) have been shown to be the most predominant symptoms among women seeking help for PMS. When comparing retrospective and prospective ratings in a community sample a discrepancy was found in which symptoms were the most common. Retrospectively, irritability was the most common mental symptom while prospectively, fatigue was the most common (Woods 1982).

Some women experience a positive mental change premenstrually at least in some respects. In the study by Stewart on women attending a gynecologist for a well woman visit, about one third of the women stated a tendency to clean or tidy and get things done as positive (Stewart 1989). More energy, performing better at work and more creative ideas were other examples of positive premenstrual change in the same study.

**Physical symptoms**

Among physical symptoms feeling of swelling is the most common reported retrospectively (Coppen & Kessel 1963, Steiner 1980, Andersch 1986, Hallman 1986, Stewart 1989, Mortola 1990, Warner 1990). When comparing retrospective and prospective ratings, swelling was most often reported retrospectively and headache prospectively (Woods 1982). Food cravings is another often mentioned physical symptom (Dalton 1984, Stout 1986a, Stewart 1989, Mortola 1990) by Dalton explained as an effect of altered glucose tolerance resulting in relative hypoglycemia and followingly increased appetite.

Breast tenderness is also a symptom often reported but all women do not regard that as negative but rather positive because they feel more attractive when their breasts become more voluminous (Stewart 1989).

**Sexual symptoms**

Sexuality has been reported to be both increased and decreased premenstrually in different women and it is most likely so, that some women experience a greater sexual interest during the premenstrual days and others can't stand the thought of sex.

In the retrospective study by Stewart, 37% of the women experienced an increased sexual interest premenstrually, while 20% stated a decreased sexual interest (Stewart 1989). Another retrospective study showed that 22% of women experienced maximum libido just before menstruation and 22% just after (Hart 1960).

In a prospective study it was shown that female-initiated sexual behaviour peaked in the ovulatory phase and that a majority of women reported a heightened sexual arousal and sexual pleasure during the premenstruum (Harvey 1987). Another recent prospective study showed that women's sexual interest was more related to whether the next day was a working day or a holiday than to phase of the menstrual cycle (Silber 1989a). Schreiner-Engel has studied the female sexual arousability and found no relationship to the gonadal hormones and the menstrual cycle (Schreiner-Engel 1980).

When concentrating on women actively seeking help for PMS it was shown by Sanders and co-workers that there was a significant decline in sexual feelings during the luteal phase compared with the follicular phase. The same study showed no significant difference in sexual feelings between the follicular and luteal phase in PMS women not actively seeking help and nor in controls (Sanders 1983). This finding points at the difference between women with severe PMS in need of medical help and women with PMS symptoms found in community-surveys. A study comparing retrospective and prospective data found no
significant difference in rating of sexual drive between the two methods used, but found in the prospective data a significant decrease in sexual drive premenstrually (Rapkin 1988). Otherwise most studies do not give information about sexual changes, simply because the rating-scales in use do not include sexual parameters.

Etiology

There is no single symptom, physical or mental that is specific for PMS. All symptoms are in one way or another part of other syndromes and this leaves many tracks open to theories and speculations about the etiology. For example, some symptoms can be interpreted as part of an affective disorder, some as part of a compulsive disorder and others as a disturbance in water balance.

Hormonal?

A lot of research has been done over the years to find the cause of premenstrual symptoms, but the closest we have come is to establish that in one way or another it has something to do with ovulation or at least the formation of a corpus luteum (Bäckström 1983, Haskett 1987, Hammarbäck 1988, Hammarbäck 1991).

No clear cut hormonal factor has yet been isolated as the cause of PMS although there has not been a lack of suggestions (for reviews Bancroft 1985, Rubinow 1989). All hormones, in one way or another involved in the reproductive system have been under suspicion, but none has in repeated, controlled studies been proven as the one causing PMS. Also hormones involved in the water-electrolyte balance have been suggested as the cause of PMS but no clear evidence have yet been presented in that matter.

Maybe the reason for this "failure" is the shortcoming of the diagnostic procedure in being able to separate women with real PMS from those with mental disorders or social problems using the menstrual cycle as the scape-goat for their discomfort in life. Many ethiological studies are based on retrospective ratings or case history and in that way we don't get pure PMS material of patients to study. This, and the lack of internationally accepted inclusion-criteria for PMS studies, is probably also the reason why there are often contradictory results between different studies. Until now there has not even been a generally accepted definition of PMS, both with respect to symptoms required and the definition of the premenstrual period, which also contributes to the confusion.

Another problem is that blood samples for hormonal analysis are drawn at different stages of the menstrual cycle in different studies, leading to conflicting results, since all hormones involved are known to fluctuate during the cycle.

Psychosocial?

Many different theories have been presented over the years with different psychological explanations for premenstrual mood disturbance. For example a fear of becoming pregnant in conflict with the thought of maybe not being pregnant was proposed as the reason for premenstrual depression by Karin Homey (Homey 1967). There have also been theories about premenstrual depression as a reaction to the coming "unclean" menstrual flow passed from one generation to the next (Goldschmidt 1934). PMS has been found more commonly in women who had a poor relationship with their mother at the time of menarche (Shainess 1961). In a review article about psychosocial aspects of the premenstrual syndrome Bernsted and co-workers (Bernsted 1984) states that "from a psychological point of view these symptoms reflect an impoverishment of the ego in relation to feminine self-
acceptance and identification with the mother”. Also other workers have suggested an association between a negative attitude towards menstruation and the feminine role (Levitt 1967, Berry 1972). In the study by Berry and McGuire there was however no relationship between the acceptance of sexual role and premenstrual tension but rather with menstrual distress and dysmenorrhea (Berry 1972). The widespread picture of how a woman is supposed to feel premenstrually is another suggested explanation (Parlee 1974).

The theories about a negative attitude towards menstruation and the feminine role as the cause of PMS has however been opposed by workers showing that women with PMS are no different in that matter compared with other women (Watts 1980, Stout 1985). However, in Watts’ study it was shown a relationship between PMS and a negative attitude towards body, genitals, sex and masturbation (Watts 1980).

Hicks and co-workers have investigated the relationship between type A-B behaviour and PMS and found that type A women retrospectively reported that they experienced about 50% more symptoms premenstrually than type B women did (Hicks 1986). This can be explained by an increased sensitivity in type A women for all kinds of feelings and therefore they also experience more symptoms premenstrually. Another plausible explanation can of course be that type A women actually do have more PMS symptoms than type B women.

The role of psychosocial stress events in premenstrual symptoms has been evaluated. In a study of undergraduate students it was shown that the experience of stressful life-events was of more importance than the phase of the menstrual cycle on mood symptoms while physical symptoms were more related to cycle phase (Wilcoxon 1976). In contrast, a recent study comprising women with well-defined severe PMS showed that there was no association between the severity of the symptoms, physical or mental, and the amount of psychosocial stress (Beck 1990).

Neurotic personality?

The theory about PMS as an expression of a neurotic personality has been widespread and some studies have supported these theories while others have been contradictory. The reason for this confusion may be the fact that in most studies the patients have been included in the study on the basis of their case-history and that there has not been any further discrimination between those really having PMS and those just claiming to have it.

In a retrospective community-study by Coppen and Kessel a significant correlation between neuroticism as measured by the Maudsley Personality Inventory (MPI) and the premenstrual symptoms irritability, depression, tension, headache and swelling was found (Coppen and Kessel 1963). In a study on volunteers Taylor found that a high Eysenck Personality Inventory (EPI) neuroticism score correlated with high scores on the Daily Symptom Rating Scale (DSRS) affect subscale and with the presence of two or more criteria for severe PMS (Taylor 1979 b). Yet another study comprising volunteers showed a relation between menstrual complaints and neurotic and paranoid tendencies (Levitt 1967). Abraham found that PMS sufferers had higher scores than controls for neuroticism, anxiety and depression, that the scores were higher premenstrually compared with the follicular phase, but that most of the women did not have scores outside the normal range (Abraham 1989). Watts found that retrospectively diagnosed PMS patients had higher scores compared with controls on the State-Trait Anxiety Inventory (STAI-Trait) and on the EPI neuroticism scale (Watts 1980).
Affective disorder?

The possibility of PMS being an affective disorder has been discussed in several reports and some workers have even shown a correlation between PMS and major affective disorder (Endicott 1981, Halbreich 1985b, Stout 1985, Hallmans 1986, Pearlstein 1990). A retrospective study by Stout and co-workers (Stout 1986b) found that women seeking help for PMS met criteria for lifetime psychiatric diagnoses of dysthymia but also phobia, obsessive-compulsive and somatization disorder at statistically significant higher rates than women in a community sample. In a recent prospective study it was shown that a high lifetime history of not only depression but also panic disorder, suicide attempts and substance abuse occurred in PMS women but only when the entire group of patients was investigated altogether. When patients with a current DSM-III-R mental disorder were excluded there were few significant differences compared with controls (Harrison 1989a). Pearlstein and co-workers also found a 29% prevalence, which is twice the normal, of postpartum depression in women with prospectively confirmed PMS or LLPDD (Late Luteal Phase Dysphoric Disorder) as it is labelled by the authors (Pearlstein 1990). Supporting the suggestion that PMS is an affective disorder is the finding that women with PMS symptoms merely of depressive nature have beneficial effect of antidepressants (Harrison 1989 b, Eriksson 1990). It has also been shown that patients with rapid-cycling bipolar affective disorder have an increased tendency to have more severe forms of PMS (retrospectively) than controls and that rapid-cyclers with PMS tend to have more frequent episodes (Price 1986). Theories have been raised suggesting PMS as a predictor of major depressive disorder later in life and this was shown in two studies on college students (Wetzel 1975, Schuckit 1975). In both studies the confirmation of premenstrual symptoms was however made only retrospectively which makes the results not entirely trustworthy.

Contradictory findings

Several studies have at least partly contradicted the theory about PMS and its association to psychiatric disorder. A prospective study on a group of women seeking help for PMS showed that women with pure PMS (symptoms only during the luteal phase), don't have higher scores for neuroticism in the EPI compared with normals. It was also shown that women with symptoms during the whole cycle but with an aggravation premenstrually, had higher neuroticism-score than normals and than women with "pure PMS" (Hammarbäck 1989a). This finding is supported by the results of a prospective study by West, including women giving a case history of PMS, showing that those with a postmenstrual mental symptom relief of 75% or more had significantly fewer past episodes of psychiatric treatment than women who had less than 75% relief of mental symptoms (West 1989).

Sanders found no significant difference between PMS patients and controls in neuroticism-scores as reflected in the EPI (Sanders 1983) and neither did Stout using the MMPI (Minnesota Multiphasic Personality Inventory) (Stout 1985). Wendestam used the CPRS (Comprehensive Psychopathological Rating Scale) for retrospective diagnosis of PMS and found in women with PMS no correlation between grade of severity of PMS and EPI-N or EPI-E scores (Wendestam 1980 thesis).

Pearlstein and co-workers (Pearlstein 1990) found that 10% of patients with prospectively confirmed PMS or LLPDD had an axis II diagnosis with avoidant personality as the most common disturbance. This is according to the authors probably not different from a normal population. Another prospective study has shown that there is one group of women with PMS with, and another without, a current or past mental disorder, also contradicting the theory of all women with PMS as being either neurotic or depressive (Harrison 1989a).
DeJong and co-workers have in a prospective study shown a high prevalence of psychiatric illness, particularly affective disorder, in women reporting premenstrual mood changes that are not confirmed by daily ratings. In women with prospectively confirmed mood changes the prevalence of psychiatric illness was still high compared with controls but significantly lower than the group with prospectively not confirmed PMS (DeJong 1985). Severino found that PMS women without a past or current psychiatric disorder had lower severity-ratings in the nonpremenstrual parts of the cycle compared with those with a psychiatric case-history (Severino 1989).

All these studies give support to the idea that there are two major groups of women with PMS. One group has symptoms solely during the luteal phase and compared with controls shows no increase in past or current psychiatric disease and no aberration in personality tests. Another group has symptoms during the entire menstrual cycle with an increase premenstrually, a more frequent case history of psychiatric disorder and results in personality tests that deviate from normal. This points at the importance of using prospective daily ratings to be able to rightly categorize the patients and thus being able to provide them with proper medical and/or psychiatric treatment. This is extremely important also when including patients in etiological and/or treatment studies.

DSM-III-R (APA 1987, Spitzer 1989) includes criteria for what they call Late Luteal Phase Dysphoric Disorder (LLPDD) but the criteria do not separate patients with pure premenstrual symptoms from those with symptoms during the whole cycle with an exacerbation premenstrually. This must be considered as a weakness in the criteria, leading to continued confusion in PMS research if not revised.

Associated factors

There have been conflicting results about whether the prevalence of premenstrual symptoms increases with age and parity or not.

Sanders found a higher prevalence of PMS among housewives and an increasing prevalence with parity but no correlation to age (Sanders 1983). Andersch and co-workers found that the prevalence of the individual symptoms most commonly reported in their study, irritability and swelling was not related to age or parity. Anxiety and swelling of fingers were however related to age but not to parity (Andersch 1986). In a sample of volunteers Ainscough found no significant difference between age or parity and PMS (Ainscough 1990).

It has however also been shown that both the duration and the intensity of the symptoms increase with age. Hallmans found a positive relationship between higher mean age and premenstrual complaints (Hallmans 1986). A study by Warner and Bancroft showed an increase in prevalence of PMS with age and with increase in duration of natural cycles (cycles not interrupted by pregnancy or hormonal medication), a weak trend for parous women to be more likely to report PMS, a significant increase among working women compared with those with no paid job, and an association with stress (Warner 1990).

Schnurr found that women presenting with the premenstrual syndrome and having the diagnosis confirmed by prospective ratings were younger and more likely to work outside the home than women not having the diagnosis confirmed (Schnurr 1988). The reason for the discrepancies between different workers is probably that some of the studies are retrospective and some of them are prospective.
Other workers have confirmed the correlation to parity and many women report that their
PMS began after a pregnancy (Dalton 1977, Hallmans 1986, Watts 1980). If it is hormonal
changes that is the cause, or whether it is the stress of having a baby and especially several
is not known. Dalton has shown a correlation between pregnancy, complicated by pre-
eclampsia, and a subsequent development of a premenstrual syndrome (Dalton 1984). This
was contradicted by a recent study showing that women with previous pre-eclampsia are
not more liable to having PMS later in life but rather that women with present hypertension
complained more of premenstrual sadness (Andersch 1990).

An association between PMS and dysmenorrhea has been discussed and also shown in
studies (Coppen 1963, Steege 1985, Abraham 1989). Abraham suggests the explanations
that some women reporting premenstrual symptoms do in fact have dysmenorrhea with
symptoms starting before menses, that women with dysmenorrhea are more likely to
associate other symptoms with the menstrual cycle and that the dysmenorrhea occurring
each cycle may cause a mood change. In contrast to these results, two recent studies have
not shown a higher incidence of dysmenorrhea in women with PMS compared with women

Diagnosis

Cyclicity

Over the years different names have been suggested to label the cyclical mood changes
occurring in many women. The most common in use nowadays is PMS (Premenstrual
Syndrome), among clinicians, researchers as well as people in the street and therefore we
have in our work chosen this label too. During the last years the name LLPDD (Late Luteal
Phase Dysphoric Disorder) has become more and more accepted especially among workers
with a more psychiatric orientation. The label LLPDD will only be used in this thesis when
DSM-III-R is described or quoted, and in references.

Both these names as well as others suggested, state when the symptoms are supposed to
occur, namely during the late luteal phase (= premenstrually) of the menstrual cycle. If this
basal condition is not fulfilled, then we are not dealing with PMS. From this follows that
the most important matter when meeting patients seeking help for PMS, must be to
establish whether the symptoms are clustered to the late luteal phase or not.

Different workers have used different methods both regarding the collection of data and the
statistical method used to establish cyclicity. Nowadays most investigators in the field of
PMS agree on the advantage of using daily prospective ratings and with these data as base
establish if the symptoms are cyclical or not. In a following chapter different rating scales
are discussed as is the use of prospective or retrospective ratings. A brief summary of some
of the methods in use for prospective establishment of cyclicity is given in table 2.

Which of the methods that is the best to use is a matter of taste since none of them is proven
better than the others. Schnurr (1989a, 1989b) has made a comparison between effect size
(Schnurr 1988), 30-percentage change (Rubinow 1984) Mann-Whitney U-test (Hammarbäck
1989a) and trend analysis (Magos 1986) and found good agreement between all methods,
but that diagnoses based on trend analysis differed to a noticeable extent, despite
statistically significant agreement. Metcalf and co-workers have also performed such a
comparison between different methods used to detect PMS and found good agreement
(Metcalf 1989a).
Table 2. Examples of different prospective methods used to establish cyclicity in women with PMS.

<table>
<thead>
<tr>
<th>Worker</th>
<th>Rating-scale</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hammarbäck (1989a)</td>
<td>VAS</td>
<td>Mann-Whitney U-test comparing the 9 preovulatory days with the 9 premenstrual days with ( p&lt;0.05 ) as limit for significant change.</td>
</tr>
<tr>
<td>Livesey (1989)</td>
<td>VAS</td>
<td>A function consisting of the first five terms of a Fourier series is fitted to the daily VAS-scores. For significant symptom change the difference between the cycle mean score and the fitted score at a point 92% through the menstrual cycle must: 1) be significant, ( p&lt;0.05 ) in a 1-tailed Student’s t-test 2) exceed 5% of the maximum possible day score of 700.</td>
</tr>
<tr>
<td>Magos (1986)</td>
<td>MMDQ</td>
<td>Trend analysis measuring positive or negative trends indicating worsening or improvement in symptoms during the 14 premenstrual days with ( p&lt;0.05 ) as limit for statistical significance of trends.</td>
</tr>
<tr>
<td>Mortola (1990)</td>
<td>CPE</td>
<td>Symptom rated on a four-point Likert scale based on interference with ability to perform daily activities. A two-way ANOVA and Neumans-Keuls multiple range test is used to compare cycle- phases.</td>
</tr>
<tr>
<td>Rubinow (1984)</td>
<td>VAS</td>
<td>A 30% increase in negative mood during the week prior to menstruation, compared with the week following menstruation.</td>
</tr>
<tr>
<td>Schnurr (1988)</td>
<td>9-point</td>
<td>Effect size computed as the mean scale difference between post- and premenstrual phases, divided by the standard deviation of the entire cycle. Clinical significance when ES ( \geq 1.0 ).</td>
</tr>
<tr>
<td>Severino (1989)</td>
<td>DRF</td>
<td>Spectral density analysis &quot;that determines whether the magnitude of change in daily symptom ratings for a given time interval is larger than that expected from the background variability in daily symptom ratings not associated with any time interval&quot;.</td>
</tr>
<tr>
<td>Sanders, West, Beck (1983, 1989, 1990)</td>
<td>VAS</td>
<td>Menstrual cycle divided in six or three phases. Mean-scores calculated for each phase. Statistical significant cyclical changes are detected by using analysis of variance (ANOVA).</td>
</tr>
</tbody>
</table>

Several workers have shown that some women have cyclical mood and body changes but they do not experience a total relief of their symptoms postmenstrually (Rubinow 1984, Hammarbäck 1989a, West 1989, Chisholm 1990). Dalton has called this "menstrual distress" and defines it as "the presence of intermittent or continuous symptoms present throughout the menstrual cycle which increase in severity during the premenstruum or menstruation" (Dalton 1984). O’Brien uses the term "secondary premenstrual syndrome" (O’Brien 1987), Rubinow "premenstrual exacerbation" (Rubinow 1985) and Hammarbäck "Premenstrual (PM) aggravation" (Hammarbäck 1989a).

**Symptoms required?**

Since we know that more than 150 different symptoms can be involved in PMS (Moos 1969, Coyne 1984, O’Brien 1987) it is easy to understand that it is difficult to decide which symptoms should be required for diagnosis. Furthermore, the symptoms are known to vary among women and also vary within the same woman from one cycle to the next.

In DSM-III-R (APA 1987) there is though a condition that certain symptoms should be represented. When we look at the criteria (pg 22) we find that the symptoms that were found to be the most commonly reported by PMS patients (Table 1, pg 9) are also represented in the criteria, namely irritability, depression, anxiety, tension, tiredness,
breast tenderness and bloatedness. It seems therefore appropriate that whichever rating-scale we use, these symptoms ought to be included.

An interesting finding was made by Hammarbäck, namely that the positive moods included in the rating scale - relaxed, friendly and cheerful - more often showed cyclicity than the negative moods and the physical symptoms (Hammarbäck 1989 thesis). This suggests that it is advisable to include positive moods in rating scales as well as negative moods and physical symptoms to get the best accuracy.

It has been suggested that the symptoms should be divided in different groups, thus creating different premenstrual syndromes (Moos 1969, Abraham 1981, Halbreich 1982, Rubinow 1984, Endicott 1986). Accordingly there would be less risk that a women with more uncommon premenstrual symptoms, maybe lacking the classical irritability, aggressiveness and depression is, misjudged. This system has however not been generally accepted.

Severity

When establishing the diagnosis of PMS we also have to deal with the problem of the severity of the symptoms. How strong must the symptoms be to qualify the woman in question as having PMS?

The basic condition in DSM-III-R demanding significant cyclicity of the symptoms covers this partly but not entirely. A 30% increase in symptom degree from the preovulatory to the premenstrual phase is suggested as limit for significance, which means that if we use a 0-10 scale and 0 stands for lack of symptom we have the situation that a woman with a mean rating preovulatory of 1 and premenstrually of 5 would have just as much PMS as a women with the mean ratings 1 and 10 respectively. It is apparent that we need a method that easily and as objectively as possible estimates the severity of PMS and preferably also give us a parameter that is comparable between patients.

Attempts to estimate severity of PMS

There have been few attempts to find methods to estimate the severity of PMS and unfortunately some of these few workers have mixed up severity and cyclicity. Methods presented as a way to estimate severity have in fact been yet another method to establish cyclicity.

Severino and co-workers used the DRF for daily ratings which is a 0-6 graded scale, and to assess the statistical significant cyclicity they used a spectral density analysis. They also calculated a "premenstrual change score" based on the difference between the average of the daily ratings from the five days before each menstruation and the average of the daily ratings during cycle days 6-10 and the five days at midcycle. To grade the severity they counted for each patient the number of positive symptoms, meaning symptoms with significant premenstrual spectral density and a premenstrual change score of at least 0.5 in each of the two menstrual cycles. The patients were subgrouped as having mild, moderate or severe PMS (Severino 1989).

Livesey and co-workers suggested that the severity of PMS could be measured by calculating the difference between the calculated mood score at a time equal to 92% of the way through the menstrual cycle and the mean score for the whole cycle (Livesey 1989). The difference must exceed the mean score for the cycle by an amount which is both significant and greater than 5% of the maximum possible daily mood score of 700. This method does not really measure severity, but is a method for establishing cyclicity.
Metcalf and Hudson assessed severity using the mean value of three retrospective self-evaluation scores, the mean value of the daily mood scores during the last five days of the menstrual cycle expressed as a percentage of the mean for days 5-14, and the difference between the mean value of the daily physical symptom scores during the last five days of the menstrual cycle and the mean for day 5-14 (Metcalf 1985). No explanation was given in the report to why the severity of mood was calculated differently from the severity of physical symptoms.

The Calendar of Premenstrual Experiences is used by Mortola and co-workers for diagnosis of PMS. They add all the scores for all physical and behavioural symptoms to estimate the severity (Mortola 1990).

**Counting days with symptoms**

An interesting way of classifying the severity of headache has been suggested by IHS (International Headache Society). The patients note daily in a diary whether he or she has headache that very day or not and the physician then uses the number of days with headache to classify the severity (IHS 1988).

Since headache just like premenstrual symptoms is a subjective matter this could be a way to measure the severity of PMS as well. If using the VAS we can assume that the two most objective points on the scale are 0 = no symptom at all, and 10 = maximum symptom. This gives us the possibility to count the number of days with no symptoms and compare with the number of days with maximum symptoms and thus get a figure that is comparable between patients and more objective than the mean-value based on all the ratings given. As far as is known today, no such attempt to prospectively measure severity of PMS has been performed before.

**Impairment in functioning**

Apart from using daily self-ratings of specific symptoms, severity can be evaluated by considering the impairment in functioning at home and in society. The criterion for severely impaired functioning is included in the DSM-III-R (APA 1987) but the criteria do not tell us how to measure the item. Unfortunately there is no clearly objective method to put forward, instead we have to rely on the statements made by the patients.

Arfwidsson and co-workers have constructed a rating-scale for anxiety-states including ratings of capability for work and social contacts using a 0-3 graded scale shown to be reliable and easy to use (Arfwidsson 1971). One can assume that a patient not being able to work because of mood-change suffers severely from the condition she is in, and therefore we found it interesting to compare the ratings for work and social contacts with the severity-calculation based on the number of days with no symptoms related to the number of days with maximum symptoms. A strong correlation between the degree of premenstrual symptoms and incapability to work has previously been shown speaking in favour of using capability to work as a control parameter when assessing the severity of PMS (Andersch 1986).

Another way to better estimate the severity of PMS would be to get statements from the partners on how the symptoms affect the family. This can at least give us important information while developing a method to measure the severity. As far as is known no study has been performed that includes spouses ratings for establishing the severity of PMS, but Cortese and Brown have in a study of coping responses in men whose partners have PMS been close to the subject. They studied how these men chose to cope with their wives.
premenstrual change and clearly showed that the men get affected by the symptoms, or maybe rather by the way the women handle the symptoms, and that there was a difference in coping strategy depending on the severity of the PMS. Men whose partners reported severe premenstrual symptoms were more likely to seek information and outside assistance and also felt more anger about the situation (Cortese 1989).

Variation in cyclicity, symptoms and severity

Most women with PMS describe variation in their premenstrual mood and body changes from one menstrual cycle to another (Steiner 1980, Abplanalp 1983). Prospective studies comprising more than one menstrual cycle have confirmed this (Shaver 1985, Schnurr 1989, Severino 1989, Ekholm II). Shaver’s study was performed using a community-sample, not women actively seeking help for PMS and it was found that there were few premenstrual symptoms that were reported concordantly across the two cycles studied. The study by Ekholm and co-workers (II) comprising women seeking help for PMS showed variation in symptoms and severity between cycles but a high concordance in which symptoms were the most reported. A prospective study on both PMS sufferers and controls during three menstrual cycles showed that most of the PMS patients did not fulfil the criteria for PMS in all three cycles (Abraham 1989). This variation between cycles must be taken into consideration when evaluating daily symptom-ratings from a menstrual cycle, above all when a patient is included in a treatment-study. It is not sufficient to use ratings from only one cycle.

The reason for this change between cycles is probably both hormonal and psychosocial. One applicable hormonal explanation can be the occurrence of anovulatory cycles, and this is shown both when anovulatory cycles are induced and when they occur spontaneously (Hammarbäck 1988, Hammarbäck 1991). There has been a lot of speculation about fluctuation of specific hormones being responsible, and though some indications exist that the severity of PMS might depend on the hormone levels (Hammarbäck 1989b), so far no conclusive report is presented.

Psychosocially, life events such as problems in family and work can make the woman more susceptible to hormonal changes and thus play a part in causing variations in premenstrual symptoms. Since fasting and participation in sports can cause anovulation it is also likely that it indirectly could affect the symptomatology of PMS.

Retrospective or Prospective Ratings?

All studies comparing retrospective and prospective ratings have however not included patients actively seeking help for PMS, but community samples or undergraduate students, and this is important to remember. Important since it has been shown that the likelihood of prospective confirmation of reported premenstrual depression is high in those reporting severe symptoms, and much lower for those reporting mild or moderate symptoms (Endicott 1982, Halbreich 1982, Christensen 1989). A study by Freeman and co-workers, including women who were consecutively enrolled in a PMS treatment programme, showed significant agreement between the retrospective and prospective ratings (Freeman 1985).

**Stereotypic beliefs**

There exists both among men and women stereotypes and cultural beliefs about the menstrual cycle and symptoms attached to its different phases (Parlee 1974, Koeske 1975, Brooks 1977, Clarke 1978, McFarland 1989). These beliefs colour especially the retrospective ratings but cannot be totally neglected when using prospective ratings either. The patient knows in what part of the menstrual cycle she is and if she is "taught" that premenstrually you are supposed to feel bad physically and/or psychically she is more inclined to give ratings which is in line with her picture of how she should feel premenstrually. In a study by Ruble it was shown that women who thought they were premenstrual reported a higher degree of symptoms than women who were told they were intermenstrual although all of them actually were premenstrual (Ruble 1977). She explained that this was caused by learned associations and beliefs about menstrual cycle related symptoms which made the women who thought they were premenstrual exaggerate naturally fluctuating bodily states. It has also been shown that women exaggerate symptoms presumably related to the menstrual cycle when they are aware that the menstrual cycle is being studied (Englander-Golden 1978). Both studies were performed on undergraduate students, not on women seeking help for PMS which might make a big difference. It has also been shown that adolescent women do not show significantly increased state anxiety and depression during the premenstrual part of the cycle (Golub 1981), while women over 30 showed a significant increase (Golub 1976).

On the other hand, two independent studies have shown persistence of premenstrual symptoms in hysterectomized women with intact ovaries (Bäckström 1981, Silber 1989b). Since these women do not have menstrual bleedings they cannot calculate in which part of the menstrual cycle they are, and thereby it is not likely that expectations about how to feel on certain days of the menstrual cycle rule, at least not their prospective ratings.

**Recall bias**

Recall bias is of course another explanation to the discrepancy between retrospective and prospective ratings, probably because the patients are more likely to remember the days with severe symptoms and forget the days with minimal symptoms. It is also possible that when they are paid attention, they are so eager to convince the examiner what rough times they are going through every month that they tend to describe their "worst case" when given a chance. We also know from our patients that the PMS symptoms can vary between cycles (Ekholm II) and if only one cycle is rated prospectively there is a chance that this very cycle happens to be one of the easy ones with a discrepancy between case-history and the result of the prospective rating as consequence. By performing daily self-rating during at least two cycles this risk is reduced.
Response to ratings

We have also the possibility of a "placebo response" to the caretaking of the patients giving presumably lower ratings in the beginning when the placebo response is most pronounced. It has been reported that the experience of being evaluated has a therapeutic effect in itself (Abplanalp 1983, Halbreich 1985a, Keye 1988, Steege 1989) and that women report less severe symptoms after at least one cycle under careful attention to their moods and behaviour (Endicott 1982).

Visual or Verbal Rating Scale

Visual Analogue Scale

The definite break-through for the use of the Visual Analogue Scale (VAS) for prospective assessment of cyclical mood changes came with the work by Sanders and co-workers in 1983 showing that among several methods tested, the VAS was the best to use (Sanders 1983). It was easy to explain to the patients, easy for them to use giving high compliance and proved to be both a valid and reliable method. Before that the VAS had been in use for a long time for assessment of other subjective feelings such as pain, but also for measurement of mood (Aitken 1969, Bond 1974) and several workers have shown that it is a valid and highly reliable instrument (Aitken 1969, Folstein 1973, Bond 1974, Ohnhaus 1975, Maxwell 1978).

Verbal Rating Scale

For retrospective measurement of premenstrual symptoms the Menstrual Distress Questionnaire Form A (MDQ) (Moos 1968) and the Premenstrual Assessment Form (PAF) (Halbreich 1982) are the most spread Verbal Rating Scales (VRS) both using six-scale steps. The MDQ contains 47 symptom for the patient to rate and the PAF contains 95 symptoms mostly formed as statements such as "Have rapid changes in mood".

<table>
<thead>
<tr>
<th>MDQ</th>
<th>PAF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1=No experience of symptom</td>
<td>1=Not applicable, not present at all, no change from usual level</td>
</tr>
<tr>
<td>2=Barely noticeable</td>
<td>2=Minimal change</td>
</tr>
<tr>
<td>3=Present,mild</td>
<td>3=Mild change</td>
</tr>
<tr>
<td>4=Present,moderate</td>
<td>4=Moderate change</td>
</tr>
<tr>
<td>5=Present,strong</td>
<td>5=Severe change</td>
</tr>
<tr>
<td>6=Acute or partially disabling.</td>
<td>6=Extreme change</td>
</tr>
</tbody>
</table>

For prospective daily ratings the MDQ form T, the Daily Symptom Rating Scale (DSRS) (Taylor 1979a) and the PAF Daily Ratings Form (DRF) (Halbreich 1985a) are the most common VRS in use. The MDQ form T has the same scale-steps as form A and contains the same number of symptoms put up for rating. The DSRS contains 17 symptoms for rating and uses a six-step scale graded 0-5. In the DRF there are 21 items listed, it has like the others six scale steps and it is elegantly designed as a calender easy for the patients to use. Dalton uses a menstrual chart containing five given symptoms and one column for "other symptoms" with a three-step scale for ratings (Dalton 1984). Schnurr uses a nine-point scale, with 1="best ever" and 9="worst ever" (Schnurr 1988).

<table>
<thead>
<tr>
<th>DSRS</th>
<th>DRF</th>
<th>Menstrual chart</th>
</tr>
</thead>
<tbody>
<tr>
<td>0=Not at all</td>
<td>1=Not at all</td>
<td>I=Mild</td>
</tr>
<tr>
<td>1=Very little</td>
<td>2=Minimal</td>
<td>II=Moderate</td>
</tr>
<tr>
<td>2=Little</td>
<td>3=Mild</td>
<td>III=Severe</td>
</tr>
<tr>
<td>3=Moderate amount</td>
<td>4=Moderate</td>
<td></td>
</tr>
<tr>
<td>4=Large amount</td>
<td>5=Severe</td>
<td></td>
</tr>
<tr>
<td>5=Very large amount</td>
<td>6=Extreme</td>
<td></td>
</tr>
</tbody>
</table>
Feelings are subjective

A person’s feelings about moods are purely subjective in nature and as such not easily described and measured by someone else. Verbal rating scales (VRS) of different kinds are widespread but have the disadvantage that they bind the patient to a grading of feelings that is not completely adequate since feelings vary in a continuous fashion. In its classical appearance the VAS is a 10 cm long line with only the extreme points defined as absence of symptoms on the left end, and the worst experience of the symptom during an ordinary menstrual cycle at the other end. The rest of the scale-steps are totally defined by the patient and followingly as private and continuous as the feelings under measure.

Comparison VAS - VRS

Ohnhaus compared the results of measurement of pain using a VAS and a VRS and found that the patients gave higher ratings when using the VRS and that the VAS more closely assessed the actual change in pain intensity (Ohnhaus 1975). In a study where women with PMS completed a VAS and a VRS the VAS was found to be the better choice (Sanders 1983).

DSM-III-R

As both gynecologists and mental health professionals over the years have become more and more interested in the problem of PMS the need for diagnostic criteria has increased. An advisory committee was selected in 1985 to consider diagnostic criteria for PMS meant for inclusion in DSM-III-R. The committee chose to use the name Late Luteal Phase Dysphoric Disorder (LLPDD) instead of PMS since it was considered to better describe the condition according to timing and nature and also comprehend women not menstruating but still having ovarian function. The thought was that a generally accepted definition would stimulate research on both the etiology and treatment and also facilitate the communication between different researchers since they would finally speak in equal terms. There is however one big problem here to overcome. Most patients with premenstrual disability seek a gynecologist or a general practitioner for help and the DSM-III-Criteria is generally not known to them. Assumably there is also a distinction between PMS patients seeking a gynecologist or a GP and patients seeking a psychiatrist, the former group with probably more physically oriented problem.

The diagnostic criteria defines the condition regarding timing, symptoms, severity, differential diagnosis and the way to diagnose using daily ratings (APA 1987, Spitzer 1989). In the criteria nothing is said about women with symptoms during the whole menstrual cycle with an aggravation of the symptoms premenstrually. We know from several studies that these women differ in personality and psychiatric case history compared with women with more strict luteal phase symptoms (Hammarbäck 1989a, Severino 1989, West 1989) and therefore it is very important to separate these different groups of patients from each other. Otherwise we might gain misleading information from our studies and above all, the patients do not get optimal treatment.

LLPDD appears in the appendix to DSM-III-R and below the diagnostic criteria are listed as in the appendix (APA 1987).

Diagnostic Criteria for Late Luteal Phase Dysphoric Disorder

A. In most menstrual cycles during the past year, symptoms in B occurred during the last week of the luteal phase and remitted within a few days after onset of the follicular
phase. In menstruating females, these phases correspond to the week before, and a few days after, the onset of menses. (In nonmenstruating females who have had a hysterectomy, the timing of luteal and follicular phases may require measurement of circulating reproductive hormones.)

B. At least five of the following symptoms have been present for most of the time during each symptomatic late luteal phase, at least one of the symptoms being either 1, 2, 3 or 4:

1. marked affective lability, e.g., feeling suddenly sad, tearful, irritable, or angry
2. persistent and marked anger or irritability
3. marked anxiety, tension, feelings of being "keyed up", or "on edge"
4. markedly depressed mood, feelings of hopelessness, or self-deprecating thoughts
5. decreased interest in usual activities, e.g., work, friends, hobbies
6. easy fatigability or marked lack of energy
7. subjective sense of difficulty in concentrating
8. marked change in appetite, overeating, or specific food cravings
9. hypersomnia or insomnia
10. other physical symptoms, such as breast tenderness or swelling, headaches, joint or muscle pain, a sensation of "bloating", weight gain

C. The disturbance seriously interferes with work or with usual social activities or relationships with others.

D. The disturbance is not merely an exacerbation of the symptoms of another disorder, such as Major Depression, Panic Disorder, Dysthymia, or a Personality Disorder (although it may be superimposed on any of these disorders).

E. Criteria A, B, C, and D are confirmed by prospective daily self-ratings during at least two symptomatic cycles. (The diagnosis may be made provisionally prior to this confirmation.)
AIMS OF THE STUDIES

Considerations before aims

It appears from the introduction that in patients with PMS, rather little is known about the stability in premenstrual symptoms, from one cycle to the other, both regarding cyclicity, preovulatory symptoms and severity. Even less is known about how subgroups of PMS patients differ from each other concerning stability in symptom pattern. These are important factors to know more about, especially as background knowledge when treatment studies are made.

It is difficult to assess the severity of a subjective condition like PMS and even more difficult to find a measure of severity that is comparable between individuals. A procedure that allows comparison of severity between individuals is of great importance.

Change in sexual interest is often reported as a premenstrual symptom. However, most studies on the subject have been made on community samples and thus little is known about change in sexuality in women with PMS. When studies have been made regarding androgens and their relation to sexual interest premenstrually, different subgroups of PMS patients have not been separated from each other.

A number of methods to assess cyclicity in a symptom pattern are presented in the introduction, and different methods are used by different workers in the field of PMS. Comparison between different methods, applied on the same material of patients, would give important information and hopefully in the future facilitate the comparison of results from different studies.

The specific aims were as follows:

1. To study the change in cyclicity and change in preovulatory symptoms between consecutive menstrual cycles in women seeking help for PMS.
2. To study the change in severity of PMS symptoms when consecutive menstrual cycles are studied.
3. To develop a method for measuring the severity of PMS.
4. To evaluate the method developed for measurement of the severity of PMS.
5. To investigate the cyclicity of sexual symptoms in women seeking help for PMS and look for correlation with hormone levels.
6. To compare some of the diagnostic methods in use for establishment of cyclicity in women seeking help for PMS.
METHODS

Common for all works included

Patients

Common for all the original papers included in the thesis is that the patients were consecutively recruited from women actively seeking help for what they claimed to be premenstrual symptoms at the Gynecological Outpatient Department at the University Hospital in Umeå, Sweden. 82 otherwise healthy patients were recruited, each giving a case history of severely impaired functioning because of premenstrual mood, behaviour or physical change. All patients' symptoms had lasted for more than one year. Their mean age was 34.9 years (range 20-45), 75% were married or cohabiting, 78% had given birth to at least one child, 49% were working full-time as employees and 10% were housewives. The studies were approved by the ethical committee of the University in Umeå.

At the first visit the patients were asked about their psychiatric lifetime history. When entering the PMS project the patients completed an Eysenck Personality Inventory (EPI) (Eysenck 1964) and a Moos Menstrual Distress Questionaire (MDQ) (Moos 1968). They were also asked to rate the influence of the symptoms on their family, work and social lives, and in 12 cases also the spouse made this rating. An earlier developed rating scale for anxiety states was used, where 0 stands for no influence at all and 3 stands for incapability to work, join family life or social life (Arfwidsson 1971). All three forms were completed during the follicular phase of the cycle following the first visit.

Daily ratings

The patients were asked to make daily ratings of their symptoms for two consecutive menstrual cycles using a Visual Analogue Scale (VAS) previously described and tested (Sanders 1983). 54 patients completed ratings during two cycles and the rest (28 patients) during one cycle.

The extremes of the VAS were 0 and 10. The patients were instructed to use the rating 0 when there was absence of the symptom under evaluation, and the rating 10 when the symptom was at its worst during an ordinary menstrual cycle. Both limits of the scale where thus known and defined for the patient before the study was started. In total 15 symptoms were rated; five adverse moods: tension, fatigue, irritability, anxiety and depression, four positive moods: energetic, relaxed, friendly and cheerful, three physical signs: headache, swelling and breast tenderness and finally three sexual parameters: sexual feelings, pleasant sexual thoughts and unpleasant sexual thoughts.

The patients also rated on a special scale, 0-5, with defined and for all patients equal scale steps how much the symptoms influenced their work, family and social life: 0=no influence at all, 1=influence of symptoms noted by the patient herself, 2=influence noted by the family, 3=disturbed relations within the family, 4=difficulties to work and 5=not able to work. They also noted if there were any special events during the day that could have influenced their mood and whether they had taken any medicine or other drugs.

The patients were instructed to start making ratings one week prior to expected menstruation to get practice in using the scale before they got started "for real" on the first day of menstruation.
Diagnosis of PMS

The patients had previously been diagnosed, as having "Pure PMS" with symptoms only during the luteal phase, "PM aggravation" with symptoms also during the follicular phase but with an aggravation premenstrually or "Non-PMS" with no cyclical pattern in their symptoms (Hammarbäck 1989a). 12 symptoms were used for diagnostic purpose: five adverse moods, four positive moods and three physical signs. Cyclicity was tested by comparing the nine preovulatory days with the nine premenstrual days with use of the Mann-Whitney U-test. A p-value <0.05 was considered as statistically significant. Patients showing significantly higher scores during the premenstrual phase in at least 3 of 12 symptoms, were considered to have cyclical mood changes and were classified as having "Pure PMS" if the number of days with an adverse symptom was less than or equal to two during the preovulatory phase. If the patient had three or more symptomatic days with three or more adverse symptoms during the preovulatory phase she was classified as having "Premenstrual aggravation". If there was not a significant difference in ratings between the preovulatory and the premenstrual phase the patient was diagnosed as "Non-PMS".

Blood samples and definition of lutéinisation

In 33 patients blood samples were drawn daily during one cycle for assay of estradiol, progesterone and LH, and in 21 patients during two cycles. 49 patients gave blood samples every week for the same assays during two cycles.

In 37 random patients, blood samples for analysis of androstenedione, testosterone, SHBG and FSH were taken between 9.00-11.00 a.m. once in the early follicular phase (days 4-9) in the same cycle as symptom ratings were made.

Estradiol, progesterone, androstenedione and testosterone were analyzed by radioimmunoassays (Bäckström 1982). For estradiol and testosterone, a celite chromatographic step was used. Coefficients of variation between assays were 13%, 12%, 10% and 10% respectively. SHBG was assayed with an immunoradiometric technique (IRMA, Farmos diagnostica, Turku Finland) (Hammond 1985). Interassay coefficient of variation was 5.5%. Serum levels of FSH and LH were determined radio-immunologically by using a double-antibody assay (Famos diagnostica, Oulo, Finland). The standards for FSH were WHO 69/104 and human pituitary LH, WHO 68/40. Within- and between-assay coefficients of variation were 8.5% and 10.5% for FSH, 8.7% and 8.7% for LH.

Lutéinisation was assumed to have taken place if the level of one progesterone value was higher than 15 nmol/l. The probable ovulation day was calculated by using the known increase per 24 hours in the progesterone concentrations following an assumed ovulation, and the known estradiol-progesterone relationships during the days prior to ovulation. The date was verified by reverse counting of days from the onset of the following menstrual period (Guerrero 1976, Landgren 1980).

Methods specific for each paper

Paper I

Patients

54 patients who had provided daily ratings in two consecutive cycles were included. They had also completed an Eysenck Personality Inventory (EPI) (Eysenck 1964) during the preovulatory phase of the first menstrual cycle.
Statistics

The patients were diagnosed and subgrouped using the two rated cycles separately, by the method described in the beginning of this chapter.

The first step was to diagnose the two cycles separately and to investigate if the patients remained in their subgroups in both cycles and if they changed subgroup, study how they changed between the subgroups. We also made a study of the concordance in the results using Spearman's rank correlation (Rs) and the statistic Kappa (K) (Fleiss 1981).

The second step was to investigate which symptoms most commonly showed cyclicity in the two cycles. The number of patients with "significant" or "not significant" cyclicity in the two cycles were counted for each symptom.

The third step was to compare the preovulatory symptoms in the two studied cycles for the patients with "Pure PMS" and "PM aggravation". This was accomplished by counting for each adverse symptom how many patients had rated themselves as having the symptom in question for three or more days during the preovulatory 9 day period. We also used the calculation of the statistic K to study the concordance in preovulatory symptoms between the two cycles.

The results of the EPI and frequency of psychiatric case history were compared between the different subgroups using the Mann-Whitney U-test and Fischer's exact test. Both rated cycles were used and compared.

Paper II

Patients

Included in this study were 54 patients who had, for two consecutive ovulatory menstrual cycles, made daily prospective ratings. They were not aware that the ratings from the two cycles would be compared with each other.

As described in methods for paper I the patients had earlier been diagnosed and divided into subgroups according to the distribution of their symptoms (Hammarbäck 1989a). The patients classified as "Non-PMS" did not show cyclical mood changes and were only included when all 54 patients were studied together as a group.

Statistics

Statistical analysis of data was made in two steps. In the first step, the Mann-Whitney U-test was used for within-individual comparison of the ratings of each symptom between the first and second rated cycles. In the second step, the method of combining p-values (Winer 1970) was used to compare subgroups of patients. To study the change in severity the natural logarithm (ln) of the p-value is summarized for each symptom and 2xln is chi-square-distributed with df=2xN. This made it possible to note differences in ratings between cycles for the groups of patients.

To compare different statistical methods a two-way ANOVA was also performed, as ANOVA though a parametric test, is often used on VAS data.

These two tests were used to compare the two cycles with each other, first using the whole cycles and then the premenstrual parts of the cycles. Because two different statistical methods were used a p-value <0.025 was considered as statistically significant. The
premenstrual period used was the nine days before the onset of menstruation. The same statistical procedure was then performed with the patient group previously diagnosed as having "Pure PMS" and then for the "Premenstrual aggravation" group. This made it possible to study whether subgroups of patients with PMS differ in severity between consecutive cycles. Mean-values were used only for descriptive purpose.

**Paper III**

**Patients**

82 patients who were previously diagnosed for presence or absence of cyclical changes and for presence or absence of adverse symptoms during the follicular phase were included. (Hammarbäck 1989a). Two of them were excluded because of lacking data in the daily self-ratings.

**Severity-score**

The ratings for the eight adverse symptoms during the luteal phase were used to calculate a severity-score. We counted how many times the minimum rating 0 and the maximum rating ≥9 were used by each patient. The sum of the total number of times the maximum score was used was subtracted from the total number of times the minimum score was used ("severity-score" = total number of 0 score - total number of ≥9 score). When we use eight adverse symptoms this gives a total range of possible scores from -112 to +112 in a luteal phase of 14 days.

The symptoms were studied individually to show which symptoms were most and least frequently used by the patients to describe their luteal phase symptoms. The total number of times the score 0 and ≥9 was used was calculated for each symptom separately. The number of patients never using minimum or maximum scores was also calculated for each symptom.

The "severity-score" was then used to divide the patients into three subgroups using the mean value of the severity-score ± 1 SD. Patients with a score +1 SD above the mean value were classified as having mild PMS and those with a score -1 SD below the mean value were classified as having severe PMS. The patients with scores between these values were classified as having moderate PMS.

**Shorter rating-scale**

The same procedure as above was repeated but only for six adverse symptoms: swelling, breast tenderness, tension, irritability, fatigue and depression. Cross-tables were used to study concordance with the subdivision made on the basis on the longer version of the rating scale and rank-correlation was used to study the concordance in severity-scores.

**Test of correlation**

Rank-correlation was used to see if our severity-score correlated best to the number of 0-ratings or to the number of ratings ≥9.

The sum of the raw scores of each symptoms ratings during the luteal phase was compared with the severity-score to see what symptoms best correlated to the severity-score. For each symptom we also correlated the number of days without symptoms and with maximum symptoms to the severity score.
Patients and ratings

82 patients described above participated in this study but two were excluded because of lacking data in the daily self-ratings. 45 of them had made daily prospective ratings of how much their PMS influenced family, work and social life using the 0-5 graded scale. 80 patients had before they entered the study given a retrospective rating of how much they estimated the condition to influence themselves, their family, social life and work performance. The MDQ was completed by 79 patients. Finally we had material comprising 12 couples where both the women seeking help for PMS and her spouse had performed retrospective ratings on how much the PMS influenced their lives.

Comparison between ratings

The severity-score obtained in paper III was compared with results from the other ways of estimating the severity of PMS. Raw-scores for each of these ways was summarized and the mean-value ± 1 SD was used for subdivision of the patients as having mild, moderate or severe PMS. The Spearman rank-correlation was used to study correlation between the severity-score obtained for each patient and the scores obtained from the other methods used. Cross-tables were used to compare the results of the subdivision in severity-groups. Spouses ratings were compared with the other ways of estimating PMS described, but also with the woman's rating to investigate agreement within the family.

Comparison with the second menstrual cycle

54 patients had performed daily self-ratings during two consecutive menstrual cycles. The procedure of calculating the severity-score and subdividing the patients into subgroups was repeated for the second cycle. Rank-correlation and cross-tables were used to study the agreement in severity between the two cycles.

In paper II we used the symptom-score from daily VAS-ratings and applied the nonparametric Mann-Whitney U-test and the method of combined p-value (Winer 1970) to study change in ratings between consecutive menstrual cycles (Ekholm II). The change in p-value between cycles was compared with change in severity-score. Rank-correlation was used to study correlation in raw-scores and cross-tables to study if there was an agreement on which of the two cycles the patient was feeling better.

Median instead of mean-value

We also calculated the median for all the different methods used and subdivided the patients with the 25% percentile as the upper limit for severe PMS, the 75% percentile as the lower limit for mild PMS and followingly patients in between these values were referred to the group moderate PMS. We used cross-tables to study correlation to the subdivision based on the mean value.

Paper V

Patients and hormones

37 patients had given blood samples for assays of androstenedione, testosterone and SHBG early in the follicular phase (for details please see above). Besides the 12 symptoms used for diagnosis and division into subgroups 71 patients had also performed daily ratings of
three sexual parameters and completed an Eysenck Personality Inventory (EPI) (Eysenck 1964). 33 patients had both completed sexual ratings and given blood samples.

**Rating scale and daily ratings**

Daily prospective ratings of three sexual parameters - sexual feelings, pleasant sexual thoughts and unpleasant sexual thoughts were made in the same cycle as the hormonal analyses. The VAS was used for quantitation with 0 and 10 as extremes (Bancroft 1983; Sanders 1983). When rating sexual feelings, the patient was supposed to evaluate her interest in or desire for sexual activity. When rating pleasant or unpleasant sexual thoughts, the patient was supposed to think about a sexual event and then evaluate whether the reaction to this thought was pleasant or unpleasant and to what degree.

**Analysis of data**

To test the presence of cyclical changes in the sexuality scores, data were tested in two steps. In the first step, the Mann-Whitney U-test was used to compare, within each individual, the ratings of the three sexual parameters between the preovulatory phase (eight days) and the premenstrual phase (eight days). The Mann-Whitney U-test was also used for testing differences in hormone levels between the "Pure PMS group" and the "PM aggravation group".

The medians for androstenedione, testosterone and SHBG were calculated and the patients were subgrouped according to a concentration above or below the median of each analysis. Those with a level equal to the median were excluded. The intention was to determine whether there was a relation between a "high" or "low" level of androgens and SHBG respectively and the cyclicity of sexual parameters.

In the second step, the method of combined p-values (Winer 1970) was used to determine if there was any difference in the cyclical pattern in subgroups of patients with "high" or "low" levels of androstenedione, testosterone and SHBG. The results of using combined p-value were compared with results of an analysis of variance (ANOVA).

To study the correlation between the levels of androgens and SHBG and the level of sexual interest, the number of days with the minimum rating 0 or 1 and the maximum rating >9 was counted for each patient. This was made both for the premenstrual part of the cycle (8 days) and for the cycle as a whole. Mean values for the number of days with minimum and maximum ratings for each symptom were calculated separately for patients with "high" and "low" level of androstenedione, testosterone and SHBG.

The Mann-Whitney U-test was used for statistical testing of differences in number of days with minimum and maximum ratings depending on the concentrations of androgens and SHBG below or above the median. A p-value <0.05 was considered statistically significant. Mean-values were used only for description of change in symptoms.

Spearman’s rank-correlation was used to study if there was a correlation between age and androgen levels and between age and sexual interest. It was also used to study correlation between the result of the EPI and androgen levels and between the EPI and sexual interest.
**Paper VI**

**Patients and ratings**

All 82 patients were initially included but two were excluded because of lacking data in the daily self-ratings. The patients made daily self-ratings as described earlier.

**Statistical methods**

Four different statistical methods suggested as useful for detection of cyclicity in premenstrual complaints were compared. They are all meant for use on daily self-rating data and were each applied on the ratings completed by our patients. The nine preovulatory (PO) days were compared with the nine premenstrual (PM) days for each symptom separately. Since the method suggested by Rubinow with 30% increase is not distinctly described in his reports, we have chosen two ways of calculation (4a. and 4b. below).

The four methods were:

1. **Nonparametric:** A one-tailed p<0.05 level Mann-Whitney U-test was used to compare the ratings from the PO days with the ratings from the PM days (Siegel 1956).

2. **Run test:** For each symptom the median score for PO and PM days was calculated. Thereafter the run test was performed on the sequential 18 days (Siegel 1956).

3. **Effect size:** The mean difference between the PO and the PM days was divided by the standard deviation of the whole cycle. ES ≥1 was considered statistically significant (Schnurr 1988).

4a. **30% increase:** The mean PO and PM scores were calculated and if the mean PM score was 30% higher than the mean PO score the change was considered significant (Rubinow 1984).

4b. **30% of scale:** If the difference between PO and PM mean scores was more than 30% of the scale (here 3.3 scale steps) the change was considered significant (Rubinow 1984).

**Cyclicity**

If there was a significant difference between the PO and the PM days in at least three of the twelve symptoms, the patient was diagnosed as having PMS. If there were fewer than three symptoms with significant change she was considered as not having PMS. As described on page 23 the number of days with adverse symptoms during the PO phase was counted to discriminate between "Pure PMS" and "PM aggravation" patients.

The results of the diagnostic procedures were compared in cross-tables and the number of symptoms showing cyclicity was correlated using Spearman's rank-correlation.

The results of the EPI and the frequency of earlier psychiatric history were compared between the cyclic and the non-cyclic group for each method used. The statistical test used was Mann-Whitney U-test and Fischers exact test.
RESULTS

Cyclicity (paper I)

Subgroups

54 patients had produced ratings from two menstrual cycles, to which it was possible to apply our diagnostic procedure. 35 patients (65%) were allocated to the same subgroup in both cycles and 19 patients (35%) changed subgroup between the two cycles. Nine patients changed between "PM aggravation" and "Non-PMS", seven changed between "Pure PMS" and "PM aggravation", three patients changed between 'Pure PMS" and "Non-PMS". There was a significant correlation in the diagnostic subgroups between the two cycles (Spearman’s rank correlation Rs=0.648; p<0.001). The concordance in subgrouping was also significant, Kappa statistic, K=0.47 (p<0.001), showing that the concordance is more than due to chance.

When using the cycle closer to a "Non-PMS" pattern 12 patients lost their cyclical pattern compared with when diagnosis was based on the cycle with a more "ideal PMS pattern", 6 because of lower premenstrual scores in one cycle, 2 because of higher preovulatory scores, and 4 because of both lower premenstrual and higher preovulatory scores.

Symptoms

When studying the cyclicity in each symptom separately, it was shown that most patients, between 59 and 74 %, showed the same pattern of cyclicity in both cycles. Headache, tension, energetic mood and irritability showed the greatest variation between cycles and concordance was not significant. The number of symptoms showing cyclical change was counted for each patient showing a significant correlation between the two cycles (Rs=0.38; p<0.005).

Preovulatory symptoms

There was a high correlation, Rs=0.71; p<0.001, between the two cycles in number of days without adverse preovulatory symptoms. Breast tenderness and headache showed to be the least concordant and also the least frequently reported symptoms preovulatory. The concordance between cycles was higher for the presence of preovulatory symptoms discriminating between "Pure PMS" and "PM aggravation" than for the presence of cyclicity.

Neuroticism and psychiatric history (paper I, V, VI)

Difference between groups

When using the cycle closer to the "ideal PMS pattern", the median score in the neuroticism scale of the Eysenck’s Personality Inventory (EPI-N) was significantly lower in the "Pure PMS" group compared with the "PM aggravation" and "Non-PMS" groups. When the cycle most resembling an "ideal PMS pattern" was used for diagnosis and subgrouping, patients diagnosed as having "Pure PMS" had significantly lower frequency of psychiatric case-history compared with "PM aggravation" and "Non-PMS" groups. When the patients were subgrouped according to the cycle closer to the "Non-PMS" pattern, the differences between the groups disappeared. Both the difference in EPI-N scores and psychiatric history became less clear when the cycles were used in their chronological order.
Correlation to androgens and sexuality

There was no correlation between the results of the EPI-N and the levels of androgens and SHBG respectively.

Between the EPI-N and the number of days with minimum or maximum ratings for the three different sexual parameters there were significant correlations when the whole cycle was studied. Rank-score was highest for the number of days with maximum rating for pleasant sexual thoughts (Rs=-0.43, p-val <0.05). Between the EPI-N and the number of days with maximum rating of sexual feelings (Rs=-0.38, p-val <0.05), and the EPI-N and the number of days with minimum rating for pleasant sexual thoughts (Rs=0.36, p-val <0.05) there were also significant correlations. Only one significant correlation was found when the premenstrual phase was used and that was between the EPI-N and number of days with minimum pleasant sexual thoughts (Rs=0.41, p-val <0.05).

Comparison between different diagnostic methods

There was no significant difference in the median neuroticism score (EPI-N) between the patients showing cyclicity or not showing cyclicity with any of the methods tested. But, when comparing the non-cyclic group to the "Pure PMS" group there was a significant difference (p<0.05) for the nonparametric test, run test and effect size. The frequency of patients having earlier psychiatric history did not differ between non-cyclic and cyclic groups with any of the different methods. However, when the non-cyclic group was tested against the "Pure PMS" group again the nonparametric, the run test and effect size showed significant differences.

Severity (paper II, III, IV)

Comparing the whole cycles

In paper II the change in degree of PMS symptoms between consecutive cycles was studied by comparing the change in p-values. There was no significant difference between cycle 1 and cycle 2 for any of the symptoms rated when all patients were studied together in one group, either when using combined p-value or ANOVA. No change between cycles was found for the "Pure PMS" group either. When using combined P-value one symptom showed significant change in the "PM aggravation" group - the positive mood friendly, with the patients as a group feeling better during the 1st cycle than during the 2nd (p<0.005). When using the ANOVA there was also one symptom that was statistically different between the two cycles - the symptom tension (p<0.01) showing a worse situation in the first cycle.

Comparing the premenstrual phases

When all patients were studied together there was one symptom that differed between cycles both when using combined p-value and ANOVA - the symptom irritability with less of the symptom during the first cycle (p<0.005).

When using the ANOVA-test, the patients with "Pure PMS" showed some significant differences between the two cycles. The patients felt less energetic, more fatigued, depressed and tense during the first cycle compared with the second. There was also a difference for headache, with less during the first cycle, thus an opposite situation to the other symptoms with significant change. When comparing the combined p-values for the women with "Pure PMS" there was no significant difference between the cycles.
The "PM aggravation" group, showed significant change between the cycles for the adverse moods tension, irritability, fatigue and depression when using combined p-value, feeling better during the 1st cycle. The ANOVA-test gave the same result but with somewhat different p-values. This pattern was the opposite to the one found in the "Pure PMS" group when using the ANOVA.

Symptoms and ratings

In paper III an attempt was made to find an easy method for estimating the severity of PMS and hopefully get a figure comparable between patients.

The symptoms most often given the minimum score = 0 were headache and breast tenderness and among mood symptoms, anxiety. Irritability was the symptom most often rated ≥9 (= maximal degree), followed by fatigue and depression. Headache was least often rated to a maximal degree.

The frequency of minimum and maximum ratings varied considerably between the patients. Three patients had never given the rating 0 during the luteal phase for any of the eight adverse symptoms, while at the other extreme one patient had given the rating 0, 91 times. The maximum rating, ≥9, was never used by 17 patients while at the other extreme there was one patient who had given this rating 59 times during the luteal phase.

We also studied how many patients who for one day or more used the minimum rating (0) and the maximum rating (>9) for each symptom. Headache was rated 0 by 65 patients and breast tenderness by 62 patients, these being the most common symptoms to be rated 0 for one day or more. Irritability, fatigue and depression were the symptoms most frequently experienced to a maximum degree for one day or more (n=38, 37 and 37 respectively).

The severity-score

The patients varied in severity-scores from -43 to 87 with a mean 26 ± 29 (±1 SD). The distribution of the sample resembled a normal distribution. ± 1 SD was used to subdivide the patients into severity-groups based on their scores. 16 patients (20%) had a severity-score equal to or above 55 and were diagnosed as having mild PMS. 49 (61%) had a severity score between 55 and -3 and were diagnosed as having moderate, and 15 (19%) who had a severity-score equal to or below -3 were diagnosed as having severe PMS.

In the group classified as mild PMS there was an almost equal distribution of patients diagnosed as "Pure PMS" = 8, "PM aggravation" = 3 or "Non-PMS" = 5. In the moderate group there was a domination of patients with "PM aggravation" = 32 and relatively few patients with "Non-PMS" = 6. 11 patients were diagnosed as "Pure PMS". In the group classified as severe PMS there were 5 patients diagnosed as "Pure PMS", 10 as "PM aggravation" and no patients subdiagnosed as "Non-PMS".

A shorter rating scale with eight symptoms, six adverse and two positive was compared with the twelve-symptom rating-scale. Results show strong agreement with the longer version with 94% of the patients classified in the same severity-group with both scales (rs=0.92, P<0.001).

Correlation severity-score and symptoms

There was a high positive correlation between the severity-score and the number of 0-ratings (rs=0.94, p<0.001). The correlation between the severity-score and the number of
ratings $\geq 9$ showed a negative correlation but not as high as to the 0-ratings ($rs=-0.64, p<0.001$).

Symptoms showing the highest correlation to the severity-score were anxiety, tension ($rs=-0.57, p<0.001$) and irritability ($rs=-0.56, p<0.001$). Headache ($rs=-0.24, p=0.03$), and breast tenderness ($rs=-0.41, p<0.001$) showed the lowest correlation. The rank-scores for depression, fatigue and swelling were distributed between -0.43 and -0.49.

**Severity-score compared with other ratings (Table 3)**

The subdivision into severity-groups using the median instead of the mean-value gave the same results and is therefore not discussed further.

When comparing the severity-score with the results of the prospective influence rating made every day by the patient, the rank-correlation between raw-scores was -0.68 ($p<0.001$) with 62% of the patients referred to the same severity-group with both methods.

The comparison of the severity-score and the retrospective estimation of influence on family, work and social life showed that 46% of the patients were placed in the same severity-group but rank-correlation of raw-scores was low, -0.23 ($p\text{-val}<0.05$). The severity-score showed a tendency to rate the severity lower than the patients own retrospective rating of influence showed.

The MDQ placed 56% of the patients in the same subgroup as the severity-score did. There was about equal distribution by the two methods classifying the patients as having more severe PMS. The patients classified as having moderate severity showed the best agreement between the severity-score and the MDQ, with 69% being allocated to the same severity group. For mild and severe PMS the figures were 43 and 27% respectively.

Table 3. Shows in cross-tables the number of patients in the different subgroups of severity of PMS. Subdivision based on the severity-score is compared with other ways of estimating the severity. It also shows the agreement in % between the severity-score and the other methods used.

<table>
<thead>
<tr>
<th>Severity-score (n=80)</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prosp. rating of influence</strong> (n=45)</td>
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<tr>
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<tr>
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<td>21</td>
<td>4</td>
<td>62%</td>
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<td>4</td>
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<tr>
<td><strong>Retrosp. rating of influence</strong> (n=80)</td>
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</tr>
<tr>
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<td>13</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>10</td>
<td>26</td>
<td>8</td>
<td>46%</td>
</tr>
<tr>
<td>Severe</td>
<td>-</td>
<td>10</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>MDQ</strong> (n=79)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>33</td>
<td>10</td>
<td>56%</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
<td>10</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
49% of the patients were classified in the same severity-group when comparing the prospective ratings of influence on family, social life etc. with the classification based on the MDQ. When disagreeing there was an equal distribution in both directions. There was a 55% agreement between the patients retrospective estimation of how much the PMS influenced their lives and the MDQ-based judgement. In 28% of the cases the MDQ-based estimation of severity was higher than shown in the patients retrospective rating of influence on their lives. 17% of the cases showed disagreement in the opposite direction. In the comparison between prospective and retrospective ratings of influence on work, family and social life 52% showed agreement between subgroups of severity.

In 9 out of 12 couples the man and the woman agreed on how much the PMS affected the family, social life and work. The estimation made by the spouse agreed with the severity-score in 8 cases while for the women's estimation there was an agreement in 7 cases. When there was disagreement there was about equal distribution for both the men and the women on whether they had estimated the severity lower or higher than the severity-score showed.

**Comparison with second menstrual cycle (Table 4)**

54 patients had performed daily symptom-ratings during two menstrual cycles and the procedure of calculating the severity-score and subdivision in subgroups was repeated for the second cycle. 65% of the patients were classified as belonging to the same subgroup of severity in both cycles, rank-correlation = 0.67 (p<0.001, n=54). The patients that were classified differently in the two cycles showed no specific pattern in their distribution, with 11 patients having a lower severity-score in the first cycle and 8 patients having a lower severity-score in the second cycle. Patients with severe and moderate PMS showed to be more stable in their severity-score compared with those with mild PMS (Table 4). 71% of patients with "PM aggravation", 59% with "Pure PMS" and 50% with "Non PMS" were classified in the same severity-group in both cycles.

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 1</td>
<td>4 (57%)</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>Moderate</td>
<td>3</td>
<td>26 (72%)</td>
<td>7</td>
</tr>
<tr>
<td>Mild</td>
<td>-</td>
<td>4</td>
<td>4 (36%)</td>
</tr>
</tbody>
</table>

In 47 patients it was possible to compare the change in severity-score with change in p-values obtained by application of the Mann-Whitney U-test and combined p-value on the VAS-ratings. 40 patients (85%) showed the same pattern with both methods as regards which of the two cycles were the better, rank-correlation 0.72 (p<0.001).

**Sexuality and hormones (paper V)**

**Hormones**

The patients classified earlier as having "Pure PMS" had a significantly lower level of testosterone and a significantly higher level of SHBG than the "PM aggravation" group. No other differences were observed between the two groups. There was no correlation between age and androgen and SHBG levels.
Cyclicity in sexual ratings (Fig. 1 and Fig. 2)

71 patients completed the daily ratings of the three sexual parameters: sexual feelings, pleasant sexual thoughts and unpleasant sexual thoughts. Thirty-three patients had also given blood samples for androgens and SHBG.

Figure 1. Shows for all patients, with androgen and SHBG values, the mean scores for sexual feelings, pleasant sexual thoughts and unpleasant sexual thoughts (n=33). A 28-day cycle was constructed with seven days in each direction from ovulation and from the first day of menstruation.

The group as a whole showed obvious cyclicity for all three sexual symptoms that were rated. The patients experienced as a group more sexual feelings and had more pleasant sexual thoughts preovulatory than premenstrually and more unpleasant sexual thoughts premenstrually than preovulatory (Fig 1). Among the 71 patients having completed the ratings of the sexual parameters there were three patients with a positive cyclicity in the parameter "sexual feelings", that is, they experienced more sexual feelings premenstrually than preovulatory (Fig 2). 32 patients showed a negative cyclicity (a decrease premenstrually) in sexual feelings (Fig 2) and 36 did not show a cyclical pattern (Fig 2).

When divided into groups depending on the level of hormone concentrations, the cyclicity in sexual parameters remained, except for the parameter unpleasant sexual thoughts, where patients with levels of androstenedione, testosterone and SHBG above the median lost their cyclical pattern when using the Mann-Whitney U-test but using the ANOVA showed significant cyclicity all the way. The number of patients showing cyclicity in sexual parameters were fewer in the subgroups with high levels of androstenedione, testosterone and SHBG for the parameter unpleasant sexual thoughts, and Fisher's exact test against hypothesis that none showed cyclicity was not significant here while it was significant for the rest of the hormonal subgroups in all three parameters.

Severity of sexual symptoms

The comparison of number of days with minimum or maximum ratings of sexual symptoms during the premenstrual phase showed no significant difference whether the patients belonged to the group with either "high" or "low" levels of androgens and SHBG. We also made the same comparison using the whole cycle. Here, the number of days with maximum scores for sexual feelings and for pleasant sexual thoughts were significantly higher (p<0.05) in the group of patients with the plasma level of androstenedione below the median.
Figure 2. Shows the distribution of the mean scores for the sexual parameters: sexual feelings and unpleasant sexual thoughts for
a) patients with negative cyclicity (n=32)
b) patients with positive cyclicity (n=3)
c) patients with no significant cyclicity (n=36).
A 28-day cycle was constructed with seven days in each direction from ovulation and from the first day of menstruation. Included here were all patients with sexual ratings (n=71).

Comparison of methods (paper VI)

Cyclicity and symptoms

There was a strong agreement between the nonparametric Mann-Whitney U-test and effect size in establishing cyclicity. Results were actually the same with 69 patients considered to have a cyclical symptom pattern with both methods.

When using the run test, four patients differed between the nonparametric test and the run test. The mean of the premenstrual phase was, however, higher than the mean of the preovulatory phase in all four cases.

When using a 30% increase in symptom ratings, 76 patients were cyclic which is more than with any of the other methods used. The method using 30% of the scale as criteria for cyclicity was more demanding than the other tests giving a smaller number of patients (50) with cyclicity than the other methods gave.

The number of symptoms showing cyclicity for each patient was tested using Spearman’s rank-correlation and was highly correlated between the different methods with p<0.001 for all correlations. The lowest rank-score was between run test and 30% increase with rs=0.57 and the highest between effect size and the nonparametric test, rs=0.86.

The nonparametric test, the run test and effect size showed significant difference (p<0.05) in median EPI-N score and in frequency of psychiatric history between the “Pure PMS” and the non-cyclic group. Both methods using 30% increase in mean symptom score as demand for cyclicity, failed to detect this difference.
DISCUSSION

Cyclicity

Like other workers in the field of PMS we have found that when a woman seeks help for PMS, the diagnosis should be based on daily self-ratings during at least two menstrual cycles (Shaver 1985, APA 1987, Schnurr 1989). Which method is chosen for the self-ratings is a matter of taste. We have chosen to use a visual analogue scale (VAS) since it is easy to use for the patients, giving better compliance and since we think it is a valid and reliable way of measuring subjective feelings (Sanders 1983, Aitken 1969, Folstein 1973, Bond 1974, Ohnhaus 1975, Maxwell 1978).

Using the Mann-Whitney U-test to detect significant cyclicity in the symptoms (p-val < 0.05) the majority of patients (78%) had the same pattern, cyclical or not cyclical, in both of two rated menstrual cycles with 22% losing or gaining cyclicity from one cycle to the other. The patients showing significant cyclicity were diagnosed as having "Pure PMS" with only luteal phase symptoms, or "PM aggravation" with symptoms during the whole menstrual cycle and an aggravation of the symptoms premenstrually. Patients not showing a cyclical change in symptoms were diagnosed as "Non-PMS". When comparing the results of this subgrouping of the patients it was found that 65% stayed in the same subgroup in both cycles leaving 35% to change subgroup. The most common change was between the "PM aggravation group" and the "Non-PMS group". The reasons for changing subgroup can be primary life events, anovulatory cycles, a positive reaction to being under evaluation or just simply a natural fluctuation in the condition. We must allow such things to occur and therefore it is not sufficient to base the diagnosis of PMS or not PMS on only one menstrual cycle.

Many of these women live under great strain and are in need of support and accurate treatment. Some of the women seeking for PMS actually have a cyclical pattern but some of them don’t, but have other problems of psychical nature. Both groups are in need of treatment but not the same treatment and therefore we must be very thorough when we establish the diagnosis.

Many different methods for detection of cyclicity and diagnosis of PMS have been suggested. We have compared three other methods: effect size (Schnurr 1988), run test (Siegel 1956) and 30% change (Rubinow 1984) to the Mann-Whitney U-test (Hammarbäck 1989). Results were very similar, and from this study we can not recommend any of the methods in favour of the others. Run test is a very simple method to use and might therefore be an interesting method to study further. There have been earlier studies comparing different diagnostic methods for PMS and none of them either have proven any method better than the other (Metcalf 1989, Schnurr 1989).

Preovulatory symptoms

The presence of preovulatory symptoms in PMS and its significance has not been evaluated until recently. Our results, as well as others (Hammarbäck 1989a, West 1989), suggest that there is a difference in personality between women diagnosed as having "Pure PMS" with strictly premenstrual symptoms and those diagnosed as having "PM aggravation" with symptoms also during the preovulatory phase but with an exacerbation premenstrually. In our case this difference was reflected as a higher EPI-N score and as a higher frequency of earlier psychiatric history for the women with "PM aggravation. These differences were
however only significant when the cycle closer to an "ideal PMS pattern" was used for diagnosis, again pointing to the importance of using more than one cycle, and preferably then using the cycle closer to an "ideal PMS pattern" since it better discriminates between the patients. West found that women with a postmenstrual mood relief below 75% had a higher frequency of earlier psychiatric treatment or marital breakdowns and were more likely to have three or more children compared with women with postmenstrual symptom relief of more than 75% (West 1989).

When looking at the cyclical pattern for individual symptoms it was found that the presence or absence of preovulatory symptoms was a more stable factor between cycles than the presence or absence of cyclicity. We do not know the reason to this finding, but maybe it is so that the occurrence of preovulatory symptoms is more closely connected to personality, giving this stability between cycles.

The severity-score

The problem with subjective ratings is that, when trying to estimate the severity, the ratings cannot be directly compared between patients. This problem is of course not exclusive for PMS but stands for all kinds of subjective feelings.

We have made an attempt to find a method for measuring the severity of PMS, a method easy to use both for the patient and the examiner. The severity-score, obtained by counting the number of days with no symptoms and from this sum subtract the sum of days with maximum symptoms, gives us a figure which we think is comparable between individuals. We are quite aware that the severity-score is not the perfect solution to estimation of the severity of PMS since it does not take ratings between 1 and 8 on the VAS into consideration. But, we think that it might be a good start and hopefully further studies will show which scores should be counted to get an optimum result. The aim was to find a method easy to use for everybody who is working with PMS patients and the sum of 0 and ≥9 ratings can be calculated by hand. If we use all the ratings the counting gets much more complicated and not so easily handled. We also think that the absence of symptom and the maximum degree of symptom are the points on the rating-scale that are the most objective ones. The distribution of the severity-score resembles a normal distribution and this suggests a biological basis for the severity of premenstrual symptoms.

Other methods suggested for assessment of the severity of PMS (Metcalf 1985, Livesey 1989, Severino 1989, Mortola 1990) are, as far as we can understand, not able to distinguish a patient with a preovulatory score of 1 and a premenstrual score of 3 from a patient with the corresponding figures 1 and 6 using the DRF. Using the VAS there would for example not be any distinction made between a patient changing from the rating 1 preovulatory to 5 premenstrually and a patient going from the rating 1 to 10. In both examples the second patient is probably feeling much worse premenstrually in that specific symptom, compared with the first patient, but that is not revealed in the severity-classification. Using The Calendar of Premenstrual Experiences and adding all the scores for all physical and behavioural symptoms, Mortola and co-workers assess the severity of PMS (Mortola 1990). The method does however not differentiate between women experiencing few symptoms to a high degree from those with many symptoms to a low degree. This is put forward as an advantage by the workers in question but isn't it likely that a woman with few symptoms to a high degree suffers more than a woman with many symptoms to a mild or moderate degree?

There was a large range among our patients in the number of times the minimum rating 0 and the maximum ratings ≥9 were used. Seventeen patients never used the maximum
ratings and three patients never used the rating 0. We don’t know if this is due to a reluctance to use the maximum ratings, or if it simply is so that during the time they performed the ratings the symptoms weren’t that bad. The patients were instructed to use the whole scale and the definition for the maximum ratings was, that they should use it when the symptoms were the worst they usually experience during an ordinary menstrual cycle. Maybe this finding is in line with those made by other workers, that PMS patients feel better when they are under careful evaluation (Endicott 1982, Abplanalp 1983, Halbreich 1985a, Keye 1988).

Correlation-tests showed that the severity-score was more related to the number of 0-ratings than to the number of maximum ratings. This could be interpreted as if the severity-score was more correlated to symptoms more seldom experienced, which of course would be unfortunate. But, when looking at different symptoms it was shown that the symptoms with the highest correlation to the severity-score were irritability, anxiety, and tension, symptoms that are among the most frequent to be reported by PMS patients (p.c.f. pg 9, Table 1). Headache was the symptom most often rated 0 premenstrually, but it had also the lowest correlation between the severity-score and the number of 0-ratings, contradicting the thought that the severity-score would be more dependent on a lack of symptom rather than the presence.

Five patients diagnosed as having "Pure PMS" were classified as having severe PMS showing that there are patients severely inflicted by their PMS symptoms but who are free of symptoms postmenstrually. These patients did also have an impaired functioning premenstrually in work performance, family and social lives because of the symptoms.

**Evaluation of the severity-score**

To evaluate the severity-score and try its validity we compared it with other possible ways of measuring severity of PMS. The severity-score was compared with the results of the MDQ, with the results of daily ratings of influence on work, family and social life, with the results of a retrospective rating of such an influence and in 12 couples with retrospective ratings made by the spouse of the impact of the PMS on the family. The highest correlation was found between the severity-score and the prospective rating of influence on work, family and social life, with 62% of the patients in the same subgroup of severity with both methods, indicating that the severity-score is a valid instrument for measurement of the severity of PMS. The MDQ and the severity-score showed agreement in 56% of the cases and the retrospective rating of influence and the severity-score in 46% of the cases, supporting that retrospective ratings are less reliable than prospective ratings when diagnosing PMS.

But we must not forget the effect of the ratings themselves (Endicott 1982, Abplanalp 1983, Halbreich 1985a, Keye 1988) maybe giving a picture of a less severe condition in the prospective ratings. In our study it was however not confirmed that the retrospective symptom-rating, in this case the MDQ, overestimated the severity of PMS. When there was disagreement it was about equal which of the two methods estimated the condition as more severe. Several previous studies have shown that retrospective ratings overestimate the symptoms of PMS (Englander-Golden 1978, Endicott 1982, Woods 1982, Sanders 1983, Rubinow 1984, Halbreich 1985a, Metcalf 1985, Magos 1986, Rapkin 1988, Christensen 1989, West 1989, Ainscough 1990), but one important thing to remember is that some of these studies were performed on volunteers and not on patients seeking help for PMS (Englander-Golden 1978, Woods 1982, Christensen 1989, Ainscough 1990). Our results are more consistent with those (Endicott 1982, Halbreich 1982, Christensen 1989) suggesting that the more severe the form of PMS, the more reliable are the retrospective
ratings. Further support to this is the fact that among our patients with severe PMS there was none diagnosed as "Non-PMS". The fact that when calculating the severity-score we do not take ratings between 1 and 8 into consideration might also be of importance to explain the rather low correlations between retrospective ratings and the severity-score. However, the correlation was rather good between the severity-score and the prospective ratings of influence indicating that the severity-score after all is a good measure and that retrospective ratings are more unreliable than prospective ones.

Another indication that the severity-score is really measuring the severity of PMS is the results of the spouses ratings which highly agree with the severity-score. Unfortunately the material was to small to allow further conclusions.

Since many patients found the 12-symptom rating scale too long, we used only eight symptoms and calculated the severity-score to see if there was any difference in severity-classification. The results agreed strongly, showing that the 8-symptom rating-scale is a worthy replacement to the 12-symptom scale.

Change in severity between cycles

In 54 patients it was possible to calculate the severity-score for two menstrual cycles and compare the results. 65% were classified into the same severity-group in both cycles, a result exactly the same as the one from the comparison of classification in subgroups in Paper I. The 35% changing severity-group can be due to naturally occuring fluctuations in the symptoms, but also be caused by a weakness in our way of measuring the severity. Further studies will hopefully give an answer to the latter question. However, the fact that 35% changed severity-group from one cycle to the other further emphasizes the need for prospective ratings from more than one cycle when we are diagnosing PMS. Many patients spontaneously report that the degree of their PMS symptoms fluctuate between cycles and it has been suggested that these fluctuations might be of hormonal origin (Hammarbäck 1989b). Life events are probably another contributing factor to this variation in symptoms between cycles. The diagnostic method must allow such natural fluctuations to occur and when using at least two cycles as basis for diagnosis we are more sure of getting the right picture.

We also used the change in p-values to study the direction and degree of change in symptom severity when consecutive cycles were compared. When all patients were investigated together there was no change between the two cycles when the whole cycles were used, and only one change when the premenstrual parts were compared. When the patients were separated in a "Pure PMS" group and a "PM aggravation" group there was a clear difference between the two groups, with the "PM aggravation" group feeling better during the first cycle compared with the second in four out of five adverse moods, both when using combined p-value and ANOVA. The ANOVA showed an opposite pattern for the "Pure PMS" group in three adverse moods, the patients feeling worse during the first cycle. Obviously "Pure PMS" patients with strictly luteal phase symptoms and "PM aggravation" patients react differently when subject to evaluation. If the rating-procedure in itself has a therapeutic effect then the "PM aggravation" group is more susceptible to this effect or at least they respond to it more quickly than the "Pure PMS" patients. Maybe this difference in response is due to the difference in personality between the different groups of PMS patients that have been reported (Hammarbäck 1989a, West 1989, Ekholm II). However, the results again point to the importance of careful evaluation of the patients, and that patients not free from symptoms during the follicular phase should be separated from those with "Pure PMS", otherwise the results risk misinterpretation.
In 47 patients it was possible to compare the change in severity-score between cycles with the change in p-values. The p-value takes all ratings given by the patient into consideration, which is not the case with the severity-score. We found a very high correlation between the two methods with respect to in which cycle the patient was feeling better, giving us support that the severity-score is a reliable measure of the severity of PMS.

Sexuality and hormones

Results showed that women with “Pure PMS” had lower plasma testosterone than women with “PM aggravation” or “Non-PMS”. This may be an important finding since it has been shown in an earlier study that PMS women with a high level of testosterone respond better to therapy with spironolactone (Rowe 1986). If this is a correct finding, our results further emphasize the importance of separating the different subgroups of PMS patients before enrolling them into a treatment programme.

The level of SHBG was increased and has in previous studies been shown to be both decreased (Dalton 1981) and increased (Bäckström 1981) in PMS patients. Since SHBG is known to fluctuate during the menstrual cycle (Plymate 1985) and the samples were drawn at different times during the menstrual cycle in these three different studies we are not able to draw any conclusions from our finding.

The patients were divided in a "high" or "low" group depending on the level of their hormone values. When looking at the relationship between the cyclicity of sexual symptoms and levels of testosterone, androstenedione and SHBG our results suggest that women with PMS symptoms and low levels of androgens and SHBG would be more likely to have a decreased sexual interest premenstrually. This result goes in line with the finding in an earlier study showing that testosterone supplementation caused an increased libido in women with a decrease in sexual interest premenstrually (Magos 1984).

There have been earlier reports that some women experience an increased sexual interest premenstrually (Stewart 1989, Hart 1960) but among our patients only three (4.2%) showed such a pattern. None of the two referred studies included PMS patients which probably explains the great discrepancy between the results.

When studying the whole cycle it was shown that patients with a low level of androstenedione had significantly more days with maximum ratings of the parameters sexual feelings and pleasant sexual thoughts, indicating that not all patients with PMS have a low sexual interest. When testing the premenstrual part of the cycle there was no difference in number of days with maximum ratings of sexual symptoms between the groups.

The results imply that there might be an endocrinological background to the change in sexuality premenstrually in PMS patients and that women with "Pure PMS" seems to differ from those with "PM aggravation".

Neuroticism and psychiatric history

Results support the finding made by Hammarbäck (Hammarbäck 1989) that the "PM aggravation" and the "Non-PMS" group have higher scores in the EPI-N and higher frequency of psychiatric history compared with the "Pure PMS" group. The difference was mostly pronounced when the cycle with a pattern closer to an "ideal PMS pattern" was used for diagnosis. This finding emphasizes the importance of using more than one cycle for diagnosis of PMS.
Watts interpreted the findings that PMS patients had higher neuroticism and trait anxiety scores in tests, as either an effect of the syndrome causing continual tension and anxiety or, as an inadequate coping in these women in many areas of life indicated by raised neuroticism and trait anxiety scores. Our results suggest that this is not true for patients with "Pure PMS" (Watts 1980).

GENERAL CONCLUSIONS

- a majority of patients seeking help for PMS keep their symptom pattern between cycles regarding cyclicity and preovulatory symptoms
- a heterogenous group of PMS patients show no change in severity between consecutive cycles, but subgroups of PMS patients seem to react differently when subjects to evaluation, the "Pure PMS" group feeling worse during the first cycle under evaluation and the "PM aggravation" group feeling better during the first cycle
- the severity-score seems to be a reliable and valid instrument for assessment of the severity of PMS
- in general, women with PMS have a decreased sexual interest premenstrually, less pronounced in the group with high levels of androgens and SHBG. A possible hormonal difference was found between the "Pure PMS" group and the "PM aggravation" group, the former having a lower testosterone level
- the agreement was good between different methods used for diagnosis of PMS
ACKNOWLEDGEMENTS

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