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Premenstrual Syndrome: A Natural Approach to Management

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ABSTRACT: *Premenstrual syndrome (PMS) is a disorder that occurs during the luteal phase of the menstrual cycle, producing a diverse number of physical and emotional changes. The most common symptoms of PMS include bloating, backache, breast tenderness, food cravings, fatigue, irritability, and depression. The timing of the appearance and disappearance of symptoms, rather than the presence of specific symptoms, is of more importance in the diagnosis of PMS. The direct cause of PMS is unknown, although there are numerous theories relating to hormonal imbalances, nutritional insufficiencies, and psychologic factors. A nutritional approach to PMS that takes into account the complex interactions of all bodily systems that influence hormonal balance and neuroendocrine function, with an emphasis on the liver, is recommended. The nutritional factors that have been studied include vitamin B_6, magnesium, zinc, choline, vitamin E, and essential fatty acids, in addition to weight management and stress reduction. Herbal therapies have also proven beneficial in the management of PMS.*

PREMENSTRUAL SYNDROME

Cyclic symptoms in women of reproductive age have been recognized for thousands of years. First appearing in the medical literature in 1931 and originally termed "premenstrual tension," this condition has been renamed "premenstrual syndrome" (PMS) in an effort to take into account the different clinical presentations that may occur.[1] PMS did not receive much attention until the 1980s and despite an abundance of recent research, information regarding the etiology, diagnosis, and management is often contradictory and incomplete.[2]

PMS is the cyclic recurrence of a group of symptoms that appear during the luteal phase of the menstrual cycle (1 to 2 weeks prior to menses) and diminish significantly or disappear completely several days after the onset of menstruation. PMS encompasses a wide variety of symptoms; however, there are no symptoms that are unique to and diagnostic of PMS. To be diagnosed with PMS, three conditions must be met: a woman's symptoms must correspond with the luteal phase and be absent during the follicular phase of the menstrual cycle; the symptoms should have some degree of monthly recurrence; and the symptoms must be severe enough to interfere with some aspect of lifestyle. Daily records confirming the severity, impact, and timing of symptoms are essential in confirming the diagnosis and ruling out more chronic disorders.[1,3]

- **PMS Symptom Complex**

Up to 150 different symptoms have been associated with PMS, ranging from psychological symptoms such as irritability, mood swings, and depression, to physiological symptoms such as bloating, breast tenderness, and headache (Table 1).[3-5] These diverse symptoms may range from mild to incapacitating. In some women a single symptom, such as depression, may predominate, whereas others may have several symptoms.[1]

Table. 1 Symptoms of PMS

Psychological	Physiological
Irritability	Bloating
Tension	Weight gain (fluid)
Anxiety	Breast tenderness
Mood swings	Headache
Aggression	Pelvic discomfort and pain
Loss of concentration	Change in bowel habits
Depression	Increased appetite
Forgetfulness	Sugar cravings
Mental confusion and fatigue	Generalized aches and pains
Insomnia	Physical tiredness
Change in libido	Weakness
Crying spells	Clumsiness

In 1987, the American Psychiatric Association (APA) concluded that *severe* PMS is actually a psychiatric disorder and introduced a new subset of PMS entitled "late luteal phase dysphoric disorder" (LLPDD). According to the APA's definition, the essential feature of LLPDD is a pattern of clinically significant emotional and behavioral symptoms that repeatedly occur during the luteal phase of the menstrual cycle.[3,6]

- **Incidence and Impact**

PMS is one of the most common disorders of women of reproductive age.[4] Numerous epidemiologic surveys have shown PMS to consistently affect between 25% and 50% of women in this age group.[7,8] However, reports of the incidence of PMS vary from 0% to 60% depending on the diagnostic tool used to measure symptoms.[9] The incidence of PMS peaks among women age 30 to 40, but studies have shown that adolescents frequently suffer the effects of PMS as well.[10] With a large number of women in the work force, the impact of PMS on productivity as a result of absenteeism and work inefficiency undoubtedly has a huge impact on the economy.

- **Etiology**

Although the symptoms of PMS have been well defined, the etiology is still unclear. Over the years, researchers have proposed numerous theories, including excessive estrogen, progesterone deficiency, elevated prolactin, increased aldosterone, nutritional insufficiencies, and various psychologic factors (Table 2).[3,4,9,11] The lack of reproducibility of studies designed to demonstrate measurable changes in hormones associated with PMS suggests that the true etiology of PMS is the consequence of complex and poorly understood interactions between ovarian hormones, endogenous opioid peptides, neurotransmitters, prostaglandins, and the circadian, peripheral, autonomic, and endocrine systems.[4,12-15]

Table 2. PMS Etiology Theories

Excess estrogen	Prostaglandin deficiency or excess
Progesterone deficiency	Endogenous hormone allergy
Fluid retention	Endogenous opiates
Hyperprolactinemia	Psychogenic
Vitamin B_6 deficiency	Thyroid abnormality
Hypoglycemia	Serotonin deficiency

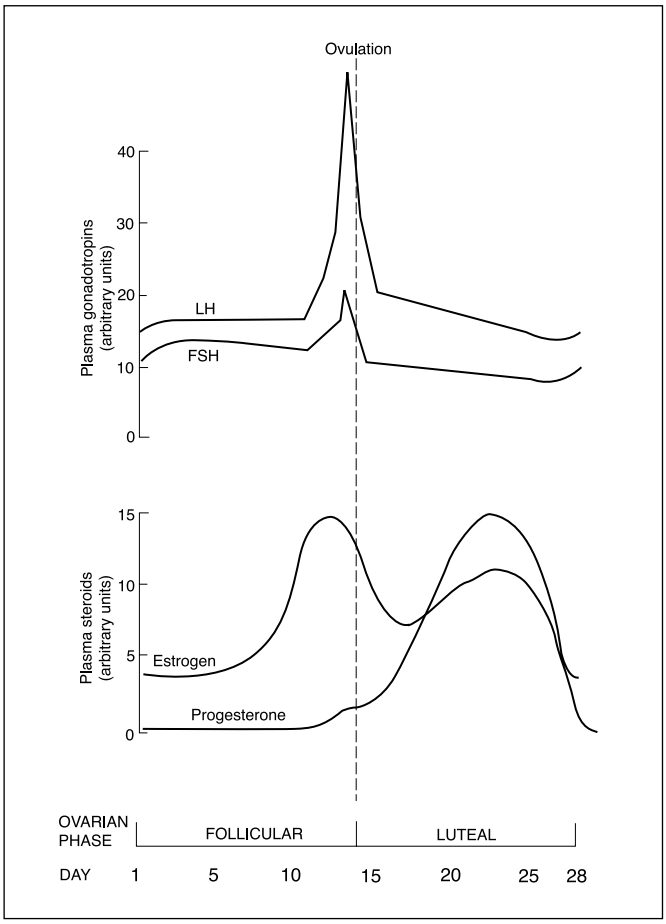
UNDERSTANDING THE MENSTRUAL CYCLE

In order to have a greater understanding of the potential etiologic factors of PMS and how nutrients affect female biochemistry, it is important to understand the menstrual cycle, neuroendocrine function, and the metabolism of estrogen, progesterone, and other hormones.

The menstrual cycle, which can be divided into a follicular phase and a luteal phase, results from complex interactions between the hypothalamus, pituitary, and ovary. This cyclical process, which requires clear communication between the participating glands, is regulated in part by complex changes in the concentrations of four hormones: follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E), and progesterone (P) (Figure 1).[16] Slight alterations in the normal cyclical elevations and/or depressions of these hormones may produce an exaggerated tissue response.[4,17-19]

The early *follicular phase*, which commences with menstruation, is characterized by high circulating levels of FSH and low levels of LH, E, and P. The high level of FSH stimulates follicular growth, E synthesis, and proliferation of the endometrium. E levels rise sharply as the maturation of the dominant follicle progresses, triggering the midcycle LH surge. The LH surge induces ovulation, which occurs 14 days before menstruation, and marks the end of the follicular phase. In the luteal phase, LH causes the granulosa cells of the ruptured follicle to luteinize and form the corpus luteum, which secretes large quantities of P and some E. The luteal phase is marked by an abrupt and transient fall in ovarian production of E and an increase in P secretion by the corpus luteum, which peaks midway through the luteal phase. LH and FSH return to previously low levels.

Figure 1. Hormonal Changes During the Normal Menstrual Cycle



Failure of ovum fertilization is associated with the degeneration of the corpus luteum and a rapid drop in circulating E and P. This fall in E and P results in disintegration and shedding of the endometrium (menstruation), marking the first day of the next cycle.[1,20]

- **Metabolism & Function of Estrogen and Progesterone**

Estrogens are a family of hormones produced predominantly by the ovaries, but also by the corpus luteum and peripheral aromatization of androgens in the liver, skin, and adipose tissues. Estradiol is the primary estrogen of ovarian origin. Increased production of estrogens may result from increased ovarian secretion, ovarian tumors, and functional cysts. However, the most common cause of estrogen excess is increased aromatization of androgens in peripheral tissues.[20,21]

Progesterone is produced and secreted by the corpus luteum at midcycle (around day 14) under the influence of luteinizing hormone (LH) from the pituitary gland. Corpus luteum production of progesterone may be dependent on a number of nutritional factors, including magnesium and vitamin E, while a deficiency may result from overconsumption of animal fats. Secondary causes of deficient corpus luteum production are defective liver, heart, or kidney function and hyperprolactinemia.[21]

Both estrogen and progesterone act synergistically to prepare the female reproductive system for pregnancy. Estrogens stimulate the growth and development of tissues involved in reproduction, such as the endometrium, and act anabolically to influence bone and cartilage growth. They also cause vasodilation and heat dissipation by affecting the peripheral blood vessels.[20] In contrast, progesterone reduces the proliferative actions of estrogen on the endometrium and converts it from proliferative to secretory in preparation for fertilization. Progestins also decrease peripheral blood flow, thereby decreasing heat loss, so that the body temperature tends to increase during the luteal phase of the menstrual cycle, which is used as an indicator of ovulation.[20]

- **Estrogen, Progesterone, and PMS**

Alterations or imbalances of the circulating ratios of estrogen and progesterone based on the time of the month can aggravate the target tissues of these hormones. This potential tissue aggravation is based on the anabolic properties of estrogen and the secretory properties of progestins (Table 3).[14]

Table 3. Action of Feminine Hormones

Estrogen Excess/Hypersensitivity May Contribute To:

- Bloating, weight gain, and water retention as a result of sodium retention.
- Excess central nervous system stimulation, producing irritability and anxiety.
- Possible histamine release, which may promote skin and allergy problems.
- Increase in pro-inflammatory prostaglandins, producing a tendency toward pain, redness, and swelling.
- Relative increase in prolactin, a hormone that can produce depression and dysphoria, breast tenderness and pain.
- Increased contraction and cramping of uterine smooth muscles.

Relative Progesterone Excess May Contribute To:

- Decreased libido.
- Water retention due to renin stimulation and aldosterone formation.
- Symptoms of excess corticosteroids.
- Depression and fatigue.
- Sedation.
- Hyperinsulinemia.

The role of increased levels of estrogen in the etiology of PMS has been described for many years and may be due to 1) an overproduction of estrogen within the body, 2) a relative increase of estrogen due to low progesterone secretion by the corpus luteum, 3) a decreased estrogen clearance rate, and/or 4) an increased target tissue sensitivity to steroid sex hormones (prostaglandin mediated).[4,8,14,17-19,21]

Progesterone excess is observed less frequently. The administration of synthetic progestins that resist liver conjugation and excretion or depressed levels of estrogen may account for true or relative progesterone elevation.[20] A relative increase in the progesterone/estrogen ratio in severely depressed, withdrawn, and suicidal PMS patients has been observed. Therefore, careful screening before administering progesterone therapy for patients exhibiting this symptom profile is advised.[14]

- **Enterohepatic Circulation and Excretion of Estrogen**

Enterohepatic circulation involves the metabolism of a substance in the liver, excretion into the bile, passage into the lumen of the intestine, reabsorption through the intestinal wall, and then return to the liver in the portal circulation. Many endogenous compounds have an enterohepatic circulation, including estrogens, folic acid, vitamin B_{12}, bile acids, cholesterol, protoporphyrin, metabolites of vitamin D, and xenobiotics.[22] Disruption at any phase of this process can contribute to an increased body burden of endotoxins, malabsorption of fat-soluble vitamins and essential fatty acids, and steroid hormone imbalances.

Several factors determine whether estrogens or other substances are secreted from the liver into the bile, including successful conjugation and optimal bile acid synthesis. The compound generally is conjugated to a polar group such as glucuronic acid, sulfate, taurine, glycine, or glutathione before secretion into bile. Glucuronidation is involved in the conjugation of estrogens as well as xenobiotics and bile acids and requires niacin, vitamin B_6, and magnesium to take place.[20] Magnesium increases glucuronyl transferase activity, an enzyme directly involved in hepatic glucuronidation of estrogen.[20]

Bile acid synthesis is dependent on the enzyme 7-alpha-reductase, the rate limiting factor in bile acid production. This enzyme, in turn, is vitamin C dependent.[20] Other cofactors determining the fate of smooth flowing bile are pantothenic acid and taurine.[22] Pantothenic acid participates in the biosynthesis of cholesterol (HMG-CoA reductase) an essential component of bile. The amino acid taurine plays a key role in bile conjugation and decreasing platelet aggregation sensitivity, which affects the circulation of the blood.[22]

The Liver

Decreased clearance rate of estrogens by the liver can be due to a variety of factors. Magnesium and B vitamin insufficiencies may decrease the liver's ability to successfully form estrogen conjugates, ultimately resulting in reductions in fecal excretion. This may explain why some physicians observe improvement in premenstrual symptoms with the administration of B-complex vitamins. Biskind et al., during the 1940s, postulated that a deficiency of B vitamins could cause a cyclical excess level of circulating estrogens because of decreased hepatic clearance, producing PMS.[23] His patients improved using B vitamins.[24] More recently, a group of researchers have been exploring the role of B-complex vitamin insufficiencies as contributing to clinical depression in young adults and the elderly.[25,26]

While individual B vitamins perform specific functions with regard to hormone regulation and neurotransmitter synthesis, a true B vitamin deficiency/PMS connection cannot be established in the average woman suffering from PMS.[13,27-29] However, mild liver dysfunction may produce enough endogenous waste to

interfere with communication between the pituitary, adrenals, and ovaries. There are many xenobiotics that are known to occupy receptor sites on the ovaries and other glands, thereby inhibiting optimal function. B vitamins are water-soluble, are eliminated from the system rapidly, and require continuous presence in the diet for optimal liver function to proceed.[20]

Hepatic function may also be compromised by fatty infiltration of the liver, which can be caused by increased alcohol consumption, or increased consumption of saturated fats. The presence of lipotropic factors in the diet, such as choline, folic acid, and vitamin B_{12}, are important elements in the prevention of hepatic lipid accumulation and in the maintenance of normal hepatic function.[22]

Alcohol, sugar, caffeine, and fatty foods can all compromise liver function. Foods that introduce exogenous estrogens, such as meat and dairy products, as well as foods commercially grown with the use of synthetic pesticides and fertilizers, will further compromise the liver and add to the estrogen burden in the body.

Another important route of estrogen excretion is as estrogen conjugates eliminated by the kidneys. Due to kidney involvement during the management of PMS, women should consume eight glasses of water daily to enhance the normal urinary excretion of estrogen conjugates.

Intestinal Tract

The gastrointestinal (GI) tract plays an important role in the balancing of estrogen within the body. After hepatic formation of estrogen glucuronide conjugates, excretion occurs via the biliary tract. The estrogen glucuronide bonds must be maintained throughout the length of the intestinal tract to have the estrogen successfully eliminated with fecal material. If the gut transit time is lengthened, there are consequent changes in the flora of the GI tract that increase the production of beta-glucuronidase-producing bacteria. Beta-glucuronidase cleaves the estrogen-glucuronide linkage and liberates biologically active estrogens, which can then be reabsorbed. Beta-glucuronidase is increased in diets high in protein and fat, resulting in increased estrogen recycling.[30]

Optimal intestinal function requires adequate digestive secretions, a high fiber intake, and an intestinal microbial balance. Goldin et al. demonstrated a positive correlation between fiber intake and fecal estrogen excretion and an inverse correlation between fecal excretion of estrogen and plasma estrogen levels in a study of vegetarian and omnivorous women.[30] These results suggest that dietary fiber can influence estrogen clearance.

- **Other Hormonal and Neuroendocrine Factors**

Dopamine and Serotonin

Dopamine and serotonin are neurotransmitters that influence mood and appetite. Ovarian hormones affect the synthesis and uptake of neurotransmitters, which can result in the manifestation of physical and behavioral symptoms of PMS. Estrogens may suppress the action of dopamine, which is a major hormonal modulator of the homeostatic balance of the active amines important for creating relaxation and mental alertness. Dopamine exerts an inhibitory effect on prolactin secretion and influences the adrenal glands and kidneys, preventing sodium and water retention.[31-34] A relative deficiency of dopamine can aggravate edema and interstitial fluid shifts during the menstrual period. Vitamin B_6, magnesium, and vitamin C are essential cofactors for the proper production of dopamine.[18,35,36]

According to recent theories, serotonin may play an important role in PMS or late luteal phase dysphoric disorder (LLPDD). One study found that compared to a control group, serotonin levels of women with PMS were significantly lower during the luteal phase, which may account for some of the psychological symptoms of PMS such as depression, anxiety, headaches, and mental confusion.[3] Low serotonin levels may also trigger early ovulation and a shift in estrogen and progesterone patterns, which could account for some of the physical symptoms of PMS such as breast tenderness, bloating, and food cravings.[3,37,38] Because exercise stimulates endorphin production it may provide some relief from PMS symptoms.[3]

Prostaglandins

Prostaglandins (PGs) are hormone-like compounds that function as mediators of a variety of physiological responses such as inflammation, vascular dilation, and immunity. They are synthesized in virtually all cells of the body, including the brain, breast, gastrointestinal tract, kidney, and reproductive tract. The anti-inflammatory series 1 PGs are derived from linoleic acid (LA), which is converted to gamma-linolenic acid (GLA), while arachidonic acid, found in animal fats, is the precursor of the pro-inflammatory series 2 PGs and leukotrienes. Imbalances in the PG series could produce inflammation in tissues, thus stimulating PMS.[8,18] Two studies have shown that women with PMS have abnormal serum levels of PGs and their precursors.[4] Lower levels of circulating PGE_1 may sensitize reproductive tissues to estrogens, producing a vulnerability to normal ovarian hormone cycling.[8]

Nutrients known to increase the conversion of EFAs to the anti-inflammatory series 1 PGs include magnesium, vitamin B_6, zinc, niacin, and vitamin C. Factors that interfere with the production of anti-inflammatory PGs include diets rich in saturated fats, alcohol consumption, and catecholamines released from the adrenal medulla during stress.[17,18]

Prolactin

Prolactin is a hormone secreted by the pituitary gland that can influence estrogen and progesterone secretion. Excess secretion of prolactin, or hyperprolactinemia, is one of many etiological factors proposed as being a potential cause of PMS.[31,39] Elevated levels of prolactin create states of dysphoria, breast tenderness, water retention, and depression, and decrease the life and action of the corpus luteum, thus decreasing the production of progesterone. Estrogens are known to enhance the release of prolactin, while dopamine inhibits prolactin secretion.[31]

Physiological factors that may promote prolactin overproduction and/or abnormal tissue sensitivity to prolactin are excess estrogen levels, stress, hypothyroid, and deficiencies of dopamine, vitamin B_6, zinc, vitamin C, and magnesium.[35,40] Dietary factors can influence elevated levels of prolactin production, such as diets high in protein and total unsaturated fats.

Endorphins

Endorphins are neuropeptide hormones of the endocrine system that participate in the regulation of diverse physiologic functions such as pain transmission, emotions, appetite control, and hormone secretion.[21] It has been postulated that a change in progesterone level or estrogen to progesterone ratio during the luteal phase of the cycle may lead to changes in endorphin activity during the days leading to menstruation. These changes in endorphin levels may have important effects on mood and behavior and, through the possible mediation of prostaglandin levels, have physical effects as well.[12] Stress-related distortions in the release of beta-endorphin may be related to some PMS symptoms.

PMS MANAGEMENT

The current treatment options for PMS vary considerably and reflect the multiple etiology theories and the complexity of hormonal interactions likely involved in PMS. They include ovulatory suppressants, progesterone, nutritional therapies, diuretics, bromocriptine, prostaglandin and melatonin inhibitors, antidepressants or other psychopharmaceuticals, and psychosocial therapies such as relaxation training, support groups, exercise, and dietary changes.[9,41] Progesterone is the most widely used treatment for PMS; however, its efficacy has been questioned.[4,14,42] Unfortunately, no one treatment has proven completely successful, and many of these therapies are not without side effects.[4,41]

In an effort to find safer, less extreme approaches to PMS management, researchers have explored the influence of diet and lifestyle modification and nutritional supplementation on female neuroendocrine function. The B-complex vitamins, magnesium, ascorbic acid, and essential fatty acids have the capability of influencing the same hormonal feedback systems as prescription treatments for PMS. However, these natural substances focus on improving the way these systems interact by influencing the transport, reception, and elimination of peptide and steroid hormone levels, rather than directly decreasing or increasing a specific hormone.

- **Nutritional Support in the Treatment of PMS**

Recent research findings increasingly suggest that nutritional factors may play significant roles in influencing both the production and metabolism of various hormones, thus playing an important role in the management of PMS. Numerous research studies have shown that nutritional supplementation may be effective in controlling symptoms of PMS.[43-46] The focus of nutritional intervention is on improving liver function, because the biochemistry of hepatic estrogen conjugation emphasizes the role that nutritional deficiencies may play in depressing the clearance rate of estrogens.

Vitamin B_6

Vitamin B_6 (pyridoxine hydrochloride) is an important cofactor for enzymes involved in estrogen conjugation in the liver; for the synthesis of several neurotransmitters including dopamine, serotonin, taurine, and norepinephrine; and for the synthesis of certain prostaglandins.[22] With decreased levels of B_6 in the body, the liver cannot conjugate estrogens, thus causing an increased blood level of estrogens. Vitamin B_6 also stimulates cell membrane transfer of magnesium and increases intracellular magnesium.

There is much documentation in the medical literature to correlate the management of PMS with vitamin B_6.[47-49] In one study, 70 women with PMS were evaluated to assess the effectiveness of B_6 on their symptoms.[49] The results suggest that B_6, in dosages ranging from 40 to 100 mg daily, is an effective and well tolerated form of treatment. It provided considerable benefit to over half of the women, relieving headaches, edema, bloatedness, depression, and irritability. In another study, Abraham and Hargrove demonstrated that 21 of 25 women with PMS receiving vitamin B_6 (500 mg/day) for three consecutive menstrual cycles in a double-blind, cross-over study showed significant clinical benefit.[48]

The liver is the primary organ responsible for the metabolism of vitamin B_6, where dietary pyridoxine is converted to its active coenzyme form, pyridoxal-5'-phosphate (PLP). This activation is dependent upon zinc, vitamin B_2, and magnesium. These nutrients, along with decreased dietary levels of pyridoxine, may play rate limiting roles in the tissue levels of the coenzyme form of B_6.[22] Because the active form of vitamin B_6 is hydrolyzed in the gut to its precursor form before it can be absorbed, the use of dietary supplements in the form of PLP, rather than pyridoxine, is not necessary.[50]

Magnesium

Because magnesium plays such an integral part in normal cell function, magnesium insufficiency may account for a wide range of PMS symptoms.[51] Studies have shown that erythrocyte magnesium levels in patients with PMS are significantly lower than that of control groups of normal women,[11,52] and magnesium supplementation may help to relieve mood-related PMS symptoms.[53]

Magnesium's role in PMS symptomatology is multifactorial because of its many roles in cellular metabolism. It is involved in 1) the synthesis of dopamine,[3,46,51] 2) estrogen conjugation by directly increasing the activity of glucuronyl transferase, an enzyme involved in the hepatic glucuronidation of estrogens,[34,46] 3) the activation of the B vitamins, especially vitamin B_6,[34] 4) energy production, 5) the synthesis of second messenger cAMP (cyclic AMP), which plays a crucial role in hormone balance,[3,20] and 6) the conversion of LA to GLA, a rate limiting step in anti-inflammatory series 1 PG synthesis.[14]

Magnesium depletion can be compounded by the use of diuretics, increased alcohol and dietary fat intakes, a high intake of dairy products, stress, and malabsorption syndromes.[3,54]

Choline

Choline acts as a methyl donor and is essential for proper liver function. As a lipotropic nutrient, it prevents the deposition of fat in the liver. Choline deficiency results in liver dysfunction, and also compromises renal function. Choline is also a precursor for the synthesis of the neurotransmitter acetylcholine, which is involved in memory and coordination, as well as phospholipids, the main components of cell membranes.[22,55]

Taurine

Taurine provides support for the liver by acting as a conjugator and detoxifier of certain xenobiotics and other exogenous toxins, in addition to endogenous compounds. Taurine may also act as a

free radical scavenger to prevent cell damage. Because vitamin B_6 is a cofactor in the biosynthesis of taurine, a B_6 deficiency can reduce taurine synthesis.[22]

Essential Fatty Acids

Essential fatty acids (EFAs), such as gamma-linolenic acid (GLA), are vital precursors of prostaglandins, which regulate the effects of sex hormones. A deficiency of EFAs, either due to inadequate linoleic acid intake or failure of normal conversion of linoleic acid to GLA, has been postulated to cause abnormal sensitivity to prolactin and the features of PMS.[46] In some studies, women treated with GLA in the form of evening primrose oil showed improvement in symptoms of depression, irritability, breast pain and tenderness, and fluid retention associated with PMS.[17,46]

A high consumption of saturated animal fats, a source of arachidonic acid, can result in an overproduction of pro-inflammatory prostaglandins. Moderate to high consumption of alcohol and deficiencies of zinc, magnesium, and vitamin B_6 also reduce GLA formation, a precursor for the anti-inflammatory prostaglandins.[56]

Phytoestrogens

Phytoestrogens are a family of compounds found in plants, especially the soybean, which have some estrogenic and/or anti-estrogenic activity.[57] In addition to their weak estrogenic effects, phytoestrogens may act as anti-estrogens by competing for estrogen-receptor sites with the more active endogenous estrogens. Women may be able to create a significant positive impact upon their hormone levels and ratios by the inclusion of soy protein in their diets.[58]

Other Nutrients

Additional nutrients that may play a role in the management of PMS include zinc, vitamin E, vitamin C, and pantothenic acid.

- **Herbs and PMS**

Botanical medicines have been used for centuries throughout the world to regulate abnormal menstrual patterns and treat the symptoms of PMS.[59-64] Throughout Europe, chaste tree berry *(Vitex agnus-castus)*, or vitex, is the number one herb used to help relieve the symptoms of PMS, such as depression, cramps, mood swings, water retention, and weight gain. Vitex tonifies the endocrine system by targeting the hypothalamus-pituitary axis and regulating the synthesis of hormones. Vitex acts directly on the pituitary gland to stimulate the secretion of LH and inhibit the secretion of FSH.[65-67] Because LH stimulates the secretion of progesterone, this leads to a normal balance between estrogen and progesterone.[65] Vitex also possesses dopaminergic properties, inhibiting the secretion of prolactin by the pituitary gland.[33,64,68]

Other herbs with a long history of use in treating women's problems include cramp bark *(Viburnum opulus)*, which relaxes the uterine muscle by acting as an antispasmodic and is used to relieve cramping, along with pain in the lower back and thighs;[58,69] salvia root *(Salvia miltiorrhiza)*, which has a long history of use in promoting blood circulation, and as a tranquilizer

Table 4. Selected Botanicals for the Treatment of PMS

Common Name *(Botanical Name)*	Country of Origin	Traditional Use	Some Active Constituents
Chasteberry Fruit *(Vitex agnus castus)*	Europe	Control and regulation of female reproductive system	Monoterpene: agnuside, euroside, aucubin; flavonoids: vitexin
Licorice Root *(Glycyrrhiza uralensis)*	China, North America, Europe	Demulcent, expectorant, anti-inflammatory, spasmolytic	Triterpene saponin: glycyrrhizin, Flavonoids: liquiritin, quercetin
Crampbark *(Viburnum opulus)*	Europe, naturalized in North America 17th century	Uterine sedative, smooth muscle relaxant, diuretic spasmolytic, cardiotonic	USP* 1894; NF** 1916-60 Arbutin, valerianic acid, tannins: anthocyanins, catechins, flavonoid
Bupleurum Root *(Bupleurum chinense)*	China	Sedative, anodyne, adaptogen	Saikosaponins A, B1-B4, C-F
Dong Quai Root *(Angelica sinensis)*	China	Antianemic, regulates menses, smooth muscle relaxant	Vitamin B_{12}, ferulic acid, ligustilide, folic acid, choline, iron
Peony Root *(Paeonia lactiflora)*	China	Antimicrobial, astringent, anti-inflammatory	Monoterpene glycosides: paeoniflorin, benzoylpaeoniflorin; sterols
Red Sage Root *(Salvia miltiorrhiza)*	China	Nervine, anxiolytic, blood regulator	Diterpene quinones: tanshinones, miltirone
Ginger Rhizome *(Zingiber officinale)*	China, Pacific Rim, India	Stimulant, carminative, digestant, anti-inflammatory	Terpenoid: zingiberene; gingerols
Wild Lettuce Leaf *(Lactuca elongata)*	North America, Europe	Relaxant, anodyne, diuretic	USP* 1820-1926 Lactucin, lactucopicrin, inulin

* United States Pharmacopoeia ** National Formulary

and sedative;[70-73] ginger root *(Zingiber officinale)*, an inhibitor of prostaglandin and leukotriene biosynthesis, has been used for thousands of years for its anti-inflammatory properties;[74,75] wild lettuce leaf *(Lactuca elongata)* has been used since ancient times for its pain-relieving and calmative effects and is used as a mild sedative;[61] and licorice root *(Glycyrrhiza uralensis)* minimizes the effects of stress by supporting the adrenal glands, and aids in digestion.[61]

- **PMS and Traditional Chinese Medicine (TCM)**

Ancient Chinese medicine has a fully developed botanical system for managing gynecological problems (Table 4).[59-64] Interestingly, one of the most commonly used TCM formulas, employing the roots of bupleurum *(Bupleurum chinense)*, dong quai *(Angelica sinensis)*, peony *(Paeonia lactiflora)*, and licorice *(Glycyrrhiza uralensis)*, focuses on liver function and strengthening the blood.[76] The traditional Chinese strategy behind this formula is to "release constrained liver ch'i," and correct "blood deficiency."[59] This parallels what may be the role of enterohepatic circulation in the management of estrogen. These plants give the liver the boost and nutrition it requires to establish the unobstructed flow of bile. Perhaps the herbs, such as dong quai, function like B complex vitamins to nourish and sustain the movement and quality of the blood. This TCM approach has proved successful for hundreds of years.

DIETARY AND LIFESTYLE INFLUENCES ON PMS

- **Diet**

Dietary factors appear to play an important role in the etiology of PMS. Compared to symptom-free women, PMS patients consume more refined sugar, refined carbohydrates, sodium, and dairy products and less B vitamins, iron, zinc, and manganese.[54] Studies have shown that vegetarian women have lower serum estrogen levels when compared to omnivorous women.[30] They found that the vegetarians consumed less total fat and more fiber than omnivores. This implies that increased dietary fiber and decreased fat intakes may be significant contributors to lowered serum estrogen levels in women.

Over time, the consumption of refined sugar may deplete the body of its reserves of chromium, manganese, zinc, magnesium, and most of the B vitamins because these nutrients are required for the metabolism of glucose.[54] Sugar also increases the tendency to hypoglycemia, particularly premenstrually, giving rise to sugar cravings, irritability, and headaches.[56] High sodium intake combined with large intakes of refined sugar can impact water retention. Refined sugar triggers insulin release, suppressing ketoacid formation and thereby causing decreased kidney clearance of excess sodium and water.[54]

Diminished liver function can actually cause an increase in circulating estrogens, thus potentiating their activity in the body. Because the liver is dependent on B vitamins to perform these functions, any lifestyle habit that depletes B vitamins will interfere with liver function. These include alcohol, caffeine, poor nutrition, and emotional and physical stress. Alcohol not only increases the body's needs for B vitamins, magnesium, and zinc, but also damages the liver, which interferes with hormone metabolism.[56]

A recommended diet centers around complex carbohydrates, including whole grains, legumes, vegetables, and fruits and the avoidance of polyunsaturated vegetable oils, refined sugar, alcohol, and caffeine-containing foods and beverages. It is also recommended to limit intake of dairy products and animal fats. Women suffering from edema should also avoid salt to reduce fluid retention.[67]

- **Obesity**

Obesity and excess adipose tissue in relation to lean body mass affect estrogen/progesterone ratios. Circulating androgens are metabolized by adipose tissue into active estrogens that influence the body balance of estrogens. Studies have shown that the extent of this conversion is significantly correlated with excessive body weight.[77] Specific dietary interventions may be very helpful in both reducing adipose aromatase activity and facilitating more desirable estrogen metabolism and excretion. Thus, a weight management program is essential in the treatment of PMS.

- **Stress**

Stress appears to exacerbate premenstrual complaints by affecting hormone production and stimulating the secretion of a range of other hormones that interfere with the sex hormones: adrenocorticortropic hormone (ACTH), cortisol, the catecholamines epinephrine and norepinephrine, and aldosterone, a corticosteroid that causes renal sodium retention.[56] The demands placed on women today may contribute to a prolonged "stress overload," which can have an adverse impact on hormonal balance and lead to symptoms of PMS. Caffeine, by increasing the effects of adrenaline, increases the effects of stress and aggravates symptoms such as anxiety, tension, irritability, and hypoglycemia.[56] Studies have shown that women who consume large amounts of caffeine are more likely to suffer from PMS.[46]

An important part of stress reduction is regular exercise, which helps to improve blood circulation and increase endorphin and neurotransmitter levels.

HEALTHY HORMONE LEVELS NOW FOR A HEALTHIER TOMORROW

Throughout a woman's life the relative production and metabolism of estrogens, as well as other endogenous messenger substances, are likely to be important in determining risk for the development of at least some endocrine-related health problems. Interventions which can help to balance these factors may not only be helpful in treating PMS, but could lower the risk for some of these hormone-related health problems in the future.

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