The Herbal Treatment of Hormonally Influenced Mood Changes (PART 2of 2)

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Menopause

Menopause literally means stopping menstruation and has occurred once a year has elapsed since the last period. Menopause that occurs between the ages of 45 and 55 is considered normal. Premature menopause is when menstruation ceases before age 40. This can occur if the ovaries fail prematurely; menopause can also be deliberately induced by drugs for medical reasons (e.g. to treat conditions such as endometriosis or uterine fibroids), or prematurely brought on by surgery, radiotherapy, chemotherapy and other drugs, or caused by certain illnesses.

The years leading up to the menopause, when hormone fluctuations begin, are often characterized by menstrual cycle changes that vary from longer or shorter cycles to totally erratic menstrual patterns. This time is known as the peri-menopause and can sometimes be accompanied by mood changes and PMS, especially PMS-D symptoms.

Etiology of menopausal mood changes

About one woman in ten experiences depression, anxiety or feelings of inadequacy around menopause, but there is some dispute as to why these symptoms occur. Some researchers believe that mood changes are related to hormone changes, others have found that these symptoms have their genesis in psychosocial factors and are more common when women have pre-existing problems, difficulties with coping generally, or PMS with mood changes.[1]

The psycho-social theory

According to this theory, a woman's attitude to menopause and aging affect her menopausal experience. Just as some women experience menopausal years with a renewed sense of self discovery and freedom, other women may experience a variety of psychologically distressing circumstances such as children leaving home, declining health, the death of a spouse and loss of social roles or support networks. These factors can spark depressive symptoms or exacerbate pre-existing mood disorders.[2] Women with a negative attitude to either menopause and/or aging were found to be much more likely to experience problems than women who saw menopause and aging as positive experiences.[3]

The hormone fluctuation theory

The theory that fluctuations in estrogen and progesterone have an effect on the brain and neurotransmitter levels is gaining considerable support due to research that has been carried out in recent years. Estrogen exerts profound effects on mood, memory and mental state through its action on a variety of neurotransmitter mechanisms in the brain. When brain estrogen levels drop due to peri-menopausal transition and menopause itself (as well as premenstrually), a drop in neurotransmitters may be affected.[4] The functional deficiency in estrogen leads to a functional deficiency in serotonin, dopamine, endorphins and noradrenaline.[5] Research has shown that estrogen stimulates a significant increase in dopamine D_2 receptors as well as an increase in the density of serotonin binding sites in areas of the brain concerned with mood, emotion, cognition and behavior.[6] In addition, during the peri-menopausal years, progesterone levels can remain normal resulting in competitive inhibition of androgen and estrogen receptors, exacerbating dysphoric states.[7] Moreover, the stress associated with mood changes can impact on adrenal function and may cause estrogen levels to drop further and aggravate menopausal symptoms.[8]

Conventional treatments resulting in increased estrogen levels or augmentation of estrogen function have proven effective in treating and preventing depression in women.[9,10] In one study, menopausal women recovering from depression had increasing levels of estrogen in their urine as they improved.[11] Conversely, a study examining depression amongst women in their 50's found that women using estrogen therapy (HRT) were more depressed than women who had never used HRT. These findings, however, could be attributed to treatment bias as a high proportion of depressed and symptomatic women were expected to seek HRT at the outset. This was borne out by the fact that the women in the study on HRT were found to have higher concurrent anti-depressant use.[12]

Fatigue can have a negative impact on depression and mood, but might not always be related to the menopause. Any of the usual causes of fatigue

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Severe Depression with Confusion/ Poor Cognition/Insomnia	
Hypericum perforatum	30
Cimicifuga racemosa	20
Rosmarinus officinalis	30
Lavandula officinalis (Lavender)	20
Dose: 7 mL BID	100 mL

The Important Herbs and Nutrients in Profile

Herbs

St John's Wort

Hypericum perforatum is one of the most widely used herbs for mild and moderate depression. *Hypericum perforatum* has been used as a nervine, astringent, expectorant and vulnerary. Grieve reports that the name Hypericum is derived from the Greek, meaning 'over an apparition,' in reference to the belief that it could cause evil spirits to flee.[19] Abnormal mental states were originally believed to be caused by evil spirits, hence the folk use of *Hypericum perforatum*.

Many of the common menopausal symptoms such as hot flushes, night sweats and depression, were once thought to be related to debility rather than hormonal disturbance and Mills reports that *Hypericum perforatum* was used traditionally for menopause as a restorative treatment.[20] Indeed, in clinical experience, *Hypericum perforatum* combined with *Vitex agnus castus* is an extremely effective treatment for most peri-menopausal mood changes. This may be due to a dual effect from *Hypericum perforatum* – the first through interaction with serotonin receptors leading to a more relaxed mood; the second on the endocrine system via the indirect improvement on estrogen levels seen when stress levels are reduced. The well-known role for *Vitex agnus castus* is as a dopaminergic analogue with the ability to influence hormone levels, but the action of *Vitex agnus castus* on dopamine receptors points to a possible additional direct action on mood.

Most practitioners will be familiar with the research on *Hypericum perforatum* proving its efficacy and safety in the treatment of depression. Despite the quantity of research to date, however, the exact mechanism of action and identification of those constituents responsible for the observed effects are still unclear. Some studies have ascertained different results, and recent investigations have questioned whether hypericin is the most active principle.[21, 22]

One study determined that the antidepressant activity of Hypericum was due to the inhibition of serotonin uptake by post-synaptic receptors.[23] Another study found Hypericum extract was able to inhibit the uptake of serotonin, dopamine and norepinephrine as well as down-regulating ß-adrenergic receptors and significantly up-regulating central serotonergic receptors. Thus the authors postulated that Hypericum elicits a similar effect to tricyclic antidepressants.[24] *Hypericum perforatum* has also been shown to reduce the expression of serotonin receptors, inhibit catechol-O-methyltransferase, weakly inhibit MAO-A & MAO-B activity and suppress interleukin-6 (indirectly inhibiting corticotrophin-releasing factor and other regulatory adrenal hormones).[25]

A recent study has shown that alcoholic extracts of Hypericum inhibit the enzyme, dopamine-β-hydroxylase responsible for the breakdown of dopamine, but have no effect on enzymes involved in the synthesis of dopamine (e.g. tyrosinase and tyrosine decarboxylase).[26]

Serotonin and Mood Changes

The neurotransmitter 5-hydroxytryptamine (5HT) or serotonin, has received significant attention in recent years regarding its role in the etiology of depression, anxiety and other nervous system disorders such as schizophrenia and obsessive-compulsive disorders. As serotonin is known to act in three major areas of the body – the GIT, blood vessels, and CNS – it has also been implicated in such diverse conditions as hypertension, obesity, stroke, migraine, and nausea.

Serotonin's effects on the CNS include control of appetite, sleep, memory and learning, mood, behavior, and endocrine regulation.[27] Serotonin acts by binding to a number of different receptors subtypes (the exact number of which continues to increase),[28] eliciting either an inhibitory or excitatory post-synaptic potential.[29] Depression that is believed to be caused by relative deficiency of serotonin can be treated through agents that stimulate its synthesis and release; inhibit its storage or re-uptake; or through mimicking its action at post-synaptic receptors.[30] *Hypericum perforatum* has been found to have an impact on serotonin uptake.

Kava Kava

Kava, *Piper methysticum*, has a long-standing traditional use amongst the inhabitants of the South Pacific Islands. As a beverage, it is ritually used to induce relaxation, improve social interaction and promote sleep. Over recent years research has been carried out on standardized extracts of Kava, which

antidepressants fail.[47] In addition, research has now identified dopaminergic overactivity as a cause of anxiety states and panic disorders.[48] In addition, dopamine appears to be affected by declining estrogen levels leading to a functional deficiency of dopamine and depressed moods.

Black Cohosh

Traditional uses of *Cimicifuga racemosa* have been for a large range of gynecological complaints, sore throats, and bronchitis and for rheumatic conditions. A vascular antispasmodic, Cimicifuga is also recommended for hypertension, owing to a blood pressure-lowering effect of one of its constituents, acteine.[49] *Cimicifuga racemosa* is now widely used by modern herbalists for menopausal symptoms including migraines and depression. It is considered to be specific for the treatment of musculoskeletal disorders that may accompany menopause, and for the treatment of hot flushes.[50] Black cohosh can also be used during adolescence for delayed menstruation caused by hormonal imbalance, especially when associated with stress and emotional factors.[51]

Recent research has shown Cimicifuga to contain three types of hormonally active substances, one of which suppresses luteinising hormone (LH) secretion after prolonged administration, and another two of which have weak estrogen-like effects. LH surges are thought to cause flushing, and the suppression of this hormone by Cimicifuga is thought to control the symptom.[52] Cimicifuga has also been studied for its effect on the vaginal cells of menopausal women. It is found to favorably alter the cells both topically and orally and reduce symptoms of vaginal dryness and irritation. These effects are not achieved rapidly, but efficacy has been shown to be equal to synthetic estrogen.[53]

Numerous clinical trials in Germany have attested to the efficacy of Cimicifuga for menopausal complaints. Thirty-six women treated in one trial reported significant improvements in hot flushes, sweating, insomnia, nervousness, irritability and depressive psychosis after 4 weeks of treatment and highly significant improvements after 12 weeks.[54] Another very similar study of 50 women, 39 of who could not take hormone therapy, also showed highly significant results. Symptoms were significantly improved after 4 and 12 weeks, with dramatic change in mood profiles, decrease in depression, tiredness, and dejection as well as increased activity.[55] A double blind study compared to low dose estrogen therapy to Cimicifuga in 80 women with menopausal symptoms. After three months, the women had significantly improved on the herb - the 0.625 mg dose of conjugated estrogen did not have an effect.[56]

Valerian

Valeriana officinalis is an aromatic plant with an historical and contemporary use as a nervine and carminative with a paradoxical use as both a sedative and a stimulant[57]- perhaps dependent on the dose. Most of the modern research carried out on *Valeriana officinalis* has been on the pharmacological and chemical constituents of the oil, though more recently the aqueous and hydro-alcoholic extracts have been examined.

Combinations of *Valeriana officinalis* and *Hypericum perforatum* have been examined in the treatment of anxiety and depression and were shown to be more effective than amitriptyline (Tryptanol) and diazepam (Valium).[58] Other research has been carried out on *Valeriana officinalis* and its active iridoids, the valepotriates, in the treatment of insomnia and other sleep disorders.

A randomized double blind study compared the use of a benzodiazepine preparation and a Hops-Valerian preparation amongst patients suffering from sleep disorders. The trial found equivalent efficacy and tolerance between the two preparations. Parameters measured included sleep quality, fitness and quality of life determined by way of questionnaires, psychometric tests, and psychopathologic scales. Unlike the Hops-Valerian preparation, the benzodiazepine preparation caused withdrawal symptoms. The authors concluded that the Hops-Valerian preparation was a sensible alternative to benzodiazepine for non-chronic and non-psychiatric sleep disorders.[59]

One study has highlighted a possible mode of action for Valerian and its relaxing effect on the nervous system. The aqueous extract of the root was found to stimulate the release of and inhibit the re-uptake of GABA. This effect was dependent on Na^{2+} in the external medium but independent of Ca^{2+}. The mechanism of GABA release was thought to be via the reversal of the GABA carrier protein.[60]

Valeriana officinalis actually contains sufficient quantities of GABA in its chemical make-up to explain some of its neurological activity.[61] However, research to date is insufficient to fully explain the sedative or neurological actions of *Valeriana officinalis* that result in the well-known improvements in insomnia, nervous tension, depression, and anxiety. Valerian combines well with *Hypericum perforatum* and *Humulus lupulus*.

Women with a negative attitude to either menopause and/or aging were found to be much more likely to experience problems than women who saw menopause and aging as positive experiences.

Clinical Findings In Diagnosis Of Depression [104]	
1	Depressed mood on a consistent basis (may also be identified, particularly in the younger population as irritability)
2	Anhedonia characterized by a loss of ability to experience interest or pleasure in all or nearly all activities.
3	Sleep disturbance, characterized by a pattern of either insomnia or hypersomnia.
4	Ruminative and persistent guilt or worthlessness.
5	Decreased energy or fatigue.
6	Poor concentration.
7	Decreased appetite with possible significant weight loss (hyperphagia can more rarely be noted).
8	Psychomotor agitation or retardation
9	Suicidal ideation with or without a plan.

Figure 4

authors were unable to determine whether the high ratios were the result of depression or whether EFA changes in tissue predated the depressive symptoms.[102] Recent research has suggested that there is an abnormal metabolism of omega-3 EFAs in depression. This is based on the findings that EFA alterations in depression are related to the inflammatory response in that illness; and that the EFA disorders persist despite successful conventional antidepressant treatment.[103]

In Conclusion

This article has focused on the hormonal connection to psychological disorders amongst women. From a holistic viewpoint, the practitioner will also be aware of a host of other causative factors in depression and anxiety including unavoidable stress in relationships or family; traumatic events; sickness or chronic pain; nutritional factors such as hypoglycemia and nutrient deficiencies; and endocrine disorders like hypothyroidism.

Depression and anxiety of any origin can be serious and debilitating disorders and need to be recognized and treated accordingly. Practitioners can evaluate the severity of symptoms through employing established medical criteria, such as the American Psychiatric Association's "Diagnostic and Statistical Manual of Mental Disorders". This manual lists nine clinical findings by which a diagnosis of clinical depression can be made (see Fig 4).

An individual is classified as clinically depressed if five or more of the symptoms are present for a minimum of two weeks, and the patient presents with either (or both) of the first two symptoms.

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