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# MENOPAUSE AND THE MIND

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Women's emotional symptoms during the menopause vary. Some have no symptoms at all, while others have mood swings, anxiety and depression. These symptoms can be frightening and surprise many women, adding to the burden of hot flushes and irregular periods.

Not only can menopause prompt uncomfortable physical symptoms, but it can also turn a woman's emotions into a pendulum, prompting moderate to severe mood swings that make a woman feel like she is in a constant state of premenstrual syndrome.

The 2015 Health & Social Care Information Report of the NHS of UK show prescriptions for antidepressant medication rising by 7.2%, with nearly 15 % of post menopausal women in the age group 45-64 taking antidepressants.[1]

## DEPRESSION

"Depressed" and "depression" are words used to describe three distinctly different conditions:

**A depressed mood** — This is a normal, brief period of feeling blue or sad that is commonly experienced and rarely requires treatment. The medical term is dysphoria.

**Depression as a symptom** — Sometimes called an adjustment reaction, this type of depression may be due to a wide variety of medical or psychological problems, or to intense reactions to life events (such as divorce, losing a job, death of a loved one). It is usually short term and most often does not require treatment, although it can progress to clinical depression. The medical term for depression that occurs most of the day, more days than not, for at least 2 years is dysthymia.

**Clinical depression** — This is a serious disorder caused by neurotransmitter imbalance in the brain. A clinical (or major) depression is a definite indication for treatment.

Unlike normal emotional experiences of sadness, loss, or passing mood states, major depression is persistent and can significantly interfere with an individual's thoughts, behaviour, mood, activity, and physical health.[2]

**Incidence of Depression**

Major depression affects nearly 5% of adult population in a given year**.** Depression is approximately twice as common in women as in men (21% vs 12.7%). Moreover, depressive episodes are more recurrent, longer, worse, and more impairing for women than for men. The racial distribution of perimenopausal depression is not known. However, in countries where older women are highly valued, women experience fewer symptoms overall during menopause.[3]

Transition to menopause and its changing hormonal milieu are strongly associated with new onset of depressed mood among women with no history of depression. Women who enter perimenopause are twice to four times more likely to have clinically significant depressive symptoms as women who had not yet made the menopausal transition.[4] An estimated 20% have depression at some point during menopause. Women with diabetes have higher incidence of depression (11.8% versus 8.4%) and anxiety (8.4% versus 6.6%) compared with women without diabetes.[5]

**Evaluating Depression**

Applying the Hospital Anxiety and Depression Scale (HADS), Center for Epidemiological Studies of Depression scale (CES-D), the Primary Care Evaluation of Mental Disorders (PRIME-MD) and Beck's Depression Inventory (BDI) are reliable and valid instruments with good psychometric properties for the measurement of psychological distress and assess depressive symptoms.

HADS developed by Zigmond and Snaith in 1983 is a simple yet reliable tool taking just 2-5 minutes to complete, containing 14 items and two subscales to assess anxiety and depression; each item is rated based on a four point scale. The maximum score for both anxiety and depression subscales is 21. Scores 0-7 is considered normal, 8-10 borderline abnormal and 11-21 is abnormal.[6]

The Center for Epidemiologic Studies Depression Scale (CESD) was created in 1977 by Laurie Radloff, and revised in 2004 by William Eaton and others. It is a 20-item measure that quantifies symptoms associated with depression, such as restless sleep, poor appetite, and feeling lonely. Response options range from 0 to 3 for each item (0 = Rarely or None of the Time, 1 = Some or Little of the Time, 2 = Moderately or Much of the time, 3 = Most or Almost All the Time). Cutoff scores (e.g., 16 or greater) that aid in identifying individuals at risk for clinical depression, with good sensitivity and specificity.[7]

The PRIME-MD consists of a two components, a one-page patient questionnaire (PQ) and a 12-page clinician evaluation guide (CEG) containing 25-questions, to assess four groups of mental disorders (mood, anxiety, alcohol, and somatoform) and eating disorders. The questions assess symptoms and signs present during the past month, plus one question about the patient's overall health. Scores of 0, 1, 2, and 3 are assigned to the response categories of “not at all,” “several days,” “more than half the days,” and “nearly every day,” respectively. Total score for the nine items ranges from 0 to 27. Total scores of 5, 10, 15, and 20 represent cutpoints for mild, moderate, moderately severe and severe depression.[8]

Created by Aaron T Beck, BDI is a 21-question multiple-choice self-report inventory,and one of the most widely used psychometric tests for measuring the severity of depression. Each question is rated on a 4-point scale ranging from 0 to 3 based on severity of each item. The maximum total score is 63. In the current 1996 version BDI-II, scores of 0-13 indicates minimal depression, 14-19 mild, 20-28 moderate depression, and 29-63 severe depression.[9]

**Risk factors for Depression**

Dysphoric mood during the early perimenopausal transition is most common in women with relatively low educational status and associated low socioeconomic status.

Societal roles and expectations may contribute to the heightened rate of depression in women. Women with particular types of stressors seem to be at increased risk for perimenopausal depression. Such stressors include the following.

- Lack of social support
- Unemployment
- Surgical menopause
- Poor overall health status

Other factors influencing depression are

- Negative mood before menopause
- Negative attitude toward menopause and aging
- Habituated to smoking
- Little or no exercise
- No partner/isolation
- A number of bothersome symptoms
- Poor self-perceived health
- Negative feelings toward partner
- A number of perceived problems
- Interpersonal stress

Stressors that tend to correspond with perimenopause and that are postulated to relate to depression include the following.

- Onset of illness in self or others
- Care of aging parents
- Changes in employment
- Change in the childbearing role
- Loss of fertility, which may be associated with a loss of an essential meaning of life
- Empty-nest syndrome – Most surveys have indicated, however, that women whose children have moved out of the house tend to report more happiness and enjoyment in life than others do
- Societal value of youth – In societies where age is valued, women tend to report having fewer symptoms at the menopause transition

**Clinical Criteria for Diagnosing Depression**

Essential criteria for major depression include depressed mood, decreased interest or pleasure in activities, or both. Additional criteria include the following.

- Increased or decreased appetite
- Weight change
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Feelings of worthlessness or guilt
- Decreased concentration

- Indecisiveness/Latency of response to questions
- Slowed thought process
- Poor eye contact
- Poor grooming or hygiene
- Diminished prosody of speech
- Suicidal ideation and plans
- Homicidal thoughts and plans
- Low energy
- Impaired concentration
- Sleep disturbances
- Weight changes
- Libido changes

**Physiological basis for Depression at Menopause**

Depression during perimenopause is partly due to declining estrogen levels as it stimulates the synthesis of neurotransmitters, the expression of receptors and influences membrane permeability. Estrogen increases the effects of the neurotransmitters serotonin and norepinephrine, both of which are most related to the physiologic cause of depression. Estrogen increases serotonin synthesis, upregulates 5-hydroxytryptamine (5-HT)-1 (5-HT1) receptors, and downregulates 5-HT2 receptors. Estrogen also increases norepinephrine activity in the brain, perhaps by decreasing reuptake and degradation through inhibition of the enzymes mono amine oxidases (MAO) and catechol O-methyltransferase (COMT). Because estrogen facilitates the actions of serotonin and norepinephrine, a decline in estrogen concentrations, in all probability, decreases levels of these hormones.

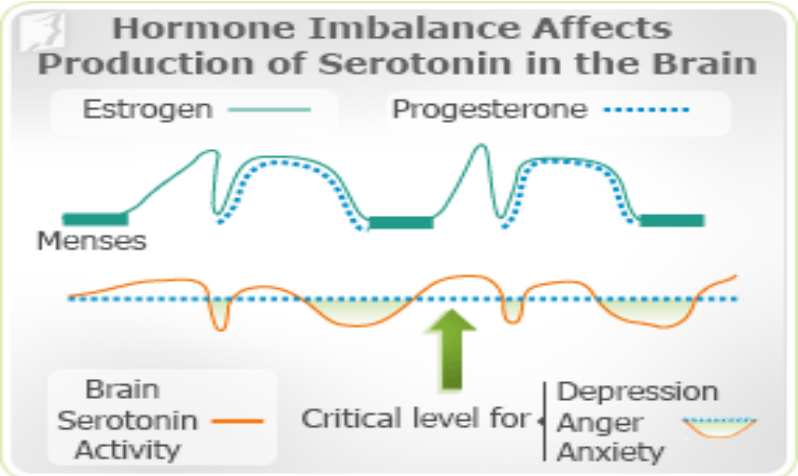


**Fig I: Female hormones and Brain Serotonin Levels.**

Increased variability of estradiol, follicle-stimulating hormone, and luteinizing hormone around the woman's own mean levels are all significantly associated with high CES-D scores. Higher testosterone levels can directly lead to higher depressive symptoms during the menopausal transition.

The strongest predictor of depressed mood is a prior history of depression, along with fluctuations in reproductive hormone levels associated with a depressed mood.

**Sleep Disorders**

Insomnia occurs in 40-50% of women during the menopausal transition, and problems associated with sleep may or may not be connected to mood disorders. Women with insomnia are more likely than others to report problems such as anxiety, stress, tension, and depressive symptoms.

Sleep disturbances during menopause have been associated with estrogen deficiency; exogenous estrogen has been shown to improve both subjective and objective sleep, attributed to a decrease in hot flashes. Elevated LH levels during late menopause produce poor sleep quality through a thermoregulatory mechanism, resulting in high core body temperatures. The sleep problems are often aggravated by vasomotor symptoms of menopause.

Rates of sleep apnea increase with age, rising from 6.5% in women aged 30-39 years to 16% in women aged 50-60 years, perhaps due to post menopausal weight gain or to decreased progesterone levels (because progesterone stimulates respiration).

Postmenopausal women experience declines in levels of melatonin and growth hormone, both of which affect sleep.

**Schizophrenia**

Schizophrenia usually manifests in young adulthood with a second peak in incidence among women aged 45-50 years; this second peak is not observed in men. There is a worsening course of schizophrenia in women during the menopausal transition suggesting that estrogen plays a modulatory role in the pathophysiology of schizophrenia.

**Panic disorder**

Panic disorder is most common in women with many physical symptoms during menopause. New-onset panic disorder and worsening of preexisting panic disorder have been observed and associated with negative life events, functional impairment, and medical comorbidity.

**Obsessive-compulsive disorder**

Fluctuations in OCD have been correlated with the menstrual cycle and with pregnancy, suggesting that hormone levels may contribute to the disorder. New-onset obsessive-compulsive disorder (OCD), a relapse of OCD, or a change in OCD symptoms may occur during menopause.

**Bipolar disorder**

Exacerbation of mood symptoms during menopause has been noted in women with preexisting bipolar disorder. Women with bipolar disorder have higher rates of depressive episodes during the menopausal transition. The frequency of depressive episodes in this population appears to be higher than during premenopausal years.

**INVESTIGATIONS FOR MOOD DISORDERS**

Thyroid-stimulating hormone (TSH) levels should be determined as hypothyroidism is an independent risk factor for depression in menopausal women.

Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels should also be measured. As ovarian production of inhibin and estrogen declines during perimenopause, LH levels begin to increase. An FSH level higher than 40 IU/L is often used as a marker of menopausal changes. Patients may begin to notice changes before laboratory values reflect the changes.

A hematocrit should be obtained; anemia can be associated with depressive-type symptoms. Dual-energy X-ray absorptiometry (DEXA) scanning is indicated to evaluate bone mineral density (BMD). Depression may be a risk factor for osteoporosis in postmenopausal women. A Mental Status Examination (MME) must be performed.

**Treatment of perimenopausal depression**

Drugs used to treat perimenopausal depression include antidepressants and hormones.

**Antidepressant therapy**

For major depression, standard antidepressants are first-line treatments. Selective serotonin reuptake inhibitors (SSRIs) are the antidepressants most commonly used in the treatment of perimenopausal depression. These drugs act by inhibiting serotonin reuptake transporters in the presynaptic neuron, making more serotonin available at the synaptic cleft. The time to onset of action is 4-6 weeks.

SSRIs are thought to be generally safe and effective. They do pose a risk of serotonin syndrome, as well as several common adverse effects (e.g. nausea, diarrhea, anorexia, excessive sweating, decreased libido or anorgasmia, headache, jitteriness, dizziness, sedation or activation, insomnia, and akathisia). Several of these medications inhibit the cytochrome P450 (CYP450) enzymes; therefore, it is prudent to check for drug interactions.

**Hormone replacement therapy**

Estrogen replacement therapy has antidepressant effects and enhances the effects of antidepressant drug treatment in perimenopausal women but not so effective in postmenopausal women. For mild depression, hormone replacement therapy alone may suffice. Estrogen has an independent antidepressant effect and may be used when traditional antidepressants fail, or when patients refuse psychotropic medications, or for those who have significant vasomotor symptoms. Women who have surgically induced menopause have an increased risk of depression, and they may be especially likely to benefit from hormone replacement therapy. The antidepressant benefit is greater in women with vasomotor symptoms, resulting in significant improvement of mood and quality of life.

In women with mild mood-disorder and symptoms that do not meet the criteria for depression, hormone replacement therapy may be considered. The effects of estrogen treatment have been studied in perimenopausal women without depression to see if it has a positive effect on mood or quality of life. Results suggest a small positive impact on mood. Among healthy women without depression, estrogen may not have a favorable effect on quality of life or mood.

**Treatment of hot flashes**

SSRIs are sometimes used to treat hot flashes. Paroxetine, controlled-release paroxetine, extended-release venlafaxine, and escitalopram may provide some benefit.

**Treatment of sleep disorders**

Estrogen may be helpful in relieving vasomotor symptoms that disrupt sleep. In a study of postmenopausal women with hot flashes, night sweats, insomnia, anxiety, or mood swings, low-dose estrogen and low-dose micronized progesterone improved sleep to a greater extent than could be explained by a reduction in vasomotor symptoms. One study using polysomnographic analysis found that isoflavone treatment is also effective in insomnia.

**Maintenance of cognitive function**

Estrogen may prevent or delay the onset of dementia, including Alzheimers disease, especially when estrogen therapy is started in younger postmenopausal women. However, the Women's Health Initiative Memory Study (WHIMS) study of postmenopausal women older than 65 years who did not have preexisting dementia, it did not show any significant improvement in global cognitive functioning when monitored by means of serial Mini Mental Status Examinations.

**Other Supportive measures**

Negative anticipation of menopause seems to be associated with elevated rates of depression and physical symptoms of menopause. Educational groups that help women learn what to expect during menopause decreases anxiety, depression, and irritability, both immediately after the group therapy and 1 year later. Patients may benefit from learning that mood symptoms are not uncommon during menopause. Providing education about depressive symptoms can help women understand their experiences and recognize depression as a treatable illness. Family members may also benefit from learning about the symptoms of major depression and the association of its onset with the menopausal transition. This information may help them understand changes they observe in their family member(s). Patients should be educated about emergency mental health services that are available in their area. They should be aware of how to obtain help if they have suicidal thoughts. Screening of postmenopausal women with diabetes for depressive and anxiety is recommended to improve their overall quality of life.

Psychiatric hospitalization is indicated for patients who are at imminent risk of harming themselves or others and for those whose depressive symptoms render them unable to care for themselves.

A healthy, balanced diet with calcium supplements is advisable. Regular exercise is also helpful in diminishing the symptoms of depression.

**Prognosis**

Depression is a significant health problem in women. According to the World Health Organization's Global Burden of Disease Study, unipolar depression is the leading cause of disease-related disability in women. Unipolar major depression is second only to ischemic heart disease in terms of associated morbidity and mortality.

The Study of Women's Health Across the Nation suggests that women are at higher risk for major depression during and immediately after the menopausal transition and that the risk is smaller when they are premenopausal.

**Dos and Donts for Depressed Perimenopausal Women**

Some tips for perimenopausal women to make it easier for them to handle their fluctuating emotions.

1. Exercise and eat healthy.
2. Find a self-calming skill to practice, such as yoga, meditation, or rhythmic breathing.
3. Avoid tranquilizers and alcohol.
4. Engage in a creative outlet that fosters a sense of achievement.
5. Stay connected with your family and community.
6. Nurture your friendships.
7. Herbal remedies such as St. John's wort etc may be tried

The following lifestyle changes, recommended by the National Institute of Mental Health, may be helpful.

a) Break large tasks into small ones, set some priorities, and do what you can as you can.
b) Participate in activities that may make you feel better such as mild exercise, going to a movie, a ballgame, or participating in religious, social, or other enjoyable activities.
c) Give it time. Expect your mood to improve gradually, not immediately. Feeling better takes time.
d) Postpone important decisions until the depression has lifted. Before deciding to make a significant transition — change jobs, get married or divorced — discuss it with others who know you well and have a more objective view of your situation.

e) Many primary care providers are not specifically trained in the management of mental health disorders, including clinical depression. Consultation with a mental health professional may be appropriate, and an expert opinion can be reassuring.

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