Major depressive disorder is a prevalent and disabling condition. The causes of mood disorders are heterogeneous, involving a complicated interplay of both psychosocial and biological variables. In an analysis of adult women, the psychosocial variables that predicted major depression appeared to result from broad pathways reflecting internalizing symptoms, externalizing symptoms and psychosocial adversity. In addition, there are significant associations between major depressive disorder and many chronic medical conditions (e.g., obesity, diabetes mellitus and hypothyroidism), underscoring the myriad biological variables that may be present in depression.

Sex-related differences in mood disorders have been frequently reported and indicate the relevance of the reproductive endocrine system in the pathogenesis and treatment of mood disorders. For example, exacerbation of depressive symptoms and recurrence of depression in women with multiple-episode depression has been reported during perimenopause. The salutary neuropsychiatric effects of gonadal steroids are implicated yet not confirmed with extant data. Although the mechanism by which estrogen might attenuate depressive symptoms is unknown, mounting evidence indicates that estrogen influences neuronal function through monoaminergic- and GABAergic-mediated systems. Estrogen is also noted to inhibit monoamine oxidase activity.

Preliminary data suggest that hormone replacement therapy (HRT) and antidepressant therapy may have overlapping molecular targets. Moreover, the putative antidepressant effects of HRT have also been reported. HRT has been prescribed for climacteric symptoms (e.g., vasomotor symptoms), and some antidepressants (e.g., serotonergic antidepressants) have been shown to alleviate the full range of climacteric symptoms. Thus, many women who experience depressive symptoms or a major depressive disorder at the time of menopause may find relief of these symptoms and even the disorder by using HRT.

With the publication in July 2002 of results indicating potential harmful effects of HRT (estrogen monotherapy), there was a dramatic reduction in HRT prescriptions. We hypothesized that the abrupt discontinuation of HRT would be associated with an increase in antidepressant usage. Fig. 1 appears to confirm the hypothesis.

We found that a significant decrease in the number of HRT prescriptions was associated with a statistically significant increase in prescriptions of serotonergic antidepressants. Others have noted associations between changes in HRT and antidepressant prescription patterns. The simultaneous increase in prescriptions of serotonergic antidepressants suggests that antidepressants are being prescribed for symptoms (psychological, physical) previously controlled with the use of HRT.

With the diminished popularity of HRT, physicians may encounter women who are experiencing depressive symptoms or actual major depressive disorders that worsen at the time of menopause. A thorough assessment is encouraged for women who present during perimenopause with disabling psychological or somatic symptoms. Symptoms indicative of major depression include feelings of hopelessness, helplessness and worthlessness, suicidal ideation and anhedonia.

If patients are found to have major depressive disorder, as defined in the DSM-IV-TR, they should be offered pharmacotherapy, psychotherapy or both. If drug therapy is chosen, standard pharmacological agents are recommended, keeping in mind that serotonergic antidepressants are also effective against climacteric symptoms. Although there is a paucity of randomized controlled trials evaluating depression-specific psychotherapy (e.g., cognitive behavioural therapy) in perimenopausal women, cognitive behavioural therapy has been proven effective in the treatment of major depressive disorder, and it avoids the burden of drug-related adverse events. The Canadian Psychiatric Association recommends both medication and psychotherapy as first-line treatment of depressive disorders. Preference for either treatment modality is influenced by the severity of illness, the availability of treatment and patient preference.

In the interim, practitioners are encouraged to be vigilant for breakthrough psychiatric and climacteric symptoms in patients discontinuing HRT and to familiarize themselves with the beneficial effects of serotonergic antidepressants on climacteric symptoms.
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Commentary

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