Relapse and Recurrence of Depression
A Practical Approach for Prevention

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Summary

Most major affective disorders are, from a longitudinal perspective, recurrent conditions. This article reviews the rationale for longer term models of antidepressant treatment, including strategies for the prevention of relapse (defined as an increase of symptoms back to a syndromal level after an initial treatment response) and recurrence (defined as the onset of a distinctly new episode of affective illness).

To prevent relapse, it is recommended that all patients whose symptoms remit during pharmacotherapy receive 4 to 6 months of continuation therapy. Those patients at increased risk for subsequent recurrent depressive episodes should be considered for an extended course of maintenance pharmacotherapy. The efficacy of tricyclic antidepressants, lithium and the selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors for the prevention of recurrent depression has been established, with the latter class having a clinical advantage in terms of common adverse effects and safety in overdose.

With each new episode of depressive illness, the risk of illness becoming more autonomous, severe and potentially refractory may increase. Thus, prophylactic treatment of patients at risk of recurrent depression remains the best way to optimise their long term outcome.
The major affective disorders are increasingly recognised as recurrent and potentially chronic conditions. Each new episode of major depressive disorder is punctuated by renewed, perhaps increased, risks of chronicity, suicide and psychosocial impairment. As a result, treatment strategies with a long term, prophylactic focus are recommended for many patients. This article will review issues pertaining to the use of long term, preventative treatment strategies for depressive states.

1. Natural History of Depression

Recent epidemiological evidence suggests that the age at onset of a first episode of mood disorder is becoming progressively younger. Moreover, the incidence of affective disorder appears to be increasing among younger cohorts. Thus, the already considerable public health impact of the affective disorders will most certainly increase in the future.

The point prevalence of chronic and recurrent cases of major affective disorder exceeds that for acute, first-episode disorders. In the 1970s, Angst et al. and Zis and Goodwin documented the likelihood of relapse and recurrence in the major affective disorders. These findings were prospectively confirmed in a series of studies conducted under the auspices of the National Institute of Mental Health Collaborative Study on the Psychobiology of Depression (as summarised by Keller and Hanks). At best, at least 50% of those who have experienced one episode of major depression will experience another at some later point. Thus, assuming a lifetime risk of major depression of 5%, an individual who has recovered from an initial episode of depression has at least a 10-fold greater risk of having another episode when compared with a person of similar age and sex who has never been clinically depressed. For recurrent (unipolar) major depression and bipolar depression, where recurrence rates of at least 70 to 90% are expected, the increase in risk of recurrence is 14- to 18-fold when compared with that in the general population. Chronic minor depressive disorders (i.e. dysthymia) are similarly associated with a marked increase in the risk of subsequent major depressive episodes.

Despite vigorous public education efforts, most depressed individuals are still likely to be either untreated or incorrectly diagnosed and/or inadequately treated. This state of affairs, while undoubtedly reinforced by societal attitudes and stigma, underscores the generally favourable short term prognosis of the mood disorders. For example, most episodes of acute major depression will last no longer than 1 year, and between 80 and 90% will have remitted within 2 years, even without specific treatment.

However, even episodes of depression of such limited duration convey many adverse economic, interpersonal and medical consequences. Furthermore, substance abuse, including that of alcohol (ethanol) and hypnosedatives, may develop during an untreated depressive episode, and depressed patients are, on average, heavier tobacco users than nondepressed individuals. Thus, for those whose depression remains untreated and who do not remit spontaneously, an ingrained pattern of chronic depression conveys even more negative prognostic implications.

While most initial episodes of depression occur at times of stress, only a minority of persons encountering such difficulties develop persistent depressive syndromes. This highlights the role of underlying psychobiological vulnerability factors in the aetiology of depression. Such risk factors include:

- a family history of affective disorder or alcoholism
- a long established pattern of maladaptive cognitive traits or interpersonal difficulties
- chronic medical problems
- a history of early trauma or abuse.

Interestingly, the relationship between stress and episodes of recurrent depression appears to be less