Chapter 2

Depression in different types of patients

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Depression in children

Depression has been estimated to have a prevalence in children of 2.5% and in adolescents of 4–8% [1]. The presentation of symptoms of depression in young people is, to a large extent, similar to that of adults, especially with respect to the presence of neurovegetative symptoms of depression. Decline in psychosocial performance (primarily in school) and reduced interest in previously enjoyed activities may be more easily detected signs that a younger individual is experiencing symptoms of depression. In addition, irritability may be more common in depressed children and adolescents than in depressed adults.

In 2003, the UK Medicine and Healthcare products Regulatory Agency (MHRA) concluded that all SSRIs, with the exception of fluoxetine, were contraindicated in the treatment of depression in young people, due to an increase in suicidal ideation, as well as dubious efficacy. In 2004, the US Food and Drug Administration (FDA) issued a "black box warning" concerning an increased risk of suicidal ideation and behavior in people under the age of 18 treated with second-generation antidepressants.

The primary analysis of randomized controlled trials (RCTs) of SSRIs that led to the FDA "black box warning" revealed an increase over baseline of roughly 2% (placebo 2% versus 4%) in suicidal ideation or behavior in people under the age of 18 given an SSRI. No children completed suicide in the RCTs included in this analysis. The difference in suicidal ideation leads to a number needed to harm (NNH) of 50. A subsequent meta-analysis of 27 RCTs of SSRIs in children and adolescents with depression, obsessive–compulsive disorder, and other anxiety disorders [2] again found no completed suicides and a smaller increase in suicidal ideation/self harm attempts with SSRIs, corresponding to an NNH of 143. The validity of using "suicidality" (meaning suicidal behaviour, ideation, or attempts) as a surrogate for suicide, as in these studies, has been criticized [3], given the relatively high incidence of suicidality in comparison to

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completed suicide. Studies of the efficacy of SSRIs in children and adolescents suggest a number needed to treat (NNT) of 5 for fluoxetine and 9 for SSRIs overall [4]. The Texas Medication Algorithm Project (TMAP) [5] considers fluoxetine, citalopram, and sertraline to be first-line medications for treatment of depression in children and adolescents, and the relatively small increase in suicidal ideation to be less significant than the benefit from treating them with SSRIs. Fluoxetine is the most highly recommended, and is still the only FDA-approved SSRI for the treatment of depression in those aged under 18. Paroxetine should be avoided in pre-adolescents.

Second-generation antidepressants such as bupropion, venlafaxine, duloxetine, and mirtazapine have little evidence to support their use in children and adolescents, and should be considered second- or third-line choices for pharmacologic treatment: the younger the child, the less the therapeutic benefit gained from second-generation antidepressants.

Alternatively, evidence-based psychotherapies such as cognitive–behavioral therapy (CBT) are also recommended, either singly or together with medication, in the treatment of depression in younger people. The combination of fluoxetine and CBT showed the most robust response in the Treatment of Adolescents with Depression Study (TADS) when compared with CBT alone or fluoxetine alone in moderately to severely depressed adolescents [6]. Fluoxetine outperformed CBT alone in this study. However, other studies [7–9] have found the combination of CBT and an SSRI to have no greater efficacy than the SSRI alone.

Depression in elderly people

The prevalence of MDDs (i.e., meeting full DSM-IV criteria) is thought to decrease with increasing age [10]. Unfortunately, rates for completed suicide increase with advancing age, to the point that people over the age of 86 have the highest suicide rate of any age group [11]. Medical burden, loss of loved ones, decreased independence, and financial hardship are thought to contribute to the likelihood of a depressive episode in elderly people.

There are difficulties in diagnosing depression in elderly people because they tend to report somatic complaints much more readily than sad mood. Other cardinal symptoms of depression, such as sleep disturbance and/or alterations in appetite or energy, can also be nonspecific changes that are common in normal aging. Depression is often comorbid with cardiovascular disease in elderly adults, and it has been suggested that circulatory problems can actually cause depressive symptoms, possibly by affecting the flow of blood to the brain. This type of depression has been termed "vascular depression,"

although this disorder is not yet recognized by the standard guidelines. *Clinically significant depression* is a category meant to capture older adults with less than full DSM-IV depressive episodes, but still meaningful depression. This diagnosis is thought to be much more common than MDD. Symptoms that can aid in identifying the depressed older adult include decreased interest (anhedonia) and social withdrawal in individuals who were previously engaged and interested in activities. Treatment in this age group is discussed in Chapter 4.

Depression in women

Women have close to twice the lifetime prevalence of depressive disorders of men [10]. Nearly all of this increased susceptibility to depression occurs during the childbearing years, from menarche to menopause. A number of variables, both psychosocial and biological, may contribute to these disparate rates of depression. As increased rates of depression in women follow ovarian function closely, estrogen has been extensively studied as a mediator of depression in women, and is, therefore, a potential agent for the treatment of depression. To date, studies of estrogen in the treatment of depression in perimenopausal and postmenopausal women have not yielded consistent findings of benefit, and ovarian hormones are not included in standard treatment recommendations for this group [12].

Depression during pregnancy can be difficult to detect, because many of the neurovegetative signs of depression are common in pregnancy. The rate of depression in pregnant women is thought to be similar to that of nonpregnant women. *Postpartum depression* follows one in eight deliveries, and can be differentiated from the benign "baby blues" by duration and severity of symptoms, and the negative impact on maternal psychosocial function. Conversely, the "baby blues" should be limited to 10 days after delivery, and psychosocial functioning should be reasonably preserved. The treatment of postpartum depression mirrors the treatment of standard depression.

Outside the reproductive-cycle–associated increase in prevalence of depression in women, few other compelling differences have been identified when comparing depression in women and men. In the STAR*D study, clinical characteristics of 2541 outpatients with major depression were compared by gender. Two-thirds of the sample were women. Women had greater symptom severity but men had more MDEs. Women were found to have greater rates of an anxiety disorder, bulimia, and somatoform disorders, as well as more suicide attempts, whereas men showed more alcohol and substance use disorders. Irritability was equally common in men and women [13].

Depression in patients with comorbid medical conditions

Depressive disorders occur more frequently in people with chronic medical conditions, and are associated with poorer long-term outcomes. Disorders of the central nervous system (CNS), such as Parkinson's disease, dementia, cerebrovascular disease (post-stroke depression [PSD], vascular dementia), and multiple sclerosis all have strong associations with depressive disorders. Chronic medical illnesses not directly affecting the CNS, such as human immunodeficiency virus (HIV), cancer, coronary artery disease, and autoimmune disorders have also been associated with higher rates of depressive disorders (see Figure 1.3). Identifying a mediator and a direction of association for these findings has been difficult.

PSD is estimated to occur in approximately a third of patients within 9 months of having a cerebrovascular accident (CVA). It can be difficult to diagnose and can mimic symptoms of depression; for example, individuals with aphasia are unable to complete a clinical interview; individuals with anosognosia may be unaware of their deficits; or individuals with physical limitations that impair the ability to engage in hedonic activities may seem to be anergic. PSD is related to poor functional outcomes, as well as poor cognitive outcomes, and its successful treatment is thought to lead to significant improvement in both cognition and function.

Depression has been linked to cardiovascular disease, as both a risk factor for developing heart disease and a predictor of increased mortality in patients with heart disease. Mediators of such an association may include inflammatory cytokines, increases in platelet thrombus formation, or alterations in sympathetic and parasympathetic tone to the cardiac conduction system.

Depression is estimated to occur in 24% of patients diagnosed with cancer. Of course, this is a highly heterogeneous group representing many types of malignancies. Pancreatic, head and neck, and breast cancer appear to have the highest rates of associated depression. Factors that can affect the emergence of depressive disorders can include the severity of the illness, disfigurement, and effects of treatment – surgical, radiation, or chemotherapeutic. Conversely, as depression is thought to lower immune system function, people with depression may be at higher risk for cancer. Successful treatment of depression in these populations can improve quality of life as well as medical outcome.

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