INTRODUCTION

Depression is a common mental disorder that presents with symptoms well beyond depressed mood. Loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, poor concentration, and a multitude of physical ailments may accompany clinical depression. These problems can become chronic or recurrent and lead to substantial impairments in an individual’s ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide, a tragic outcome associated with the loss of about 850,000 lives every year worldwide.

Depression occurs in persons of all genders, ages, and backgrounds. It is the leading cause of disability as measured by Years Lived with Disability and was the fourth leading contributor to the global burden of disease in 2000, according to the World Health Organization [1]. By the year 2020, depression is projected to rank second in the DALY’s (Disability Adjusted Life Years) calculated for all ages and both sexes [1-2]. Today, depression is already the second cause of DALY’s in the age category 15-44 years for both sexes combined [1].

Depression can be reliably diagnosed in the primary care setting. Antidepressant medications and brief structured forms of psychotherapy are effective for 60-80% of those affected with depression. However, fewer than 25% of those affected (in some countries like Lebanon, fewer than 10%) receive such treatment. Barriers to effective care include the lack of resources, lack of trained providers, and the social stigma associated with mental disorders including depression.

DEFINITION

Depression is a mood disorder that involves the body and the mind. Major depressive disorder (MDD) is a medical condition characterized by many symptoms emerging together. To be diagnosed with MDD, one must meet the criteria established in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorder (DSM-IV) [3] for MDD. Five (or more) of the symptoms must have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms should be either depressed mood or loss of interest or pleasure. The criteria are:

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful);
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others);
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day;
4. Insomnia or hypersomnia nearly every day;
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down);
6. Fatigue or loss of energy nearly every day;
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick);
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others);
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

The above symptoms should cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. Also, the symptoms must not be due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism). While depression may occur as only one single episode in a person’s lifetime, for many it is a recurrent disorder with repetitive episodes of varying severity.

There are many types of depression. Depression can be unipolar, where the mood disturbance is characterized by feeling sad or down during each episode, or it can be part of a bipolar disorder, where some episodes are characterized by depressed mood and others by euphoric and elated (or irritable) mood associated with increased levels of energy, talking a lot, spending much more money than usual, and decreased need of sleep – a state also known as
mania (or hypomania). Depression can also be seasonal, where depressed mood, low energy, and appetite change predominately in the winter months, and typically improve in spring and summer. This is known as Seasonal Affective Disorder (SAD) and is probably related to the intensity of light that reaches the brain.

In later life, depression frequently coexists with other medical illnesses and disabilities. In addition, advancing age is often accompanied by loss of key social support systems due to the death of a spouse or siblings, relocation of residence, or social isolation due to infirmity. Because of these changes, and the fact that older people normally experience functional and physiological decline, doctors and family may miss the diagnosis of depression in the elderly, hence delaying effective treatment. As a result, many seniors find themselves having to cope with symptoms that could otherwise be easily treated. In addition, depression tends to last longer in older adults. It doubles their risk of cardiac diseases and increases their risk of death from other illnesses [4], while reducing their ability to rehabilitate.

PATHOPHYSIOLOGY

The underlying pathophysiology of major depressive disorder has not been clearly defined. Clinical and preclinical trials suggest a disturbance in central nervous system (CNS) serotonin (5-hydroxytryptamine, or 5-HT) activity as a prominent factor. Other neurotransmitters implicated include norepinephrine (NE) and dopamine (DA) [5]. The role of CNS serotonin activity in the pathophysiology of major depressive disorder is suggested by the efficacy of selective serotonin reuptake inhibitors (SSRIs) in the treatment of major depressive disorder. Furthermore, studies have shown that an acute transient relapse of depressive symptoms can be produced in research subjects in remission using tryptophan depletion, which causes a temporary reduction in CNS 5-HT levels. Serotonergic neurons implicated in affective disorders are found in the dorsal raphe nucleus, the limbic system, and the left prefrontal cortex. Studies suggest that seasonal affective disorder is also mediated by changes in CNS levels of serotonin and appears to be triggered by alterations in circadian rhythm and sunlight exposure.

Vascular disease may contribute to depression by disrupting the neuronal networks involved in emotion regulation – in particular, frontostriatal pathways that link dorsolateral prefrontal cortex, orbitofrontal cortex, anterior cingulate, and dorsal cingulate [6]. Microvascular disease in other components of the limbic circuitry, in particular the hippocampus and amygdala, has also been implicated in depression.

Endocrine changes in depression are evident across the life span, but some are particular to aging. Women with a previous history of depression are at higher risk of developing depression during menopause, suggesting a role for estrogen in mood regulation. Similarly, low testosterone levels have been associated with depression in older men.

ETIOLOGY

Genetics

Genetic susceptibility plays a role in the development of major depressive disorder. Individuals with a family history of affective disorders, panic disorder, and alcohol dependence carry a higher risk for major depressive disorder. Studies such as those by Akiskal and Weller [7] and Weissman et al. [8] suggest a genetic component in the etiology of depressive disorders. Other evidence suggests that late-onset depression (after age 60 y) is an etiologically and clinically distinct syndrome [9] and that genetic factors likely play less of a role in late-onset than early-onset depression. A family history of depression is less common among older adults with depression than younger adults. However, certain genetic markers have been associated, although inconsistently, with late-onset depression, including polymorphisms of the apolipoprotein E, brain-derived neurotrophic factor (BDNF), and 5-HT transporter genes. Interestingly, these markers have also been associated with cognitive impairment, hippocampal volume, and antidepressant response, respectively.

Stressors

Although major depressive disorder can arise without any precipitating factors, stress and interpersonal losses certainly increases the risk. Psychodynamic formulations indicate that significant losses in early life predispose to major depressive disorder over the lifespan of the individual, as does mental trauma, either transient or chronic. Cognitive-behavioral models of depression posit that depression is a behavioral response to repeated stressors and that cognitive distortions (i.e., negative thoughts) contribute to and perpetuate depressed mood [9].

Chronic pain, medical illness, and psychosocial stress can also play a role in both the initiation and maintenance of major depressive disorder. Older adults may perceive medical illness as psychologically distressing, and illnesses may lead to increased disability, decreased independence, and disruption of social networks [10]. Other psychosocial risk factors for depression in late life include impaired social supports, caregiver burden, loneliness, bereavement, and negative life events [11]. Of particular interest is the association between chronic uncontrolled pain and depression, each of which can make the other worse thus initiating a cycle of escalation. The limited pharmaceutical options for pain management in Lebanon hinders the clinician’s ability to potentially arrest this vicious cycle.

Vascular depression

The vascular depression hypothesis posits that cerebrovascular disease may cause or contribute to late-life depression. Various lines of evidence support this hypothesis, including the high incidence of depression following a stroke and higher prevalence of ischemic white-matter changes in older adults with depression compared to those without [12]. Additional evidence can be found in the
bidirectional association between depression and coronary artery disease (CAD), and higher rates of depression among patients with vascular dementia than those with Alzheimer’s disease [12].

EPIDEMIOLOGY

Interest in geriatric depression has increased in recent years and several population studies have examined its prevalence, with results ranging from 1% to 20%. Methodological differences may account for this wide variability [13].

The WHO World Mental Health (WMH) Survey Initiative was launched in 2000 to obtain such data in large-scale psychiatric epidemiological surveys. Lebanon was the only Arab country included in the WMH survey (other countries have joined since). The Lebanese survey, the Lebanese Evaluation of the Burden of Ailments and Needs of the Nation (LEBANON), was undertaken by the Institute for Development, Research Advocacy and Applied Care (IDRAAC) with the Department of Psychiatry and Clinical Psychology at Balamand University, and St George Hospital University Medical Center. The primary goal was to produce nationally representative data for prevalence, correlates, and treatment of mental disorders, to raise awareness about mental illness, and to influence healthcare policy in Arab countries [14].

Based on the LEBANON study that interviewed nearly 3,000 subjects (nationally representative sample), 12.6% of the Lebanese population suffer from a lifetime prevalence of mood disorder. As for the geriatric population (65 years and older), 9.3% suffer from a lifetime prevalence of mood disorders (Fig. 1) [15].

The USA took part in the WHO World Mental Health (WMH) Survey Initiative. Nationally, 19% of the Americans suffer from a lifetime prevalence of mood disorder. As for the geriatric population, 12.4% suffer from a lifetime prevalence of mood disorder [16]. However, these rates may be higher in the community as the WMH Survey Initiative excluded people suffering from dementia. Some studies estimate that 20% to 40% of people suffering from early to moderate stages of dementia also suffer from depression.

STIGMA AND LACK OF AWARENESS OF DEPRESSION IN LEBANON AND DEVELOPING COUNTRIES

To some, the increased prevalence of depression in the United States compared to Lebanon may seem surprising. Residents of developing countries in general contend with stressors to a greater degree than in developed countries, and Lebanon is no exception. Political uncertainty, security concerns, and economic stress are the obvious constants, but in addition increasing fragmentation of family structure, limited healthcare access and social support, attitudes towards the elderly, and a widening gap between the rich and poor, all provide additional layers of stress.

One explanation lies in the stigma attached to mental illness and depression in Lebanon. Depression is often viewed as a sign of weakness—a character flaw that must be addressed by self-improvement. In some conservative societies of various religions, mental illness is considered a punishment from God for discretions committed by the family. Afflicted patients are kept away from public view, and the problem is not talked about. The shame of seeking help for depression is sometime sensed in the primary care setting, when patients present for “other” conditions, then apologetically seek help for stress and depression. It is quite possible that a sizable segment of the population remains undiagnosed and suffers in silence. In order to overcome this cultural hindrance, public awareness campaigns may prove helpful.

Another explanation would be the lack of awareness of this disorder among the public and primary care physicians alike. In the LEBANON study, people were asked if they would be ashamed to seek help for their depression and the answer was overwhelmingly in favor of seeking help. However, those that did suffer from depression often were not aware of their condition. Healthcare professionals must be vigilant and actively screen for depression, and initiate treatment when appropriate, or refer the patient when necessary.

![Figure 1](image_url)

**Figure 1**

Lifetime prevalence of mood disorder and major depression by age groups in Lebanon.[14]

MDD: Major depressive disorder. There was no statistical significance among age groups.
DEPRESSION AND THE RISK OF SUICIDE

Suicide rates are generally higher among the elderly compared to younger age groups, and are highest among elderly white males (Fig. 2). More than two thirds of suicides in the elderly take place in the context of depression, and 75% of all geriatric patients who succeed in suicide had seen their primary-care physician in the previous month [18]. Depressed elderly persons with suicidal ideation (active or passive) have higher depression ratings (i.e. severity) than depressed elders without suicidal ideation. Any suicidal ideation should be taken seriously since the elderly are less prone, compared with other age groups, to use the threat of suicide as a tool to manipulate others or as an attention-seeking measure.

In Lebanon, 4.3% of the population experienced suicidal ideation and 2% attempted suicide. As for the elderly population, 3% experienced suicidal ideation and almost 1% attempted suicide (Fig. 3). These rates were calculated from the LEBANON study [14]. It is believed, however, that these rates may be an underestimation of the actual rates due to moral, religious, and social reasons. Until the present time, there is no official suicide registry in Lebanon. Frequently, the cause of death (when due to suicide) is changed on official death certificates.

DIAGNOSIS

The differential diagnosis for depression includes other psychiatric disorders such as dysthymia and bipolar disorder, CNS diseases such as Parkinson’s disease and neoplastic lesions, endocrine disorders such as hypothyroidism and hyperthyroidism, drug-related conditions such as alcohol abuse or side effects of β-blockers, infectious disease such as syphilis, and sleep-related disorders. When indicated, alternative diagnoses and secondary causes of depression must be ruled out by appropriate tests. Complete blood count, serum electrolytes, blood urea nitrogen,
creatinine, serum toxicology screen, and thyroid function tests should be considered in the initial workup of depression.

Depression is a clinical diagnosis. In addition to a thorough history and physical examination, standardized screening tests can be used to screen for depression and bipolar disorder. The most widely used tests are the Hamilton Depression Rating Scale (HDRS) [19] and the Geriatric Depression Scale (GDS) [20]. While many instruments of varying degree of sophistication exist to measure depression, the GDS, first created by Yesavage et al. in 1983, has been tested and used extensively in the older population. It is a brief questionnaire in which participants are asked to respond to the 30 questions by answering “yes” or “no” in reference to how they felt on the day of administration. Scores of 0-9 are considered normal, 10-19 indicate mild depression and 20-30 indicate severe depression. The GDS may be used with healthy, medically ill, and mild to moderately cognitively impaired older adults. It has been extensively used in the community, acute and long-term care settings, and in research. The GDS was found to have 92% sensitivity and 89% specificity when evaluated against the DSM-IV diagnostic criteria. Validity and reliability of the tool have been supported through both clinical practice and research.

However, the GDS is not a substitute for a diagnostic interview by mental health professionals. It is a useful screening tool in the clinical setting to facilitate assessment of depression in older adults especially when baseline measurements are compared to subsequent scores.

Also, it is important to understand that the results obtained from the use of any depression rating scales are imperfect in any population, especially elderly patients.

COMORBIDITIES

Commonly, depression in the elderly is accompanied by other medical illnesses. A threshold or sub-threshold psychiatric disorder was detected in 42.5% of all patients consulting general practitioners [21]. Increased longevity of the elderly is accompanied by an increase in chronic medical problems such as osteoarthritis, chronic pain, sensory impairment, or debility. Quality of life may be compromised by the morbidity associated with these conditions, which, in turn, can contribute to further depression. It is also well documented that depression has direct bearing on physical health. As a result, an escalating cycle may develop where failing health triggers further depression, and depression worsens medical illness and disability [22].

For example, symptoms of depression affect between 20% and 25% of diabetics – nearly twice the prevalence of non-diabetics. In a cohort study of more than 78,000 women older than 54 years, investigators found a 35% increased risk of any cause of death for those with diabetes, a 44% increased risk for those with depression, and twice the risk of death for those with both conditions compared to their counterparts with neither [23]. Even after demographic variables, body mass index, smoking status, alcohol intake, physical activity, and comorbidities (including hypertension, hypercholesterolemia, heart diseases, stroke, and cancer) were adjusted for, women who had both conditions still had the highest relative risks for all cause mortality and cardiovascular mortality [23].

Regarding coronary artery disease, worsening depression in patients suffering from heart failure is associated with a doubling of the risk for cardiac-related hospitalization or death [24].

A significant increase in poor cardiovascular outcomes is seen regardless of any changes in the status of heart failure, suggesting that depression exerted the biggest influence on the increased risk. Moreover, depression is three times more common in patients after an acute myocardial infarction than in the general community [25].

Recognizing depression in an older patient with a host of medical ailments is not always straightforward. It is, therefore, not surprising that the diagnosis is often missed in the primary-care settings. However, when the diagnosis of depression is made correctly, and effective treatment is started, studies have shown that patients’ functional ability improve even though their underlying medical condition has not changed.

TREATMENT

A wide range of effective treatments are available for the management of major depressive disorder. Medication alone can relieve symptoms, and brief psychotherapy (e.g., cognitive-behavioral therapy, interpersonal therapy) has also been shown in clinical trials to be an effective treatment option, either alone or in combination with medication.

In 2011, the American Psychiatric Association (APA) updated its Practice Guideline for the Treatment of Patients with Major Depressive Disorder [26]. The guideline emphasizes the need to customize treatment for each patient based on a careful assessment of symptoms (including depression rating scale measurements) as well as an analysis of therapeutic benefits and side effects. Treatment should maximize patient function within specific and realistic goals. The initial treatment modality should be determined by clinical assessment, comorbidities, stressors, patient preference, and responses to previous treatments.

Medications

Currently, six classes of antidepressants exist on the market: selective serotonin reuptake inhibitors (SSRIs), selective serotonin/norepinephrine reuptake inhibitors (SNRIs), atypical antidepressants, tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs) and recently melanorenergic agonists. A detailed discussion of these medications is beyond the scope of this review.

■ Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) have the advantage of easy dosing and relatively low toxicity in overdose. This class includes: fluoxetine, fluvoxamine,
Selective serotonin/norepinephrine reuptake inhibitors

Atypical antidepressants

Monoamine oxidase inhibitors

Melatonergic agonists

Tricyclic antidepressants

The SSRIs are greatly preferred over the other classes of antidepressants due to their superior tolerability and more benign safety profile. The recommendation as first-line agents is supported by the 2011 APA guideline. Common adverse effects include gastrointestinal upset, sexual dysfunction, and changes in energy level (i.e., fatigue, restlessness). The SSRIs are not as problematic in patients with cardiac disease, as they do not appear to exert any effect on blood pressure, heart rate, cardiac conduction, or cardiac rhythm. Because the adverse effect profile of SSRIs is favorable, improved compliance over other agents is promoted.

Selectivity serotonin/norepinephrine reuptake inhibitors

Selective serotonin/norepinephrine reuptake inhibitors (SNRIs), which include venlafaxine, desvenlafaxine, and duloxetine, can be used as first-line agents, particularly in patients with significant fatigue or pain syndromes associated with the episode of depression. SNRIs also have an important role when used sequentially as second-line agents in patients who have not responded to SSRIs.

Atypical antidepressants

Atypical antidepressants effectively augment therapy in major depressive disorder. These agents include buproprion, mirtazapine, and trazodone. This group also shows low toxicity in overdose and may have an advantage over the SSRIs by causing less sexual dysfunction and GI distress.

Tricyclic antidepressants

These agents have a long record of efficacy in the treatment of depression and have the advantage of lower cost. They are used less commonly at present because of the need to titrate the dose to a therapeutic level, and due to their considerable side effects and toxicity in overdose.

Monoamine oxidase inhibitors

Monoamine oxidase inhibitors (MAOIs) are quite effective in a broad range of affective and anxiety disorders, and include phenelzine and tranylcypromine. Because of the risk of hypertensive crisis, patients administered MAOIs must follow a low-tyramine diet. Other adverse effects include insomnia, anxiety, postural hypotension, weight gain, and sexual dysfunction. Due to their side effect profile, MAOIs are rarely used at the present time.

Melatonergic agonists

This is the newest class of antidepressants, and currently includes only one molecule agomelatine. This drug was approved for treatment of depression by the European Medicines Agency (EMEA) in 2009, but has not gained FDA approval due to concerns with efficacy (but not safety). Agomelatine is a melatonergic agonist. It is indicated for the treatment of major depressive episodes in adults. Only limited clinical data is available on the use of agomelatine in elderly patients (≥ 65 years old) with major depressive disorder. Therefore, caution should be exercised when prescribing it to those patients [27].

Psychotherapy

The National Institute of Mental Health (NIMH) collaborative study (non-geriatric-age adults) reported that psychotherapy was equivalent in efficacy to antidepressant medication for all but the most severe cases of depressions [28]. If the depression occurs in the context of psychosocial stressors, psychotherapy may be all that is necessary to achieve a remission of depressive symptoms in an older person willing to engage in self-reflection. For those with more severe depression that includes considerable vegetative symptoms, such as disorganized sleep or significant weight loss, an antidepressant is also often required. Since depression is always experienced in a social context, with frequent disruption of interpersonal relationships, combined treatment with antidepressant medication and psychotherapy often seems the most reasonable choice. A psychotherapeutic component to treatment strategies can also help ensure adherence to a medication regimen, as well as educate the patient about the symptoms and mechanisms of depression in order to place the patient’s social dysfunction in a rational perspective. Several short-term psychotherapy approaches have been developed for the elderly. A full description is beyond the scope of this review but can be found elsewhere [29].

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is a very effective treatment for depression; it is usually undertaken after several medication trials have failed or when a patient is severely vegetative or suicidal. In 1938, the question of inducing seizures as treatment for depression was explored after it was noted that epileptic patients who were depressed showed a marked improvement in mood after a seizure. Treatment with ECT for depression was found to be successful [30]. Despite a long history attesting to the safety and efficacy of this intervention (particularly with the advent of neuromuscular blocking agents), ECT continues to suffer from negative connotations in the public mind. Misguided impressions are based more in popular culture, such as the graphic depiction of the process in movies, rather than in clinical facts. As a result, ECT may be shunned as a treatment option, when, in fact, in select patients it can be as (or more) effective than pharmacological intervention.

Typically, 6 to 12 ECT treatments are required for an antidepressant response. Maintenance antidepressant medication is begun upon completion. Unilateral ECT causes less memory loss and confusion compared with bilateral ECT and is attempted first. Patients with coexisting dementia are prone to post-ECT confusion and may require a longer time-interval between treatments. Some centers offer outpatient maintenance ECT for patients who cannot be stabilized on antidepressant medication.

A common myth is that ECT causes permanent memory damage. The seizure induced by ECT certainly causes temporary interference with the laying down of new memory, such that patients often have impaired recall of events experienced immediately prior to their ECT treat-
ment. However, long-term follow-up studies have not demonstrated any difference in memory at six months after a completed course of ECT, compared with baseline [31].

**Hospitalization**

Depressed geriatric patients should be considered for inpatient psychiatric hospitalization if they are suicidal, have complex medical problems, are candidates for ECT, show severe psychotic symptoms, or do not have an adequate social support system. A specialized geriatric psychiatry unit is preferred in order to maximize the benefit of a trained multidisciplinary team of psychiatrists, internists, nurses, and psychologists to address the patient’s needs.

**CONCLUSION**

Research, improved awareness, and treatment advances have revolutionized the care of depressed elderly persons in the last fifteen years. With current resources and knowledge, optimism has justifiably replaced therapeutic nihilism. The current task at hand is to educate the public in general, and all healthcare workers in particular, about the availability of effective treatments. Depression should never be considered normal, neither in childhood nor in later life.

**REFERENCES**