

Depression: When and How to Treat a Debilitating Disease



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Learning Objectives

Upon completion of this course, you should be able to:

- ▶ Describe the pathophysiology of the various forms of depression
- ▶ Describe the pharmaceutical and nonpharmaceutical options for treating various types of depression
- ▶ Identify criteria for referring patients to a mental health professional

For information on how to earn CE contact hours, see inside front cover. To view disclosure information, see page 5. Participation in this self-study activity should be completed in about 1 hour.

Course ID: AB0436

An estimated 4.6% to 8.6% of patients seen by primary care professionals suffer from depression and only about one-third to one-half of those depression cases are detected during a consultation. Changes in the way healthcare is delivered make it more important than ever for primary care professionals to assume responsibility for the diagnosis and treatment of this common disorder. This article provides an overview of the pharmacologic options for treating the many forms of this debilitating disease. Criteria for deciding when to refer a patient to a mental health professional are also discussed.

Introduction

Mood or affective disorders are characterized by a disturbance in the regulation of mood, behavior, or affect. They are subdivided into 3 categories: depressive disorders, depression in association with a medical illness or substance abuse, and bipolar disorders. Depression is a leading cause of disability worldwide, and it is

the third most common reason for consultation in primary care.^{1,2} Despite the frequency in which depression is seen and the availability of effective interventions, the diagnosis and treatment of depression by nonspecialist healthcare professionals often does not follow current guidelines,^{3,4} and many individuals suffering from depression receive no treatment for their

symptoms.⁵⁻⁷ As a result, patient outcomes are compromised.⁸⁻¹³

Definition

Depression is now recognized as a multi-system disorder affecting both brain and body. Depression causes alterations in the endocrine, cardiovascular, and immune systems and results in changes in bone metab-

ABBREVIATIONS	
ADD	attention deficit disorder
ECT	electroconvulsive therapy
EPS	extra pyramidal symptoms
IPT-D	interpersonal psychotherapy for depression
MAOI	monoamine oxidase inhibitor
OD	overdose
REM	rapid eye movement
SSRI	selective serotonin reuptake inhibitor
TCA	tricyclic antidepressant

olism as well.¹⁴⁻¹⁶ Several different types of depressive disorders exist; a more detailed explanation of the signs and symptoms associated with each of type is addressed in Course 1 on the accompanying CD.

Major depression

Major depression is defined as depressed mood occurring on a daily basis for a minimum of 2 weeks. (See Table 1.¹⁷) Episodes can be characterized by apathy, indifference, sadness, or irritability. Associated signs and symptoms include changes in sleep patterns, appetite, and weight; motor agitation or retardation; fatigue; impaired concentration and decision-making; feelings of shame or guilt; and thoughts of death or dying. Depressed patients often report a profound loss of pleasure in all enjoyable activities. They frequently exhibit early morning awakening and often notice a diurnal variation in mood, with more extreme feelings of sadness earlier in the day. Approximately 15% of the population experiences a major depressive episode at some point in life, and 6% to 8% of all outpatients in primary care settings satisfy the diagnostic criteria for this disorder.¹⁷

Dysthymia

Dysthymia consists of a pattern of chronic (at least 2 years), ongoing, mild depressive symptoms that are less severe and less disabling than those noted in major depression. Patients may exhibit a profile of pessimism, disinterest, and low self-esteem; this disorder exists in about 5% of patients seen in primary care practice.

Minor depression

Minor depression is a diagnosis used for

individuals who experience at least 2 symptoms for 2 weeks but do not meet the full criteria for major depression. Despite its name, minor depression is associated with significant morbidity and mortality.

Unipolar depressive disorder

Unipolar depressive disorder usually begins in early adulthood and recurs episodically during a person's lifetime. Fifty percent of people with unipolar depression who experience 1 episode have at least 1 or more recurrences.

Seasonal affective disorder

A seasonal pattern of depression manifests with the onset and remission of episodes

at predictable times of the year. This disorder is more common in women and symptoms include anergy, fatigue, weight gain, and episodic carbohydrate craving.

Bipolar disorder

Bipolar disorder is characterized by unpredictable swings in mood, from mania (or hypomania) to depression. Some patients suffer from recurrent attacks of mania. Half of patients with bipolar disorder present with a mixture of psychomotor agitation and activation, with dysphoria, anxiety, or irritability. In patients diagnosed with bipolar II disease, the full criteria for mania are lacking, but depression episodes are separated by periods of mild

TABLE 1. CRITERIA FOR MAJOR DEPRESSIVE DISORDERS

Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either: (1) depressed mood or (2) loss of interest or pleasure. Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

- Depressed mood most of the day, nearly every day, as indicated by either subjective report (eg, feels sad or empty) or observation made by others (eg, appears tearful)
- 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)
- Significant weight loss when not dieting or weight gain (eg, a change of >5% of body weight in a month), or decrease or increase in appetite nearly every day.
- Insomnia or hypersomnia nearly every day
- Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
- Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
- 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 symptoms do not meet the criteria for a mixed episode

The symptoms cause clinically significant stress or impairment in social, occupational, or other important areas of functioning

The symptoms are not due to the direct physiologic effects of a substance (eg, a drug of abuse, a medication) or a general medical condition (eg, hypothyroidism)

The symptoms are not better accounted for by bereavement; ie, after the loss of a loved one, the symptoms persist for >2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation

Diagnostic and Statistical Manual of Mental Disorders, 4th ed.¹⁷

activation and increased energy. Patients with cyclothymic disease experience numerous hypomanic periods of short duration followed by clusters of depressive symptoms. Bipolar disease affects about 1% of the population of the United States and is usually diagnosed between the ages of 20 and 30 years.

Depression associated with medical illness
Depression that occurs in the context of a medical illness can be difficult to diagnose and can be related to several causes. Virtually every class of medication includes some agents that can cause depression. Depressive symptoms often follow unstable angina, myocardial infarction, or heart transplant, which impairs rehabilitation and leads to higher morbidity and mortality rates. Evidence also exists indicating that depression increases a patient's risk of developing coronary artery disease;¹⁸ in patients with cancer, depression rates are approximately 25%. Neurologic disorders, diabetes mellitus, hypothyroidism, chronic obstructive pulmonary disease, and chronic hepatitis C infection are also associated with depression.

A recent development in the treatment of depression is the recognition that depression is a recurrent or chronic disorder.¹⁹ Evidence from longitudinal studies indicates that about 80% of patients who experience a major depressive disorder will have at least 1 more episode during their lifetimes.¹⁹ While this may be unwelcome news for patients suffering from depression, the good news is that newer medications for the treatment of depression have been developed that offer simple dosing schedules, favorable adverse-effect profiles, and less risk of overdose.²⁰

Exercise 1

A patient presents with enough symptoms to make a diagnosis of depression according to the DSM-IV. Which of the following must first be ruled out before making the diagnosis of major depression?

- History of overeating
- Family history of depression
- Current substance abuse
- All of the above

Answer on page 24.

Pathophysiology of Depression

Recent progress has been made in identifying the neural circuits and neurochemicals involved in the vulnerability toward depressive illness.²¹ Neuroimaging studies have revealed abnormalities in several regions of the prefrontal cortex, amygdala, and hippocampus.²² Abnormalities in the regulation of neurotransmitters, including serotonin, norepinephrine, dopamine, glutamate, and γ -aminobutyric acid, and hormones and neuropeptides, such as cortisol, corticotrophin-releasing hormone, neuropeptide Y, and substance P, have also been reported.²³ These findings have contributed to the development of novel antidepressants, but none has resulted in a specific biomarker or diagnostic test for the disease. Vulnerability genes for depression have not been identified, although recently several genes for other neuropsychiatric disorders have been found;²⁴ these findings have provided the basis for the development of currently available antidepressants.

Life stress and biological susceptibility are also believed to play important roles in the onset of a depressive disorder.²⁵⁻²⁷ Kindling refers to repeated, intermittent, subthreshold stimulation that evokes increasingly widespread biochemical and physiologic manifestations culminating in a progression of behavioral abnormalities, which if sufficiently repeated, become spontaneous. This theory explains why depression often begins with a major stressful event, but later patients can relapse even if they are not exposed to a stressful event. Kraepelin observed that untreated bipolar illness tends to be progressive, and that initial episodes of mania and depression may be precipitated by stressors, but with repetition may occur more autonomously and with a shorter interval. In 1921, he made a classic observation about a patient who became depressed "...after the death first of her husband, next of her dog, and then of her dove."²⁸ Not only is there evidence of stress sensitization (an increasing sensitivity to psychosocial stressors), but there is now also strong evidence of episode sensitization (the increased vulnerability to recurrence with shorter well-intervals as a function of the number of prior episodes). However, with appropriate psychotherapeutic

and pharmacotherapeutic intervention, episodes and episode progression can be prevented.²⁹

Pharmacologic Treatment

Treatment of depression is based on balancing short-term symptom remission with long-term maintenance strategies for preventing recurrence. One study reported that approximately 28% of patients with a new prescription for antidepressants stopped taking the medication during the first month of therapy. Of the group of patients who were compliant until the end of the first month, when they were interviewed at the end of the third month, 44% of them had stopped taking their antidepressants. Only severe side effects, which were few, were associated with early noncompliance, suggesting that noncompliance is not highly associated with issues of tolerability.³⁰

Poor concordance with medication regimens can arise from inadequate counseling regarding the need for antidepressants.³¹ Several educational strategies targeted at healthcare professionals and innovative methods of organizing and providing healthcare have been proposed to improve the recognition and management of depression in nonspecialist settings such as primary care.^{32, 33} The most successful interventions include frequent visits during the first 4 to 6 weeks of treatment, supplemental educational materials, and psychological support. Although there are many effective antidepressants, none is ideal. Figure 1 outlines an approach to choosing an agent for a patient. A good approach to choosing the right antidepressant involves matching the patient's preferences and medical history with the drug's metabolic and side effect profiles. Table 3¹⁸ lists some strategies for managing side effects related to antidepressants.

Types of Antidepressants

MAOIs

The monoamine oxidase inhibitors (MAOIs) were some of the first antidepressants developed. The neurotransmitters responsible for mood, primarily norepinephrine and serotonin, are also known as monoamines. Monoamine oxidase is an enzyme that breaks down these substances. MAOIs inhibit this enzyme, thereby increasing the supply of norepinephrine and serotonin.

TABLE 2. ANTIDEPRESSANTS

Name	Usual Daily Dose, mg	Side Effects	Comments
SSRIs			
Fluoxetine (Prozac)	10–80	Headache; nausea and other GI effects; jitteriness; insomnia; sexual dysfunction; can affect plasma levels of other meds (except sertraline); akathisia rare	Once-daily dosing, usually in am; fluoxetine has very long half-life; must not be combined with MAOIs
Sertraline (Zoloft)	50–200		
Paroxetine (Paxil)	20–60		
Fluvoxamine (Luvox)	100–300		
Citalopram (Celexa)	20–60		
Escitalopram (Lexapro)	10–30		
TCAs			
Amitriptyline (Elavil)	150–300	Anticholinergic (dry mouth, tachycardia, constipation, urinary retention, blurred vision); sweating; tremor; postural hypotension; cardiac conduction delay; sedation; weight gain	Once-daily dosing, usually qhs; blood levels of most TCAs available; can be lethal in O.D. (lethal dose=2g); nortriptyline best tolerated, especially by elderly
Nortriptyline (Pamelor)	50–200		
Imipramine (Tofranil)	150–300		
Desipramine (Norpramin)	150–300		
Doxepin (Sinequan)	150–300		
Clomipramine (Anafranil)	150–300		
Mixed Norepinephrine/Serotonin Reuptake Inhibitors			
Venlafaxine (Effexor)	75–375	Nausea; dizziness; dry mouth; headaches; increased blood pressure; anxiety and insomnia	Bid-tid dosing (extended release available); lower potential for drug interactions than SSRIs; contraindicated with MAOIs
Mirtazapine (Remeron)	15–45	Somnolence; weight gain; neutropenia rare	Once daily dosing
Mixed-Action Drugs			
Bupropion (Wellbutrin)	250–450	Jitteriness; flushing; seizures in at-risk patients; anorexia; tachycardia; psychosis	Tid dosing, but sustained release also available; fewer sexual side effects than SSRIs or TCAs; may be useful for adult ADD
Trazodone (Desyrel)	200–600	Sedation; dry mouth; ventricular irritability; postural hypotension; priapism rare	Useful in low doses for sleep because of sedating effects with no anticholinergic side effects
Nefazodone (Serzone)	300–600	Sedation; headache; dry mouth; nausea; constipation	Once-daily dosing; no effect on REM sleep, unlike other antidepressants
Amoxapine (Asendin)	200–600	Sexual dysfunction	Lethality in overdose; EPS possible
MAOIs			
Phenelzine (Nardil)	45–90	Insomnia; hypotension; anorgasmia; weight gain; hypertensive crisis; tyramine cheese reaction; lethal reactions with SSRIs; serious reactions with narcotics	May be more effective in patients with atypical features or treatment-refractory depression
Tranylcypromine (Parnate)	20–50		
Isocarboxazid (Marplan)	20–60		

Reus VI, 1995¹⁸

The MAOIs are highly effective, particularly in atypical depression, but the risk of hypertensive crisis following intake of tyramine-containing foods or psychomimetic drugs makes them inappropriate as first-line agents. Common side effects include orthostatic hypertension, weight gain, insomnia, and sexual dysfunction. MAOIs should not be taken concomitantly with selective serotonin reuptake inhibitors (SSRIs) because of the risk of serotonin syndrome, or with tricyclic antidepressants (TCAs) because of possible hyperadrenergic effects.¹⁹

TCAs

Tricyclic antidepressants (TCAs) are one of the oldest classes of antidepressants and are still used extensively. Before the introduction of SSRIs, TCAs were the standard treatment for depression. However, they are associated with more side effects than the newer antidepressants. In patients who are depressed, decreased amounts of noradrenaline and serotonin are released from nerve cells. TCAs prevent this reabsorption of noradrenaline and serotonin back into the nerve cells. This prolongs the mood-lightening effect of any released noradrenaline and serotonin and in this way helps to relieve depression.

Although TCAs have some disadvantages, some advantages are associated with these drugs. The existence of generic equivalents makes them inexpensive. Additionally, there is a well-defined relationship between dose, plasma level, and therapeutic response for several of the TCAs, particularly nortriptyline, imipramine, and deipramine;¹⁸ the principal side effects associated with TCAs are antihistamine (sedation) and anticholinergic (constipation, dry mouth, urinary hesitancy, and blurred vision. Cardiac toxicity due to conduction block can also occur, but this is uncommon when the drugs are taken at therapeutic levels. Nevertheless, TCAs are contraindicated in patients with serious cardiovascular risk factors.

SSRIs

The serotonergic system modulates mood, emotion, sleep, and appetite and is implicated in the control of numerous behavioral and physiologic functions. Decreased serotonergic neurotransmission has been proposed to play a key role in depression. The selective serotonin

reuptake inhibitors (SSRIs) are drugs that selectively and powerfully inhibit serotonin reuptake and result in a potentiation of serotonergic neurotransmission. One of the advantages of these drugs is that they have low toxicity if taken in overdose. They were developed to replace TCAs, which can be toxic, for the treatment of depression.

Newer medications

Four newer medications that do not fit into the other categories are bupropion, nefazodone, venlafaxine, and mirtazapine. Bupropion is a novel antidepressant whose mechanism of action is thought to involve enhancement of adrenergic function. It has no anticholinergic, sedating, or orthostatic side effects and has a low incidence of sexual side effects. It may, however, be associated with stimulant-like side effects, may lower seizure threshold, and has an exceptionally short half-life. An extended-release preparation is available.

Nefazadone is a selective 5HT₂ receptor antagonist that also inhibits the presynaptic reuptake of serotonin and norepinephrine. Its side effects are similar to those of the SSRIs, and twice-daily dosing produces steady-state levels in 4 to 5 days. The drug is structurally related to trazodone, which is used for its sedative rather than its antidepressant effects. Nefazadone appears to produce a lower incidence of sexual side effects than the SSRIs.

Venlafaxine, like imipramine, blocks the reuptake of both norepinephrine and serotonin, but it produces relatively few of the side effects associated with the traditional tricyclics. Unlike the SSRIs, it has a relatively linear dose-response curve. Patients taking venlafaxine should be monitored for a possible increase in diastolic blood pressure.

Mirtazapine, a tetracyclic antidepressant that has a unique spectrum of activity, is the most recently released of the newer

TABLE 3. MANAGEMENT OF ANTIDEPRESSANT SIDE EFFECTS

Symptoms	Comments and Management Strategies
Nausea, loss of appetite	Usually short-lived and dose-related; consider temporary dose reduction or administration with food and antacids
Diarrhea	Famotidine, 20–40 mg/d
Constipation	Wait for tolerance; try diet change, stool softener, exercise; avoid laxatives
Sexual dysfunction	Consider dose reduction; drug holiday
Anorgasmia/impotence; impaired ejaculation	Bethanechol, 10–20 mg, 2 h before activity, or cyproheptadine, 4–8 mg 2 h before activity, or bupropion, 100 mg bid or amantadine, 100 mg bid/tid
Orthostasis	Tolerance unlikely; increase fluid intake, use calf exercises/support hose; fludrocortisone, 0.025 mg/d
Anticholinergic	Wait for tolerance
Dry mouth, eyes	Maintain good oral hygiene; use artificial tears, sugar-free gum
Tremor/jitteriness	Antiparkinsonian drugs not effective; use dose reduction/slow increase; lorazepam, 0.5 mg bid, or propranolol, 10–20 mg bid
Insomnia	Schedule all doses for the morning; trazodone, 50–100 mg qhs
Sedation	Caffeine; schedule all dosing for bedtime; bupropion, 75–100 mg in afternoon
Headache	Evaluate diet, stress, other drugs; try dose reduction; amitriptyline, 50 mg/d
Weight gain	Decrease carbohydrates; exercise; consider fluoxetine
Loss of therapeutic benefit over time	Related to tolerance? Increase dose or drug holiday; add amantadine, 100 mg bid, buspirone, 10 mg tid, or pindolol, 2.5 mg bid
Reus VI, 1995 ¹⁸	

medications. It increases noradrenergic and serotonergic neurotransmission through a blockade of central α_2 -adren-
 ergic receptors and postsynaptic 5HT₂
 and 5HT₃ receptors. Because it is strongly
 antihistaminic, it may produce sedation.

Other Therapeutic Options

Electroconvulsive therapy

Researchers have found that electro-
 convulsive therapy (ECT) is at least as
 effective as medication but is reserved for
 individuals whose depression is severe or
 for those who cannot take antidepressant
 medication.³⁴ ECT is often effective in
 cases in which antidepressant medica-
 tion does not provide sufficient symptom
 relief. In recent years, ECT has improved;
 a muscle relaxant is given before ECT
 treatment, which is performed under
 general anesthesia. Electrodes are placed
 at precise locations on the patient's head
 to deliver electrical impulses. The stimu-
 lation causes a brief seizure in the brain.
 For full therapeutic benefit, several ECT
 sessions are required.

Transcranial magnetic stimulation is an
 investigational treatment of depression
 that has been shown to be effective in
 controlled clinical trials; however, it is
 uncertain whether these results are clini-
 cally relevant. Vagus-nerve stimulation
 appeared to be effective in treatment-
 resistant depression in an initial open
 study, but it failed in a controlled trial.

Psychotherapy

While interpersonal therapy and
 cognitive-behavioral therapy have been
 most studied with depressed patients,
 brief psychodynamic therapy recently,
 using vigorous controlled studies, shows
 promising results.^{35,36} Other studies stress
 the quality of the therapy as the key to
 preventing relapse.^{34,37} Therapy may be
 particularly helpful for patients with dys-
 thymia, as 50% either do not respond to
 treatment or refuse to take it.³⁸

The potential efficacy of psychotherapy
 has been the subject of numerous
 scientific studies since the mid-1980s.³⁹

Since that time, 2 major forms of
 psychotherapy—cognitive and interper-
 sonal—have been found to be equally
 effective and equally rapid in their initial
 response. However, longer periods of
 therapy appear to be associated with
 better long-term outcomes.⁴⁰ Cognitive
 behavior therapy, first described by Beck
 and colleagues,⁴¹ involves the restructur-
 ing of cognitive distortions and automatic
 negative thoughts that patients commonly
 develop in response to long-standing
 depression. The second form of psycho-
 therapy, interpersonal psychotherapy
 for depression (IPT-D), is based on the
 work of Gerald Klerman and colleagues.⁴²
 IPT-D uses a standardized series of 12 to
 16 weekly sessions described in a treat-
 ment manual; therapy focuses on inter-
 personal problems and conflicts that arise
 as a result of chronic depression, such as
 the inability to assert oneself or unwilling-
 ness to take risks. This type of therapy,
 which helps patients learn how to disen-
 tangle the long-standing effects of chronic
 depression from their core character,
 has been found to be effective in 65% of
 patients with dysthymia.³⁸

Combined pharmacotherapy and psychotherapy

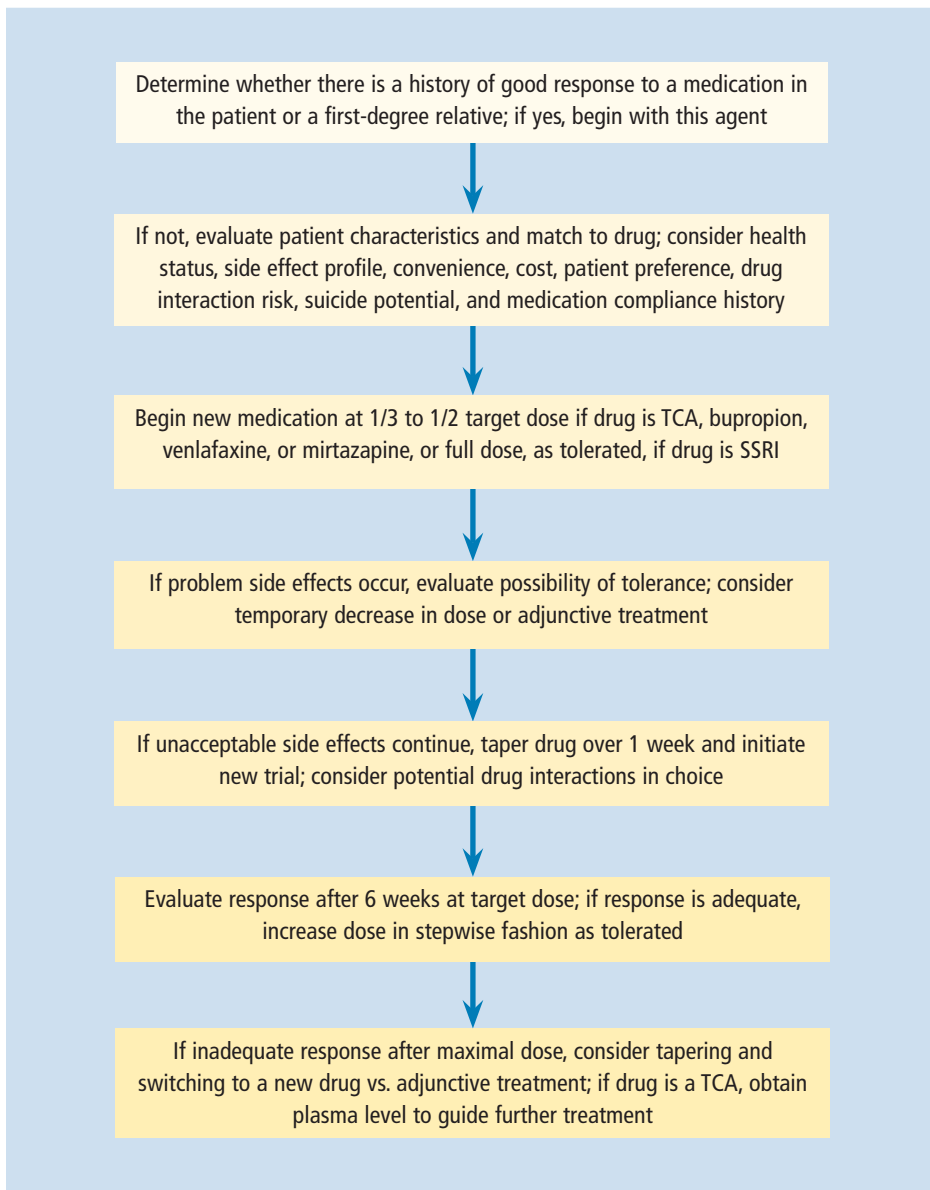
A study was conducted to compare the
 efficacy of antidepressants with that of
 antidepressants plus psychotherapy in
 the treatment of depression.⁴³ Patients
 were randomized to 2 groups—one
 group received antidepressants alone
 (n=84) and one group received combined
 therapy (n=83). The antidepressant pro-
 tocol provided for 3 successive steps in
 case of intolerance or inefficacy: fluox-
 etine, amitriptyline, and moclobemide.
 The combined group received, in addi-
 tion to pharmacotherapy, 16 sessions of
 short psychodynamic supportive psycho-
 therapy. In 24 weeks, 40% of the patients
 who began the pharmacotherapy stopped
 taking the medication and 22% of those
 receiving the combined therapy stopped
 taking the medication. The difference in
 success rates was statistically significant,
 favoring combined therapy, in 23%,
 31%, and 62% of the patients after 8, 16,
 and 24 weeks of treatment, respectively.
 At week 24, the mean success rate was
 40.7% in the pharmacotherapy group
 and 59.2% in the combined therapy
 group. If patients believed that combined
 treatment was significantly more accept-

TABLE 4. CLINICAL PHARMACOLOGY OF MOOD STABILIZERS

Agent and Dosing	Side Effects and Other Effects
Lithium Starting dose: 300 mg bid or tid Therapeutic blood level: 0.8–1.2 meq/L	<ul style="list-style-type: none"> ■ Common side effects: Nausea/anorexia/diarrhea, fine tremor, thirst, polyuria, fatigue, weight gain, acne, folliculitis, neutrophilia, hypothyroidism ■ Blood level is increased by thiazides, tetracyclines, and NSAIDs ■ Blood level is decreased by bronchodilators, verapamil, and carbonic anhydrase inhibitors ■ Rare side effects: Neurotoxicity, renal toxicity, hypercalcemia, ECG changes
Valproic acid Starting dose: 250 mg tid Therapeutic blood level: 50–125 µg/mL	<ul style="list-style-type: none"> ■ Common side effects: Nausea/anorexia, weight gain, sedation, tremor, rash, alopecia ■ Inhibits hepatic metabolism of other medications ■ Rare side effects: Pancreatitis, hepatotoxicity, Stevens-Johnson syndrome
Carbamazepine/ oxcarbazepine Starting dose: 200 mg bid for carbamazepine, 150 bid for oxcarbazepine Therapeutic blood level: 4– 12 µg/mL for carbamazepine	<ul style="list-style-type: none"> ■ Common side effects: Nausea/anorexia, sedation, rash, dizziness/ataxia ■ Carbamazepine, but not oxcarbazepine, induces hepatic metabolism of other medications ■ Rare side effects: Hyponatremia, agranulocytosis, Stevens-Johnson syndrome
Lamotrigine Starting dose: 25 mg/d	<ul style="list-style-type: none"> ■ Common side effects: Rash, dizziness, headache, tremor, sedation, nausea ■ Rare side effect: Stevens-Johnson syndrome

Reus VI, 1995¹⁸

FIGURE 1. GUIDELINES FOR THE MEDICAL MANAGEMENT OF MAJOR DEPRESSIVE DISORDER¹⁸



able, they were significantly less likely to drop out of combined therapy and, ultimately, they were significantly more likely to recover. The authors concluded that combined therapy is preferable to pharmacotherapy in treating ambulatory patients with major depression.

Exercise 2

Research has found that the most productive therapy for a nonsuicidal depressed patient is:

- a. Treatment with medication alone
- b. Treatment with talk therapy alone
- c. A combination of pharmacotherapy and psychotherapy
- d. Inpatient treatment

Answer on page 24.

Other controlled trials have also shown that cognitive-behavioral and interpersonal therapy are effective in improving psychological and social adjustment and that a combined approach is more successful in most patients. All patients with suicidal ideation should be immediately referred to a psychiatric clinician, such as an advanced practice psychiatric nurse, psychologist, clinical social worker, or psychiatrist; in all patients, the response to therapy should be evaluated at 2 months and a decision about continuation of or changes in treatment should be made at that time.¹⁸

Treatment of Bipolar Disorder

Mood stabilizers are used in the treat-

TABLE 5. CONSENSUS GUIDELINES ON THE DRUG TREATMENT OF ACUTE MANIA AND BIPOLAR DEPRESSION⁴⁴

Condition	Preferred Agents
Euphoric mania	Lithium
Mixed/dysphoric mania	Valproic acid
Mania with psychosis	Valproic acid with olanzapine, conventional antipsychotic, or risperidone
Hypomania	Lithium, lamotrigine, or valproic acid alone
Severe depression with psychosis	Venlafaxine, bupropion, or paroxetine plus lithium plus olanzapine, or risperidone; consider ECT
Severe depression without psychosis	Bupropion, paroxetine, sertraline, venlafaxine, or citalopram plus lithium
Mild to moderate depression	Lithium or lamotrigine alone; add bupropion if needed

Sachs GS et al, 2000⁴⁴

ment of bipolar disorder to control the mood swings of the manic and depressed phases of the disorder. (See Table 4.¹⁸) Lithium carbonate is the mainstay of treatment in bipolar disorder; however, sodium valproate and olanzepine are equally effective in acute mania, and lamotrigine is effective in bipolar depression. The recurrent nature of bipolar disorder makes maintenance therapy necessary. A sustained blood lithium level of at least 0.8 mEq/L is important for optimal prophylaxis and has been shown to reduce risk of suicide. Compliance is frequently a problem and requires the assistance and education of concerned family members. Antidepressant medications are sometimes required for breakthrough depression, but they should be avoided during maintenance therapy because they can precipitate mania or accelerate the cycle frequency. Consensus guidelines for the treatment of acute mania and bipolar depression are described in Table 5.⁴⁴

Exercise 3

A man presents to your outpatient practice appearing depressed and talking about suicide. What is your first step in treating this patient?

- a. Prescribe an SSRI antidepressant
- b. Perform labs to check for an underlying medical condition
- c. Recommend ECT
- d. Refer to a psychiatric clinician

Answer on page 24.

Conclusion

Depression is a multisystem disorder seen in 4.6% to 8.6% of patients seen in primary practice. About one-third to one-half of cases of depression is detected; however, even when the disease is identified, patient outcomes are often poor. Finding the right antidepressant, taking the time to ensure that the patient understands and agrees to the goals of therapy, and referring patients for psychotherapy as needed are all steps that can improve outcomes for patients with this debilitating disease. ■

Answers

Exercise 1

A patient presents with enough symptoms to make a diagnosis of depression according to the DSM-IV. Which of the following must first be ruled out before making the diagnosis of major depression?

- a. History of overeating
- b. Family history of depression
- c. Current substance abuse
- d. All of the above

Answer: c. In order to make the diagnosis of major depression, it must be established that the symptoms “are not due to the direct physiologic effects of a substance (eg, a drug of abuse, a medication) or a general medical condition.”

Exercise 2

Research has found that the most productive therapy for a nonsuicidal depressed patient is:

- a. Treatment with medication alone
- b. Treatment with talk therapy alone
- c. A combination of pharmacotherapy and psychotherapy
- d. Inpatient treatment

Answer: c. Combined therapy is preferable to either treatment alone, resulting in a greater success rate and better adherence to treatment.

Exercise 3

A man presents to your outpatient practice appearing depressed and talking about suicide. What is your first step in treating this patient?

- a. Prescribe an SSRI antidepressant
- b. Perform labs to check for an underlying medical condition
- c. Recommend ECT
- d. Refer to a psychiatric clinician

Answer: d. Immediate intervention is needed. An advanced practice psychiatric nurse, psychologist, clinical social worker, or psychiatrist are all good referrals.

For information on how to earn CE contact hours, see inside front cover.

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