Depressive Disorders

http://lifeskillssouthflorida.com/what-we-treat/depressive-disorders/

Depressive disorders are characterized by sadness severe enough or persistent enough to interfere with function and often by decreased interest or pleasure in activities. Exact cause is unknown but probably involves heredity, changes in neurotransmitter levels, altered neuroendocrine function, and psychosocial factors. Diagnosis is based on history. Treatment usually consists of drugs, psychotherapy, or both and sometimes electroconvulsive therapy.

The term depression is often used to refer to any of several depressive disorders. Three are classified in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Text Revision (DSM-IV-TR) by specific symptoms:

- Major depressive disorder (often called major depression)
- Dysthymia
- Depressive disorder not otherwise specified

Two others are classified by etiology:

- Depressive disorder due to a general physical condition
- Substance-induced depressive disorder

Depressive disorders occur at any age but typically develop during the mid-teens, 20s, or 30s. In primary care settings, as many as 30% of patients report depressive symptoms, but < 10% have major depression.

The term depression is often used to describe the low or discouraged mood that results from disappointments or losses. However, a better term for such a mood is **demoralization**. The negative feelings of demoralization, unlike those of depression, resolve when circumstances or events improve; the low mood usually lasts days rather than weeks or months, and suicidal thoughts and prolonged loss of function are much less likely.

Etiology

Exact cause is unknown, but genetic and environmental factors contribute.

Heredity accounts for about half of the etiology (less so in late-onset depression). Thus, depression is more common among 1st-degree relatives of depressed patients, and **concordance** between identical twins is high. Also, genetic factors probably influence the development of depressive responses to adverse events.

Other theories focus on changes in neurotransmitter levels, including abnormal regulation of cholinergic, catecholaminergic (noradrenergic or dopaminergic), and serotonergic (5-hydroxytryptamine) neurotransmission. Neuroendocrine dysregulation may be a factor, with particular emphasis on 3 axes: hypothalamic-pituitary-adrenal, hypothalamic-pituitary-thyroid, and growth hormone.

Psychosocial factors also seem to be involved. Major life stresses, especially separations and losses, commonly precede episodes of major depression; however, such events do not usually cause lasting, severe depression except in people predisposed to a mood disorder.

People who have had an episode of major depression are at higher risk of subsequent episodes. People who are introverted and who have anxious tendencies may be more likely to develop a depressive disorder. Such people often do not develop the social skills to adjust to life pressures. Depression may also develop in people with other mental disorders.

Women are at higher risk, but no theory explains why. Possible factors include greater exposure to or heightened response to daily stresses, higher levels of monoamine oxidase (the enzyme that degrades neurotransmitters considered important for mood), higher rates of thyroid dysfunction, and endocrine changes that occur with menstruation and at menopause. In postpartum depression, symptoms develop within 4 wk after delivery; endocrine changes have been implicated, but the specific cause is unknown.

In seasonal affective disorder, symptoms develop in a seasonal pattern, typically during autumn or winter; the disorder tends to occur in climates with long or severe winters.

Depressive symptoms or disorders may accompany various physical disorders, including thyroid and adrenal gland disorders, benign and malignant brain tumors, stroke, AIDS, Parkinson's disease, and multiple sclerosis (see Table 1: Mood Disorders: Some Causes of Symptoms in Depression and Mania). Certain drugs, such as corticosteroids, some β-blockers, interferon, and reserpine, can also result in depressive disorders. Abuse of some recreational drugs (eg, alcohol, amphetamines) can lead to or accompany depression. Toxic effects or withdrawal of drugs may cause transient depressive symptoms.

Table 1

Some Causes of Symptoms in Depression and Mania

Type of Disorder	Depression	Mania
Connective tissue	SLE	Rheumatic fever SLE
Endocrine	Addison's disease	Hyperthyroidism

	Cushing's disease Diabetes mellitus Hyperparathyroidism Hyperthyroidism Hypothyroidism Hypopituitarism Hypogonadism	
Infectious	AIDS General paresis (parenchymatous neurosyphilis) Influenza Infectious mononucleosis TB Viral hepatitis Viral pneumonia	AIDS General paresis Influenza St. Louis encephalitis
Neoplastic	Cancer of the head of the pancreas Disseminated carcinomatosis	
Neurologic	Cerebral tumors Complex partial seizures (temporal lobe) Head trauma Multiple sclerosis Parkinson's disease Sleep apnea Stroke (left frontal)	Complex partial seizures (temporal lobe) Diencephalic tumors Head trauma Huntington's disease Multiple sclerosis Stroke
Nutritional	Pellagra Pernicious anemia	
Other*	Coronary artery disease Fibromyalgia Renal or hepatic failure	
Pharmacologic	Amphetamine withdrawal Amphotericin B Anticholinesterase insecticides Barbiturates β-Blockers (some, eg, propranolol) Cimetidine Corticosteroids Cycloserine Estrogen therapy Indomethacin Interferon Mercury	Amphetamines Certain antidepressants Bromocriptine Cocaine Corticosteroids Levodopa Methylphenidate Sympathomimetic drugs

	Methyldopa Metoclopramide Oral contraceptives Phenothiazines Reserpine Thallium Vinblastine Vincristine	
Mental	Alcoholism and other substance use disorders Antisocial personality Anxiety disorders Dementing disorders in the early phase Schizophrenic disorders	

*Depression commonly occurs in these disorders, but no causal relationship has been established.

Symptoms and Signs

Depression causes cognitive, psychomotor, and other types of dysfunction (eg, poor concentration, fatigue, loss of sexual desire, loss of pleasure), as well as a depressed mood. Other mental symptoms or disorders (eg, anxiety and panic attacks) commonly coexist, sometimes complicating diagnosis and treatment.

Patients with all forms of depression are more likely to abuse alcohol or other recreational drugs in an attempt to self-treat sleep disturbances or anxiety symptoms; however, depression is a less common cause of alcoholism and drug abuse than was once thought. Patients are also more likely to become heavy smokers and to neglect their health, increasing the risk of development or progression of other disorders (eg, COPD).

Depression may reduce protective immune responses. Depression increases risk of cardiovascular disorders, MIs, and stroke, perhaps because in depression, cytokines and factors that increase blood clotting are elevated and heart rate variability is decreased—all potential risk factors for cardiovascular disorders.

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Major depression (unipolar disorder): Periods (episodes) that include ≥ 5 mental or physical symptoms and last ≥ 2 wk are classified as major depression. One of the symptoms must be sadness deep enough to be described as despondency or despair (often called depressed mood) or loss of interest or pleasure in usual activities (anhedonia). Other mental symptoms include feelings of worthlessness or guilt, recurrent thoughts of death or suicide, and a reduced ability to concentrate. Physical symptoms include changes in weight or appetite, loss of energy, fatigue, psychomotor retardation or agitation, and sleep disorders (eg, insomnia, hypersomnia, early morning awakening). Patients may appear miserable, with tearful eyes, furrowed brows, down-turned corners of the mouth, slumped posture, poor eye contact, lack of facial expression, little body movement, and speech changes (eg, soft voice, lack of prosody, use of monosyllabic words). Appearance may be confused with Parkinson's disease. In some patients, depressed mood is so deep that tears dry up; they report that

they are unable to experience usual emotions and feel that the world has become colorless and lifeless. Nutrition may be severely impaired, requiring immediate intervention. Some depressed patients neglect personal hygiene or even their children, other loved ones, or pets.

Major depression is often divided into subgroups:

- **Psychotic:** This subgroup is characterized by delusions, often of having committed unpardonable sins or crimes, of harboring incurable or shameful disorders, or of being persecuted. Patients with delusions may also have auditory or visual hallucinations (eg, hearing accusatory or condemning voices). If only voices are described, careful consideration should be given to whether the voices represent true hallucinations.
- **Catatonic:** This subgroup is characterized by severe psychomotor retardation or excessive purposeless activity, withdrawal, and, in some patients, grimacing and mimicry of speech (echolalia) or movement (echopraxia).
- **Melancholic:** This subgroup is characterized by loss of pleasure in nearly all activities, inability to respond to pleasurable stimuli, unchanging emotional expression, excessive or inappropriate guilt, early morning awakening, marked psychomotor retardation or agitation, and significant anorexia or weight loss.
- **Atypical:** This subgroup is characterized by a brightened mood in response to positive events and rejection sensitivity, resulting in depressed overreaction to perceived criticism or rejection, feelings of leaden paralysis or anergy, weight gain or increased appetite, and hypersomnia. Symptoms tend to worsen as the day passes.

Dysthymia: Low-level or sub-threshold depressive symptoms that persist for ≥ 2 yr are classified as dysthymia. Symptoms typically begin insidiously during adolescence and follow a low-grade course over many years or decades (diagnosis requires a course of ≥ 2 yr); dysthymia may intermittently be complicated by episodes of major depression. Affected patients are habitually gloomy, pessimistic, humorless, passive, lethargic, introverted, hypercritical of self and others, and complaining. Patients with chronic depressive states, whether dysthymia or chronic major depression, are also more likely to have

underlying anxiety, substance use, or personality (ie, borderline personality) disorders.

Depression not otherwise specified (NOS): Clusters of symptoms that do not meet criteria for other depressive disorders are classified as depression NOS. For example, minor depressive disorder may involve ≥ 2 wk of any of the symptoms of major depression but fewer symptoms than the 5 required for diagnosing major depression. Brief depressive disorder involves the same symptoms required for diagnosing major depression but lasts only 2 days to 2 wk. Premenstrual dysphoric disorder involves a depressed mood, anxiety, and decreased interest in activities but only during most menstrual cycles, beginning in the luteal phase and ending within a few days after onset of menses.

Mixed anxiety-depression: Although not considered a type of depression in DSM-IV-TR, this condition, also called anxious depression, refers to concurrent mild symptoms common to anxiety and depression. The course is usually chronically intermittent. Because depressive disorders are more serious, patients with mixed anxiety-depression should be treated for depression.

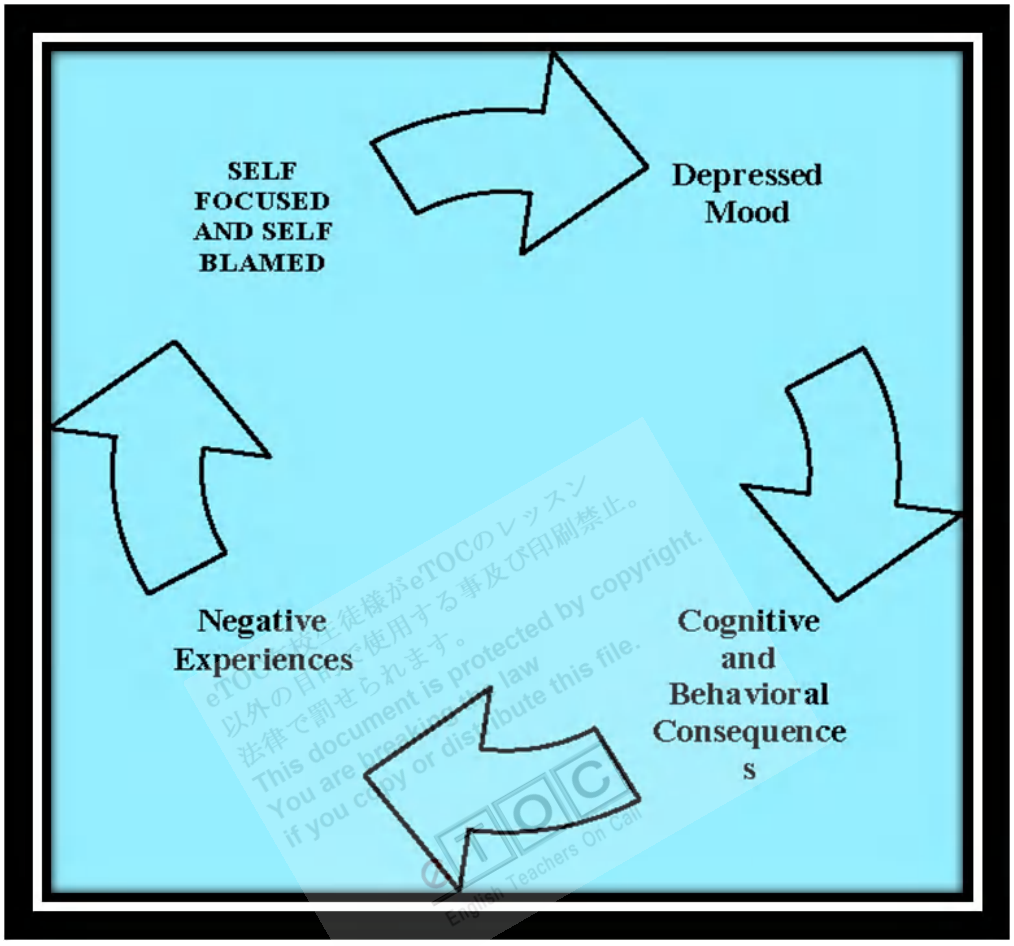
Diagnosis

- Clinical criteria (DSM-IV-TR)
- CBC, thyroid-stimulating hormone, vitamin B_{12}, and folate levels to rule out physical disorders that can cause depression

Diagnosis is based on identifying the symptoms and signs (see above). Several brief questionnaires are available for screening. They help elicit some depressive symptoms but cannot be used alone for diagnosis. Specific close-ended questions help determine whether patients have symptoms required by DSM-IV-TR criteria for diagnosis of major depression.

Severity is determined by the degree of pain and disability (physical, social, occupational) and by duration of symptoms. A physician should gently but directly ask patients about any thoughts and plans to harm themselves or others. Psychosis and catatonia indicate severe depression. Melancholic

features indicate severe or moderate depression. Coexisting physical conditions, substance abuse disorders, and anxiety disorders may add to severity.



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Differential diagnosis: Depressive disorders must be distinguished from demoralization. Other mental disorders (eg, anxiety disorders) can mimic or obscure the diagnosis of depression. Sometimes more than one disorder is present. Major depression (unipolar disorder) must be distinguished from bipolar disorder.

In elderly patients, depression can manifest as dementia of depression (formerly called pseudodementia), which causes many of the symptoms and signs of dementia such as psychomotor retardation and decreased concentration. However, early dementia may cause depression. In general, when the diagnosis is uncertain, treatment of a depressive disorder should be tried.

Differentiating chronic depressive disorders, such as dysthymia, from substance abuse disorders may be difficult, particularly because they can coexist and may contribute to each other.

Physical disorders must also be excluded as a cause of depressive symptoms. Hypothyroidism often causes symptoms of depression and is common, particularly among the elderly. Parkinson's disease, in particular, may manifest with symptoms that mimic depression (eg, loss of energy, lack of expression, paucity of movement). A thorough neurologic examination is needed to exclude this disorder.

Testing: No laboratory findings are pathognomonic for depressive disorders. Tests for limbic-diencephalic dysfunction are rarely indicated or helpful. However, laboratory testing is necessary to exclude physical conditions that can cause depression. Tests include CBC, TSH levels, and routine electrolyte, vitamin B_{12}, and folate levels. Testing for illicit drug use is sometimes appropriate.

Treatment

- Support
- Psychotherapy
- Drugs

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Symptoms may remit spontaneously, particularly when they are mild or of short duration. Mild depression may be treated with general support and psychotherapy. Moderate to severe depression is treated with drugs, psychotherapy, or both and sometimes electroconvulsive therapy. Some patients require a combination of drugs. Improvement may not be apparent until after 1 to 4 wk of drug treatment.

Depression, especially in patients who have had > 1 episode, is likely to recur; therefore, severe cases often warrant long-term maintenance drug therapy. Most people with depression are treated as outpatients. Patients with significant suicidal ideation, particularly when family support is lacking, require hospitalization, as do those with psychotic symptoms or physical debilitation.

Depressive symptoms in patients with substance abuse disorders often resolve within a few months of stopping substance use. Antidepressant treatment is much less likely to be effective while substance abuse continues.

If a physical disorder or drug toxicity could be the cause, treatment is directed first at the underlying disorder. However, if the diagnosis is in doubt or if symptoms are disabling or include suicidal ideation or hopelessness, a therapeutic trial with an antidepressant or a mood-stabilizing drug may help.

Initial support: Until definite improvement begins, a physician should see patients weekly or biweekly to provide support and education and to monitor progress. Telephone calls may supplement office visits.

Patients and loved ones may be worried or embarrassed about the idea of having a mental disorder. The physician can help by explaining that depression is a serious medical disorder caused by biologic disturbances and requires specific treatment and that the prognosis with treatment is good. Patients and loved ones should be reassured that depression does not reflect a character flaw (eg, laziness, weakness). Telling patients that the path to recovery often fluctuates helps them put feelings of hopelessness in perspective and improves adherence.

Encouraging patients to gradually increase simple activities (eg, taking walks, exercising regularly) and social interactions must be balanced with acknowledging their desire to avoid activities. The physician can suggest that patients avoid self-blame and explain that dark thoughts are part of the disorder and will go away.

Psychotherapy: Psychotherapy, often as cognitive-behavioral therapy (individual or group), alone is often effective for milder forms of depression. Cognitive-behavioral therapy is increasingly used to combat the inertia and self-defeating mental set of depressed patients. However, cognitive-behavioral therapy is most useful when combined with antidepressants to treat moderate to severe depression. Cognitive-behavioral therapy may improve coping skills and enhance gains by providing support and guidance, by removing cognitive distortions that prevent adaptive action, and by encouraging patients to gradually resume social and occupational roles. Couple therapy may help reduce conjugal tensions and disharmony. Long-term psychotherapy is usually unnecessary except for patients who have long-term interpersonal conflicts or who are unresponsive to brief therapy.

Selective serotonin reuptake inhibitors (SSRIs): These drugs prevent reuptake of serotonin (5-hydroxytryptamine [5-HT]). SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. Although these drugs have the same mechanism of action, differences in their clinical properties make selection important. SSRIs have a wide therapeutic margin; they are relatively easy to administer, with little need for dose adjustment (except for fluvoxamine).

By preventing reuptake of 5-HT presynaptically, SSRIs result in more 5-HT to stimulate postsynaptic 5-HT receptors. SSRIs are selective to the 5-HT system but not specific for the different 5-HT receptors. They stimulate 5-HT_1 receptors, with antidepressant and anxiolytic effects, but they also stimulate 5-HT_2 receptors, commonly causing anxiety, insomnia, and sexual dysfunction, and 5-HT_3 receptors, commonly causing nausea and headache. Thus, SSRIs can paradoxically relieve and cause anxiety.

A few patients may seem more agitated, depressed, and anxious within a week of starting SSRIs or increasing the dose. Patients and their loved ones should be warned of this possibility and instructed to call the physician if symptoms worsen with treatment. This situation should be closely monitored because some patients, especially younger children and adolescents, become increasingly suicidal if agitation, increased depression, and anxiety are not detected and rapidly treated. Recent studies have determined that children, adolescents, and young adults have an increased rate of suicidal ideation, suicide gestures, and suicide attempts during the first few months of taking SSRIs (the same concern may apply to serotonin modulators, serotonin-norepinephrine reuptake inhibitors, andnorepinephrine-dopamine reuptake inhibitors); physicians must balance this risk with clinical need.

Sexual dysfunction (especially difficulty achieving orgasm but also decreased libido and erectile dysfunction) occurs in one third or more of patients. Some SSRIs cause weight gain. Others, especially fluoxetine, may cause anorexia in the first few months. SSRIs have few anticholinergic, adrenolytic, and cardiac conduction effects. Sedation is minimal or nonexistent, but in the early weeks of treatment, some patients tend to be sleepy during the day. Loose stools or diarrhea occurs in some patients.

Drug interactions are relatively uncommon; however, fluoxetine, paroxetine, andfluvoxamine can inhibit cytochrome P-450 (CYP450) isoenzymes, which can lead to serious drug interactions. For example, these drugs can inhibit the metabolism of certain β-blockers, including propranolol and metoprolol, potentially resulting in hypotension and bradycardia. Discontinuation symptoms (eg, irritability, anxiety, nausea) can occur if the drug is stopped abruptly; such effects are less likely with fluoxetine.

Serotonin modulators (5-HT_2 blockers): These drugs block primarily the 5-HT_2 receptor and inhibit reuptake of 5-HT and norepinephrine. Serotonin modulators include nefazodone, trazodone, and mirtazapine. Serotonin modulators have antidepressant and anxiolytic effects but do not cause sexual dysfunction. Unlike most antidepressants, nefazodone does not suppress REM (rapid eye movement) sleep and produces restful sleep. Nefazodone can

significantly interfere with drug-metabolizing liver enzymes and has been associated with liver failure. Trazodone is related to nefazodone but does not inhibit 5-HT reuptake presynaptically. Unlike nefazodone, trazodone has caused **priapism** (in 1/1000) and, as an α_1-noradrenergic blocker, may cause **orthostatic** (postural) **hypotension**. It is very **sedating**, so its use in antidepressant doses (> 200 mg/day) is limited. It is most often given in 50- to 100-mg doses at bedtime to depressed patients with **insomnia**.

Mirtazapine inhibits 5-HT reuptake and blocks α_2-adrenergic autoreceptors, as well as 5-HT_2 and 5-HT_3 receptors. The result is increased serotonergic function and increased noradrenergic function without sexual dysfunction or nausea. It has no cardiac adverse effects, has minimal interaction with drug-metabolizing liver enzymes, and is generally well tolerated, although it does cause sedation and weight gain, mediated by H_1 (histamine) blockade.

Serotonin-norepinephrine reuptake inhibitors: These drugs (eg, venlafaxine, duloxetine) have a dual 5-HT and norepinephrine mechanism of action, as do tricyclic antidepressants. However, their toxicity approximates that of SSRIs. Nausea is the most common problem during the first 2 wk; modest dose-dependent increases in BP occur with high doses. Discontinuation symptoms (eg, irritability, anxiety, nausea) often occur if the drug is stopped suddenly. Duloxetine resembles venlafaxine in effectiveness and adverse effects.

Norepinephrine-dopamine reuptake inhibitors: By mechanisms not clearly understood, these drugs favorably influence catecholaminergic, dopaminergic, and noradrenergic function. They do not affect the 5-HT system.

Bupropion is currently the only drug in this class. It can help depressed patients with concurrent attention-deficit/hyperactivity disorder or cocaine dependence and those trying to stop smoking. Bupropion causes hypertension in a very few patients but has no other effects on the cardiovascular system. Bupropion can cause seizures in 0.4% of patients taking doses > 150 mg tid (or > 200 mg sustained-release [SR] bid or > 450 mg extended-release [XR] once/day); risk is increased in patients with bulimia. Bupropion does not have sexual adverse effects and interacts little with co-administered drugs, although it does inhibit

the CYP2D6 hepatic enzyme. Agitation, which is common, is considerably attenuated by using the SR or XR form.

Heterocyclic antidepressants: This group of drugs, once the mainstay of treatment, includes tricyclic (tertiary amines amitriptyline and imipramine and their secondary amine metabolites nortriptyline and desipramine), modified tricyclic, and tetracyclic antidepressants. Acutely, these drugs increase the availability of primarily norepinephrine and, to some extent, 5-HT by blocking reuptake in the synaptic cleft. Long-term use downregulates α_1-adrenergic receptors on the postsynaptic membrane—a possible final common pathway of their antidepressant activity.

Although effective, these drugs are now rarely used because overdose causes toxicity and they have more adverse effects than other antidepressants. The more common adverse effects of heterocyclics are due to their muscarinic-blocking, histamine-blocking, and α_1-adrenolytic actions. Many heterocyclics have strong anticholinergic properties and are thus unsuitable for the elderly and for patients with benign prostatic hypertrophy, glaucoma, or chronic constipation. All heterocyclics, particularly maprotiline and clomipramine, lower the threshold for seizures.

Monoamine oxidase inhibitors (MAOIs): These drugs inhibit the oxidative deamination of the 3 classes of biogenic amines (norepinephrine, dopamine, 5-HT) and other phenylethylamines. MAOIs have little or no effect on normal mood. Their primary value is for treating refractory or atypical depression when SSRIs, tricyclic antidepressants, and sometimes even electroconvulsive therapy is ineffective.

MAOIs marketed as antidepressants in the US (eg, phenelzine, tranylcypromine ,isocarboxazid) are irreversible and nonselective (inhibiting MAO-A and MAO-B). Another MAOI (selegiline), which inhibits only MAO-B at lower doses, is available as a patch.

MAOIs that inhibit MAO-A and MAO-B can cause hypertensive crises if a sympathomimetic drug or food containing tyramine or dopamine is ingested concurrently. This effect is called the cheese reaction because mature cheese

has a high tyramine content. MAOIs are used infrequently because of concern about this reaction. The lower dosage of the selegiline patch is considered safe to use without specific dietary restrictions, unless the dosage must be higher than starting levels (a 6-mg patch). More selective and reversible MAOIs (eg,moclobemide, befloxatone), which inhibit MAO-A, are not yet available in the US; they are relatively free of these interactions. To prevent hypertension and febrile crises, patients taking MAOIs should avoid sympathomimetic drugs (eg, pseudoephedrine), dextromethorphan,reserpine, and meperidine as well as malted beers, Chianti wines, sherry, liqueurs, and overripe or aged foods that contain tyramine or dopamine (eg, bananas, fava or broad beans, yeast extracts, canned figs, raisins, yogurt, cheese, sour cream, soy sauce, pickled herring, caviar, liver, extensively tenderized meats). Patients can carry 25-mg tablets of chlorpromazine and, as soon as signs of such a hypertensive reaction occur, take 1 or 2 tablets as they head to the nearest emergency department.

Common adverse effects include erectile dysfunction (least common with tranylcypromine), anxiety, nausea, dizziness, insomnia, pedal edema, and weight gain. MAOIs should not be used with other classes of antidepressants, and at least 2 wk (5 wk with fluoxetine, which has a long half-life) should elapse between use of the 2 classes of drugs. MAOIs used with antidepressants that affect the 5-HT system (eg, SSRIs, nefazodone) may cause neuroleptic malignant syndrome (malignant hyperthermia, muscle breakdown, renal failure, seizures, and eventual death. Patients who are taking MAOIs and who also need antiasthmatic or antiallergic drugs, a local anesthetic, or a general anesthetic should be treated by a psychiatrist plus an internist, a dentist, or an anesthesiologist with expertise in neuropsychopharmacology.

Drug choice and administration: Choice of drug may be guided by past response to a specific antidepressant. Otherwise, SSRIs are often the initial drugs of choice. Although the different SSRIs are equally effective for typical cases, certain properties of the drugs make them more or less appropriate for certain patients.

If one SSRI is ineffective, another SSRI can be substituted, but an antidepressant from a different class may be more likely to help.Tranylcypromine in high doses (20 to 30 mg po bid) is often effective for depression refractory to sequential trials of other antidepressants; it should be given by a physician experienced in use of MAOIs. Psychologic support of patients and loved ones is particularly important in refractory cases.

Insomnia, a common adverse effect of SSRIs, is treated by reducing the dose or adding a low dose of trazodone or another sedating antidepressant. Initial nausea and loose stools usually resolve, but throbbing headaches do not always go away, necessitating a change in drug class. An SSRI should be stopped if it causes agitation. When decreased libido, impotence, or anorgasmia occur during SSRI therapy, dose reduction may help, or a change can be made to another drug class.

SSRIs, which tend to stimulate many depressed patients, should be given in the morning. Giving the entire heterocyclic antidepressant dose at bedtime usually makes sedatives unnecessary, minimizes adverse effects during the day, and improves adherence. MAOIs are usually given in the morning and early afternoon to avoid excessive stimulation.

Therapeutic response with most classes of antidepressants usually occurs in about 2 to 3 wk (sometimes as early as 4 days or as late as 8 wk). For a first episode of mild or moderate depression, the antidepressant should be given for 6 mo, then **tapered** gradually over 2 mo. If the episode is severe or is a recurrence or if there is suicidal risk, the dose that produces full **remission** should be continued during maintenance.

For psychotic depression, imipramine appears to be more effective than monotherapy with antidepressants from other classes; dosing this drug can be guided by steady-state plasma levels. The addition of an antipsychotic may improve the likelihood of response, but antipsychotic monotherapy appears to be ineffective.

Continued therapy with an antidepressant for 6 to 12 mo (up to 2 yr in patients > 50) is usually needed to prevent relapse. Most antidepressants,

especially SSRIs, should be tapered off (by decreasing the dose by about 25%/wk) rather than stopped abruptly; stopping SSRIs abruptly may result in discontinuation syndrome (nausea, chills, muscles aches, dizziness, anxiety, irritability, insomnia, fatigue). The likelihood and severity of withdrawal varies inversely with the half-life of the SSRI.

Medicinal herbs are used by some patients. St. John's wort (see Dietary Supplements: St. John's Wort) may be effective for mild depression, although data are contradictory. St. John's wort may interact with other antidepressants and other drugs. A number of placebo-controlled studies of ω-3 supplementation, used as **augmentation** or as monotherapy, have suggested that eicosapentaenoic acid 1 to 2 g once/day has useful antidepressant effects.

Electroconvulsive therapy (ECT): Severe suicidal depression, depression with agitation or psychomotor retardation, delusional depression, or depression during pregnancy is often treated with ECT if drugs are ineffective. Patients who have stopped eating may need ECT to prevent death. ECT is also effective for psychotic depression. Response to 6 to 10 ECT treatments is usually dramatic and may be lifesaving. Relapse after ECT is common, and drug therapy is often maintained after ECT is stopped.

Phototherapy: Phototherapy is best known for its effects on seasonal depression but can also be effective in other types of depression. Treatment can be provided at home with 2,500 to 10,000 lux at a distance of 30 to 60 cm for 30 to 60 min/day (longer with a less intense light source). In patients who go to sleep late at night and rise late in the morning, phototherapy is most effective in the morning, sometimes supplemented with 5 to 10 min of exposure between 3 PM and 7 PM. For patients who go to sleep and rise early, phototherapy is most effective between 3 PM and 7 PM.

Other therapies: Psychostimulants (eg, dextroamphetamine, methylphenidate) are sometimes used, often with antidepressants; however, they have not been well studied in controlled clinical trials.

Vagus nerve stimulation involves intermittently stimulating the vagus nerve via an implanted pulse generator. It may be useful for depression refractory to other treatments but usually takes 3 to 6 mo to be effective.

Deep brain stimulation and transcranial magnetic stimulation are still under study

Reference: http://www.merckmanuals.com

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