

## Eastside Psychiatric Services

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# Depression

## Introduction

Everyone experiences some unhappiness, often as a result of a change, either in the form of a setback or a loss, or simply, as Freud said, "everyday misery." The painful feelings that accompany these events are usually appropriate, necessary, and transitory, and can even present an opportunity for personal growth. However, when depression persists and impairs daily life, it may be an indication of a depressive disorder. Severity, duration, and the presence of other symptoms are the factors that distinguish normal sadness from a depressive disorder.

Depression has been alluded to by a variety of names in both medical and popular literature for thousands of years. Early English texts refer to "melancholia," which was for centuries the generic term for all emotional disorders. Depression is now referred to as a mood disorder, and the primary subtypes are major depression, dysthymia (chronic and usually milder depression), and atypical depression. Other important forms of depression are premenstrual dysphoric disorder (PDD or PMDD) and seasonal affective disorder (SAD).

The other major mood disorder is bipolar disorder, or manic-depressive illness, which is characterized by periods of depression alternating with episodes of excessive energy and activity. Bipolar disorder is not discussed in this report; see *Well-Connected Report #66 Bipolar Disorder*.

## Major Depression

In major, or acute, depression, at least five of the symptoms listed below must occur for a period of at least two weeks, and they must represent a change from previous behavior or mood. Depressed mood or loss of interest must be present.

1. Depressed mood on most days for most of each day. (Irritability may be prominent in children and adolescents.)
2. Total or very noticeable loss of pleasure most of the time.
3. Significant increases or decreases in appetite, weight, or both.
4. Sleep disorders, either insomnia or excessive sleepiness, nearly every day.
5. Feelings of agitation or a sense of intense slowness.
6. Loss of energy and a daily sense of tiredness.
7. Sense of guilt or worthlessness nearly all the time.
8. Inability to concentrate occurring nearly every day.

## 9. Recurrent thoughts of death or suicide.

In addition, other criteria must be met:

- The symptoms listed above do not follow or accompany manic episodes (such as in bipolar disorder or other disorders).
- They impair important normal functions (such as work or personal relationships).
- They are not caused by drugs, alcohol, or other substances.
- They are not caused by normal grief.

A long-term study conducted in 1997 found that episodes of major depression usually last about 20 weeks. Between 30% and 40% of depressed patients experience sudden attacks of anger that they describe as uncharacteristic and inappropriate.

## Dysthymia (Chronic Depression)

Dysthymia, or chronic depression, afflicts 3% to 6% of the general population and is characterized by many of the same symptoms that occur in major depression; symptoms of dysthymia are less intense and last much longer, at least two years. The symptoms of dysthymia have been described as a "veil of sadness" that covers most activities. Possibly because of the duration of the symptoms, patients who suffer from chronic minor depression do not exhibit marked changes in mood or in daily functioning, although they have low energy, a general negativity, and a sense of dissatisfaction and hopelessness.

*Double Depression.* Often, symptoms become more severe over time. In one long-term study, nearly all patients with dysthymia suffered at least one episode of major depression superimposed on chronic depression (sometimes called double depression) at some time in their life. Some experts believe that such double depression should be considered as part of the natural course of dysthymic disorder. Women may be more susceptible to double depression. In one study, more than one-third of those who recovered from dysthymia relapsed within five years.

## Atypical Depression

About a third of patients with depression have atypical depression. Symptoms include overeating and oversleeping. Such patients tend to have a feeling of being weighed down and react strongly to rejection. It tends to occur more in women, unmarried people, and those with other emotional disorders, such as anxiety or substance abuse. It also may impair functioning more severely than ordinary depression does.

## Seasonal Affective Disorder

Seasonal affective disorder (SAD) is characterized by annual episodes of depression during fall or winter that remit in the spring or summer. Other SAD symptoms include fatigue, a tendency to overeat (particularly carbohydrates) and to oversleep in winter. A minority of individuals with SAD has the more common depressive symptoms of *undereating* and being sleepless. SAD tends to last about five months in those who live in the northern part of the U.S.

It should be noted that seasonal changes affect many people's moods, regardless of gender and whether or not they have SAD. Simply being mildly depressed during the winter does not mean that one has SAD. Living in a northern country with long winter nights does not guarantee a higher risk for depression. One small intriguing study, in fact, found that people with SAD who were left-handed became depressed in the spring and summer and their spirits rose in the fall and winter months. This suggests that changes in light may not be the only contributor to SAD.

## Causes

The causes of depression are not fully known. Most likely a combination of genetic, biologic, and environmental factors are at work.

## Genetic Factors

Because depression runs in families, and has a strong genetic component, there is compelling evidence that it is a biologic phenomenon. Data from family, twin, adoption, and genetic studies have confirmed this. Studies have found that first-degree relatives of patients with depression are two to six times more likely to develop the problem than individuals without a family history.

## Biologic Factors

Evidence now strongly supports the theory that depression has a biologic basis and that certain brain chemicals and neural pathways responsible for regulating mood and associated behaviors are altered.

*Neurotransmitter Abnormalities.* The basic biologic causes of depression are strongly linked to abnormalities in the delivery of certain key neurotransmitters (chemical messengers in the brain).

- *Serotonin.* Perhaps the most important neurotransmitter in depression is serotonin. Among other functions, it is important for feelings of well-being. One 2003 study indicated that serotonin improves a person's ability to pick up emotional cues from other people, which is important for healthy relationships. Another study further suggested that people deficient in serotonin were less likely to take risks for high rewards than those with normal levels.
- *Other Neurotransmitters.* Other neurotransmitters possibly involved in depression include acetylcholine and catecholamines, a group of neurotransmitters that consists of dopamine, norepinephrine, and epinephrine (also called adrenaline). Corticotropin-releasing factor (CRF), which is believed to be a stress hormone and a neurotransmitter, is thought to be involved in depression and anxiety. Increased CRF concentrations appear to interact with serotonin and have been detected in patients with either depression or anxiety.

The degree to which these chemical messengers are disturbed is determined by other factors, such as light, structural abnormalities in the brain, sleep disorders, or genetic susceptibility. For example, researchers have identified a defect in the gene known as SERT, which regulates serotonin and has been linked to depression.

*Reproductive Hormones.* In women, the female hormones estrogen and progesterone most likely play a role in depression. [ See Box Depression in Women.]

## Insomnia and Sleep Disorders

Studies estimate that 20% of people with insomnia suffer from major depression and 90% of people with depression have insomnia. Although stress and depression are major causes of insomnia, insomnia may also increase the activity of the hormones and pathways in the brain that can *produce* emotional problems. Even modest alterations in waking and sleeping patterns can have significant effects on a person's mood. Persistent insomnia may actually be a symptom of later emotional disorders in some cases.

## Depression as Adaptive Strategy

Some experts theorize that low mood is an adaptive response to situations in which expectations fail to match achievements (such as with an unrequited love affair, career failure, or a challenge of authority). In its healthy state, the pain this response causes provides both an incentive to disengage and a passive, withdrawn state that allows a period of thought before changing direction. Depression as a disorder (characterized by pervasive pessimism, low self-esteem and total lack of initiative) may develop if there are constant unachievable objects or goals and there are no positive relationships to help a person change direction. (Such cases could certainly occur in highly competitive societies that lack strong social support and where the media holds up unattainable

images as desirable.) Such a theory does not, however, rule out biologic or other factors that can contribute to depressive disorders.

## Depression in Women

Women, regardless of nationality or socioeconomic level, have significantly higher rates of depression than do men. The causes of such higher rates appear to be a mix of biologic and cultural factors.

### Hormonal Fluctuations and Life Stages

Extreme hormonal shifts can trigger emotional swings in all women. The role of hormones in depression is not clear, however, and is mostly based on observations of depression during specific stages in female development. Female hormones undoubtedly play some role in premenstrual dysphoria, postpartum depression, and SAD. These forms of depression recede or stop after menopause.

*Early Puberty.* Girls who go through puberty early (reaching the midpoint at 11 years or younger) are more likely to experience depression during adolescence than girls who mature later.

*Premenopause.* Premenopausal women between the ages of 20 and 45 were most susceptible to depression, with 22% of this age group reporting symptoms of major depression. Specifically, premenstrual dysphoric disorder (severe depression before a period) affects an estimated 3% to 8% of women during their reproductive years. [ See *Well-Connected Report # 79 Premenstrual Syndrome.*]

*Perimenopause.* Depression often occurs around menopause (the perimenopausal period), when, in addition to hormonal changes, other factors such as cultural pressures favoring young women, sudden recognition of aging, and sleeplessness are involved. In one study, more than half of perimenopausal women were diagnosed with major depression. Women who suffered depression before menopause may also have a risk for entering the premenopausal period at a slightly earlier age than women without depression.

*Postmenopause.* Once women pass into the postmenopausal period, studies suggest that average depression scores are nearly as low as those in premenopausal women. In fact, many women report that after menopause, previous bouts of depression, particularly when caused by seasonal changes or premenopausal syndrome, recede or stop completely.

### Premenstrual Dysphoric Disorder

The syndrome of severe depression, irritability, and tension before menstruation is known as premenstrual dysphoric disorder (PDD or PMDD), also called late-luteal dysphoric disorder. It affects an estimated 3% to 8% of women in their reproductive years. A diagnosis of PDD depends on having five or more standard symptoms of major depression that occur during most menstrual cycles, with symptoms worsening a week or so before the menstrual period and resolving afterward. PMDD has features of both anxiety and depression disorders, although experts increasingly believe it is a distinct disorder with specific biochemical abnormalities. [For more information, see *Well-Connected Report #79 Premenstrual Disorder.*]

### Depression and Pregnancy

*Depression During Pregnancy.* Pregnancy is certainly an occasion of great celebration for most women most of the time. However, emotions during that time are not always straightforward, and depression is a common (although most often a temporary) companion. A 2001 study found that depression during pregnancy was more common than depression after pregnancy, with the highest depression scores occurring in week 32.

Prenatal depression can affect a mother's sleep, physical activity, adherence to care, and appetite—all of which can affect the unborn child. Some research suggests that depression during pregnancy may pose a risk for later language and behavior problems in the child later on.

*Miscarriage.* Miscarriage poses a very high risk for depression, particularly in the first month after the loss. Older women with no previous successful pregnancies and those with a history of depression are at particular risk during this time. (There has been some concern that depression increases the risk for miscarriage in the first place, but a 2003 study found no evidence to support this, at least in the first 22 weeks.)

*Postpartum Depression.* Most new mothers experience weeping, irritability, and confusion for a few days following childbirth. Such symptoms, known as the "baby blues," are not considered to be indicators of postpartum depression, however, unless they persist in severe form nearly every day for more than a week or two.

Postpartum depression can first develop as long as three months after delivery. Studies have reported that between 8% and 20% of women have diagnosable postpartum depression within that time. In one study, 5% of these women had suicidal thoughts. (It should be noted that many male partners of new mothers also suffer from depression around the birth of a child.)

Studies have not found any association between a higher risk for postpartum depression and a woman's educational level, the gender of the child, whether or not she breastfeeds, whether or not the pregnancy was planned, or whether the delivery was vaginal or cesarean. The rapid decline of reproductive hormones that accompany childbirth is likely to play the major role in postpartum depression in susceptible women. Fluctuating thyroid hormones can also contribute to depression. Different studies have suggested that women who are more sensitive to hormone fluctuations and so at greater risk for postpartum depression have one or more of the following conditions:

- A history of prior depressive episodes.
- A family history of mood disorders.
- Stressful life events (such as being a new mother and having an infant with medical problems).
- Lack of social support or feeling as if it is lacking.

*Treatment During and After Pregnancy.* Although a mother's depression during and after pregnancy can have serious effects on her child, treatment is problematic.

Psychotherapy is helpful in the short term of women with postpartum depression but may not be any more helpful than routine care from a physician in the long run.

Physicians are reluctant to give antidepressants to pregnant women. Encouraging studies to date, however, suggest that selective serotonin reuptake inhibitors (SSRIs) do not pose a higher than normal risk for miscarriage or birth defects or later problems in the offspring. High doses, however, may reduce birth weight. Also, taken late in pregnancy, however, SSRIs may affect serotonin levels in the newborn. Studies on the effects on infants of nursing women taking SSRIs report very low levels of the medications in blood but no observable negative effects on the babies. More research is needed, however, and most physicians advise women to avoid, if possible, any medications during pregnancy and nursing.

### **The Theory of Affiliate Behaviors and Oxytocin**

Depression in women is more likely to follow interpersonal problems, while in men depression tends to be attributed to stressful life events. One theory about the higher risk of depression in women concerns affiliate behaviors, which are those that involve activities surrounding relationships, and a peptide called oxytocin (OT).

Oxytocin is found in mammals and stimulates uterine contraction during labor and milk release

during nursing. And evidence suggests it may also play a role in affiliate behaviors such as maternal caregiving and sexual bonding after puberty. Under primitive conditions, the release of OT after puberty coincided with early mating and breeding. In modern cultures, however, there is typically a long delay between puberty and childbirth. Some experts theorize that release of OT and the subsequent inability to mate and procreate creates feelings of loss and separation in women that can lead to depression.

This theory is backed up by some studies suggesting that young women most vulnerable to depression are those who are also most sensitive to separation from parents, friends, or loved ones.

### **Social and Economic Factors in Women**

The role that work, marriage, and children play in a woman's depression is complex. Many women feel that they must be everything to everyone and at the same time feel as if they are no one at all. Such a self-image is common and should be strongly considered as a major contributor to depression in many women, particularly those who work and have small children. The following are results of studies suggesting the difficulty of assessing the relationship between a woman's social status and depression, however.

In a report on women worldwide issued by the World Health Organization in 1996, married women with children had a higher risk for depression than did married childless women, single women, or single or married men.

A survey of women in the Boston area reported, however, that women between the ages of 36 and 44 who had children were significantly less likely to be depressed than childless women. And the more children they had, the less depressed they tended to be. This study targeted older premenopausal women. The difference between this study and others may be due to the presence of older children, who might add a supportive emotional network, rather than dependent toddlers.

The perceived low status and isolation accompanying the role of housewife may play a role in a young mother's depression. A European study reported that depression increased in men and fell in women between 1980 and 1995, a period coinciding with more women entering the work force. (Work outside the home that fails to provide social support, however, will not necessarily help protect against depression.)

Other studies in the U.S. have reported that grandmothers who care for their grandchildren and mothers of toddlers, regardless of whether they worked outside the home or not, have a very high risk for depression.

## **Risk Factors**

According to a major 2003 survey, more than 16% of Americans experience major depression disorder over the course of their lifetimes. Furthermore, an estimated 13 to 14 million Americans experience major depression each year. Depression is second only to high blood pressure as a chronic condition encountered by primary care physicians. Depression is an illness that can afflict anyone, regardless of age, race, class, or gender, and it is sometimes referred to as the common cold of mental illness. Although some evidence suggests the depression has increased over recent decades, one 40-year analysis found the overall rate to be holding steady, although the burden of depression may be shifting to women younger than 45.

## **Gender and Depression**

*Depression in Women.* At any given time, 5% to 9% of women are depressed, compared to 1% to 3% of men. In one study, nearly half of all women surveyed had experienced depression at some point in their lives and over half of those who suffered from it had sought treatment. Women are also more apt to have multiple types

of depression (dysthymia and major depression). [For more information, see *Box Depression in Women.*]

*Depression in Men.* Depression is not rare in men. In fact, prepubescent boys are more likely than girls of the same age to be depressed. Older men are also at much higher risk for suicide and, as with women, they are at risk for health complications of depression. Some evidence suggests that men are more apt than women to mask their depression by using alcohol, which may result in a lower reported (but not actual) incidence of depression in men. Some Swedish experts have suggested that men with depression might be identified with the following indicators:

- Low tolerance to stress.
- Behaviors such as "acting out" and being impulsive.
- A history of alcohol or substance abuse.
- A family history of depression, alcohol abuse, or suicide.

## Age and Depression

*Depression in Children and Adolescents.* An Australian study reported that 2.1% of girls and 3.7% of boys between the ages six and 12 experienced depression during the course of a year. Others studies report that between 4% and 8% of teenagers suffer from depression. Depression before puberty is more likely to occur in boys and after puberty in girls. [For more information, see *Depression in Children.*]

*Depression in the Elderly.* Studies have suggested that, in general, a third of the elderly population is depressed. [For more information, see *Depression in the Elderly.*]

## Social Status and Economic Considerations

The role of society and economics has specific implications for women. [ See *Box Depression in Women.*] Being in a low socioeconomic group is a major risk factor for depression in anyone. Money, of course, allows greater access to good medical care, but this factor does not fully explain the higher rates of depression in impoverished people. People at any income level are likely to be depressed if they have poor health and are socially isolated. Some studies suggest that Western cultural attitudes that link income to social status may play a significant role in the connection between poverty and depression:

- In one British study, actual poverty or unemployment increased the duration of any existing depression, but it did not appear to play any important causal role. Feelings of financial insecurity, however, both caused and prolonged depression.
- Another study reported that Mexican adults who immigrated to America had half the psychiatric illnesses as did Mexican-Americans born in the U.S., regardless of their income. But the longer the immigrants lived in the US, the greater their risk for psychiatric problems. Traditional influences of Mexican culture and social ties, then, appeared to protect newly arrived immigrants from mental illness, even when they were poor. Eventually, however, the consequences of Americanization added to poverty and led to feelings of alienation and inferiority.

## Family History

Depression in family members increases the risk for depression in other family members. For example, studies report that depression for even one or two months in a mother increases the risk for depression in her children. The more severe the maternal depression, the higher the risk for depression in the children. In a perpetuating cycle, being depressed as a child increases the risk for depression during adulthood. In such cases, genetic or environmental factors or both may be responsible. Spouses of partners with depression are themselves at higher risk for depression.

## Consequences of Loss and Trauma

Patients who have had serious bouts of depression usually cite a stressful life event as the precipitating factor for their illness. Adverse events during childhood pose a higher risk for depression in adulthood. In one study, parental divorce, physical abuse, and frightening experiences were particularly associated with onset of depression in adulthood. Only divorce was associated with recurrence, however.

Adverse events in adulthood also trigger depression. Losing a spouse through divorce or death is a major risk factor for depression in anyone. In fact, recent loss of a loved one is the most frequently reported precipitant of acute depression. All major (and even minor) losses, however, cause grief reactions. People who develop acute or chronic depression after a loss may have predisposing factors, including genetic or biologic ones, which make them more vulnerable. The existence or absence of a strong social network of family, friends, or both also has a major positive or negative effect, respectively, on recovery. Most people are able to cope with the emotional pain and eventually move beyond it without becoming chronically depressed. [ See Ruling out Grief and Loneliness *under* Diagnosis.]

Traumatic events such as abuse or even natural disasters can cause severe immediate or delayed depression from which recovery takes a long time.

## Accompanying Medical Disorders

*Severe or Chronic Medical Conditions.* Any chronic or serious illness that is life threatening or out of a person's control can lead to depression.

*Thyroid Disease.* Thyroid disease can cause depression; however, it may be misdiagnosed as depression and go undetected.

*Headaches.* Studies have reported a strong association between depression and headaches, including chronic tension-type and migraine. Some experts believe that a syndrome of migraine headaches (and also possibly tension-type), anxiety, and depression, is caused by common factors, such as abnormalities in chemical messengers, particularly dopamine or serotonin.

*Stroke.* Having a stroke increases the risk of developing depression.

## Medications

A number of drugs taken for chronic problems cause depression. Among them are pain relievers for arthritis, cholesterol-lowering drugs, medications for high blood pressure and heart problems, and bronchodilators used for asthma and other lung disorders.

## Smoking

There is a significant association between cigarette smoking and a susceptibility to depression. People who are prone to depression face a 25% chance of becoming depressed when they quit smoking, and this increased risk persists for at least six months. What's more, depressed smokers are unlikely to stop smoking. Only about 6% remain smoke-free after a year. Smokers with a history of depression are not encouraged to continue smoking, but rather to keep a close watch on recurrence of depressive symptoms if they do stop smoking. The antidepressant bupropion (Wellbutrin), which is approved for helping people quit smoking (marketed under the name Zyban), is proving to be very useful in helping smokers to quit.

## Anxiety Disorder

Chronic depression is a frequent companion to anxiety disorders. In one study, up to 96% of patients with depressive disorders experienced concurrent anxiety. More than two-thirds of people with obsessive-compulsive disorder, a common anxiety disorder, also suffer from depression.

## Personality Characteristics and Disorders

Some evidence suggests that certain personality styles, which include an intense need for close relationships and concern for disapproval or need for control, pose a high risk for depression, particularly after an adverse life event. In line with these findings, the following specific *personality disorders* have been associated not only to a first episode of depression, but also to relapses:

- A person with *borderline personality disorder* acts impulsively and has a poor self-image and unstable relationships. In one study, patients with borderline personality disorder and major depression were more likely than those with either condition alone to plan and attempt suicide.
- An individual with an *avoidant personality* avoids strangers and unfamiliar situations.

(Personality disorders, as opposed to emotional disorders, are those with abnormal behavioral patterns rather than abnormal emotions.)

## Insomnia and Sleep Disorders

Sleep abnormalities are an integral part of depressive disorders, with more than 90% of depressed patients experiencing insomnia. Although stress and depression are major causes of insomnia, insomnia may also increase the activity of the hormones and pathways in the brain that can *produce* emotional problems. Even modest alterations in waking and sleeping patterns can have significant effects on a person's mood. Persistent insomnia may even predict the future development of emotional disorders. Some investigators, in fact, are exploring the possibility of preventing psychiatric disorders by early recognition and treatment of insomnia.

## Risk Factors for Seasonal Affective Disorder

Seasonal affective disorder (SAD) affects about one in 20 adults. About 80% of people who suffer from SAD are women. People who live in the north are more apt to experience SAD than are Southerners.

## Complications of Depression

Depression is often chronic, with episodes of recurrence and improvement. Approximately one-third of patients with a single episode of major depression will have another episode within one year after discontinuing treatment, and more than 50% will have a recurrence at some point in their lives. Depression is more likely to recur if the first episode was severe or prolonged, or if there have been recurrences. To date, even newer antidepressants have failed to achieve permanent remission in most patients with major depression, although the standard medications are very effective in treating and preventing acute episodes.

## Risk for Suicide

About 90% of suicides are due to treatable disorders, most commonly depression or substance abuse. People with depression have up to a 15% risk for suicide, with the highest risk in patients who are hospitalized for depression. Some studies indicate that atypical depression poses a higher risk for suicide than typical depression and that dysthymia may pose a higher risk than episodic major depressive disorder. Depressed men are more likely to commit suicide than depressed women, and in the U.S. and around the world, suicide is most common in men older than 60. Suicidal preoccupation or threats of suicide should always be treated seriously in anyone, however. [For the risk of suicide in young people or the elderly, see *Depression in the Elderly* or *Depression in Children*.]

## Effect on Physical Health

Major depression in the elderly or in people with serious illness seems to reduce their survival rates, even independently of any accompanying illness. In one study, even minor depression was associated with a higher risk for a shorter life in men (although not in women). Decreased physical activity and social involvement certainly play a role in the association between depression and illness severity. Some research also suggests, however, that depression produces biologic factors, such as low serotonin levels, which trigger stress-related responses in the body that cause blood clotting problems, inflammation, and damage to organs and cells.

*Effect on Heart Disease and Other Age-Related Problems.* Many studies have now reported strong associations between depression and a worse and even shorter old age. Depression increases the incidence and severity of heart attacks, stroke, and death after these events. Depression is also associated with mental decline and even osteoporosis in older people. [For more detailed discussion, see Depression in the Elderly.]

*Obesity.* Both obesity and depression are increasing in American. In a 2002 study, for instance, adolescents who were depressed had a high risk for obesity. The conditions may have common risk factors. For example, being in a lower social and economic group increases the risk for both obesity and depression. Low physical activity may also be a common factor. Few studies have investigated common biologic or behavioral factors.

*Increasing Sensations of Pain.* Depression coincides with high pain scores in people with chronic pain, such as those arthritis or fibromyalgia.

*Cancer.* The relationship between depression and cancer has been explored for years with only a few clear-cut associations (e.g., with pancreatic cancer). Certainly depression and anxiety can have a profound impact on quality of life in cancer patients. A 2002 study reported a worse outlook in cancer patients with a history of depressive symptoms -- but not in patients whose depression occurred after the illness.

## Impact on Daily Activities and Relationships

*Effects of Parental Depression on Children.* Depression in parents can have profound effects on their children. It not only increases the risk for depression in their children, but, according to one study, it may even increase a child's risk for many medical conditions (e.g., urinary and genital disorders, headaches, lung problems).

*Effects on Marriage.* In one survey, nearly half of people who suffered from psychiatric disorders before or during their first marriage were divorced, compared to a divorce rate of 36% in those who never suffered from emotional disorders. Spouses of partners with depression are themselves at higher risk for depression.

*Effect on Work.* Depression is well known to adversely affect a person's work life. It significantly increases the risk for unemployment and lower income. Major depression, according to a major 2003 survey, accounts for nearly half of the nation's excess lost productive time (in most cases because of reduced performance at work). Workers with depression also lose significantly more time due to ill health than non-depressed workers. Such lost time is estimated to cost the country billions of dollars each year.

## Substance Abuse

*Alcohol and Drug Abuse.* It is estimated that up to 25% of people with alcohol or drug abuse problems also have major depression. Studies on the connections between alcohol dependence and depression have still not resolved whether one causes the other or if they both share some common biologic cause.

*Smoking.* Depression is a well-known risk factor for smoking, and it increases the danger of starting young. Indeed, nicotine may stimulate receptors in the brain that improve mood in certain people with genetically induced depression.

## Diagnosis

Most people who are depressed do not seek psychiatric help and must rely on their family doctor. Unfortunately, it is often difficult for a primary care physician to recognize the problem if the patient does not bring it up directly.

Patients themselves may be unable to sense or admit their own depression. In one study, although 21% of patients who visited their family physicians were depressed, only 1% described their problem as depression.

Depression can also be confused with other medical illnesses. Weight loss and fatigue, for example, accompany many conditions, some serious, but they can also occur with depression.

Although not all patients who visit their physician should be screened for depression, individuals who have certain factors might ask their doctor if they should be screened for depression. For example, the following people may be at higher risk and therefore warrant a screening test:

- People with a family or personal history of depression.
- Patients with multiple medical problems.
- Patients with physical symptoms that have no clear medical cause.
- Patients with chronic pain.
- Individuals who visit their physician more frequently than expected.

## Screening Tests

A mental health specialist, such as a psychiatrist, social worker, or psychologist, is the best source for a diagnosis of depression. Such health professionals may administer a screening test such as the Beck Depression Inventory or the Hamilton Rating Scale, which consist of about 20 questions that assess the individual for depression. Studies are finding that even computerized phone interviews are valuable as screening tools for depression. It is important to note, however, that these tests are limited, and mental health professionals generally diagnose depression based on symptoms and other criteria. [For diagnostic criteria, see Introduction.]

Note: Specific groups may present different symptoms of depression. People from nonwestern countries are more apt to report physical symptoms (such as headache, constipation, weakness, or back pain) related to the depression, rather than mood-related symptoms. [ See Depression in Children *and* Depression in the Elderly.]

## Ruling Out Grief and Loneliness

*Grief.* The symptoms of grief (bereavement) and depression have much in common; indeed, it may be difficult to separate the two. Grief, however, is considered to be a healthy and important emotional response for dealing with loss, and it generally follows a characteristic path:

- Grief normally has a limited duration. In people without any co-existing emotional disorder, bereavement usually lasts between three and six months.
- The grieving person typically endures a succession of emotions that include shock and denial, loneliness, despair, social alienation, and anger.
- The recovery period following this process, during which the individual becomes re-involved with life, takes about the same amount of time as the bereavement cycle.

If the grief is still severe after this period, however, it may affect a person's health or increase the risk for on-going depression. Some experts suggest that such a severe persistent grieving state be categorized as a separate psychologic diagnosis, termed complicated grief disorder, which would be related to post-traumatic stress syndrome and require special treatment.

*Loneliness.* Like grief, loneliness is a condition that may often be mistaken for depression. In fact, while loneliness and depression often go hand in hand, some researchers believe that some people with loneliness may be effectively treated for depression. Of course, every person feels loneliness now and then. Debilitating loneliness, however, is often characterized by misery, a feeling of hollowness, unrealistic expectations for one's life, and feeling removed from others. Shy people may be more prone to loneliness. Psychotherapy of various kinds may help people address and allay loneliness.

## Treatment

Depression is a treatable illness, with many therapeutic options available. Increasingly, professionals are

viewing major depression as a chronic illness (i.e., the condition nearly always returns when treatment is stopped treatment). Therefore, medical intervention and help must be ongoing.

Patients with chronic depression have a number of options, including psychotherapy, antidepressants, or both. Of note, a 2002 study suggested that newer antidepressants and psychotherapy affected the same regions of the brain, which indicates they have a similar mechanism of action. The majority of people with acute depression respond to either the first or second trial of therapy.

In general, the treatment choice depends on the degree and type of depression and other accompanying conditions. It also may depend on age, pregnancy status, or other individual factors. [ See Depression in Children, Depression in the Elderly, and Depression in Women.]

Unfortunately, an important 2003 study reported that even if the depression is diagnosed, only about 20% of Americans with major depression are receiving adequate treatment. Most patients are treated by their family doctor, who may not have sufficient information or training on dosages or specific agents that would be best suited for individual cases. Even worse, about half people with depression, particularly the elderly, do not receive any therapy at all. Lack of health insurance is a major factor in these low treatment rates.

*Patients with Major Depression.* A number of studies have supported a combination of cognitive behavioral therapy (CBT) plus antidepressants (typically an SSRI, such as Prozac) given for at least 60 days. CBT is used to resolve any residual symptoms after medication has been started. Some studies estimate that only 40% of people with chronic depression respond to medications alone compared to 60% who are given combination treatment.

For those who fail medications and psychotherapy, other techniques, such as electroconvulsive therapy (ECT), are safe and effective. In recent years, experimental procedures, such as vagus nerve stimulation and repetitive transcranial magnetic stimulation, have also been found to be effective in some cases of treatment-resistant depression.

*Patients with Minor Depression.* Patients with minor depression (fewer than five symptoms that persist for less than two years) may respond well to watchful waiting and supportive care. For example, one study found that newer antidepressants were only modestly helpful in older patients with mild depression. Supportive care that consists only of brief and occasional counseling sessions with the family doctor may be as helpful as antidepressants in some cases.

*Patients with Depression and Other Psychiatric Problems.* Other psychiatric problems often coexist with depression. If patients also suffer from anxiety, treating the depression first often relieves both problems. Those with more severe psychiatric problems, such as bipolar disorder or schizophrenia, require specialized treatments.

*Patients with Depression and Medical Conditions.* Depression can worsen many medical conditions and may even increase mortality rates from some disorders, such as heart attack and stroke. Depression, then, should be aggressively treated in anyone with a serious medical problem.

*Patients with Depression and Substance Abuse Problems.* Treating depression in patients who abuse alcohol or drugs is important and can sometimes help patients quit.

## Choosing a Therapist

Most people with depression can be treated in an office setting by a psychiatrist or other therapist. Infrequently, the level of dysfunction may be serious enough to warrant hospitalization to provide protection from further deterioration or self-harm.

*Mental Health Professionals.* The only health professionals who can prescribe antidepressants are the following:

- Psychiatrists. (These are mental health professionals with MD degrees.)
- Any medical physician with an MD.
- Some psychiatric nurse clinicians.

Although other mental health professionals cannot prescribe drugs, most therapists have arrangements with a psychiatrist for providing medications to their patients. In general, mental health professionals are categorized by their training:

- Psychoanalysts tend to have a degree in psychiatry, psychology, or social work as well as several years of training at a psychoanalytic institute.
- Psychologists have graduate-level training, including an internship in a mental healthcare facility.
- A clinical social worker has a master's degree and two years of supervised experience in mental health and human services.
- Advanced-practice psychiatric nurses have a master's degree and can provide therapeutic services.

#### *Tips for Selecting a Therapist:*

- Patients can locate a mental health professional in their area by asking their doctor for a referral or by contacting a mental health organizations. [ See Resources.]
- The patient should describe problems briefly but specifically over the phone to any prospective therapist to get a sense of whether he or she will suit the patient's needs.
- An advanced degree does not necessarily guarantee quality therapy. The patient's belief in his or her health provider may be the most important component in recovery, as indicated by studies reporting that placebos relieve depression in about a third of patients and in some cases actually work better than psychotherapy.
- Patients should not be shy about considering a change in their therapist if they lack confidence in their current one.

## Depression in the Elderly

Although depression in the elderly is very common, the aging process itself is unlikely to be the cause in most cases. An Italian study, for example, indicated that the very old (people who lived beyond 90 years of age) were no more likely to be depressed than younger adults. (The rate was 10% in both groups.) Studies on the cause or extent of depression in the elderly are not clear-cut.

The severity of depression in elderly patients is strongly associated with poor health and with less ability to function. In one study of older adults undergoing rehabilitation, half of whom were depressed, as their function improved so did their mood.

Anyone who experiences cumulative negative life events, physical illness, the death of a loved one, impaired functioning, or loss of independence can become deeply depressed. The elderly are at highest risk for such events. Interestingly, in this regard, one study suggested that pessimistic elderly people are less prone to depression than their optimistic peers -- possibly because pessimists are more likely expect and therefore adapt to negative experiences than those with an optimistic personality.

## Diagnosing Depression in the Elderly

Because of the complex relationship between depression, drug interactions, and serious physical illness in the elderly, an accurate diagnosis in this group is important but not always straightforward. The characteristic symptoms of depression are not always present or readily apparent in older people:

- Some older people may be aware of their depression but believe that nothing can be done about it.
- Many elderly people who are depressed may report only physical symptoms (aches and pains) or other mood states (confusion, agitation, anxiety, and irritability) related to depression rather than depression itself.
- Often they are unable or unwilling to express their feelings or are even unaware that they are depressed.

- Their symptoms are often ignored or confused with other ailments common in the elderly, including Parkinson's or Alzheimer's disease, dementia, thyroid disorders, arthritis, stroke, cancer, heart disease, and other chronic conditions.
- Depression is also a side effect of many drugs that are commonly prescribed for the elderly. It is often very difficult, then, to determine if the patient's depression is a psychologic reaction to the illness, caused by the disease itself, or completely independent from the medical condition. Both physical and emotional conditions should be considered in making a diagnosis in older people.

## Physical and Mental Consequences of Depression in the Elderly

Many studies have now reported strong associations between even mild depression and poorer quality of life as well as a shorter lifespan.

*Risk for Suicide in the Elderly.* Suicide in the elderly is the third-leading cause of death related to injury. Men account for 81% of these suicides, with divorced or widowed men at highest risk.

*Effects of Depression on the Ability to Function.* A 2000 study indicated that even mild depressive symptoms in people aged 65 and above are associated with a higher risk of becoming disabled and having a lower chance of recovery.

*Heart Disease and Heart Attacks.* Depression increases the severity of a heart attack and may even impair a patient's response to medication for heart disease. Although people with heart disease may certainly become depressed, this does not explain entirely the link between the two problems. The data are now suggesting that depression itself may be a true risk factor for heart disease as well as its increased severity. A number of studies have suggested that depression has biologic effects on the heart, including a higher risk for blood clotting, changes in heart rate, and impaired blood flow to the heart (particularly in response to mental stress). A study in 2001, for example, reported an association between depression and a greater risk for death from heart problems even in people without a history of heart disease. A 2002 study reported a higher risk for heart failure in women -- although not in men -- with depression. It should be noted that simply treating depression does not improve survival rates after a heart attack --only treating heart disease does this.

The more severe the depression, the more dangerous to the health, although even mild depression, including feelings of hopelessness, experienced over many years, may harm the heart, even in people with no early signs of heart disease.

*Stroke.* Depression has also been linked to a higher risk for having a stroke and lower survival rates after one. In one 2000 study, for example, patients with severe depression had a 73% higher risk for stroke, and those with moderate depression had a 25% higher risk than average. The risk for stroke in depressed African Americans in the study was notable, 160% higher than average. Furthermore, a 2001 study confirmed that self-reported negative mood symptoms correlated with increased mortality up to two years after a stroke. Some research has suggested that injuries in the brain after a stroke can cause depression, although a 2003 study reported the same rates of depression after a stroke as after a heart attack. More research is needed to determine if some common factors in both events may increase the risk for depression.

*Mental Decline.* Depression in the elderly is associated with a decline in mental functioning, regardless of the presence of dementia. Depression may be a predictor or even a cause of Alzheimer's disease. Brain scans in the elderly, for example, have reported greater atrophy in the brains of depressed individuals than in those of nondepressed ones.

*Osteoporosis.* Some studies have linked past and current major depression with bone-density loss in women. One explanation for this association is that depressed women have higher levels of the stress hormone cortisol, which may contribute to bone density loss.

## Treating Depression in the Elderly

Some experts recommend only psychotherapy or attention intervention for elderly patients with mild depression.

In many older patients, a regular exercise program may be sufficient to improve mood.

Ideally, elderly people with more serious depression should be treated with a combination of psychotherapy and antidepressants on an ongoing basis. And the treatment should be ongoing. Unfortunately, such intensive treatment is not often available to elderly patients. Furthermore, even with this approach, many elderly patients do not achieve remission or even significant improvement.

The use of antidepressants in the elderly can also be problematic:

- Tricyclics are as effective and less expensive than SSRIs, but they have more adverse effects. Specifically, they pose a higher risk for adverse effects on the heart and possibly the lungs. (The older tricyclics, e.g., amitriptyline and imipramine, have other severe side effects in older adults.)
- SSRIs have fewer side effects than tricyclics. A 2002 study using sertraline (Zoloft) suggested it was safe and effective for treating depression in heart attack patients. Of possible significance for people with heart disease or stroke are studies suggesting that SSRIs may reduce the risk for blood clotting and so help protect the heart. More research on the effects of SSRIs on the heart is needed. Contrary to common belief, SSRIs do not appear to pose any lower risk for falls than the older tricyclic antidepressants. (The effect of the newer antidepressants on falling is not yet known.) In any case, patients with Parkinson's may want to avoid SSRIs because they can increase the risk for tremor and other symptoms of the disease.

## Depression in Children and Adolescents

Depressed children often suffer in silence, and depression may be evident only from reports of problems in school. It is also often difficult for adults to believe that children can be chronically depressed. Symptoms for depression in children often differ from those in adults and may include the following:

- An inability to enjoy favorite activities.
- Persistent sadness.
- Increased irritability.
- Complaints of physical problems, such as headaches and stomachaches.
- Poor performance in school.
- Persistent boredom.
- Low energy.
- Poor concentration.
- Changes in eating and/or sleeping patterns.
- A greater tendency to bully others. (Anxious children are more often bullied.)

## Risk Factors for Depression in Children and Adolescents

Depression can occur in children of all ages, including preschoolers, although adolescents have the highest risk (about 20%). Risk factors for depression in young people include having parents, particularly mothers with depression. Early negative experiences and exposure to stress also pose a risk for depression. Sometimes depression develops after a physical illness. In adolescents, feeling alienated from parents is a strong predictor for depression.

## Consequences of Depression in Children and Adolescents

*Outlook for Future Emotional Problems.* Adolescents who have depression are at significantly higher risk for substance abuse, recurring depression, and other emotional problems such as bipolar disorder in adulthood.

*Risk for Suicide in Adolescents.* Suicide is the third most common cause of death among adolescents, and is one of the most devastating events that can happen to a family. Suicide is most commonly associated with depression in young people but it is also commonly associated with anxiety, psychosis, substance abuse, or impulsivity. More girls attempt suicide but more boys succeed, most often because they choose guns or violent methods while girls tend to overdose, which is more treatable. Nevertheless, attempts are major risk factors for

a later suicide. Any expression of suicidal intent should be treated very seriously.

The following are danger signs in young people:

- Withdrawal from friends.
- Sudden decrease in school performance.
- Loss of interest in activities that were previously pleasurable.
- Unusual irritability.
- Unusual changes in sleep or eating habits.

Risk factors for suicide include a history of neglect or abuse, history of deliberate self-harm, a family member who committed suicide (nearly always one who shared a common mood disorder), access to firearms, are in communities where there have been recent outbreaks of suicide in young people. A romantic break-up is often the trigger for a suicidal attempt in teenagers. Feeling connected with parents and family protected young people with depression in one study, regardless of gender or ethnicity.

In one study, adolescents failed to seek help for suicidal thoughts for the following reasons:

- They believed nothing would help.
- They were reluctant to tell anyone they had problems.
- They thought it was a sign of weakness to seek help.
- They did not know where to go.

Parents should not hesitate to seek professional help for their children if they suspect they are thinking about killing themselves. This is a medical emergency and requires immediate treatment.

Behavioral therapies and antidepressants are promising treatments for preventing suicide but need study. It is important to note that there has been a decline in adolescent suicides over the past decade, which some experts attribute to the increased use of antidepressants in this population. Reports in the popular press of an increased risk for suicide with SSRIs are unproven and a 2003 study found no association between SSRIs and suicide.

## Treating Depression in Children and Adolescents

Studies suggest that when children or adolescents are treated, up to 80% recover. Still, between 25% and 50% of such young people have a recurrence of depression within two years of the first episode.

*Mild to Moderate Depression.* Children and adolescents with mild to moderate depression should receive psychotherapy before medications are tried. Cognitive therapy may be the best approach for children and adolescents with depression. (It may even be helpful in preventing depression in young people whose parents have a history of depression.) One study suggested, however, that there was very little difference in success rates among three major forms of psychotherapy: cognitive-behavioral therapy, family therapy, or supportive therapy. All achieved about an 80% recovery, with a 30% recurrent rate an average of 4 months after recovery.

*Severe Depression.* The American Academy of Child and Adolescent Psychiatry recommends the SSRI antidepressants for children and adolescents with very severe depression that does not respond to psychotherapy. Many SSRIs appear to be safe and effective, but at this time Prozac is the only one to be approved for children over seven and for adolescents. Some of the newer antidepressants, such as nefazodone and venlafaxine, may also be safe and effective in children.

(Tricyclic antidepressants do not tend to be beneficial in adolescents and children and they have many side effects. MAOIs are also not commonly prescribed.)

For optimal results, SSRIs should be combined during the early acute phase with a mixture of psychotherapies, including cognitive-behavioral, interpersonal, and psychodynamic therapies. Initial drug treatments should continue for at least six months, and a maintenance phase should last another year or longer.

Of some concern is a 2002 study suggesting that SSRIs may delay or impair growth in children. More research is needed on this issue. Reports in the popular press of an increased risk for suicide with SSRIs are unproven. Still, the FDA warns physicians to stay alert to any signs of suicidal thought or behavior in people taking SSRIs. [For more information, see *Box Suicide and SSRIs*.]

## Drug Treatment Guidelines

*Active Antidepressants Versus Placebo.* Antidepressants are effective in many patients, but there are some problems in gauging their success. Determining the true value of an antidepressant medication is difficult because between some of their benefits are attributed to the placebo effect. Placebos themselves can achieve a 35% response. Experts point out that people who respond to placebos still show poorer social functioning than those who respond to medication. An interesting 2002 study used electroencephalography (EEG) and reported that placebos and active antidepressants affected different parts of the brains in people who responded to one or the other. (No part of the brain was affected in people who did not respond to either a placebo or an active drug.)

*Major Classes of Antidepressants.* The primary target of most major antidepressant drug classes is the transport of the important neurotransmitters serotonin and norepinephrine. Such drug classes are the following:

- Selective serotonin-reuptake inhibitors (SSRIs). These have become the standard antidepressants. They are effective and have very moderate side effects. Some may be beneficial in treating anxiety and certain subtypes of depressive disorders unresponsive to previous agents, including premenstrual dysphoric disorder and seasonal affective disorder, atypical depression, and recurrent brief depression.
- Tricyclic antidepressants (TCAs). These are effective but can have severe adverse effects, particularly in older people.
- Monoamine oxidase inhibitors (MAOIs), including newer selective MAOIs. MAOIs are the most effective antidepressants for atypical depression, but have some severe side effects and require restrictive dietary rules.
- Drugs generally referred to as "designer antidepressants" specifically target specific neurotransmitters (brain chemicals) other than or in addition to serotonin. Many are being proving to be effective in patients who do not respond to standard antidepressants or in specific patients, such as smokers who want to quit or patients with chronic pain.
- The herbal remedy St. John's wort is included as a separate category, since it is unregulated and its chemical classification has not yet been determined.

A great deal of leeway exists in choosing an appropriate antidepressant. Overall, they seem to be equally effective, although cost, individual responses, and side effects vary widely.

*Approach and Duration of Initial Treatment.* The guidelines for the duration of an initial antidepressant regimen is as follows:

- Patients should start at a low dose, which is increased over a period of five to 10 days.
- Some experts recommend that the patients see their physician every one to two weeks until substantial improvement occurs. It is important to note, however, that it may take four to six weeks before a patient experiences the effects of any antidepressant.
- Side effects usually diminish within one to four weeks. (Exceptions may be weight gain and sexual dysfunction.)
- If no improvement occurs within three to four weeks, however, and the patient is not overly distressed by side effects, an alternative agent may be tried. More than 80% of patients respond to some antidepressant, although specific agents are helpful for only about half of patients. This suggests that if one medication fails, another has a good chance of being helpful. Newer agents with different mechanisms are being developed that are improving response rates.
- In general, patients should continue taking antidepressants for at least six months after symptom relief to help prevent relapse. (Patients who improve within two weeks of taking medications may not require lengthy treatment.)

*Treating Recurrence.* Recurrence of depression is very common. About a third of patients will relapse after a

first episode within a year of ending treatment, and more than half will experience a recurring bout of depression at some point during their lives. Among those at highest risk for early relapse and who may require ongoing antidepressants are the following:

- Patients with at least two episodes of major depression or major depression that lasts for two years or longer before initial treatment.
- Patients who continue to have low-level depression for seven months after starting antidepressant treatments.

In one study, 41% of patients relapsed after they stopped treatment compared to only 18% who had continued their antidepressants. Patients, then, may need maintenance therapy. Experts disagree, however, on the optimal length or the appropriate dosage of maintenance therapy. Some patients may need to stay on antidepressants for a year or two--or even indefinitely. Some experts recommend withdrawing from medication after a year. (This should be gradual, over two to three months.) If depression recurs, then the patients should go back on the antidepressants.

There is no risk for addiction with current antidepressants, and many of the common antidepressants, including most standard SSRIs, have been proven safe when taken for a number of years.

*Common Side Effects of Most Antidepressants.* No matter how well a drug treats depression, the ability of the patient to tolerate its side effects strongly influences his or her compliance with therapy. Lack of compliance is probably the major barrier to success. According to one study, as many as 70% of elderly depressed patients did not adhere to antidepressant drug regimens. Side effects can be avoided or moderated if any regimen is started at low doses and built up over time. Although specific side effects are discussed under individual drugs, there are a few that are common to many of them:

- Sexual dysfunction is a common side effect of nearly all the standard antidepressants and some of the newer drugs. These side effects can be particularly distressing for patients on maintenance treatment who otherwise feel well. Some of the newer antidepressants, such as mirtazapine, bupropion, or nefazodone, may be effective alternatives without as high a risk for this problem. Sildenafil (Viagra), used for erectile dysfunction in men, may help reverse sexual dysfunction from antidepressants in both men and women. It does not heighten sexual interest, however.
- An increased risk of oral health problems caused by dry mouth is associated with long-term use of most antidepressants. The risks appear to be highest with some of the new designer antidepressants, with the use of multiple drugs, and with the presence of oral infections. Patients can increase salivation by chewing gum, taking vitamin C tablets, using saliva substitutes, and rinsing the mouth frequently. (In one small study, drinking coffee reduced dry mouth associated with tricyclic antidepressants.)
- Virtually all antidepressants have complicated interactions with other drugs; some are very serious. A few are mentioned in the individual drug discussions below, but many are not, and patients should inform the physician of any drugs they are taking, including over-the-counter medications.
- Nearly all antidepressants are metabolized in the liver, so anyone with liver abnormalities should use them with caution.
- Abrupt withdrawal from many antidepressants can produce severe side effects; no antidepressant should be stopped abruptly without consultation with a physician.

### Suicide and SSRIs

Over the years, there have been some reports of a higher risk for suicide with the use of SSRIs, including fluoxetine (Prozac) and paroxetine (Paxil, Seroxat). Of particular concern have been reports of a greater risk for suicide in young people taking paroxetine. The evidence to support these fears is generally very weak.

An eight-year study helped lay to rest the very early reports of an association between fluoxetine and an increased risk for suicidal thoughts and behavior. In this study, there was actually an insignificant reduction in suicidal risk. A more recent study in 2003 found no higher risk in people taking SSRIs than in those taking a placebo. Intensive research is continues to determine if SSRIs pose a risk for suicide in anyone.

Still, the FDA advises physicians to be alert to any suicidal thinking and behaviors in people on antidepressants. There is some evidence to suggest that antidepressants might revitalize suicidal attempts in patients who were too despondent before treatment to make the effort. SSRIs may also pose a higher risk for impulsivity, which may increase the risk for suicide in young people with depression and other conditions, such as attention deficit disorder.

Experts warn that caregivers and physicians should be vigilant for any signs of suicidal intent during the early acute phases of treatment. Depression itself, in any case, increases the risk for suicidal thoughts and behavior.

Patients should be aware of any suicidal thoughts and should seek help immediately.

## Selective Serotonin-Reuptake Inhibitors

Selective serotonin-reuptake inhibitors (SSRIs) are now the first-line treatment of major depression. They work by increasing levels of serotonin in the brain. SSRIs include fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil, Asimia, Seroxat), fluvoxamine (Luvox), citalopram (Celexa, Cipramil), and escitalopram (Lexapro, Cipralext). There are no significant differences among SSRI brands in effectiveness for treating major depressive disorder, although individual drugs may have different side effects or benefits for specific patients. For example, Lexapro and newer forms of paroxetine may have more specific effects than other SSRIs and so have fewer side effects. SSRIs also appear to be safe and effective for many young people with major depression, but at this time Prozac is the only one of these agents to be approved for children over seven and adolescents.

Because they act on serotonin specifically, SSRIs have fewer side effects than the older antidepressants, which have more widespread effects in the body. Patients taking SSRIs report not only relief of depressive symptoms but also better relationships with other people.

*Candidates for SSRIs.* SSRIs appear to help people with the following conditions:

- Mild to moderately severe major depression.
- Seasonal affective disorder.
- Dysthymia.
- Severe premenstrual syndrome and premenstrual dysphoric disorder (PMDD). A repackaged form of fluoxetine (Sarafem) is the first SSRI specifically FDA-approved for PMDD. Other SSRIs and newer antidepressants, however, are also proving to be effective.
- Anxiety disorders.
- Bulimia.
- Impulsive and aggressive behaviors in psychiatric patients and in people with no mental health problems.

*Duration of Effectiveness and Use.* SSRIs take, on average, two to four weeks to be effective in most adults. They may take even longer, up to 12 weeks, in the elderly and in those with dysthymia. By 14 weeks, depression should be in remission in everyone who responds to the drugs. Unfortunately, recurrence is common once the drugs are stopped. Studies to date have indicated that the standard SSRIs are probably safe, although it is still unclear which patients would most benefit from on-going medication. Some experts recommend withdrawing from medication after a year. If depression recurs, then the patients should go back on the antidepressants.

*Drug Interactions.* SSRIs interact with numerous drugs, and caution should be taken that the physician is well informed of any other medications the patient is taking. In rare cases, taking them with other drugs that affect serotonin levels may result in a reversible narrowing of the blood vessels in the brain causing "explosive headache" and possible seizures or even stroke. Such agents include other antidepressants, anti-migraine agents, decongestants, diet pills, St. John's wort, ecstasy, cocaine, and methamphetamine.

*Side Effects of SSRIs.* Side effects include the following:

- Nausea and gastrointestinal (GI) symptoms. These effects usually wear off over time.
- Agitation, insomnia, mild tremor, and impulsivity occur in 10% and 20% of people who take SSRIs, these symptoms may be particularly problematic in patients who also suffer from anxiety, sleeplessness, or both. Such side effects may persist. On the other hand, about 20% of SSRI-treated patients experience drowsiness, which may be counteracted by taking the medication at bedtime. Newer SSRIs, such as escitalopram (Lexapro), may have fewer of these adverse effects.
- Dry mouth is common and can increase the risk for cavities and mouth sores.
- Lack of motivation, fatigue, and mental dullness.
- Flu-like symptoms
- Headache.
- Weight gain. Some weight loss during the first few weeks of treatment may occur, but over time patients on maintenance treatment typically return to their pretreatment weight or gain weight. Weight gain varies depending on the SSRI. For example, in one study patients who took paroxetine (Paxil) experienced five times the weight gain as those who took citalopram (Celexa). Patients should be encouraged to maintain a low-calorie diet and to exercise. They should be aware that some of the weight-loss medications, notably sibutramine (Meridia), can have serious interactions with SSRIs.
- Sexual side effects. Sexual dysfunction, including delayed or loss of orgasm and low sexual drive, is now a well-known side effect of SSRIs. One 2002 study suggested that men report higher rates of sexual problems but sexual dysfunction may actually be more severe in women. It should be noted, however, that in one 2001 study, sexual desire *increased* in 20% of women and 27% of men taking the SSRI. In patients with normal sexual function, only about 15% of patients experienced greater sexual dysfunction, which was generally mild to moderate and mostly took the form of less sexual interest. Taking a supervised drug "holiday" on the weekend may improve sexual function during that time. (Withdrawal symptoms may develop and include return of depression, sleep problems, exhaustion, and dizziness.) Some of the newer SSRIs or designer antidepressants may cause less severe impairment of sexual function. Sildenafil (Viagra), used for erectile dysfunction in men, may help reverse sexual dysfunction from antidepressants in both men and women. It does not heighten sexual interest, however.
- Bleeding. There is an increased risk for bleeding, notably gastrointestinal bleeding, particularly in people who take NSAIDs (such as aspirin and ibuprofen) regularly or in people who require blood thinning agents. Elderly people taking these drugs should take the lowest dose possible, and those with heart problems should be monitored closely.
- There have been some reports of worsened glaucoma in patients taking SSRIs. This is a very rare complication and it isn't clear that there is a causal relationship. Patients with glaucoma who take SSRIs should have their eyes examined regularly.
- Over the years, some patients taking SSRIs have reported a group of side effects, known as extrapyramidal symptoms, which are similar to those in Parkinson's disease and affect the nerves and muscles controlling movement and coordination. They are uncommon, and when they develop they tend to occur within the first month of treatment.
- There is a higher risk for hip fracture, particularly during the early days of treatment (although not as high as with tricyclics).
- High doses may cause hallucinations, confusion, changes in blood pressure, stiffness, and irregular heart beats. Death from overdose is extremely rare.
- The effects of long-term use of SSRIs in young people are not clear. There have been case reports of myoclonus (uncontrolled muscle jerks) with long-term use. In addition, there is some concern that SSRIs may limit growth in children.

*Drug Interactions.* Serious interactions can occur with other antidepressants, such as tricyclics and, of particular note, monoamine oxidase inhibitors (MAOIs) ( *see below*). Other serious interactions have occurred with meperidine (Demerol) and illegal substances (such as LSD, cocaine, or ecstasy). People who take SSRIs may drink alcohol in moderation, although the combination may compound any drowsiness experienced with SSRIs, and some SSRIs increase the effects of alcohol.

*Withdrawal Symptoms.* Dizziness, muscle weakness or pain, odd sensations in the limbs, nausea, loose stools, visual disturbances, irritability, insomnia, mood worsening, and headaches have been known to occur with sudden discontinuation of SSRIs. The symptoms are more likely to occur with antidepressants with shorter half-lives as compared with fluoxetine, which has a long half-life. Reducing the dose of the antidepressant before stopping it is recommended.

## Designer Antidepressants

A number of drugs have now been developed that target other neurotransmitters, such as norepinephrine or dopamine, alone or in addition to serotonin. In general, the advantages of the new designer antidepressants are as follows:

- They may be more tolerable than the older tricyclic compounds and even some SSRIs, although long-term side effects are not fully known in this group.
- Most of these drugs have fewer adverse effects than SSRIs on sexual function, and some people have even reported enhanced sexuality with some of them.
- They may be more effective than SSRIs for severely depressed patients.
- Some of these agents are helpful for additional problems, such as insomnia, fibromyalgia and similar chronic pain syndromes, or smoking, that may affect people with depression.

They do share some side effects, including dizziness and dry mouth, with other antidepressants. Comparison studies are needed, however, to determine if any of these drugs are superior to standard SSRIs in treating different stages or aspects of depression. Combinations may prove to be the most effective approach.

*Dual Inhibitors.* Dual inhibitors act directly on two neurotransmitters -- norepinephrine and serotonin. They improve bladder capacity and may be helpful for people who also suffer from urinary incontinence. They also may help patients with chronic pain syndromes or fibromyalgia. On the basis of a review of the literature, in 2002 an expert panel concluded that simultaneous targeting of both serotonin and norepinephrine was currently the optimal approach for patients who failed standard antidepressant therapies.

- Venlafaxine (Effexor) is similar to Prozac in effectiveness and tolerability for most patients. It has a faster action, however. As with the SSRIs, venlafaxine impairs sexual function. Although clinical trials have shown that the drug is safe and effective in most people, of concern are recent reports of changes in blood pressure and heart conduction abnormalities, which may cause serious problems in elderly patients. Some patients report severe withdrawal symptoms, including dizziness and nausea. It can also cause uterine and vaginal bleeding unrelated to menstruation.
- Duloxetine (Cymbalta) also acts on both serotonin and norepinephrine. An estimated 65% of patients with major depressive disorder will respond to this drug, and 43% will go into remission. It also may help patients with chronic pain syndromes, such as fibromyalgia, and those with stress incontinence. To date, side effects are mild and include dry mouth, nausea, and sleepiness. No significant hypertension has been reported. It also appears to pose a lower risk for sexual dysfunction than standard SSRIs.
- Milnacipran (Ixel) is a similar agent but not yet approved in the U.S. It is specifically being researched for helping people with fibromyalgia and other pain syndromes.

*Other Antidepressants with Multiple Effects on Neurotransmitters.* Other antidepressants are available with different actions. For example, nefazodone and mirtazapine may enhance both serotonin and norepinephrine indirectly. These agents may provide relief from insomnia and anxiety, which are common in many depressed patients. (SSRIs and dual inhibitors generally pose a *higher* risk for insomnia.) Bupropion has weak effects on serotonin, norepinephrine, and possibly dopamine.

- Bupropion (Wellbutrin, Zyban) has weak effects on the reuptake of serotonin, norepinephrine, and dopamine--a third important neurotransmitter. The actions affect dopamine may be responsible for its benefits in helping smokers to quit. (Dopamine is important in feelings of reward.) Bupropion causes less sexual dysfunction than SSRIs. About 25% of patients experience initial weight loss. Side effects include restlessness, agitation, sleeplessness, headache, rashes, stomach problems, and in rare cases, menstrual irregularities (rare), hallucinations and bizarre thinking. High doses can be toxic and may cause dangerous heart arrhythmias. Seizures have also been reported, usually in patients with eating disorders (anorexia or bulimia) or those with risk factors for seizures.
- Nefazodone (Serzone) is more rapidly effective and has fewer distressing side effects, including sexual dysfunction, than SSRIs. The drug can also be combined with SSRIs or psychotherapies for improved response. Nefazodone is one of the few antidepressants that has a positive effect on sleep efficiency. The drug may cause an abrupt drop in blood pressure after standing up suddenly. Of concern are rare cases of liver failure in patients taking nefazodone.
- Mirtazapine (Remeron) is a unique antidepressant known as a 5-HT<sub>2</sub> blocker. It may indirectly enhance the effects of both serotonin and norepinephrine. Compared to some common SSRIs, studies are indicating that it becomes effective more rapidly and has stronger early actions against anxiety in

patients who suffer both disorders. It also improves sleep. Patients may be able to safely switch directly from an SSRI to mirtazapine without having to do through a withdrawal period. It has a lower incidence of sexual dysfunction than many other antidepressants. It may elevate cholesterol and triglyceride levels slightly. It also causes blurred vision and may cause slight weight gain.

**Selective Noradrenaline Reuptake Inhibitor.** Reboxetine (Edronax, Vestra) is at least equal to Prozac in reducing depression and improving social functioning. In one study, however, more patients taking reboxetine dropped out (12% versus 7% for Prozac) because of side effects. It typically causes insomnia during the first week of treatment that resolves over time. Reboxetine is available in other countries, but the FDA has not approved it for marketing in the U.S.

## Tricyclic Antidepressants

Before the introduction of SSRIs, tricyclics had been the standard treatment for depression.

Tricyclics are sometimes referred to as belonging to one of two categories: tertiary or secondary amines:

- Tertiary amines include amitriptyline (Elavil, Endep) and imipramine (Tofranil).
- Secondary amines include desipramine (Norpramin) and nortriptyline (Pamelor, Aventyl). Secondary amines may have fewer side effects, including drowsiness, than tertiary amines, but they are as toxic in high amounts.

Less commonly used or investigative tricyclics include doxepin (Sinequan), amoxapine (Asendin), maprotiline (Ludiomil), protriptyline (Vivactil), trimipramine (Surmontil), mianserin (Bolvidon), and dothiepin (Prothiaden).

Tricyclics are as effective for treating depression but they have more adverse effects. They may offer benefits for many people with dysthymia, who generally do not respond to SSRIs. In one clinical trial, men responded far better to the tricyclic imipramine (Tofranil) than they did to the SSRI sertraline (Zoloft).

**Side Effects of Tricyclics.** Side effects are fairly common with these medications. In fact, in an analysis of studies, more tricyclic users discontinued their drugs due to side effects than did SSRI or MAOI users. Those most often reported include the following:

- Dry mouth. (One intriguing study suggested that drinking coffee may help reduce this side effect.)
- Constipation.
- Blurred vision.
- Sexual dysfunction.
- Weight gain.
- Difficulty urinating.
- Drowsiness (varies by drug).
- Dizziness. Blood pressure may drop suddenly when sitting up or standing.

Tricyclics can have serious, although rare, side effects:

- They tend to cause disturbances in heart rhythm, which can pose a danger for some patients with certain heart diseases. One study comparing nortriptyline with paroxetine, an SSRI, reported nine times more adverse cardiac events with the use of the tricyclic than with the SSRI.
- Also of concern is a study reporting that tricyclics, particularly imipramine, may be responsible for 10% of cases of a lung disease called idiopathic pulmonary fibrosis (IPF), which can cause lung inflammation and scarring. Initial symptoms are breathlessness and dry cough. The two newer tricyclics, mianserin and dothiepin, also increased the risk.
- Tricyclics can be fatal with an overdose.
- A 2000 study showed a small increased risk for non-Hodgkin's lymphoma associated with tricyclic use.

Side effects and their severity may vary among the tricyclics. Examples are the following:

- In one study, mianserin, a newer tricyclic, improved sexual dysfunction caused by SSRIs.
- Protriptyline can cause sun sensitivity, and people who take this should take precautions against sunlight when they go outdoors.

## Monoamine Oxidase Inhibitors (MAOIs)

Monoamine oxidase inhibitors (MAOIs) block the enzyme monoamine oxidase, which has negative effects on many of the neurotransmitters that are important for well-being. MAOIs include phenelzine (Nardil), isocarboxazid (Marplan), and tranylcypromine (Parnate). Because these agents can have very severe side effects, they are usually indicated only when other antidepressants prove ineffective.

Newer MAOIs, such as selegiline (Eldepryl, Movergan), also known as deprenyl, and moclobemide (Aurorix, Manerix), target only one form of the MAOI enzyme. They may be effective without the significant side effects of the older MAOIs for patients with dysthymia. One interesting 2002 study reported that selegiline delivered from a skin patch was effective and safe for patients with major depression. At this time moclobemide is not available in the U.S.

*Candidates for MAOIs.* They may be effective for the following conditions:

- Atypical depression.
- Eating disorders.
- Post-traumatic stress disorder.
- Borderline personality.

*Side Effects.* MAOIs commonly cause the following side effects:

- Orthostatic hypotension (a sudden drop in blood pressure upon standing).
- Drowsiness or insomnia.
- Dizziness.
- Sexual dysfunction. (Of note, however, in one 2000 study, only 1.9% of patients taking the newer European MAOI moclobemide reported sexual dysfunction related to their antidepressant compared to 21.6% of patients taking SSRIs.)
- The most serious side effect is severe hypertension, which can be brought on by eating certain foods having a high tyramine content. Such foods include aged cheeses, most red wines, sauerkraut, vermouth, chicken livers, dried meats and fish, canned figs, fava beans, and concentrated yeast products.
- MAOIs may also cause birth defects and should not be taken by pregnant women.
- Very dangerous side effects can occur from interactions with other antidepressants, including SSRIs. There should be at least a two to five-week break between taking MAOIs and other antidepressants. MAOIs can have serious interactions with other drugs as well, including some common over-the-counter cough medications, psychostimulants (such as Ritalin), and decongestants.

## Azapirones

Azapirones, including buspirone (BuSpar) and gepirone (Ariza, Variza), act on serotonin receptors called 5-HT (1A). Buspirone is primarily used to treat anxiety disorders, but they may have benefits for depression—particularly gepirone in extended release formulations. Studies on gepirone indicate that it may help some people with major and atypical depression. Buspirone (BuSpar) has shown benefits in treating resistant depression when added to the SSRIs citalopram or fluoxetine. More research is needed to determine the role of these agents in depression.

## St. John's Wort and Other Herbal Remedies

*General Guidelines.* St. John's wort (*Hypericum perforatum*) is an herbal remedy that may help some patients with mild to moderate depression. It is not clear, however, how significant the benefits are. Some, but not all, studies report that it is more effective than placebo. Notably, a 2002 study reported no differences between St.

John's wort and placebo for patients with moderate depression. A 2000 study on similar patients, however, reported that it was as effective as a tricyclic.

Even if studies were consistent, this herbal substance is not regulated and there is no guarantee of quality in any brands currently available. In fact, in a 2003 study, out of 54 St. John's products bought in Canada and the US, only two products contained concentrations of the active ingredients that fell within 10% of the claims on the labels. [ See *Box Warnings for Alternative and So-Called Natural Remedies Used in Depression.*]

At this time, the following guidelines are recommended:

- People with severe depression should not take this remedy without a physician's guidance. Even those with mild depression should not use St. John's wort without consulting a physician. Children and pregnant or nursing women should not take this substance.
- People should purchase brands only from well-established manufacturers until regulations have been established for this and other herbal remedies.
- Although no dose levels have been established, trials indicate that 300 milligrams taken three times a day may be effective. (Patients should check with a knowledgeable physician.)
- It takes between two and three weeks for the drug to have an effect.
- Early studies had suggested that the herbal substance might act in the same way as chemical MAOIs, but the MAO-like activity of St. John's wort appear to be minimal. Still, some experts suggest avoiding large amounts of foods and substances that have tyramine, such as red wine, meat, and aged cheese.
- It should not be combined with other antidepressants.

*Side Effects.* Side effects include nausea, dry mouth, allergic reactions, and fatigue, although, in general, side effects are uncommon. In one study, only 1.1% of patients discontinued the agent because of side effects. Some people have reported temporary nerve damage after sun exposure, specifically pain and tingling on sun-exposed areas, although a 2001 study found that sun sensitivity reactions were low. Some laboratory studies suggest high doses may impair fertility in men.

*Interactions.* St. John's wort may increase the risk for bleeding when used with anti-clotting agents or with other natural or standard medications that thin blood, such as warfarin or high doses of vitamin E. They may interact with oral contraceptives in women. Notably the herbal agent appears to reduce the effectiveness of certain cancer chemotherapy agents and HIV treatments. In fact, one study indicated that it might alter enzymes that cause a reduction in effectiveness of about half of all common medications.

### **Warnings for Alternative and So-Called Natural Remedies Used in Depression**

Alternative or natural remedies are not regulated and their quality is not publicly controlled. In addition, any substance that can affect the body's chemistry can, like any drug, produce side effects that may be harmful.

There have been a number of reported cases of serious and even lethal side effects from herbal products. In addition, some so-called natural remedies were found to contain standard prescription medications. Most problems reported occur in herbal remedies imported from Asia.

Other herbal or natural remedies being studied for depression are S-adenosylmethionine (SAMe), valerian, and kava. Some studies have reported some benefits from SAMe, but in general research is much weaker on these agents than on St. John's wort and they have some problems. In addition to warnings on St. John's wort discussed above, other herbal remedies used for depression may have problems. The following are examples:

- *Valerian.* Valerian has sedative qualities. This herb is listed on the FDA's list of generally safe products. Of note, however, its effects could be dangerously increased if it is used with standard sedatives. Other interactions and long-term side effects are unknown. Side effects

include vivid dreams. It should be noted that high doses of valerian can cause blurred vision, excitability, and changes in heart rhythm.

- **Kava.** Some evidence suggests that kava may relieve anxiety in some people. Although a few studies done on this herb generally report that it is safe, there have been reports of liver failure and death from this medication. Those at highest risk are those with existing impaired liver function. Other side effects include itchy, scaly skin, muscle weakness, and problems with coordination. It also interacts dangerously with certain medications, including alprazolam, an anti-anxiety drug. And it increases the potency of certain other drugs, including other sleep medications, alcohol, and antidepressants.

Even if studies report positive benefits from herbal remedies, most, to date, are very small. In addition, the substances used in such studies are, in most cases, not those being marketed to the public. The following website is building a database of natural remedy brands that it tests and rates. Not all are yet available ([www.ConsumerLab.com](http://www.ConsumerLab.com) ▶▶).

## Augmentation Strategies

Augmentation strategies generally involve the use of drugs not typically thought of as antidepressants in combination with a standard antidepressant. Such strategies are being used for patients who fail standard therapies or who need to quickly speed up the response of the antidepressant. Augmentation therapies include use of the following:

- Mood stabilizers like lithium, carbamazepine, and divalproex sodium.
- Newer antipsychotic drugs (such as risperidone).
- Psychostimulants. Standard psychostimulants include dextroamphetamine (Dexedrine) and methylphenidate (Ritalin). A newer psychostimulant, modafinil (Provigil, Alertec), is also showing promise for augmenting antidepressants. It may also pose less risk for abuse.
- Thyroid hormones. In one small study, high doses of thyroid hormone combined with an antidepressant had very mild side effects and were very effective in half of severely depressed treatment-resistant patients. Another study reported good results when thyroid hormone was followed by small doses of lithium.
- Beta-blockers. Pindolol (Visken), a beta-blocker normally used for heart disease, is proving to be effective in hastening the response of antidepressants. In one study, after ten days, nearly half the patients taking the combination was in remission compared to 25% of patients taking only Paxil. In the study on Prozac, patients reached a sustained response within 19 days on the combination compared to 29 days with Prozac alone.

## Psychotherapy

Among the various psychotherapies, cognitive-behavioral therapy at this time appears to be the most effective approach for most adult patients. A 2000 study suggested that there was very little difference among major psychotherapeutic approaches -- cognitive-behavioral therapy, family therapy, and supportive therapy. There are other effective therapies as well, such as problem-solving therapy, and interpersonal therapy.

Psychoanalytic or psychodynamic approaches have not been helpful. (Based on Freudian theory, psychodynamic psychotherapy concentrates on working through unresolved conflicts from one's childhood. Depression is viewed as a grieving process for the loss of a parent or other significant person or for the loss of their love.)

In any case, if psychotherapy is being used along without medications, benefits should be evident within eight weeks and symptoms should be fully resolved by 12 weeks. If these conditions are not met, then the patient should strongly consider antidepressant agents.

## Cognitive Behavioral Therapy

In a major analysis of four randomized comparative studies, cognitive behavior therapy was as effective as

antidepressants in treating severe depression for many patients. Much of the success of psychologic therapy, in any case, depends on the skill of the therapist. Many studies suggest that combining cognitive therapy with antidepressants offer the greatest benefits for many patients, particularly for dysthymia (chronic depression). Some studies also report that in these patients the benefits of cognitive therapy persist for these patients after treatment has ended, with the risk of relapse reduced by up to 50%.

*Best Candidates.* Cognitive therapy may be particularly helpful for the following patients:

- Patients with atypical depression.
- Adolescents with mild symptoms of major depression.
- Women with non-psychotic postpartum depression.
- Children of parents with the disorder. In this case, therapy should involve the whole family.
- Cognitive therapy does not appear to be as beneficial as antidepressants for most patients with dysthymia.

*Approach.* This approach focuses on identification of distorted perceptions that patients may have of the world and themselves, on changing these perceptions, and on discovering new patterns of actions and behavior. These perceptions, known as schemas, are negative assumptions developed in childhood that can precipitate and prolong depression. Cognitive therapy works on the principle that these schemas can be recognized and altered, thereby changing the response and eliminating the depression.

- First, the patient must learn how to recognize depressive reactions and thoughts as they occur, usually by keeping a journal of feelings about, and reactions to, daily events.
- The patient is often given "homework" that tests old negative assumptions against reality and demands different responses.
- Then, the patient and therapist examine and challenge these entrenched and automatic reactions and thoughts.
- As the patient begins to understand the underlying falseness of the assumptions that cause depression, he or she can begin substituting new ways of coping.

Over time, such exercises help build confidence and eventually alter behavior. Patients may take group or individual cognitive therapy. Cognitive therapy is a time-limited treatment, typically lasting 12 to 14 weeks. Extending this period, however, may help prevent relapse. In one study, therapy was continued for 10 sessions over an additional eight months. This extended treatment significantly reduced the risk of recurrence. In fact, some experts believe that short-term therapy is not at all effective for patients with chronic or relapsing psychiatric disorders.

## Interpersonal Therapy (IPT)

Based in part on psychodynamic theory, interpersonal therapy acknowledges the childhood roots of depression, but focuses on symptoms and current issues that may be causing problems. IPT is not as specific as cognitive or behavioral therapy, and all work is done during the sessions. The therapist seeks to redirect the patient's attention, which has been distorted by depression, toward the daily details of social and family interaction. The goals of this treatment method are improved communication skills and increased self-esteem within a short period (three to four months of weekly appointments) of time. Among the forms of depression best served by IPT are those caused by distorted or delayed mourning, unexpressed conflicts with people in close relationships, major life changes, and isolation.

## Supportive Psychotherapy or Attention Intervention

The intent of supportive psychotherapy or attention intervention is to provide the patient with a nonjudgmental environment by offering advice, attention, and sympathy. Supportive therapy appears to be particularly helpful for improving compliance with medications by giving reassurance, especially when setbacks and frustration occur. A 2000 study reported that it was as effective as other therapies for depressed adolescents.

## Problem Solving Therapy

Problem solving therapy trains patients to address current problems by breaking them into smaller manageable parts. They then identify the steps they should make toward positive change. It involves six individual sessions, and some evidence suggests it is as effective as medication in some patients with major depression.

## Other Treatments

### Electroconvulsive Therapy

Electroconvulsive therapy (ECT), commonly called shock treatment, has received bad press, in part for its potential memory-depleting effect, since it was introduced in the 1930s. ECT has been refined over the years and is now considered to be the most effective treatment for severe depression. It is effective more than 90% of the time in patients with mood disorders. Maintenance ECT may also be effective in preventing relapse. In one 2000 study, continued use of ECT in responsive patients, along with long-term antidepressant use, prevented relapse in 73% of patients after five years compared to 18% in patients on antidepressants alone.

*Candidates for ECT.* About 40,000 Americans receive ECT each year; many are elderly women who are psychiatric inpatients. Many experts urge that ECT be used earlier in the course of major depression, although most insurers or HMOs will not pay for early treatment. ECT may be beneficial for the following patients with severe depression:

- Patients who cannot, for any reason, take antidepressant drugs.
- Suicidal patients.
- Elderly patients who are psychotic and depressed.
- Pregnant women with severe depression.
- Patients with certain heart problems.
- Young patients who fit the adult criteria for ECT.

*The Procedure.* In general, hospitalization is not necessary for the treatment. ECT involves the following:

- A muscle relaxant and short-acting anesthetic are administered.
- A small amount of electric current is sent to the brain, causing a generalized seizure that lasts for about 40 seconds.
- Most patients receive six treatments, spaced every two to five days. Others receive up to 15 treatments, followed by six to 12 additional treatments spaced every other week or longer for another two to four months.

This procedure is associated with a great deal of anxiety and the patient should be reassured. One form of ECT called right unilateral ECT (RUL ECT) may provide equal therapeutic benefits to more traditional bilaterally applied forms of the therapy, and more importantly, may have a less potentially deleterious effect on memory.

*Side Effects.* Side effects of ECT may include temporary confusion, memory lapses, headache, nausea, muscle soreness, and heart disturbances. Administering the drug naloxone immediately before ECT may help reduce its adverse effects on concentration and some (but not all) memory impairment. Concerns about permanent memory loss appear to be unfounded. One study that used brain scans before and after ECT found no evidence of cell damage. In another small study of teenagers who had undergone ECT for severe mood disorders, only one of 10 reported memory impairment more than three years after the treatment.

### Phototherapy

Phototherapy is recommended as the first-line treatment for seasonal affective disorder (SAD).

*The Procedure.* The procedure is noninvasive and simple. It is best performed immediately after waking in the morning. The patient sits a few feet away from a box-like device that emits very bright fluorescent light (10,000 lux) for about 30 minutes every day.

Some people report mood improvement as early as two days after treatment. In others depression may not lift for three or four weeks. (If no improvement is experienced after that, then the depression is probably caused by other factors.)

*Side Effects.* Side effects include headache, eye strain, and irritability, although these symptoms tend to disappear within a week. Patients taking light-sensitive drugs (e.g., those used for psoriasis), certain antibiotics, or antipsychotic drugs should not use light therapy. Patients should be examined by an ophthalmologist before undergoing this treatment.

## Cingulotomy

A surgical technique called cingulotomy interrupts the cingulate gyrus, a bundle of nerve fibers in the front of the brain, by applying heat or cold. A variation of this procedure using MRI scans to guide the surgeon produced long-term improvement in 53% to 78% of patients with severe intractable depression. The procedure is generally safe with few serious complications; it does not affect intellect or memory.

## Transcranial Magnetic Stimulation

Transcranial magnetic stimulation (TMS) employs high frequency magnetic pulses that target affected areas of the brain. The intention is similar to electroconvulsive therapy (ECT) but, unlike ECT it is more precise and has the potential of having the same benefits as ECT. A 2001 meta-analysis reported that it was superior to sham treatments, although it was not clear whether benefits were significant. Investigators continue to try various techniques that might produce consistent improvements.

## Vagus Nerve Stimulation

Vagus nerve stimulation (VNS) is procedure that is effective for certain patients with epilepsy, and is now showing some success in treating intractable depression

VNS involves implanting a battery-powered device under the skin in the upper left of the chest. The neurologist programs the device to deliver mild electrical stimulation to the vagus nerve. (The patient may also pass a magnet over the device to give it an extra dose if they sense a seizure coming on.) The two vagus nerves are the longest nerves in the body. They run along each side of the neck, then down the esophagus to the gastrointestinal tract. The vagus nerve travels to areas of the brain that control functions such as sleep and mood.

Studies report response rates of 35% to 46% in appropriate candidates with treatment-resistant depression. (It is not likely to be effective in patients who have failed to respond to multiple antidepressants.) It is typically used for three months. A 2002 study suggested that longer-term use (about a year) might improve results.

Vagal stimulation can cause shortness of breath, hoarseness, sore throat, coughing, ear and throat pain, or nausea and vomiting. These side effects can be reduced or eliminated by reducing the intensity of stimulation. Long-term studies on epilepsy patients are reporting no serious adverse side effects, although the treatment may cause lung function deterioration in people with existing lung disease.

## Acupuncture

Some evidence suggests that acupuncture may help in relieving depression in some women. Small studies, including one in 2001, have found it comparable to medications or psychotherapy. Larger studies are required to confirm its benefits.

## Sleep Deprivation

Research suggests that even one night of total sleep deprivation can reduce depression 40% to 60% of the

time. Improvement in mood generally occurs during the night or on the following day. About 10% to 15% of people who respond to this treatment have reduced depression only after fully sleeping again. Some people may respond to sleep deprivation that occurs only in the second half of the night (3:00 to 6:00 AM). It should be noted that in 2% to 7% of cases depression may worsen after sleep deprivation.

## Lifestyle Changes

### Dietary Factors

*Carbohydrates and Tryptophan.* Some people report relief from depression by eating foods or diet supplements that boost levels of tryptophan, an amino acid involved in the production of serotonin. A high-carbohydrate drink available over the counter called PMS Escape, for example, increases tryptophan levels and may alleviate depression associated with premenstrual syndrome for about three hours. Simply eating a high amount of carbohydrates, however, is not a solution for depression. In fact, a 2002 study found a correlation between high sugar consumption and higher rates of depression, although there is no evidence to suggest a causal association.

(Important Note: Impurities found in diet supplements containing L-tryptophan itself have caused cases of eosinophilia-myalgia syndrome, a condition that elevates certain white blood cells and can be fatal. Supplements containing L-tryptophan are currently banned in the U.S. by the FDA.)

*Fish Oil.* Some evidence suggests that an imbalance in the ratio of specific fatty acids (omega-6 to omega-3) may increase the risk for depression. Both are polyunsaturated fats but omega-6 fatty acids are mostly found in corn, safflower, soybean, and sunflower oil and omega-3 fatty acids are found in fish oil, canola oil, soybeans, flaxseed, and certain nuts and seeds. One study reported more depression in patients who had higher ratios of foods rich in omega 6 compared to those containing omega 3 fatty acids. (This imbalance has also been associated with heart disease.) The bottom line may be to increase intake of omega-3 rich foods, such as fish, nuts, and canola oil, and reduce consumption of foods containing omega-6 fatty acids, such as corn and sunflower oils. Such a dietary approach is healthy in any case. Experts have been investigating whether eating fish or taking fish oil supplements can reduce depression. The best results have been from supplements of 1 g of ethyl-eicosapentanoic acid (E-EPA), a compound in fish oil.

*Caffeine.* Studies have found an association between moderate consumption of caffeinated beverages and a lower incidence of suicide, indicating that coffee or tea might help reduce depression. One study supported the findings for a lower risk for suicide with moderate coffee intake but reported a *higher* risk for suicide with high coffee consumption. In such cases, coffee may not be the cause of the higher risk; women who drink such large amounts of coffee may be self medicating their depression. Heavy coffee use may also coincide with a higher risk for abuse of other substances, such as alcohol or cigarettes, which may increase the risk for suicide.

*Vitamins and Other Supplements.* Certain B vitamins have been associated with some protection against depression.

- Vitamin B-3 (niacin) is important in the production of tryptophan and is produced from processing vitamin B3 (niacin). Dietary sources of niacin include oily fish (such as salmon or mackerel), pork, chicken, dried peas and beans, whole grains, seeds, and dried fortified cereals.
- Vitamin B-12 and calcium supplements may help reduce depression that occurs before menstruation. A 2001 study also suggested that calcium might help prevent postpartum depression.
- Folate, a B vitamin, may enhance the effectiveness of SSRIs and other antidepressants.

### Exercise

Increasingly studies are reporting major benefits from exercise for people with depression. The following are some examples:

- A 2002 study reported that 55% of older women with depression that did not respond to medication

improved with 10 weeks of exercise. (Only a third of women who did not exercise improved during that time.)

- A 2000 study reported that 30 minutes of brisk exercise three times a week may be just as effective as medication in relieving the symptoms of mild to moderate depression and reduces the risk of relapse.
- A 1999 study on exercise in the elderly reported that after 26 weeks, exercise was as effective as antidepressants. (Antidepressants relieved depression earlier, however.)
- One study found that teenagers who were active in sports have a greater sense of well being than their sedentary peers; the more vigorously they exercised, the better their emotional health.

Specific exercises may be particularly beneficial:

**Aerobics.** Either brief periods of intense training or prolonged aerobic workouts can raise chemicals in the brain, such as endorphins, adrenaline, serotonin, and dopamine that produce the so-called runner's high. And, of course, weight loss and increased muscle tone can boost self-esteem.

**Yoga.** Yoga practice, which involves rhythmic stretching movements and breathing have been found to positively affect mood and may have clinical potential as a technique for improving and stabilizing mood. One study, in fact, suggested that men actually may have better results with yoga than with aerobic exercise. In the study men experienced significantly lower levels of tension, fatigue, and anger after yoga than after swimming. (Yoga and swimming tended to produce equal benefits in women.)

## Social Support

A strong network of social support is both important for prevention and recovery from depression. Support from family and friends must be healthy and positive; one study of depressed women showed, however, that overprotective as well as very distant parenting was associated with a slow recovery from depression. Studies indicate that people with strong spiritual faiths have a lower risk for depression. Such faith does not require an organized religion. People with depression might find solace from less structured sources, such as those that teach meditation or other methods for obtaining spiritual self-fulfillment.

## Resources

- [www.depression.org](http://www.depression.org) -- National Foundation for Depressive Illness (800-239-1265)
- [www.ndmda.org](http://www.ndmda.org) -- National Depressive and Manic-Depressive Association (800-826-3632)
- [www.nimh.nih.gov](http://www.nimh.nih.gov) -- National Institute of Mental Health (800-64-PANIC)
- [www.nami.org](http://www.nami.org) -- National Alliance for the Mentally Ill (800-950-6264)
- [www.emotionsanonymous.org](http://www.emotionsanonymous.org) -- Emotions Anonymous (612-647-9712)
- [www.cognitivetherapynyc.com](http://www.cognitivetherapynyc.com) -- American Institute for Cognitive Therapy (212-308-2440)
- [www.aabt.org](http://www.aabt.org) -- Association for the Advancement of Behavior Therapy (800-685-AABT)
- [www.psych.org](http://www.psych.org) -- The American Psychiatric Association (202-682-6000)
- [www.dotcomsense.com](http://www.dotcomsense.com) -- The American Psychological Association (800-964-2000)
- [www.socialworkers.org](http://www.socialworkers.org) -- The National Association of Social Workers (202-408-8600)
- [www.apna.org](http://www.apna.org) -- The American Psychiatric Nurses Association (202-857-1133)
- [www.sltbr.org](http://www.sltbr.org) -- Society for Light Treatment and Biological Rhythms
- [www.chss.iup.edu/postpartum](http://www.chss.iup.edu/postpartum) -- Postpartum Support International
- [www.depressionafterdelivery.com](http://www.depressionafterdelivery.com) -- Depression after Delivery
- [www.aacap.org](http://www.aacap.org) -- American Academy of Child and Adolescent Psychiatry
- [www.mentalhelp.net](http://www.mentalhelp.net) -- Mental Health Net
- [www.cognitivetherapy.com](http://www.cognitivetherapy.com) -- Information on cognitive therapy
- [www.mentalhealth.com](http://www.mentalhealth.com) -- Free encyclopedia of mental health information
- [www.1-800-therapist.com](http://www.1-800-therapist.com) or [www.4therapy.com/locator](http://www.4therapy.com/locator) -- Find a therapist
- [www.4therapy.com/consumer/assessment](http://www.4therapy.com/consumer/assessment) -- Assess your depression

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