

What is major depression?

Major depression is a serious medical illness affecting 15 million American adults or approximately 5-8 percent of the adult population in a given year. Unlike normal emotional experiences of sadness, loss or passing mood states, major depression is persistent and can significantly interfere with an individual's thoughts, behavior, mood, activity and physical health. Among all medical illnesses, major depression is the leading cause of disability in the United States and many other developed countries.

Depression occurs twice as frequently in women as in men for reasons that are not fully understood. More than one-half of those who experience a single episode of depression will continue to have episodes that occur as frequently as once or even twice a year. Without treatment, the frequency of depressive illness as well as the severity of symptoms tends to increase over time. Left untreated, depression can lead to suicide.

Major depression, also known as clinical depression or unipolar depression, is only one type of depressive disorder. Other depressive disorders include dysthymia (chronic, less severe depression) and bipolar depression (the depressed phase of bipolar disorder). People who have bipolar disorder experience both depression and mania. Mania involves unusually and persistently elevated mood or irritability, elevated self-esteem and excessive energy, thoughts and talking.

What are the symptoms of major depression?

The onset of the first episode of major depression may not be obvious if it is gradual or mild. The symptoms of major depression characteristically represent a significant change from how a person functioned before the illness. The symptoms of depression include:

- persistently sad or irritable mood
- pronounced changes in sleep, appetite and energy
- difficulty thinking, concentrating and remembering
- physical slowing or agitation
- lack of interest in or pleasure from activities that were once enjoyed
- feelings of guilt, worthlessness, hopelessness and emptiness
- recurrent thoughts of death or suicide
- persistent physical symptoms that do not respond to treatment, such as headaches, digestive disorders and chronic pain

When several of these symptoms of depressive illness occur at the same time, last longer than two weeks and interfere with ordinary functioning, professional treatment is needed.

What are the causes of major depression?

There is no single cause of major depression. Psychological, biological and environmental factors may all contribute to its development. Whatever the specific causes of depression, scientific research has firmly established that major depression is a biological, medical illness.

Norepinephrine, serotonin and dopamine are three neurotransmitters (chemical messengers that transmit electrical signals between brain cells) thought to be involved with major depression. Scientists believe that if there is a chemical imbalance in these neurotransmitters, then clinical states of depression result. Antidepressant medications work by increasing the availability of neurotransmitters or by changing the sensitivity of the receptors for these chemical messengers.

Scientists have also found evidence of a genetic predisposition to major depression. There is an increased risk for developing depression when there is a family history of the illness. Not everyone with a genetic predisposition develops depression, but some people probably have a biological make-up that leaves them particularly vulnerable to developing depression. Life events, such as the death of a loved one, a major loss or change, chronic stress and alcohol and drug abuse, may trigger episodes of depression. Some illnesses such as heart disease and cancer and some medications may also trigger depressive episodes. It is also important to note that many depressive episodes occur spontaneously and are not triggered by a life crisis, physical illness or other risks.

How is major depression treated?

Although major depression can be a devastating illness, it is highly treatable. Between 80-90 percent of those diagnosed with major depression can be effectively treated and return to their usual daily activities and feelings. Many types of treatment are available and the type chosen depends on the individual and the severity and patterns of his or her illness. There are three well-

established types of treatment for depression: medications, psychotherapy and electroconvulsive therapy (ECT). For some people who have a seasonal component to their depression, light therapy may be useful. These treatments may be used alone or in combination. Additionally, peer education and support can promote recovery. Attention to lifestyle, including diet, exercise and smoking cessation, can result in better health, including mental health.

Medication

It often takes two to four weeks for antidepressants to start having an effect and six to 12 weeks for antidepressants to have their full effect. The first antidepressant medications were introduced in the 1950s. Research has shown that imbalances in neurotransmitters like serotonin, dopamine and norepinephrine can be corrected with antidepressants. The FDA regularly approves different medicines; visit www.fda.gov for the most current list. Four groups of antidepressant medications are most often prescribed for depression:

- Selective serotonin reuptake inhibitors (SSRIs) act specifically on the neurotransmitter serotonin. They are the most common agents prescribed for depression worldwide. These agents block the reuptake of serotonin from the synapse to the nerve, thus artificially increasing the serotonin that is available in the synapse (this is functional serotonin, since it can become involved in signal transmission, the cardinal function of neurotransmitters). SSRIs include fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), citalopram (Celexa), escitalopram (Lexapro) and fluvoxamine (Luvox).
- Serotonin and norepinephrine reuptake inhibitors (SNRIs) are the second-most popular antidepressants worldwide. These agents block the reuptake of both serotonin and norepinephrine from the synapse into the nerve (thus increasing the amounts of these chemicals that can participate in signal transmission). SNRIs include venlafaxine (Effexor) and duloxetine (Cymbalta).
- Bupropion (Wellbutrin) is a very popular antidepressant medication classified as a norepinephrine-dopamine reuptake inhibitor (NDRI). It acts by blocking the reuptake of dopamine and norepinephrine.
- Mirtazapine (Remeron) works differently from the compounds discussed above. Mirtazapine targets specific serotonin and norepinephrine receptors in the brain, thus indirectly increasing the activity of several brain circuits.
- Tricyclic antidepressants (TCAs) are older agents seldom used now as first-line treatment. They work similarly to the SNRIs, but have other neurochemical properties which result in very high side effect rates, as compared to almost all other antidepressants. They are sometimes used in cases where other antidepressants have not worked. TCAs include amitriptyline (Elavil, Limbitrol), desipramine (Norpramin), doxepin (Sinequan), imipramine (Norpramin, Tofranil), nortriptyline (Pamelor, Aventyl) and protriptyline (Vivactil).
- Monoamine oxidase inhibitors (MAOIs) are also seldom used now. They work by inactivating enzymes in the brain which catabolize (chew up) serotonin, norepinephrine and dopamine from the synapse, thus increasing the levels of these chemicals in the brain. They can sometimes be effective for people who do not respond to other medications or who have “atypical” depression with marked anxiety, excessive sleeping, irritability, hypochondria or phobic characteristics. However, they are the least safe antidepressants to use, as they have important medication interactions and require adherence to a particular diet. MAOIs include phenelzine (Nardil), isocarboxazid (Marplan) and tranylcypromine sulfate (Parnate).
- Nonantidepressant adjunctive agents. Often psychiatrists will combine the antidepressants mentioned above with each other (we call this a “combination”) or with agents which are not antidepressants themselves (we call this “augmentation”). These latter agents can include the atypical antipsychotic agents [aripiprazole (Abilify), olanzapine (Zyprexa), quetiapine (Seroquel), ziprasidone (Geodon), risperidone (Risperdal)], buspirone (Buspar), thyroid hormone (triiodothyronine or “T3”), the stimulants (methylphenidate (Ritalin), dextroamphetamine (Aderall)), dopamine receptor agonists (pramipexole (Mirapex), ropinirole (Requip)), lithium, lamotrigine (Lamictal), s-adenosyl methionine (SAME), pindolol and steroid hormones (testosterone, estrogen, DHEA).

Individuals living with mental illness and their families must be cautious during the early stages of medication treatment because normal energy levels and the ability to take action often return before mood improves. At this time—when decisions are easier to make, but depression is still severe—the risk of suicide may temporarily increase.

Psychotherapy

There are several types of psychotherapy that have been shown to be effective for depression including cognitive-behavioral therapy (CBT) and interpersonal therapy (IPT). Research has shown that mild to moderate depression can often be treated successfully with either of these therapies used alone. However, severe depression appears more likely to respond to a combination of psychotherapy and medication.

- Cognitive behavioral therapy (CBT) helps to change the negative thinking and unsatisfying behavior associated with depression, while teaching people how to unlearn the behavioral patterns that contribute to their illness.
- Interpersonal therapy (IPT) focuses on improving troubled personal relationships and on adapting to new life roles that may have been associated with a person's depression.
- Electroconvulsive therapy (ECT) is a highly effective treatment for severe depressive episodes. In situations where medication, psychotherapy and a combination of the two prove ineffective or work too slowly to relieve severe symptoms such as psychosis or thoughts of suicide, ECT may be considered. ECT may also be considered for those who for one reason or another cannot take antidepressant medications.

What are the side effects of the medications used to treat depression?

Different medications produce different side effects and people differ in the type and severity of side effect they experience. About 50 percent of people who take antidepressant medications experience some side effects, particularly during the first weeks of treatment. Side effects that are particularly bothersome can often be treated by changing the dose of the medication, switching to a different medication or treating the side effect directly with additional medications. Rarely, serious side effects such as fainting, heart problems or seizure may occur, but they are almost always treatable.

- Tricyclic antidepressants (TCAs) cause side effects that include dry mouth, constipation, bladder problems, sexual problems, blurred vision, dizziness, drowsiness, skin rash and weight gain or loss.
- Monoamine oxidase inhibitors (MAOIs). Individuals taking MAOIs may have to be careful about eating certain smoked, fermented or pickled foods, drinking certain beverages or taking some medications because they can cause severe high blood pressure in combination with the medication. A range of other, less serious side effects occur including weight gain, constipation, dry mouth, dizziness, headache, drowsiness, insomnia and sexual side effects (problems with arousal or satisfaction).
- SSRIs and SNRIs tend to have fewer and different side effects, such as nausea, nervousness, insomnia, diarrhea, rash, agitation or sexual side effects (problems with arousal or orgasm).
- Bupropion generally causes fewer common side effects than TCAs and MAOIs. Its side effects include restlessness, insomnia, headache or a worsening of preexisting migraine conditions, tremor, dry mouth, agitation, confusion, rapid heartbeat, dizziness, nausea, constipation, menstrual complaints and rash.

Reviewed by Dr. Ken Duckworth, NAMI Medical Director, September 2009