

THE PHARMA INNOVATION

Depression - Symptoms, Causes, Medications and Therapies

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Depression is the most common of the affective disorders; it may range from a very mild condition, bordering on normality, to severe (psychotic) depression accompanied by hallucinations and delusions. Worldwide, depression is a major cause of disability and premature death. When the negative reactions to life's situations become repetitively intense and frequent we develop symptoms of depression. Life throws up innumerable situations, which we greet with both negative and positive emotions such as excitement, frustration, fear, happiness, anger, sadness. Depression is prevalent among all age groups, in almost all walks of life. Indians are among the world's most depressed. According to a World Health Organization-sponsored study, while around 9% of people in India reported having an extended period of depression within their lifetime, nearly 36% suffered from what is called Major Depressive Episode (MDE). MDE is characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy and poor concentration, besides feeling depressed. Lowest prevalence of MDE was in China (12%). The average age of depression in India is 31.9 years compared to 18.8 years in China, and 22.7 years in the US. The female: male ratio was about 2:1. "WHO ranks depression as the fourth leading cause of disability worldwide and projects that by 2020, it will be the second leading cause.

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INTRODUCTION: Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an

individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide, a tragic fatality associated with the loss of about 850 000 lives every year. Depression is the leading cause of disability as measured by YLDs and the 4th leading contributor to the global burden of disease (DALYs) in 2000. By the year 2020, depression is projected to reach 2nd place of the ranking of DALYs calculated for all ages, both sexes. Today, depression is already the 2nd cause of DALYs in the age category 15-44 years for both

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sexes combined. Depression occurs in persons of all genders, ages, and backgrounds. Depression is a disorder of the brain. There are a variety of causes, including genetic, environmental, psychological, and biochemical factors. Depression usually starts between the ages of 15 and 30, and is much more common in women. Women can also get postpartum depression after the birth of a baby. Some people get seasonal affective disorder in the winter. Depression is one part of disorder. There are effective treatments for depression, including antidepressants and talk therapy. Most people do best by using both. Depression is common, affecting about 121 million people worldwide. Depression is among the leading causes of disability worldwide. Depression can be reliably diagnosed and treated in primary care. Fewer than 25 % of those affected have access to effective treatments. Depression can be reliably diagnosed in primary care. Antidepressant medications and brief, structured forms of psychotherapy are effective for 60-80 % of those affected and can be delivered in primary care. However, fewer than 25 % of those affected (in some countries fewer than 10 %) receive such treatments. Barriers to effective care include the lack of resources, lack of trained providers, and the social stigma associated with mental disorders including depression. Research by 20 different researchers, says depression affects nearly 121 million people worldwide. It is the second contributor to shorter lifespan for individuals in the 15-44 age group.

DEPRESSION SYMPTOMS¹⁻⁵

Depression symptoms include:

- Feelings of sadness or unhappiness
- Irritability or frustration, even over small matters
- Loss of interest or pleasure in normal activities
- Reduced sex drive
- Insomnia or excessive sleeping
- Changes in appetite — depression often causes decreased appetite and weight loss, but in some people it causes increased cravings for food and weight gain
- Agitation or restlessness — for example, pacing, hand-wringing or an inability to sit still
- Irritability or angry outbursts
- Slowed thinking, speaking or body movements
- Indecisiveness, distractibility and decreased concentration
- Fatigue, tiredness and loss of energy — even small tasks may seem to require a lot of effort
- Feelings of worthlessness or guilt, fixating on past failures or blaming yourself when things aren't going right
- Trouble thinking, concentrating, making decisions and remembering things
- Frequent thoughts of death, dying or suicide
- Crying spells for no apparent reason
- Unexplained physical problems, such as back pain or headaches

Depression affects each person in different ways, so symptoms caused by depression vary from person to person. Inherited traits, age, gender and cultural background all play a role in how depression may affect you.

Depression symptoms in children and teens

Common symptoms of depression can be a little different in children and teens than they are in adults.

- In younger children, symptoms of depression may include sadness, irritability, hopelessness and worry.
- Symptoms in adolescents and teens may include anxiety, anger and avoidance of social interaction.
- Changes in thinking and sleep are common signs of depression in adolescents and adults but are not as common in younger children.
- In children and teens, depression often occurs along with behavior problems and other mental health conditions, such as

anxiety or attention-deficit/hyperactivity disorder (ADHD).

- Schoolwork may suffer in children who are depressed.

Depression symptoms in older adults

Depression is not a normal part of growing older, and most seniors feel satisfied with their lives. However, depression can and does occur in older adults. Unfortunately, it often goes undiagnosed and untreated. Many adults with depression feel reluctant to seek help when they're feeling down.

- In older adults, depression may go undiagnosed because symptoms — for example, fatigue, loss of appetite, sleep problems or loss of interest in sex — may seem to be caused by other illnesses.
- Older adults with depression may have less obvious symptoms. They may feel dissatisfied with life in general, bored, helpless or worthless. They may always want to stay at home, rather than going out to socialize or doing new things.
- Suicidal thinking or feelings in older adults is a sign of serious depression that should never be taken lightly, especially in men. Of all people with depression, older adult men are at the highest risk of suicide.

SIGNS AND SYMPTOMS OF DEPRESSIVE DISORDER⁶

1. A depressive disorder is a syndrome (group of symptoms) that reflects a sad and/or irritable mood exceeding normal sadness or grief. More specifically, the sadness of depression is characterized by a greater intensity and duration and by more severe symptoms and functional disabilities than is normal.
2. Depressive signs and symptoms are characterized not only by negative thoughts, moods, and behaviors but also by specific changes in bodily functions (for example, crying spells, body aches, low energy or libido, as well as problems with eating, weight, or sleeping). The functional changes of clinical depression are often called neurovegetative signs. This means that the nervous system changes in the brain cause many physical symptoms that result in diminished participation and a decreased or increased activity level.
3. Certain people with depressive disorder, especially bipolar depression (manic depression), seem to have an inherited vulnerability to this condition.
4. Depressive disorders are a huge public-health problem, due to its affecting millions of people. About 10% of adults, up to 8% of teens and 2% of preteen children experience some kind of depressive disorder.
 - The statistics on the costs due to depression in the United States include huge amounts of direct costs, which are for treatment, and indirect costs, such as lost productivity and absenteeism from work or school.
 - Adolescents who suffer from depression are at risk for developing and maintaining obesity.
 - In a major medical study, depression caused significant problems in the functioning of those affected more often than did arthritis, hypertension, chronic lung disease, and diabetes, and in some ways as often as coronary artery disease.
 - Depression can increase the risks for developing coronary artery disease, HIV, asthma, and many other medical illnesses. Other complications of depression include its tendency to increase the morbidity (illness/negative health effects) and mortality (death) from these and many other medical conditions.
 - Depression can coexist with virtually every other mental health illness, aggravating the status of those who suffer the combination

of both depression and the other mental illness.

- Depression in the elderly tends to be chronic, has a low rate of recovery, and is often undertreated. This is of particular concern given that elderly men, particularly elderly white men have the highest suicide rate.
5. Depression is usually first identified in a primary-care setting, not in a mental-health practitioner's office. Moreover, it often assumes various disguises, which causes depression to be frequently underdiagnosed.
 6. In spite of clear research evidence and clinical guidelines regarding therapy, depression is often undertreated. Hopefully, this situation can change for the better.
 7. For full recovery from a mood disorder, regardless of whether there is a precipitating factor or it seems to come out of the blue, treatment with medication and/or electroconvulsive therapy (ECT) and psychotherapy are necessary.

TYPES OF DEPRESSION

Depressive disorders are mood disorders that come in different forms, just as do other illnesses, such as heart disease and diabetes. Three of the most common types of depressive disorders are discussed below. However, remember that within each of these types, there are variations in the number, timing, severity, and persistence of symptoms. There are also differences in how individuals experience depression based on age.

Major depression

Major depression is characterized by a combination of symptoms that last for at least two weeks in a row, including sad and/or irritable mood (see symptom list), that interfere with the ability to work, sleep, eat, and enjoy once-pleasurable activities. Difficulties in sleeping or

eating can take the form of excessive or insufficient of either behavior. Disabling episodes of depression can occur once, twice, or several times in a lifetime.

Dysthymia

Dysthymia is a less severe but usually more long-lasting type of depression compared to major depression. It involves long-term (chronic) symptoms that do not disable but yet prevent the affected person from functioning at "full steam" or from feeling good. Sometimes, people with dysthymia also experience episodes of major depression. This combination of the two types of depression is referred to as double-depression.

Bipolar disorder (manic depression)

Another type of depression is bipolar disorder, which encompasses a group of mood disorders that were formerly called manic-depressive illness or manic depression. These conditions show a particular pattern of inheritance. Not nearly as common as the other types of depressive disorders, bipolar disorders involve cycles of mood that include at least one episode of mania or hypomania and may include episodes of depression as well. Bipolar disorders are often chronic and recurring. Sometimes, the mood switches are dramatic and rapid, but most often they are gradual. When in the depressed cycle, the person can experience any or all of the symptoms of a depressive disorder. When in the manic cycle, any or all of the symptoms listed later in this article under mania may be experienced. Mania often affects thinking, judgment, and social behavior in ways that cause serious problems and embarrassment. For example, indiscriminate or otherwise unsafe sexual practices or unwise business or financial decisions may be made when an individual is in a manic phase.

A significant variant of the bipolar disorders is designated as bipolar II disorder. (The usual form of bipolar disorder is referred to as bipolar I

disorder.) Bipolar II disorder is a syndrome in which the affected person has repeated depressive episodes punctuated by what is called hypomania (mini-highs). These euphoric states in bipolar II do not fully meet the criteria for the complete manic episodes that occur in bipolar I.

CAUSES OF DEPRESSION⁷⁻⁹

Some types of depression run in families, indicating that a biological vulnerability to depression can be inherited. This seems to be the case, especially with bipolar disorder. Families in which members of each generation develop bipolar disorder have been studied. The investigators found that those with the illness have a somewhat different genetic makeup than those who do not become ill. However, the reverse is not true. That is, not everybody with the genetic makeup that causes vulnerability to bipolar disorder will develop the illness. Apparently, additional factors, possibly a stressful environment, are involved in its onset and protective factors are involved in its prevention.

Major depression also seems to occur in generation after generation in some families, although not as strongly as in bipolar I or II. Indeed, major depression can also occur in people who have no family history of depression.

An external event often seems to initiate an episode of depression. Thus, a serious loss, chronic illness, difficult relationship, financial problem, or any unwelcome change in life patterns can trigger a depressive episode. Very often, a combination of genetic, psychological, and environmental factors is involved in the onset of a depressive disorder. Stressors that contribute to the development of depression sometimes affect some groups more than others. For example, minority groups who more often feel impacted by discrimination are disproportionately represented. Socioeconomically disadvantaged groups have higher rates of depression compared to their advantaged counterparts. Immigrants to the United States may be more vulnerable to

developing depression, particularly when isolated by language.

Regardless of ethnicity, men appear to be particularly sensitive to the depressive effects of unemployment, divorce, low socioeconomic status, and having few good ways to cope with stress. Women who have been the victim of physical, emotional, or sexual abuse, either as a child or perpetrated by a romantic partner are vulnerable to developing a depressive disorder as well. Men who engage in sex with other men seem to be particularly vulnerable to depression when they have no domestic partner, do not identify themselves as homosexual, or have been the victim of multiple episodes of antigay violence. However, it seems that men and women have similar risk factors for depression for the most part.

Nothing in the universe is as complex and fascinating as the human brain. The 100-plus chemicals that circulate in the brain are known as neurochemicals or neurotransmitters. Much of our research and knowledge, however, has focused on four of these neurochemical systems: norepinephrine, serotonin, dopamine, and acetylcholine. In the new millennium, after new discoveries are made, it is possible that these four neurochemicals will be viewed as the "black bile, yellow bile, phlegm, and blood" of the 20th century.

Different neuropsychiatric illnesses seem to be associated with an overabundance or a lack of some of these neurochemicals in certain parts of the brain. For example, a lack of dopamine at the base of the brain causes Parkinson's disease. Alzheimer's dementia seems to be related to lower acetylcholine levels in the brain. The addictive disorders are under the influence of the neurochemical dopamine. That is to say, drugs and alcohol work by releasing dopamine in the brain. The dopamine causes euphoria, which is a pleasant sensation. Repeated use of drugs or alcohol, however, desensitizes the dopamine system, which means that the system gets used to the drugs and alcohol. Therefore, a person needs more drugs or alcohol to achieve the

same high feeling. Thus, the addicted person takes more substance but feels less and less high and increasingly depressed.

Certain medications used for a variety of medical conditions are more likely than others to cause depression as a side effect. Specifically, some medications that are used to treat high blood pressure, cancer, seizures, extreme pain, and to achieve contraception can result in depression. Even some psychiatric medications like some sleep aids and medications to treat alcoholism and anxiety can contribute to the development of depression.

Many mental-health conditions or developmental disabilities are associated with depression as well. Individuals with anxiety, attention deficit hyperactivity disorder (ADHD), substance abuse, and developmental disabilities may be more vulnerable to developing depression.

The different types of schizophrenia are associated with an imbalance of dopamine (too much) and serotonin (poorly regulated) in certain areas of the brain. Finally, the depressive disorders appear to be associated with altered brain serotonin and norepinephrine systems. Both of these neurochemicals may be lower in depressed people. Please note that depression is "associated with" instead of "caused by" abnormalities of these neurochemicals because we really don't know whether low levels of neurochemicals in the brain cause depression or whether depression causes low levels of neurochemicals in the brain.

What we do know is certain medications that alter the levels of norepinephrine or serotonin can alleviate the symptoms of depression. Some medicines that affect both of these neurochemical systems appear to perform even better or faster. Other medications that treat depression primarily affect the other neurochemical systems. The most powerful treatment for depression, electroconvulsive therapy (ECT), is certainly not specific to any particular neurotransmitter system. Rather, ECT, by causing a seizure, produces a generalized brain activity that probably releases massive amounts of all of the neurochemicals.

Women are twice as likely to become depressed as men. However, scientists do not know the reason for this difference. Psychological factors also contribute to a person's vulnerability to depression. Thus, persistent deprivation in infancy, physical or sexual abuse, clusters of certain personality traits, and inadequate ways of coping (maladaptive coping mechanisms) all can increase the frequency and severity of depressive disorders, with or without inherited vulnerability.

The effect of maternal-fetal stress on depression is currently an exciting area of research. It seems that maternal stress during pregnancy can increase the chance that the child will be prone to depression as an adult, particularly if there is a genetic vulnerability. It is thought that the mother's circulating stress hormones can influence the development of the fetus' brain during pregnancy. This altered fetal brain development occurs in ways that predispose the child to the risk of depression as an adult. Further research is still necessary to clarify how this happens. Again, this situation shows the complex interaction between genetic vulnerability and environmental stress, in this case, the stress of the mother on the fetus.

Postpartum depression

Postpartum depression (PPD) is a condition that describes a range of physical and emotional changes that many mothers can have after having a baby. PPD can be treated with medication and counseling. Talk with your health-care practitioner right away if you think you have PPD.

There are three types of PPD women can have after giving birth:

1. **The so-called "baby blues"** happen in many women in the days right after childbirth. A new mother can have sudden mood swings, such as feeling very happy and then feeling very sad or angry. She may cry for no reason and can feel impatient, irritable, restless, anxious, lonely, and sad. The baby blues may last only a few hours or as long as one to two weeks after delivery. The baby blues do not

always require treatment from a health-care provider. Often, joining a support group of new moms or talking with other moms helps.

- 2. Postpartum depression (PPD)** can happen a few days or even months after childbirth. *PPD can happen after the birth of any child, not just the first child.* A woman can have feelings similar to the baby blues -- sadness, despair, anxiety, irritability -- but she feels them much more strongly than she would with the baby blues. PPD often keeps a woman from doing the things she needs to do every day. When a woman's ability to function is affected, this is a sure sign that she needs to see her health-care provider right away. If a woman does not get treatment for PPD, symptoms can get worse and last for as long as one year. While PPD is a serious condition, it can be treated with medication and counseling.
- 3. Postpartum psychosis** is a very serious mental illness that can affect new mothers. This illness can happen quickly, often within the first three months after childbirth. Women can experience psychotic depression, in that the depression causes them to lose touch with reality, have auditory hallucinations (hearing things that aren't actually happening, like a person talking), and delusions (seeing things differently from what they are in reality). Visual hallucinations (seeing things that aren't there) are less common. Other symptoms include insomnia (not being able to sleep), feeling agitated (unsettled) and angry, strange feelings and behaviors, as well as having suicidal or homicidal thoughts. Women who have postpartum psychosis need treatment right away and almost always need medication. Sometimes women are put into the hospital because they are at risk for hurting themselves or someone else, including their baby.

DEPRESSION DIAGNOSE ¹³

People who wonder if they should talk to their health professional about whether or not they have depression may consider taking a depression self-test, which asks questions about depressive symptoms. In thinking about when to seek medical advice about depression, the sufferer can benefit from considering if the sadness lasts more than two weeks or so or if the way they are feeling significantly interferes with their ability to function at home, school, or work and in their relationships with others. The first step to obtaining appropriate treatment is accurate diagnosis, which requires a complete physical and psychological evaluation to determine whether the person may have a depressive illness, and if so, what type. As previously mentioned, certain medications, as well as some medical conditions, can cause symptoms of depression. Therefore, the examining physician should rule out (exclude) these possibilities through an interview, physical examination, and laboratory tests. Many primary-care doctors use screening tools, symptoms tests, for depression, which are usually questionnaires that help identify people who have symptoms of depression and may need to receive a full mental-health evaluation.

The doctor usually asks about alcohol and drug use and whether the patient has had thoughts about death or suicide. Further, the history often includes questions about whether other family members have had a depressive illness, and if treated, what treatments they received and which were effective.

A diagnostic evaluation also includes a mental-status examination to determine if the patient's speech, thought pattern, or memory has been affected, as often happens in the case of a depressive or manic-depressive illness. As of today, there is no laboratory test, blood test, or X-ray that can diagnose a mental disorder. Even the powerful CT, MRI, SPECT, and PET scans, which can help diagnose other neurological disorders such as stroke or brain tumors, cannot detect the subtle and complex brain changes in psychiatric illness. However, these techniques are

currently useful in research on mental health and perhaps in the future they will be useful for diagnosis as well.

CAUSES, INCIDENCE, AND RISK FACTORS¹⁴

The exact cause of depression is not known. Many researchers believe it is caused by chemical changes in the brain. This may be due to a problem with your genes, or triggered by certain stressful events. More likely, it's a combination of both.

Some types of depression run in families. But depression can also occur if you have no family history of the illness. Anyone can develop depression, even kids.

The following may play a role in depression:

- Alcohol or drug abuse
- Certain medical conditions, including underactive thyroid, cancer, or long-term pain
- Certain medications such as steroids
- Sleeping problems
- Stressful life events, such as:
 - Breaking up with a boyfriend or girlfriend
 - Failing a class
 - Death or illness of someone close to you
 - Divorce
 - Childhood abuse or neglect
 - Job loss
 - Social isolation (common in the elderly)

TALK THERAPY

Talk therapy is counseling to talk about your feelings and thoughts, and help you learn how to deal with them.

Types of talk therapy include:

- Cognitive behavioral therapy teaches you how to fight off negative thoughts. You will learn how to become more aware of your symptoms and how to spot things that make your depression worse. You'll also be taught problem-solving skills.
- Psychotherapy can help you understand the issues that may be behind your thoughts and feelings.
- Joining a support group of people who are sharing problems like yours can also help. Ask your therapist or doctor for a recommendation.

OTHER TREATMENTS FOR DEPRESSION

- Electroconvulsive therapy (ECT) is the single most effective treatment for severe depression and it is generally safe. ECT may improve mood in those with severe depression or suicidal thoughts who don't get better with other treatments. It may also help treat depression in those who have psychotic symptoms.
- Transcranial magnetic stimulation (TMS) uses pulses of energy to stimulate nerve cells in the brain that are believed to affect mood. There is some research to suggest that it can help relieve depression.
- Light therapy may relieve depression symptoms in the winter time. However, it is usually not considered a first-line treatment.

EXPECTATIONS (PROGNOSIS)

Some people with major depression may feel better after taking antidepressants for a few weeks. However, many people need to take the medicine for 4 - 9 months to fully feel better and prevent the depression from returning.

For people who have repeated episodes of depression, quick and ongoing treatment may be needed to prevent more severe, long-term depression. Sometimes people will need to stay on medications for long periods of time.

COMPLICATIONS

People who are depressed are more likely to use alcohol or illegal substances.

Complications of depression also include:

- Increased risk of physical health problems
- Suicide

PREVENTION

Do not drink alcohol or use illegal drugs. These substances can make depression worse and might lead to thoughts of suicide.

Take your medication exactly as your doctor instructed. Ask your doctor about the possible side effects and what you should do if you have any. Learn to recognize the early signs that your depression is getting worse.

The following tips might help you feel better:

- Get more exercise
- Maintain good sleep habits
- Seek out activities that bring you pleasure
- Volunteer or get involved in group activities
- Talk to someone you trust about how you are feeling

- Try to be around people who are caring and positive

TREATMENTS FOR DEPRESSION ¹²⁻¹⁴

Regardless of the medication that may be used to treat depression, practitioners have become more aware that different ethnic groups may have different responses and have different risks for side effects than others.

Antidepressant medications Selective serotonin reuptake inhibitors (SSRIs) are medications that increase the amount of the neurochemical serotonin in the brain. (Remember that brain serotonin levels are often low in depression.) As their name implies, the SSRIs work by selectively inhibiting (blocking) serotonin reuptake in the brain. This block occurs at the synapse, the place where brain cells (neurons) are connected to each other. Serotonin is one of the chemicals in the brain that carries messages across these connections (synapses) from one neuron to another.

The SSRIs work by keeping serotonin present in high concentrations in the synapses. These drugs do this by preventing the reuptake of serotonin back into the sending nerve cell. The reuptake of serotonin is responsible for turning off the production of new serotonin. Therefore, the serotonin message keeps on coming through. It is thought that this, in turn, helps arouse (activate) cells that have been deactivated by depression, thereby relieving the depressed person's symptoms.

SSRIs have fewer side effects than the tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs), which are discussed below. SSRIs do not interact with the chemical tyramine in foods, as do the MAOIs, and therefore do not require the dietary restrictions of the MAOIs. Also, SSRIs do not cause orthostatic hypotension (sudden drop in blood pressure when sitting up or standing) and heart-rhythm disturbances, like the TCAs do. Therefore, SSRIs are often the first-line

treatment for depression. Examples of SSRIs include fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa), fluvoxamine (Luvox), and escitalopram (Lexapro).

SSRIs are generally well tolerated, and side effects are usually mild. The most common side effects are nausea, diarrhea, agitation, insomnia, and headache. However, these side effects generally go away within the first month of SSRI use. Some patients experience sexual side effects, such as decreased sexual desire (decreased libido), delayed orgasm, or an inability to have an orgasm. Some patients experience tremors with SSRIs. The so-called serotonergic (meaning caused by serotonin) syndrome is a serious neurologic condition associated with the use of SSRIs. It is characterized by high fevers, seizures, and heart-rhythm disturbances. This condition is very rare and has been reported only in very ill psychiatric patients taking multiple psychiatric medications.

All patients are unique biochemically. Therefore, the occurrence of side effects or the lack of a satisfactory result with one SSRI does not mean that another medication in this group will not be beneficial. However, if someone in the patient's family has had a positive response to a particular drug, that drug may be the preferable one to try first.

Dual-action antidepressants: The biochemical reality is that all classes of medications that treat depression (MAOIs, SSRIs, TCAs, and atypical antidepressants) have some effect on both norepinephrine and serotonin, as well as on other neurotransmitters. However, the various medications affect the different neurotransmitters in varying degrees.

Some of the newer antidepressant drugs, however, appear to have particularly robust effects on both the norepinephrine and serotonin systems. These medications seem to be very promising, especially for the more severe and chronic cases of depression. (Psychiatrists, rather than family practitioners, see such cases most frequently.) Venlafaxine (Effexor), duloxetine (Cymbalta) and desvenlafaxine (Pristiq) are three of

these dual-action compounds. Effexor is a serotonin reuptake inhibitor that, at lower doses, shares many of the safety and low side-effect characteristics of the SSRIs. At higher doses, this drug appears to block the reuptake of norepinephrine. Thus, venlafaxine can be considered an SNRI, a serotonin and norepinephrine reuptake inhibitor. Cymbalta and Pristiq tend to act as equally powerful serotonin reuptake inhibitors and norepinephrine reuptake inhibitors regardless of the dose. They are, therefore, also considered SNRIs.

Mirtazapine (Remeron), another antidepressant, is a tetracyclic compound (four-ring chemical structure). It works at somewhat different biochemical sites and in different ways than the other drugs. It affects serotonin, but at a postsynaptic site (after the connection between nerve cells). It also increases histamine levels, which can cause drowsiness. For this reason, mirtazapine is given at bedtime and is often prescribed for people who have trouble falling asleep. Like the SNRIs, it also works by increasing levels in the norepinephrine system. Other than causing sedation, this medication has side effects that are similar to those of the SSRIs but to a lesser degree in many cases.

Atypical antidepressants are so named because they work in a variety of ways. Thus, atypical antidepressants are not TCAs, SSRIs, or SNRIs, but they are effective in treating depression for many people nonetheless. More specifically, they increase the level of certain neurochemicals in the brain synapses (where nerves communicate with each other). Examples of atypical antidepressants include nefazodone (Serzone), trazodone (Desyre 1), and bupropion (Wellbutrin). The United States Food and Drug Administration (FDA) have also approved bupropion for use in weaning from addiction to cigarettes. This drug is also being studied for treating attention deficit disorder (ADD) or attention deficit hyperactivity disorder (ADHD). These problems affect many children and adults and restrict their ability to manage their impulses and activity level, focus, or concentrate on one thing at a time.

Lithium (Eskalith, lithobid), valproate (Depakene, Depakote), carbamazepine (Epitol, Tegretol), and lamotrigine (Lamictal) are mood stabilizers and anticonvulsants. They have been used to treat bipolar depression. Certain antipsychotic medications, such as ziprasidone (Geodon), risperidone (Risperdal), quetiapine (Seroquel), aripiprazole (Abilify), asenapine (Saphris), and paliperidone (Invega), may treat psychotic depression. They have also been found to be effective mood stabilizers and are therefore sometimes used to treat bipolar depression, usually in combination with other antidepressants.

Monoamine oxidase inhibitors (MAOIs) are the earliest developed antidepressants. Examples of MAOIs include phenelzine (Nardil) and tranylcypromine (Parnate). MAOIs elevate the levels of neurochemicals in the brain synapses by inhibiting monoamine oxidase. Monoamine oxidase is the main enzyme that breaks down neurochemicals, such as norepinephrine. When monoamine oxidase is inhibited, the norepinephrine is not broken down and, therefore, the amount of norepinephrine in the brain is increased.

MAOIs also impair the ability to break down tyramine, a substance found in aged cheese, wines, most nuts, chocolate, and some other foods. Tyramine, like norepinephrine, can elevate blood pressure. Therefore, the consumption of tyramine-containing foods by a patient taking an MAOI drug can cause elevated blood levels of tyramine and dangerously high blood pressure. In addition, MAOIs can interact with over-the-counter cold and cough medications to cause dangerously high blood pressure. The reason for this is that these cold and cough medications often contain drugs that likewise can increase blood pressure. Because of these potentially serious drug and food interactions, MAOIs are usually only prescribed after other treatment options have failed.

Tricyclic antidepressants (TCAs) were developed in the 1950s and '60s to treat depression. They are called tricyclic

antidepressants because their chemical structures consist of three chemical rings. TCAs work mainly by increasing the level of norepinephrine in the brain synapses, although they also may affect serotonin levels. Doctors often use TCAs to treat moderate to severe depression. Examples of tricyclic antidepressants are amitriptyline (Elavil), protriptyline (Vivactil), desipramine (Norpramin), nortriptyline (Aventyl, Pamelor), imipramine (Tofranil), trimipramine (Surmontil), and perphenazine (Triavil).

Tetracyclic antidepressants are similar in action to tricyclics, but their structure has four chemical rings. Examples of tetracyclics include maprotiline (Ludiomil) and mirtazapine (Remeron), a drug that was discussed above under dual-action antidepressants. TCAs are safe and generally well tolerated when properly prescribed and administered. However, if taken in overdose, TCAs can cause life-threatening heart-rhythm disturbances. Some TCAs can also have anticholinergic side effects, which are due to the blocking of the activity of the nerves that are responsible for control of the heart rate, gut motion, visual focus, and saliva production. Thus, some TCAs can produce dry mouth, blurred vision, constipation, and dizziness upon standing. The dizziness results from low blood pressure that occurs upon standing (orthostatic hypotension). Anticholinergic side effects can also aggravate narrow-angle glaucoma, urinary obstruction due to benign prostate hypertrophy, and cause delirium in the elderly. TCAs should also be avoided in patients with seizure disorders or a history of strokes.

Stimulants such as methylphenidate (Ritalin) or dextroamphetamine (Dexedrine) are used primarily for the treatment of depression that is resistant to other medications. The stimulants are most commonly used along with other antidepressants or other medications, such as mood stabilizers, antipsychotics, or even thyroid hormone. They are sometimes used alone but rarely. The reason they are usually used sparingly and with other medications for depression is that unlike the other medications, they may induce an

emotional rush and a high in both depressed and nondepressed people. Therefore, the stimulants are potentially addictive drugs.

Electroconvulsive therapy (ECT)

In the ECT procedure, an electric current is passed through the brain to produce controlled convulsions (seizures). ECT is useful for certain patients, particularly for those who cannot take or have not responded to a number of antidepressants, have severe depression, and/or are at a high risk for suicide. ECT often is effective in cases where trials of a number of antidepressant medications do not provide sufficient relief of symptoms. This procedure probably works, as previously mentioned, by a massive neurochemical release in the brain due to the controlled seizure. Often highly effective, ECT relieves depression within one to two weeks after beginning treatments in many people. After ECT, some patients will continue to have maintenance ECT, while others will return to antidepressant medications or have a combination of both treatments.

Over the years, the technique of ECT has been much improved. The treatment is given in the hospital under anesthesia so that people receiving ECT do not hurt themselves or feel pain. Most patients undergo six to 10 treatments. An electrical current is passed through the brain to cause a controlled seizure, which typically lasts for 20 to 90 seconds. The patient is awake in five to 10 minutes. The most common side effect is short-term memory, which resolves quickly. ECT can usually be safely done as an outpatient procedure.

Psychotherapies

Many forms of psychotherapy are effectively used to help depressed individuals, including some short-term (10 to 20 weeks) therapies. *Talking* therapies (psychotherapies) help patients gain insight into their problems and resolve them through verbal give-and-take with the therapist. *Behavioral* therapists help patients

learn how to obtain more satisfaction and rewards through their own actions. These therapists also help patients to unlearn the behavioral patterns that may contribute to their depression.

Interpersonal and cognitive/behavioral therapies are two of the short-term psychotherapies that research has shown to be helpful for some forms of depression. Interpersonal therapists focus on the patient's disturbed personal relationships that both cause and exacerbate the depression. Cognitive/behavioral therapists help patients change the negative styles of thinking and behaving that are often associated with depression.

Psychodynamic therapies are sometimes used to treat depression. They focus on resolving the patient's internal psychological conflicts that are typically thought to be rooted in childhood. Long-term psychodynamic therapies are particularly important if there seems to be a lifelong history and pattern of inadequate ways of coping (maladaptive coping mechanisms) in negative or self-injurious behavior.

GENERAL APPROACH TO TREATING DEPRESSION¹³

In general, the severe depressive illnesses, particularly those that are recurrent, will require antidepressant medications (or ECT in severe cases) along with psychotherapy for the best outcome. If a person suffers one major depressive episode, he or she has a 50% chance of a second episode. If the individual suffers two major depressive episodes, the chance of a third episode is 75%-80%. If the person suffers three episodes, the likelihood of a fourth episode is 90%-95%. Therefore, after a first depressive episode, it might make sense for the patient to gradually come off medication. However, after a second and certainly after a third episode, most clinicians will have a patient remain on a maintenance dosage of the medication for an extended period of years, if not permanently.

Patience is required because the treatment of depression takes time. Sometimes, the doctor will

need to try a variety of antidepressants before finding the medication or combination of medications that is most effective for the patient. Sometimes, the dosage must be increased to be effective.

In choosing an antidepressant, the doctor will take into account the patient's age, his/her other medical conditions, and medication side effects. Doctors often use one of the SSRIs initially because of their lower severity of side effects compared to the other classes of antidepressants. Side effects of SSRI medications can be further minimized by starting them at low doses and gradually increasing the doses to achieve full therapeutic effects. For those patients who do not respond after taking a SSRI at full doses for six to eight weeks, doctors generally switch to a different SSRI or another class of antidepressants. For patients whose depression failed to respond to full doses of one or two SSRIs or whom could not tolerate those medications, doctors will then try medications from another class of antidepressants. Some doctors believe that antidepressants with dual action (action on both serotonin and norepinephrine), such as duloxetine (Cymbalta), (Cymbalta), mirtazapine (Remeron), venlafaxine (Effexor), and desvenlafaxine (Pristiq), may be effective in treating patients with severe depression that is treatment resistant. Other options include bupropion (Wellbutrin, Wellbutrin SR, Wellbutrin XL, Zyban), which has action on dopamine (another neurotransmitter). Sometimes doctors may use a combination of antidepressants from different classes. Also, new types of antidepressants are constantly being developed, and one of these may be the best for a particular patient.

If the depressed person is taking more than one medication for depression or medications for any other medical problem, each of the patient's doctors should be made aware of the other prescriptions. Many of these medications are cleared from the body (metabolized) in the liver. This means that the multiple treatments can interact competitively with the liver's biochemical clearing systems. Therefore, the actual blood

levels of the medications may be higher or lower than would be expected from the dosage. This information is especially important if the patient is taking anticoagulants (blood thinners), anticonvulsants (seizure medications), or heart medications, such as digitalis (Crystodigin). Although multiple medications do not necessarily pose a problem, all of the patient's doctors may need to be in close contact to adjust dosages accordingly.

Patients often are tempted to stop their medication too soon, especially when they begin feeling better. It is important to keep taking medication therapy until the doctor says to stop, even if the patient feels better beforehand. Doctors often will continue the antidepressant medications for at least six to 12 months because the risk of depression quickly returning when treatment is stopped decreases after that period of time in those people experiencing their first depressive episode. Some medications must be stopped gradually to give the body time to adjust (see discontinuation of antidepressants below). For individuals with bipolar disorder or chronic major depression, medication may have to become a part of everyday life for an extended period of years in order to avoid disabling symptoms.

Antidepressant medications are not habit-forming, so there need not be concern about that. However, as is the case with any type of medication prescribed for more than a few days, antidepressants must be carefully monitored to ensure that the patient is getting the correct dosage. The doctor will want to check the dosage and its effectiveness regularly.

If the patient is taking MAOIs, certain aged, fermented, or pickled foods must be avoided, like many wines, processed meats, and cheeses. The patient should obtain a complete list of prohibited foods from the doctor and keep it available at all times. The other types of antidepressants require no food restrictions. Remember that some over-the-counter cold and cough medicines can also cause problems when taken with MAOIs.

People should never mix medications of any kind (prescribed, over the counter, or borrowed) without consulting their doctor. The dentist or any other medical specialist who prescribes a drug should be informed that the patient is taking antidepressants. Some drugs that are harmless when taken alone can cause severe and dangerous side effects when taken with other drugs. This may also be the case for individuals taking supplements or herbal remedies. Some drugs, such as alcohol (including wine, beer, and hard liquor), tranquilizers, narcotics or marijuana, reduce the effectiveness of antidepressants and should be avoided. These and other drugs can also be dangerous when the person's body is either intoxicated with or withdrawing from their effects due to increasing the risk of seizure in combination with antidepressant medications.

Antianxiety drugs such as diazepam (Valium), alprazolam (Xanax), and lorazepam (Ativan) are not antidepressants, but they are occasionally prescribed alone or with antidepressants for a brief period of anxiety. However, they should not be taken alone for depressive disorder. Furthermore, the antianxiety drugs should be phased out as soon as the antidepressant and antianxiety effects of the antidepressant medications begin to work, which is usually in four to six weeks.

Finally, the doctor should be consulted concerning any questions about a medication or problem that the patient believes is medication-related.

VITAMIN D CAN REDUCE RISK OF DEPRESSION IN CHILDREN¹⁴

- Parents, please note -- make sure that your child is exposed to adequate sunlight and consume a diet rich in vitamin B, for a new study says that these will reduce their risk of suffering from depression in later life.
- Researchers at the University of Bristol have carried out the study and found that

children with low levels of vitamin D are more likely to suffer from mental health problems such as depression in their teenage years.

- However, the study says those who get adequate vitamin D have 10 per cent lower risk of developing depression, the 'Daily Mail' reported.
- For their study, the researchers looked at vitamin D levels in more than 2,700 children when they were aged nine and 13. Those with the lowest levels of vitamin D were more likely to show signs of depression.
- Children with higher levels were also more likely to show a decline in depressive symptoms in their teenage years.
- The study investigated levels of two forms of the vitamin -- D2 and D3 -- and found the strongest anti-depression link with D3, say the researchers.
- Vitamin D is mainly made by the action of sunlight on the skin. It's also abundant in oily fish like tuna.

CONCLUSION

Indians are the world's most depressed people with nearly 36 per cent suffering from Major Depressive Episode (MDE), the cluster of symptoms of depression, according to a WHO-sponsored study. The study found that people living in wealthier nations like Netherlands, France and the US were less happy and more depressed than those in poorer ones. Netherlands with an average 33.6 per cent case of MDE came second while France and US were placed on third and fourth positions with 32.3 per cent and 30.9 per cent cases respectively. In India, around 9 per cent of people reported having an extended period of depression within their lifetime and nearly 36 per cent suffered from MDE. The average age of depression in India is 31.9 years

compared to 18.8 years in China, and 22.7 years in the US. The study, published in the BMC Medicine journal, is based on interviews of more than 89,000 people in 18 different countries. One in seven people (15 per cent) in high-income countries is likely to get depression over their lifetime, compared with one in nine (11 per cent) in middle and low-income countries, the study says. MDE is characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy and poor concentration, besides feeling depressed. WHO ranks depression as the fourth leading cause of disability worldwide and projects that by 2020, it will be the second leading cause. Women are twice as likely to suffer depression as men and the loss of a partner, whether from death or divorce, was a main factor, the study reveals. Depression affects over 120 million people worldwide. It can interfere with a person's ability to work, make relationships difficult, and destroy quality of life. In severe cases it leads to suicide, causing 850,000 deaths a year. Psychotherapy can be delivered, to individuals, groups, or families by mental health professionals, including psychotherapists, psychiatrists, psychologists, clinical social workers, counselors, and suitably trained psychiatric nurses. With more complex and chronic forms of depression, a combination of medication and psychotherapy may be used.

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