

Depression

A plain-English guide for you and your family

WHAT IS HAPPENING

Normally, your brain uses chemical messengers called serotonin, norepinephrine, and dopamine to keep your mood steady, help you enjoy things, and control sleep, appetite, and energy. Think of these chemicals like a three-way balance that keeps you feeling okay and able to bounce back from hard days. When depression happens, this balance breaks. Genes you were born with, stressful life events like losing someone you love or going through trauma, medical illness, or even some medicines can all lower these brain chemicals or make the brain less able to use them. When serotonin, norepinephrine, and dopamine drop or stop working right, you feel sad most of the day, nearly every day, for at least two weeks. You lose interest in things you used to enjoy — even favorite hobbies or time with loved ones feel flat. Your sleep changes; you might sleep too much or wake up at three in the morning and cannot fall back asleep. Your appetite shifts; you might eat much less or much more than usual. You feel exhausted even after rest. It is hard to focus, make decisions, or remember things. You might feel worthless or guilty about things that are not your fault. In the most serious cases, you might think about death or hurting yourself. Sometimes your body hurts too — headaches, stomach pain, or aches with no clear cause — because the same brain chemicals that control mood also control how your body senses pain. Depression is a real medical condition, not weakness or something you can just snap out of. The good news is it can be treated with therapy like cognitive behavioral therapy, which teaches your brain new thinking patterns, or medication, which raises those low brain chemicals back up, or both. If you or someone you know is thinking about suicide, call 988, the Suicide and Crisis Lifeline, right away. Help is available twenty-four seven, and depression can get better with the right support.

What you might feel

- Feeling sad, empty, or hopeless most of the day, nearly every day
- Loss of interest or pleasure in activities you used to enjoy
- Trouble sleeping (sleeping too much or too little)
- Feeling tired or having very low energy almost every day
- Changes in appetite or weight (eating much more or much less than usual)

- Trouble concentrating, remembering things, or making decisions
- Feeling worthless or excessively guilty about things
- Moving or speaking more slowly than usual, or being restless and unable to sit still
- Thoughts of death or suicide, or a plan to hurt yourself

Call the doctor right away if...

- Thoughts of suicide, a plan to hurt yourself, or telling others you want to die
- Hearing voices or seeing things that are not there (psychotic depression)
- Complete inability to care for yourself — not eating, not getting out of bed, not speaking
- Rapid weight loss or severe malnutrition from not eating
- New confusion, severe memory loss, or fast worsening of thinking (may signal severe depression or another medical cause)

What the care team will do

- Complete a suicide risk assessment using a screening tool like the Columbia Suicide Severity Rating Scale; remove access to firearms, pills, or other lethal means if any suicidal thoughts are present
- Ask about all current medications, alcohol use, and when the last dose of any psychiatric medication was taken; watch for signs of serotonin syndrome (confusion, fast heart rate, high blood pressure, sweating, muscle twitching) if the patient is on multiple antidepressants
- Check vital signs, weight, and hydration status; look at skin turgor (pinch test) and mucous membranes to assess for dehydration
- Assess ability to perform basic self-care: bathing, eating, taking medications, getting out of bed; document exactly what the patient can and cannot do independently
- Screen for psychotic symptoms by asking if the patient hears voices, sees things others do not see, or has beliefs that seem unusual; observe for talking to self, responding to internal stimuli, or paranoid statements
- Document sleep pattern for the past week: hours of sleep per night, time to fall asleep, nighttime awakenings, and daytime naps
- Educate the patient that antidepressant medication takes 4 to 6 weeks to work fully; the first changes will be better sleep and energy, then mood improves last
- Connect the patient with a therapist trained in cognitive behavioral therapy (CBT) or interpersonal psychotherapy (IPT); give printed resources or app-based CBT tools if in-person therapy is not immediately available

Medicines you may be given — and why

Sertraline (Zoloft)

Depression happens when serotonin — a brain messenger that steadies mood, sleep, and appetite — runs too low or doesn't stick around long enough between nerve cells. Normally, after serotonin carries its message across the gap (synapse) between two cells, the sending cell vacuums it back up through a pump to recycle it. Sertraline blocks that vacuum pump. With the pump blocked, serotonin stays in the gap longer, giving the receiving cell more time to catch the signal. Over four to six weeks, this stronger signaling helps the brain's mood circuits rebalance, lifting sadness, worry, and low energy.

Escitalopram (Lexapro)

Escitalopram works the same way as sertraline: it blocks the serotonin vacuum pump (the SERT transporter) so serotonin stays active longer in the gaps between brain cells. This lets the receiving cells catch a stronger mood signal. Over several weeks, the brain's mood circuits rebalance, lifting sadness, worry, and tiredness. Escitalopram is the purified, more active half of an older drug (citalopram), so it often works at lower doses with fewer side effects.

Fluoxetine (Prozac)

Fluoxetine blocks the serotonin vacuum pump so serotonin stays in the synapse longer, boosting mood signals between nerve cells. What makes fluoxetine different is its very long half-life — it stays in your body for days (even weeks) after each dose. This slow build-up and slow washout means fewer withdrawal symptoms if you miss a dose or stop, but it also means side effects may linger longer if they occur, and it takes longer to fully leave your system when switching to a different medicine.

Venlafaxine (Effexor XR)

Depression can involve two brain messengers: serotonin (which steadies mood, sleep, and appetite) and norepinephrine (which boosts energy, focus, and alertness). Venlafaxine blocks the vacuum pumps for both, so they stay in the synapse longer. This gives a double boost — steadying mood and lifting energy — which can help people who didn't get enough relief from an SSRI that only targets serotonin. At lower doses, it mostly affects serotonin; at higher doses, it adds norepinephrine.

Duloxetine (Cymbalta)

Duloxetine blocks the vacuum pumps for both serotonin (the mood and sleep messenger) and norepinephrine (the energy and alertness messenger), so both stay active longer in the gaps between nerve cells. This steadies mood and boosts energy. Duloxetine also works in the spinal cord to dampen pain signals, which is why it helps with physical pain that often comes with

depression — like chronic aches, nerve pain (such as diabetic neuropathy), or fibromyalgia pain.

Bupropion (Wellbutrin)

Unlike SSRIs, bupropion does not touch serotonin. Instead, it blocks the vacuum pumps for norepinephrine (the energy and alertness messenger) and dopamine (the motivation and reward messenger), so both stay active longer in the synapse. This makes it especially helpful for people whose depression shows up as low energy, no motivation, trouble focusing, or feeling 'flat' inside. Because it doesn't affect serotonin, bupropion usually does not cause weight gain, emotional numbness, or sexual side effects — common problems with SSRIs.

Mirtazapine (Remeron)

Mirtazapine works differently from SSRIs and SNRIs. It blocks alpha-2 receptors on nerve cells — these receptors normally act like brakes, slowing down the release of serotonin and norepinephrine. With the brakes off, nerve cells release more of both messengers. Mirtazapine also blocks certain serotonin receptors (5-HT₂ and 5-HT₃) that cause nausea, anxiety, and sexual side effects, and it blocks histamine receptors (H₁), which calms the nervous system and helps with sleep. This makes it especially helpful for people with depression who can't eat, can't sleep, or feel very anxious.

Lithium (Lithobid, Eskalith)

Lithium is a simple natural element (a soft, silvery metal salt, like sodium or potassium) that steadies the wild ups and downs of nerve cell signaling in the brain. It works inside nerve cells to balance second-messenger systems (chemical pathways like inositol and protein kinases that pass signals along inside the cell). This keeps nerve cells from firing too much or too little. Lithium also boosts brain-derived neurotrophic factor (BDNF), a growth protein that helps brain cells grow, connect, and repair. It's used when depression keeps coming back, when other medicines don't work, when depression is part of bipolar disorder, or when suicide risk is high — lithium lowers the risk of suicide more than almost any other treatment.

Aripiprazole (Abilify)

When an antidepressant alone doesn't lift depression enough (treatment-resistant depression), adding a low dose of aripiprazole can boost the response. Aripiprazole is called a 'dopamine partial agonist' — it fine-tunes dopamine (the motivation and reward messenger) by acting as a stabilizer rather than simply blocking or boosting. Where dopamine is too high, aripiprazole lowers it a bit; where it's too low, it raises it a bit. It also modulates serotonin receptors. This balancing act helps lift mood, motivation, and energy when depression is stubborn.

Quetiapine (Seroquel)

Quetiapine blocks several different receptors — serotonin (especially 5-HT_{2A}), dopamine (D₂), histamine (H₁), and norepinephrine (alpha-1 and alpha-2) — which helps calm an overactive stress response, steady mood swings, and improve sleep. At low doses (25–100 mg), it's very sedating and mainly used to help with sleep and anxiety in depression. At higher doses (300 mg and up), it can lift depression on its own (monotherapy) or boost another antidepressant (add-on therapy). One of its breakdown products (norquetiapine) blocks the norepinephrine reuptake pump, adding an antidepressant effect.

Esketamine (Spravato nasal spray)

Esketamine works faster than traditional antidepressants — often within hours to days instead of weeks. It blocks a receptor called NMDA (N-methyl-D-aspartate), which normally controls the flow of glutamate, the brain's main 'go' signal that excites nerve cells. When NMDA receptors are blocked, there's a brief surge of glutamate release. This surge triggers a burst of brain-derived neurotrophic factor (BDNF), a growth protein that helps brain cells quickly form new connections (synapses) and repair damaged mood circuits. Think of it like jump-starting a stalled car — the quick jolt gets the engine running again. Esketamine is used for severe, treatment-resistant depression (when two or more antidepressants have failed) or for major depression with acute suicidal thoughts when fast action is critical.

Where this information comes from

- APA Practice Guideline for the Treatment of Patients with Major Depressive Disorder (2010, reaffirmed 2015)
- U.S. Preventive Services Task Force (USPSTF) Depression Screening Recommendation (2023)
- DSM-5-TR (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision)
- Cochrane Depression, Anxiety and Neurosis Group

Last reviewed: 2026-07-07