

Migraine

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THE STORY IN ONE SENTENCE

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“Migraine is a problem with both nerves and blood vessels—the outer layer of the brain gets too electrically excited. Treatment means either stopping attacks when they start or preventing them from ever beginning.”

Normal anatomy — the body's job

Normally, the cortex (the outer layer of the brain) keeps its electrical signals steady and damped, so no wild waves of activity ripple across it. The trigeminal nerve—the main pain nerve in your head—and the blood vessels around the brain and its covering (the meninges, the protective layers wrapping the brain) stay quiet, signaling pain only if there's real injury. Keep that picture in your head, because the weird findings in migraine only make sense as a change from this calm state.

BODY'S JOB

The cortex runs smooth, steady electrical pulses to think, see, and move without random noise. The trigeminal nerve watches the blood vessels and meninges for danger—swelling, stretch, or inflammation—and only fires if something truly threatens the brain. The blood vessels stay stable in size and don't leak inflammatory chemicals. This balance keeps your head pain-free and your senses clear.

1. Cortex sends calm, steady electrical signals—no wild waves.
2. Trigeminal nerve sits quiet, monitoring blood vessels and meninges for real threats.
3. Blood vessels around the brain stay stable—no swelling, no chemical leak.
4. CGRP (calcitonin gene-related peptide, the pain-and-swelling messenger) stays low.

5. Result: no headache, no sensory distortion, clear thinking.

What breaks

In migraine, the brain's electrical brake fails, letting a wave of overexcitement—cortical spreading depression—roll across the cortex. That wave flips on the trigeminal nerve like a fire alarm, which then dumps CGRP and other inflammatory chemicals onto the blood vessels and meninges, making them swell and scream pain. Once started, the pain signals spread and amplify (sensitization), so even normal touch or light feels unbearable. Triggers—stress, skipped meals, hormone swings (especially estrogen drops before a period), lack of sleep, certain foods (aged cheese, wine, MSG), weather changes, bright lights—can set off the cascade in people whose brains are wired to overreact.

CLINICAL TERM

Cortical spreading depression (a self-propagating wave of neuronal and glial depolarization followed by suppression) underlies aura. Activation of the trigeminovascular system (trigeminal nerve endings on intracranial vessels and meninges) with release of CGRP (calcitonin gene-related peptide) and other neuropeptides drives vasodilation and neurogenic inflammation, producing pain. Central and peripheral sensitization amplify nociceptive signaling. Genetic susceptibility and environmental triggers (stress, sleep disturbance, hormonal fluctuation, dietary factors, barometric pressure changes) lower the threshold for attack initiation.

How the body compensates

The body doesn't really compensate for migraine—it just endures the storm. Vital signs usually stay normal because migraine itself doesn't threaten blood pressure, breathing, or heart rate. The danger is missing the slow slide into medication overuse headache (MOH, rebound headaches from taking pain meds too often) or overlooking a different, serious cause (stroke, meningitis, tumor) that mimics migraine. A stable-looking patient who is using triptans or painkillers more than 10 days a month is heading toward rebound headaches and worsening attacks. Watch the trend—frequency, severity, medication use—not just one snapshot.

1. Vital signs (blood pressure, pulse, oxygen) stay normal during most migraine attacks—migraine is a pain disorder, not a circulatory or breathing crisis.
2. The body tries to shut down input—patients seek dark, quiet rooms—to reduce sensory overload hitting the sensitized brain.
3. Nausea and vomiting occur because the brainstem pain centers activate the vomiting center nearby; this is the brain's way of saying 'emergency,' even though it doesn't help.

4. The dangerous middle: frequent attacks lead to more medication use (triptans, NSAIDs like ibuprofen, opioids), which paradoxically lowers the threshold for the next attack, creating medication overuse headache (MOH).
5. The crash point to watch for: taking acute migraine medication (triptan, combination painkiller, opioid) more than 10 days per month for three months raises the risk of MOH and transforms episodic migraine (occasional attacks) into chronic daily headache (headache 15 or more days each month).
6. You could also miss another serious cause: sudden 'thunderclap' headache (worst headache of your life in seconds), fever with stiff neck, new headache after age 50, headache with weakness or confusion, or headache after head trauma all demand imaging (CT or MRI) or lumbar puncture (spinal tap) to rule out stroke, bleed, infection, or tumor.
7. Migraine with aura (especially in women who smoke or use estrogen-containing birth control) slightly raises stroke risk, so counsel on quitting smoking and considering non-estrogen contraception.
8. Look at the trajectory—are attacks getting more frequent, lasting longer, or requiring more medication?—not just one visit. A stable patient on a downhill slope is not really stable.

Domino effect

1. Premonitory phase (warning phase): yawning, mood changes (irritability or feeling unusually happy), food cravings, neck stiffness, tiredness. — Hours to days before the headache, the hypothalamus (the brain's master control center for sleep, appetite, and mood, deep in the middle of the brain) starts firing abnormally, sending out warning signals that the migraine system is winding up—these are not imagined; they are real brain changes you can see on imaging.
2. Aura phase (in about 25% of people with migraine): visual zigzags or blind spots, tingling that spreads up an arm, slurred speech, sometimes weakness. — Cortical spreading depression—a slow wave of electrical silence—creeps across the occipital cortex (vision area at the back of the brain), parietal cortex (sensation area on the side), or frontal/temporal cortex (speech area on the front and side) at 2–5 millimeters per minute, causing reversible symptoms that march and then fade as the wave passes; this is electrical noise, not a stroke, so it leaves no permanent damage.

3. Headache phase: unilateral (one-sided), throbbing pain that builds over hours and lasts 4–72 hours if untreated. — The cortical spreading depression activates the trigeminal nerve in the brainstem (the thick stalk connecting the brain to the spinal cord), which releases CGRP (calcitonin gene-related peptide, a powerful pain and swelling messenger) and substance P (another pain chemical) onto the meningeal blood vessels (vessels in the protective layers around the brain), making them swell and fire pain signals back to the thalamus (the brain's relay station for sensation, deep inside) and then up to the cortex, where you feel the throb.
4. Light sensitivity (Photophobia) (light hurts), sound sensitivity (phonophobia) (sound hurts), osmophobia (smells are unbearable), and nausea/vomiting. — Central sensitization spreads through the brainstem and thalamus, so normal light, sound, and smell signals are now read as painful; the vomiting center in the medulla (the lowest part of the brainstem, where it meets the spinal cord) fires because it sits right next to the pain pathways—nausea is collateral damage, not separate sickness.
5. Allodynia (pain from things that shouldn't hurt): even gentle touch on the scalp or face feels painful; combing hair or wearing glasses hurts. — Peripheral sensitization makes trigeminal nerve endings fire at the slightest touch, and central sensitization amplifies those signals, so non-painful input is now registered as pain—this is a sign the attack is deep and may be harder to stop.
6. Postdrome phase (migraine hangover): tiredness, mental fog, mood changes, muscle aches for hours to a day after the headache fades. — The chemical storm—CGRP release, serotonin (a mood and pain-regulating brain messenger) depletion, inflammatory peptides, and hours of pain signaling—exhausts the brain's energy stores (ATP, the cell's fuel molecule) and leaves the system in recovery mode, like the calm after a seizure.
7. Return to baseline (in episodic migraine, fewer than 15 headache days per month) or progression to chronic migraine (15 or more headache days per month) if triggers are not managed or medication overuse develops. — Most people with migraine reset completely between attacks—no brain damage occurs. But frequent attacks, medication overuse (more than 10 days per month), or untreated comorbidities (other conditions that make things worse, like depression, sleep pauses in breathing (apnea), obesity) can lower the threshold further, transforming episodic migraine into chronic daily headache, where the brain stays in a sensitized state and never fully calms.

8. Each piece points backward: postdrome ← pain sensitization ← CGRP release ← trigeminal activation ← cortical spreading depression ← hypothalamic priming ← genetic susceptibility plus trigger. — None of this is random. One upstream break—hyperexcitable migraine circuitry (a brain wired to overreact electrically and chemically)—explains every downstream finding. The body is not trying to help; it is stuck in a maladaptive pain loop. Understanding the sequence lets you interrupt it early (acute treatment with triptans, NSAIDs, or CGRP blockers) or raise the threshold to prevent it (prophylaxis with beta-blockers, anticonvulsants, antidepressants, or CGRP monoclonal antibodies).

Symptoms · what the patient feels, and why

- Pounding pain on one side of the head that throbs with each heartbeat: Blood vessels around the brain swell and press on pain nerves. The trigeminal nerve (the main pain wire in the face and head) sends strong pain signals to the brain, creating that pulsing ache that matches your pulse.
- Nausea or vomiting: The brainstem (the command center at the base of your brain) gets stirred up during a migraine and triggers the vagus nerve (the big nerve that controls your stomach and gut). This makes your stomach churn and can make you throw up.
- Light hurts your eyes (photophobia): During a migraine, the thalamus (the brain's relay station for senses) becomes extra sensitive and overreacts to normal light. Even dim light feels too bright and painful.
- Sound hurts your ears (phonophobia): The same thalamus overload makes normal sounds feel unbearably loud. The auditory cortex (the brain's hearing center) processes sound too intensely, so quiet noises feel like shouting.
- Physical activity makes the pain worse: Moving around increases blood flow and raises pressure inside the already-swollen blood vessels around the brain, which pushes harder on the pain nerves and cranks up the throbbing.
- Aura before or during the headache (flashing lights, zigzag lines, blind spots, numbness, or trouble speaking): A wave of brain activity called cortical spreading depression (a slow ripple of nerve cells firing, then going quiet) moves across the occipital cortex (the back part of the brain that handles vision) and sometimes the sensory or speech areas. This temporary disruption creates the strange visual or sensory symptoms.
- Headache that lasts 4 to 72 hours if untreated: The migraine process (blood vessel swelling, nerve inflammation, and chemical imbalances like low serotonin, a brain messenger that steadies mood and pain signals) takes time to start and time to calm down. Without medicine, the body usually resets itself within three days.

- Sudden, explosive 'thunderclap' headache that peaks in seconds: This is NOT a migraine. It can signal a burst blood vessel in the brain (subarachnoid bleeding (hemorrhage), bleeding into the space around the brain) or blocked veins (cerebral venous clot formation (thrombosis), a clot stopping blood from draining out of the brain). It demands immediate imaging to rule out life-threatening bleeding or clots.
- New weakness, numbness, vision loss, or confusion that lasts beyond the aura phase: True migraine aura goes away within an hour. If it lasts longer or causes new deficits, it may be a stroke (a blocked artery cutting off blood and oxygen to part of the brain) or another serious brain problem, not a migraine.
- Fever, stiff neck, or confusion along with the headache: These signs suggest meningitis (infection or inflammation of the meninges, the protective lining around the brain and spinal cord) or encephalitis (infection inside the brain itself). Migraines do not cause fever or a stiff neck.

Focused exam

- Throbbing, pulsing headache on one side of the head: The pounding matches the heartbeat because blood vessels around the brain are widening and squeezing over and over. One-sided throbbing is the hallmark of migraine and points away from tension headache (which presses both sides like a tight band) or sinus headache (which aches over the cheeks and forehead).
- The person hides in a dark, quiet room during the attack: Light and sound feel unbearable because the trigeminal nerve (the main pain highway feeding the head and face) is firing too hard, making the brain extra sensitive to every sight and sound. When someone wants to shut out the world, that strongly points to migraine, not a mild everyday headache.
- Nausea or vomiting during the headache: Migraine stirs up the area postrema (the brain's vomit center in the brainstem), because the same nerve signals that drive head pain also trigger the stomach. This tells you the attack is real and strong, not just a regular headache.
- Aura that comes before or during the headache—zigzag lights, blind spots, tingling, trouble finding words—and fully goes away within an hour: Aura is cortical spreading depression: a slow wave of overactive nerve cells marching across the surface of the brain (the cortex), followed by a quiet zone. It is reversible and almost always means migraine. If the symptoms do NOT go away, or if they come on suddenly without a slow march, worry about stroke instead.

- Normal neurologic exam between attacks—no weakness, no lasting numbness, no slurred speech, no confusion, no fever, no stiff neck: Migraine is a primary headache disorder: nothing is permanently broken in the brain; the wiring just misfires sometimes. If you find weakness that stays, fever, a stiff neck, or confusion, you are dealing with something else (stroke, meningitis, tumor, bleeding) and must act immediately.
- Early warning signs 12 to 24 hours before the headache—yawning over and over, mood swings, craving certain foods, feeling very tired: These early clues tell you the hypothalamus (the brain's control center for sleep, hunger, and hormones) is already shifting before the pain starts. Recognizing this phase helps the person predict attacks and take medicine early, when it works best.

Diagnostics · every test answers a question

- MRI or CT of the brain (with and without contrast if red-flag symptoms are present—sudden worst headache of life, new neurologic deficit, fever, age > 50 with new headache) → Is there a dangerous structural problem in the brain causing the headache, such as a tumor, bleeding, stroke, or infection?
- Lumbar puncture (spinal tap) with opening pressure measurement → Is there bleeding in the fluid around the brain (subarachnoid bleeding (hemorrhage)), infection (meningitis), or high pressure inside the skull (idiopathic intracranial high blood pressure (hypertension))?
- Complete blood count (CBC) with differential and inflammatory markers (ESR, CRP) → Is there an infection, inflammation, or another body-wide illness driving the headache?
- Thyroid-stimulating hormone (TSH) and complete metabolic panel (sodium, calcium, glucose, kidney and liver function) → Is a hormone imbalance or electrolyte problem worsening or triggering the headaches?
- Red blood cell (Erythrocyte) sedimentation rate (ESR) and temporal artery biopsy (if giant cell arteritis is suspected) → Is there inflammation of the temporal artery (giant cell arteritis) causing the headache?

Treatment logic

- Triptan (sumatriptan 100 mg by mouth, rizatriptan 10 mg, or sumatriptan 6 mg injection) taken at the start of headache pain → Triptans activate serotonin 1B and 1D receptors (docking sites on blood vessels and nerve endings), shrinking swollen vessels and blocking the release of CGRP (calcitonin gene-related peptide—the main pain messenger in migraine). This stops the pain cascade before it spreads. They work best if taken early, before pain becomes severe.

- NSAIDs (ibuprofen 400–800 mg, naproxen 500–550 mg) or acetaminophen 1000 mg for mild-to-moderate migraine → These medicines block cyclooxygenase (COX) enzymes, which cuts down on prostaglandins (chemicals that open blood vessels and amplify pain signals). This reduces inflammation and pain around the brain's blood vessels and offers quick relief for less severe attacks.
- Antiemetic (metoclopramide 10 mg IV or by mouth, or prochlorperazine 10 mg IV or IM) given with acute migraine treatment → These medicines block dopamine receptors (docking sites in the brain) in the area postrema (the brain's vomit center) and the chemoreceptor trigger zone, stopping nausea and vomiting. They also speed up stomach emptying, which helps the gut absorb triptans or pain medicine faster and makes them work better.
- Daily preventive medicine (propranolol 80–240 mg, topiramate 50–200 mg, amitriptyline 25–100 mg at bedtime, or CGRP monoclonal antibody like erenumab 70–140 mg monthly injection) if 4 or more migraines per month or if attacks are disabling → Beta-blockers like propranolol calm overactive nerve firing. Topiramate quiets electrical activity in the cortex (the brain's outer layer). Amitriptyline raises serotonin and norepinephrine (brain messengers that steady mood and pain control). CGRP antibodies block calcitonin gene-related peptide (the main pain molecule in migraine). All of these lower the brain's sensitivity to triggers and cut attack frequency by 50% or more over weeks to months.
- Trigger avoidance and lifestyle habits—regular sleep schedule, staying hydrated, managing stress, avoiding known food triggers like aged cheese or alcohol, eating regular meals → Removing or limiting migraine triggers—such as skipped meals (which drop blood sugar and stress the hypothalamus), poor sleep (which disrupts the brain's control center for hormones and alertness), dehydration, stress, and hormonal swings—reduces how often the brain's excitability threshold is crossed and an attack is kicked off.
- OnabotulinumtoxinA (Botox) injections—155 to 195 units across 31 to 39 sites in the head and neck every 12 weeks—if chronic migraine (15 or more headache days per month) persists despite other preventives → Botox blocks acetylcholine (the chemical that tells muscles to contract) at nerve and muscle junctions around the head and neck, quieting the overactive pain signals sent along the trigeminal nerve to the brain. It also blocks CGRP and substance P (another pain messenger) from being released by nerve endings.
- Gepant (ubrogepant 50–100 mg or rimegepant 75 mg by mouth) as acute treatment if triptans fail, cause side effects, or are contraindicated → Gepants block CGRP receptors (the docking sites for calcitonin gene-related peptide) directly, stopping the pain signal without narrowing blood vessels. This makes them safe for people with heart disease or stroke risk, who cannot take triptans.

Medications

Ibuprofen or naproxen (NSAIDs) · Nonsteroidal anti-inflammatory drug (NSAID)

Blocks an enzyme called COX (cyclooxygenase, the factory in cells that makes swelling chemicals). COX makes prostaglandins, tiny chemicals that puff up blood vessels and turn on pain signals. By shutting down COX, the drug shrinks the swelling in blood vessels around the brain and quiets the pain.

1. When a migraine starts, COX inside cells near the brain's blood vessels churns out prostaglandins.
2. Prostaglandins make the vessels swell and poke the pain nerves next to them.
3. The NSAID locks onto COX and stops it from making any more prostaglandins.
4. With fewer prostaglandins floating around, swelling goes down and pain signals fade.

SAFETY WATCH

Can upset your stomach or cause ulcers if you use it often or at high doses. · May raise blood pressure a bit. · Can harm your kidneys if you take high doses for a long time or if you are dehydrated. · Avoid if you have had stomach bleeding or severe kidney disease. · Using NSAIDs more than 10–15 days per month can cause rebound headaches (medication-overuse headache).

Acetaminophen (paracetamol, Tylenol) · Analgesic (pain reliever)

Turns down pain signals in the brain and spinal cord. The exact steps are still being studied, but acetaminophen seems to block a brain version of the COX enzyme and may also boost the body's own pain-damping pathways. It quiets the sensation of pain without fighting swelling.

1. Acetaminophen enters the brain and spinal cord.
2. It blocks an enzyme (likely COX-2 in the brain) that makes pain chemicals.
3. It may also nudge the body's endocannabinoid system (natural pain-damping signals) to work harder.
4. Pain signals become weaker, so the headache feels less intense.

SAFETY WATCH

Safe at normal doses—up to 3,000 mg per day for adults (some guidelines say up to 4,000 mg, but staying under 3,000 is safer)—but too much seriously damages your liver. · Never mix with alcohol; both stress the liver and together they can cause liver failure. · Check the labels on cold medicines, sinus pills, and sleep aids; many already contain acetaminophen, so you can accidentally take too much. · Using acetaminophen more than 10–15 days per month can cause rebound headaches.

Sumatriptan, rizatriptan, eletriptan, zolmitriptan (triptans) · Triptan (selective serotonin 5-HT_{1B/1D} receptor agonist)

Triptans mimic serotonin (a brain messenger that steadies mood and blood vessels) and lock onto special docking sites called 5-HT_{1B} and 5-HT_{1D} receptors. Turning on 5-HT_{1B} receptors squeezes swollen blood vessels back to normal size. Turning on 5-HT_{1D} receptors on nerve endings stops the nerves from dumping out pain chemicals like CGRP (calcitonin gene-related peptide, a powerful swelling and pain signal) and substance P (another pain messenger).

1. During a migraine, blood vessels around the brain swell and the trigeminal nerve releases CGRP and substance P.
2. The triptan binds to 5-HT_{1B} receptors on blood vessel walls and makes them squeeze back to normal width.
3. It also binds to 5-HT_{1D} receptors on trigeminal nerve endings and blocks the release of CGRP and substance P.
4. With less CGRP and substance P around, swelling stops and pain signals stop traveling up to the brain, so the headache fades.

SAFETY WATCH

Can cause a tight or heavy feeling in the chest, throat, or neck (usually harmless muscle tightness, not your heart, but tell your doctor if it happens). · Do not use if you have heart disease, uncontrolled high blood pressure, or have had a stroke, because triptans squeeze blood vessels everywhere, including the heart. · Do not take within 24 hours of ergotamine (another migraine drug) or another triptan—stacking them can dangerously narrow vessels. · Using triptans more than 10 days per month can cause medication-overuse headache (rebound headaches).

Ubrogepant (Ubrelvy), rimegepant (Nurtec ODT) · CGRP receptor antagonist (oral 'gepant')

Blocks the docking site (receptor) for CGRP (calcitonin gene-related peptide, a chemical that nerves release during a migraine to make blood vessels swell and send pain signals). By sitting

in the receptor and not letting CGRP plug in, the drug stops CGRP from causing swelling and pain.

1. During a migraine, the trigeminal nerve dumps large amounts of CGRP into the tissues around blood vessels.
2. CGRP normally docks onto its receptor and triggers blood vessels to swell and nerves to fire pain signals.
3. The gepant locks onto the CGRP receptor first, blocking CGRP from binding.
4. Without CGRP's signal, swelling stops and pain pathways quiet down, so the headache fades.

SAFETY WATCH

Generally well tolerated; the most common side effect is nausea. · Avoid if you have severe liver disease. · Do not use with strong CYP3A4 inhibitors (certain antibiotics like clarithromycin and antifungals like ketoconazole) without your doctor's approval—they can raise gepant levels too high. · Using gepants more than 10 days per month may cause medication-overuse headache (rebound), though the risk appears lower than with triptans or NSAIDs.

Lasmiditan (Reyvow) · Selective serotonin 5-HT_{1F} receptor agonist ('ditan')

Turns on the 5-HT_{1F} receptor, which sits on nerves in the trigeminal pain pathway but NOT on blood vessels. By activating this receptor, lasmiditan calms the trigeminal nerve's electrical activity and blocks it from sending pain signals to the brain. Because it does not touch blood vessels, it is safe for people with heart disease who cannot take triptans.

1. Migraine pain signals race along the trigeminal nerve and up into the brainstem.
2. Lasmiditan binds to 5-HT_{1F} receptors on those nerve fibers.
3. Turning on the receptor dials down the nerve's electrical firing and stops it from releasing pain chemicals.
4. Pain signals are blocked before they reach higher brain centers, so the headache stops.

SAFETY WATCH

Can cause significant dizziness and drowsiness—do NOT drive or operate machinery for at least 8 hours after taking it (FDA black-box warning). · May cause a brief feeling of tingling or warmth. · Avoid alcohol while using lasmiditan; together they increase dizziness and sedation. · Using lasmiditan more than 10 days per month may cause medication-overuse headache.

Metoclopramide (Reglan) or prochlorperazine (Compazine) · Dopamine D₂ receptor antagonist; antiemetic and prokinetic

Blocks dopamine receptors in two key places. First, in the chemoreceptor trigger zone (the brain's nausea alarm, sitting in the brainstem), blocking dopamine turns off nausea signals. Second, in the stomach and upper intestine, blocking dopamine allows the stomach muscles to squeeze and push food forward. Migraines often slow or stop the stomach (gastroparesis), so these drugs restart digestion and stop vomiting.

1. During a migraine, the brainstem's vomiting center becomes overactive and the stomach slows down or stops moving food.
2. The drug blocks dopamine D₂ receptors in the chemoreceptor trigger zone, turning off nausea signals before they reach the vomiting center.
3. It also blocks dopamine in the gut, which normally tells stomach muscles to relax; without dopamine's brake, the muscles can squeeze and move food normally again.
4. Nausea fades and the stomach works, so you can keep down water and other migraine medicine.

SAFETY WATCH

Can rarely cause muscle spasms, restlessness, or trouble sitting still (extrapyramidal symptoms, or EPS), especially in children and young adults. These reverse when you stop the drug. · Long-term use (months to years) carries a small risk of tardive dyskinesia (involuntary chewing or tongue movements that may not go away)—avoid using these drugs every day for chronic prevention. · May cause drowsiness. · Prochlorperazine can lower blood pressure when you stand up; rise slowly from sitting or lying down. · Metoclopramide carries an FDA black-box warning about tardive dyskinesia; use the lowest dose for the shortest time needed.

Propranolol (Inderal), metoprolol (Lopressor, Toprol-XL), atenolol (Tenormin) · Beta-adrenergic receptor antagonist (beta-blocker)

Blocks beta receptors that normally respond to adrenaline (epinephrine, the body's stress hormone). In the brain's blood vessels, this keeps them from over-dilating (opening too wide). It may also stabilize the electrical excitability of the cerebral cortex, making cortical spreading depression (the slow wave that triggers migraines) less likely to start. Steadying heart rate and blood pressure also lowers migraine triggers like stress and adrenaline surges.

1. Beta receptors normally make blood vessels and nerve cells more reactive to stress hormones like adrenaline.
2. The beta-blocker sits on these receptors and blocks adrenaline from binding.

3. Blood vessels stay steady instead of swinging wide open, and nerve cells are less likely to fire the abnormal spreading wave that triggers a migraine.
4. Over weeks to months, the brain's threshold for starting a migraine rises, so attacks happen less often.

SAFETY WATCH

Can make you feel tired or slow your heart rate and lower your blood pressure. · May worsen asthma or chronic obstructive pulmonary disease (COPD)—avoid non-selective beta-blockers like propranolol if you have reactive airway disease; cardioselective ones like metoprolol or atenolol are safer but still use caution. · Can mask the warning signs of low blood sugar (hypoglycemia) in people with diabetes—you may not feel your heart race when sugar drops. · May worsen depression in some people. · Do not stop suddenly after long-term use; taper slowly over a week or two to avoid rebound high blood pressure and fast heart rate.

Topiramate (Topamax) · Antiepileptic drug (anticonvulsant, used for migraine prevention)

Works on several brain pathways at once to calm overactive neurons. It boosts GABA (gamma-aminobutyric acid, the brain's main calming signal), blocks glutamate (the brain's main excitatory signal), and stabilizes voltage-gated sodium and calcium channels (the electrical gates on nerve cells). It also slightly blocks carbonic anhydrase (an enzyme in cells). Together, these actions raise the threshold for cortical spreading depression, so the migraine wave is less likely to start.

1. Neurons in the cortex can become hyperexcitable, making cortical spreading depression (the slow electrical ripple that triggers a migraine) more likely.
2. Topiramate increases GABA activity, which puts the brakes on neuron firing.
3. It blocks glutamate receptors, cutting down excessive excitatory signals that push neurons to fire.
4. It stabilizes sodium and calcium channels, preventing the rapid, repeated firing that kicks off the migraine wave.
5. With neurons calmer and less excitable, the brain's migraine threshold rises and attacks happen less often.

SAFETY WATCH

Can cause tingling in fingers and toes (paresthesias, usually harmless but annoying). · May cause weight loss and decreased appetite. · Can rarely cause kidney stones—drink plenty of water (8 glasses a day) to lower risk. · May cause cognitive side effects: trouble finding words, slowed thinking, or memory problems ('foggy thinking'). These often improve if the dose is raised slowly. · Can harm a developing baby (increased risk of cleft lip/palate and lower birth weight); use reliable birth control and talk to your doctor before getting pregnant. · Rarely can cause metabolic acidosis (acid building up in the blood) (too much acid in the blood) or acute angle-closure glaucoma (sudden eye pain and vision loss—seek emergency care).

Amitriptyline (Elavil), nortriptyline (Pamelor) · Tricyclic antidepressant (TCA)

Blocks the reuptake pumps that normally pull serotonin and norepinephrine (two brain messengers) back into nerve cells after they deliver their message. With the pumps blocked, serotonin and norepinephrine stay active longer in the synapse (the gap between nerve cells). Extra serotonin stabilizes blood vessels and mood circuits; extra norepinephrine strengthens the descending pain-control pathways (the brain's natural pain-damping system that runs from the brainstem down the spinal cord). Over weeks, this steady boost raises the migraine threshold.

1. Normally, after serotonin and norepinephrine deliver their signal, pumps pull them back into the sending nerve cell to be recycled.
2. Amitriptyline or nortriptyline blocks those pumps, so serotonin and norepinephrine hang around in the synapse longer.
3. Extra serotonin stabilizes blood vessels in the meninges and steadies mood circuits, reducing migraine triggers.
4. Extra norepinephrine boosts the brain's descending pain-damping system, which quiets pain signals traveling up the spinal cord.
5. Over 4–8 weeks, this steady increase in neurotransmitters reduces migraine frequency and may lower pain intensity during attacks.

SAFETY WATCH

Can cause dry mouth, constipation, blurred vision, and urinary retention (anticholinergic effects from blocking acetylcholine receptors). · May cause drowsiness and weight gain—usually taken at bedtime so drowsiness helps you sleep. · Rarely can affect heart rhythm (prolonged QT interval); your doctor may check an EKG before starting, especially if you have heart disease. · Can lower the seizure threshold slightly (rarely causes seizures unless you are already at risk). · Avoid if you have untreated narrow-angle glaucoma, recent heart attack, or severe heart block. · Nortriptyline causes fewer side effects than amitriptyline (less anticholinergic and sedation) and is often preferred.

Divalproex sodium (Depakote), valproate · Antiepileptic drug (anticonvulsant, used for migraine prevention)

Boosts GABA (gamma-aminobutyric acid, the brain's main calming signal) by blocking the enzyme that breaks GABA down and by increasing the enzyme that makes GABA. It also blocks voltage-gated sodium channels and may block T-type calcium channels on neurons. Together, these actions calm overactive nerve cells and raise the threshold for cortical spreading depression, so migraines start less often.

1. Valproate inhibits GABA transaminase (the enzyme that breaks down GABA) and activates glutamic acid decarboxylase (the enzyme that makes GABA), so GABA levels rise.
2. Higher GABA activity calms neurons and makes them less likely to fire rapidly.
3. Valproate also blocks sodium channels, preventing the repeated high-frequency firing that can trigger cortical spreading depression.
4. With neurons stabilized and less excitable, the brain's migraine threshold rises and attacks happen less often.

SAFETY WATCH

Can cause nausea, weight gain, and tremor. · Can cause hair thinning or loss (usually temporary). · Rarely can harm the liver (hepatotoxicity), especially in children under 2 or people with certain genetic enzyme defects; your doctor will check liver tests periodically. · Rarely can cause pancreatitis (sudden severe stomach pain—seek emergency care). · Causes serious birth defects (neural tube defects, lower IQ, autism spectrum disorder) and should NOT be used in women of childbearing age unless no other option works and reliable birth control is in place (FDA black-box warning). · Can lower platelet count (cells that help blood clot); your doctor will check blood counts.

Candesartan (Atacand), other angiotensin receptor blockers (ARBs) · Angiotensin II receptor blocker (ARB)

Blocks the AT₁ receptor for angiotensin II (a hormone that narrows blood vessels and raises blood pressure). By blocking this receptor, blood vessels stay relaxed and blood pressure drops. In the brain, steadier blood flow and lower vascular reactivity may reduce the trigger for cortical spreading depression. The exact migraine-prevention mechanism is still being studied, but calmer blood vessels and lower stress on the vascular system likely raise the migraine threshold.

1. Angiotensin II normally docks onto AT₁ receptors and squeezes blood vessels, raising blood pressure and making vessels reactive.
2. Candesartan blocks the AT₁ receptor, so angiotensin II cannot bind.
3. Blood vessels stay relaxed, blood pressure drops, and vascular reactivity decreases.
4. Steadier cerebral blood flow and calmer vessels may reduce the likelihood of cortical spreading depression, lowering migraine frequency over several weeks.

SAFETY WATCH

Can cause dizziness or lightheadedness, especially when standing up, because it lowers blood pressure. · Can raise potassium levels—your doctor will check bloodwork, especially if you have kidney disease or take other medicines that raise potassium. · Do NOT use during pregnancy (can harm or kill the developing baby); stop immediately if you become pregnant. · Rarely can worsen kidney function, especially if you are dehydrated or have pre-existing kidney disease.

OnabotulinumtoxinA (Botox) · Botulinum toxin type A (neurotoxin used for chronic migraine prevention)

Injected into specific muscles around the head, neck, and shoulders, botulinum toxin blocks the release of acetylcholine (the signal that makes muscles contract) AND blocks the release of pain chemicals—CGRP (calcitonin gene-related peptide), substance P, and glutamate—from sensory nerve endings. This calms overactive peripheral branches of the trigeminal nerve and occipital nerves (pain nerves of the head), stopping them from bombarding the brainstem with migraine signals. By quieting these sensory nerves at their endings, the toxin prevents central sensitization (the wind-up of pain pathways in the brainstem and spinal cord) and reduces migraine days.

1. Tiny amounts of botulinum toxin (5 units per site, 155–195 units total) are injected into muscles and near sensory nerves in a standard pattern around the head and neck.
2. The toxin enters nerve terminals and cleaves a protein called SNAP-25, which nerve cells need to release chemical messengers from tiny storage bubbles (vesicles).

3. Without SNAP-25, acetylcholine release stops, so muscles relax slightly.
4. More importantly, the toxin also stops sensory nerves from releasing CGRP, substance P, and glutamate, so the trigeminal and occipital nerves stop sending a constant barrage of pain signals to the brainstem.
5. Over 10–14 days the effect builds, and migraine days per month drop by about 50% in people with chronic migraine (15 or more headache days per month, with at least 8 being migraines).

SAFETY WATCH

Most common side effects are neck pain, headache (usually mild and temporary), and muscle weakness at injection sites. · Rarely can cause eyelid droop (ptosis) if toxin spreads to nearby muscles; this usually resolves in a few weeks. · Do not use if you have a skin infection at the injection sites or an allergy to any botulinum toxin product. · Avoid if you have myasthenia gravis, Lambert-Eaton syndrome, or amyotrophic lateral sclerosis (ALS)—conditions where nerve-muscle communication is already impaired. · Very rarely, botulinum toxin can spread beyond the injection site and cause serious symptoms (trouble swallowing, breathing, speaking)—seek emergency care if these occur.

Erenumab (Aimovig), fremanezumab (Ajovy), galcanezumab (Emgality), eptinezumab (Vyepti) · Monoclonal antibody targeting CGRP or its receptor

These are laboratory-made antibodies (immune proteins designed to lock onto one target) that either bind directly to CGRP molecules floating in the blood and tissues (fremanezumab, galcanezumab, eptinezumab) or block the CGRP receptor on cells (erenumab). CGRP (calcitonin gene-related peptide) is a powerful pain and swelling signal released by the trigeminal nerve during migraines. By locking onto CGRP or its receptor, these antibodies stop CGRP from sending its signal. Because antibodies are large proteins, they stay in the bloodstream for weeks, providing steady, long-lasting prevention without going through the liver or kidneys much.

1. The antibody is injected under the skin (subcutaneous, monthly or quarterly) or into a vein (eptinezumab only, IV infusion every 3 months).
2. It circulates in the blood and binds tightly to CGRP molecules (fremanezumab, galcanezumab, eptinezumab catch free CGRP before it can dock) or to the CGRP receptor on cells (erenumab blocks the docking site).
3. CGRP can no longer trigger blood vessel swelling or activate pain pathways.
4. The antibody stays active for 4 weeks (monthly dosing) or 12 weeks (quarterly dosing), keeping CGRP activity low and migraine frequency down by about 50% in people with episodic or chronic migraine.

SAFETY WATCH

Injection-site reactions (redness, swelling, itching) are common but usually mild and go away in a day or two. · Constipation is the most common body-wide side effect, especially with erenumab (happens in about 10–15% of people). · Rarely, muscle cramps or muscle spasms. · Very rarely, severe constipation with serious complications has been reported—drink plenty of water, eat fiber, and tell your doctor if you have fewer than 3 bowel movements per week. · Very safe overall with few drug interactions because antibodies do not go through liver enzymes (cytochrome P450) much and are broken down by normal protein recycling. · Expensive; insurance prior authorization usually required.

Red flags

- Sudden thunderclap headache that peaks in seconds (may be bleeding in the brain)
- New weakness, vision loss, numbness, or confusion that does not go away (may be a stroke)
- Fever, stiff neck, or confusion (may be meningitis or encephalitis)
- Headache after age 50 for the first time (may be giant cell arteritis, an inflamed artery in the temple, or a brain tumor)
- Worsening headaches in someone with cancer, HIV, or a weakened immune system (may be infection or spread of cancer to the brain)

Nursing priorities

1. Place the patient in a quiet, dark room and minimize noise, bright lights, and interruptions — Migraine involves sensitization of the trigeminal nerve (main face and head nerve) and brain pathways that process light and sound, so reducing sensory stimulation decreases pain signals and nausea
2. Give prescribed triptan medication (sumatriptan or rizatriptan) or NSAID as soon as possible in the headache phase — Triptans work by constricting dilated blood vessels and blocking pain pathways in the trigeminal nerve; early treatment stops central sensitization (pain amplification in the brain) and gives better relief than delayed dosing
3. Administer anti-nausea medicine (metoclopramide or prochlorperazine) before or with pain medication — Migraine causes gastroparesis (stomach paralysis) that slows absorption of oral medicines; anti-emetics (anti-nausea drugs) restore gut motility and also have pain-relieving effects by blocking dopamine
4. Monitor for medication overuse by documenting how many days per month the patient uses acute headache medicine — Taking acute migraine medicine more than 10 days per month causes rebound headaches through changes in pain receptors in the brain and nervous system, creating a cycle of worsening migraines

5. Assess for red flag symptoms including sudden onset, fever, neurologic deficits, altered mental status, or neck stiffness before giving migraine treatment — These warning signs indicate life-threatening conditions like subarachnoid bleeding (hemorrhage), meningitis, or stroke that mimic migraine but need immediate imaging and different emergency treatment
6. Educate the patient to keep a headache diary tracking frequency, triggers, and medicine use to guide preventive therapy decisions — Four or more migraines per month cause significant disability and meet criteria for daily preventive medicine (propranolol, topiramate, amitriptyline, or CGRP inhibitors) that reduce attack frequency by stabilizing brain excitability
7. Teach patients to identify and avoid personal migraine triggers such as specific foods, sleep changes, stress, or hormonal fluctuations — Triggers lower the threshold for cortical spreading depression (the brain wave that starts migraine) by affecting neurotransmitter balance, blood vessel tone, and inflammatory pathways

Sources

- American Headache Society 2024 Migraine Guidelines
- International Headache Society ICHD-3 Classification
- American Academy of Neurology 2023
- Cochrane Review on Migraine Management

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