

Migraine

A plain-English guide for you and your family

WHAT IS HAPPENING

Normally, your brain keeps its electrical activity steady and calm, and the blood vessels around your brain stay quiet. The trigeminal nerve—the big nerve that carries pain signals from your head—sits silently unless there's real danger. In migraine, that calm breaks. A wave of electrical and chemical change rolls across the outer layer of your brain—called cortical spreading depression—and turns on pain signals from the trigeminal nerve and the blood vessels it watches. A chemical called CGRP (calcitonin gene-related peptide, a messenger that opens blood vessels and screams 'pain!') floods the area, making vessels swell and nerves fire. That creates the throbbing headache, usually on one side, that can last hours or even days. Before the headache, you might yawn a lot, crave certain foods, or feel moody—those are warning signs the system is winding up. Some people see zigzag lines, feel tingling, or have trouble speaking—that's the aura, caused by the electrical wave moving across the brain. After the headache fades, you're wiped out and foggy—the postdrome—because your brain just survived a chemical storm. Triggers like stress, missed sleep, hormone changes, certain foods, or weather shifts can set the whole cascade off. None of this is random; each piece points back to one upstream break: the brain's pain and blood vessel system firing when it shouldn't.

What you might feel

- Pounding pain on one side of the head that throbs with each heartbeat
- Nausea or vomiting
- Light hurts your eyes (photophobia)
- Sound hurts your ears (phonophobia)
- Physical activity makes the pain worse
- Aura before or during the headache (flashing lights, zigzag lines, blind spots, numbness, or trouble speaking)
- Headache that lasts 4 to 72 hours if untreated
- Sudden, explosive 'thunderclap' headache that peaks in seconds
- New weakness, numbness, vision loss, or confusion that lasts beyond the aura phase

- Fever, stiff neck, or confusion along with the headache

Call the doctor right away if...

- 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)

What the care team will do

- Place the patient in a quiet, dark room and minimize noise, bright lights, and interruptions
- Give prescribed triptan medication (sumatriptan or rizatriptan) or NSAID as soon as possible in the headache phase
- Administer anti-nausea medicine (metoclopramide or prochlorperazine) before or with pain medication
- Monitor for medication overuse by documenting how many days per month the patient uses acute headache medicine
- Assess for red flag symptoms including sudden onset, fever, neurologic deficits, altered mental status, or neck stiffness before giving migraine treatment
- Educate the patient to keep a headache diary tracking frequency, triggers, and medicine use to guide preventive therapy decisions
- Teach patients to identify and avoid personal migraine triggers such as specific foods, sleep changes, stress, or hormonal fluctuations

Medicines you may be given — and why

Ibuprofen or naproxen (NSAIDs)

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.

Acetaminophen (paracetamol, Tylenol)

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.

Sumatriptan, rizatriptan, eletriptan, zolmitriptan (triptans)

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).

Ubrogepant (Ubrelvy), rimegepant (Nurtec ODT)

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.

Lasmiditan (Reyvow)

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.

Metoclopramide (Reglan) or prochlorperazine (Compazine)

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.

Propranolol (Inderal), metoprolol (Lopressor, Toprol-XL), atenolol (Tenormin)

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.

Topiramate (Topamax)

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.

Amitriptyline (Elavil), nortriptyline (Pamelor)

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.

Divalproex sodium (Depakote), valproate

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.

Candesartan (Atacand), other angiotensin receptor blockers (ARBs)

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.

OnabotulinumtoxinA (Botox)

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.

Erenumab (Aimovig), fremanezumab (Ajovy), galcanezumab (Emgality), eptinezumab (Vyepti)

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.

Where this information comes from

- 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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