

# Encephalitis

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## THE STORY IN ONE SENTENCE

A virus sneaks into brain tissue—or the body's defense system mistakenly attacks the brain—and both cause the brain to swell inside the hard skull.

“The brain swells from infection or from the body attacking itself by mistake. Doctors give acyclovir (an antiviral medicine) right away to stop the deadliest virus while tests figure out the exact cause.”

## Normal anatomy — the body's job

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The brain is a soft, delicate organ that controls everything you think, feel, and do. It sits inside a hard skull and floats in a clear fluid called cerebrospinal fluid (CSF) that cushions it like bubble wrap. A special barrier—the blood-brain barrier—lines the tiny blood vessels inside the brain and acts like a strict security gate: it lets oxygen and sugar through to feed brain cells but blocks most germs, toxins, and even many medicines.

## BODY'S JOB

The brain sends electrical signals between billions of nerve cells (neurons) to make your heart beat, your lungs breathe, your muscles move, and your mind think and remember. The blood-brain barrier keeps infections out by filtering what crosses from blood into brain tissue. Cerebrospinal fluid absorbs shocks (like when you bump your head) and washes away waste products. Normally, viruses circulating in your blood cannot cross the barrier into brain tissue, so the brain stays sterile and works smoothly.

1. Blood carries oxygen and nutrients to the brain through tiny vessels called capillaries.
2. The blood-brain barrier (made of tightly packed cells lining those vessels) filters what crosses from blood into brain tissue—only safe, small molecules like oxygen and sugar get through.
3. Brain cells (neurons) use that oxygen and sugar to fire electrical signals that control your whole body—movement, breathing, heartbeat, thoughts, and memories.

4. Cerebrospinal fluid bathes the brain and spinal cord, cushioning them against bumps and flushing out waste products into the bloodstream.
5. The skull is a rigid, closed box—any swelling inside has nowhere to go, so pressure rises and squeezes the soft brain tissue against the hard bone.

## What breaks

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A virus breaks through the blood-brain barrier and starts copying itself inside brain cells, killing them. Or the immune system gets confused and makes antibodies that attack the brain's own neurons by mistake. Either way, brain tissue swells, electrical signals misfire, and normal thinking, memory, and movement fall apart.

### CLINICAL TERM

Encephalitis is inflammation of the brain parenchyma (the actual brain tissue made of neurons). The most common infectious cause in the United States is herpes simplex virus type 1 (HSV-1), which reactivates from the trigeminal ganglion (a nerve cluster near the face where the virus hides after childhood infection) and travels into the temporal lobes (the parts of the brain on the sides, near your ears, that handle memory, emotion, and language). Other viral causes include varicella-zoster virus (the chickenpox virus that hides in nerve roots), enteroviruses (spread by fecal-oral contact), West Nile virus, and other arboviruses (viruses spread by mosquitoes or ticks). Autoimmune encephalitis happens when the body makes antibodies that attack receptors or proteins on neurons—common types include anti-NMDA receptor encephalitis (often in young women, sometimes triggered by an ovarian teratoma) and acute disseminated encephalomyelitis (ADEM, often after a viral infection or vaccination, more common in children). The inflammation causes neurons to swell, blood vessels to leak fluid into brain tissue, and the whole brain to swell inside the rigid skull, raising intracranial pressure. Misfiring neurons cause seizures (abnormal, chaotic electrical storms). Damaged temporal lobes cause memory loss, confusion, bizarre behavior, and personality changes. If swelling is severe, brain tissue can herniate (shift downward through the opening at the skull base), crushing the brainstem (which controls breathing and heart rate) and causing coma or death.

## How the body compensates

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The body tries to wall off the infected or attacked area, send more immune cells to fight the virus or calm the attack, and keep vital functions (breathing, heartbeat) going. But these efforts cause more swelling and can spiral into danger—rising pressure inside the skull chokes off blood flow, and continuous seizures exhaust the brain's energy reserves. Early on, vital signs (blood pressure, pulse, oxygen level) may look normal even as brain cells are dying, so

you must watch closely for worsening confusion, new weakness, repeated seizures, or drowsiness as red flags that compensation is failing.

1. {'what': 'Immune cells (white blood cells) rush to the infected or attacked brain area.', 'why': 'The immune system detects the virus or the mistaken attack and floods brain tissue with white blood cells and antibodies to kill the virus or stop the autoimmune reaction. But this immune response itself releases inflammatory chemicals (cytokines) that cause blood vessels to leak fluid, adding to brain swelling.'}
2. {'what': 'Blood vessels in the brain dilate (widen) to deliver more oxygen and immune cells.', 'why': 'Wider vessels mean more blood flow, bringing oxygen and immune fighters to damaged tissue. But dilated vessels leak more fluid into the surrounding brain, increasing swelling and pressure inside the rigid skull.'}
3. {'what': 'Body temperature rises—fever often reaches 102–104°F (39–40°C).', 'why': 'The immune system raises body temperature to help kill viruses and speed up immune reactions. High fever makes you feel miserable (severe headache, chills, body aches) and can lower the seizure threshold, making seizures more likely.'}
4. {'what': 'The brain tries to maintain blood flow despite rising pressure inside the skull.', 'why': 'As swelling increases intracranial pressure, the body raises blood pressure to push blood through squeezed vessels and keep oxygen reaching brain cells. But if pressure keeps climbing, blood flow eventually drops, and brain tissue starts to die from lack of oxygen (ischemia).'}
5. {'what': 'Seizures may start as brief, isolated misfires, then become continuous (status epilepticus).', 'why': '"Damaged, irritated neurons fire chaotically at first in short bursts—brief seizures lasting seconds to a few minutes. If inflammation spreads or pressure rises, the electrical storm never stops (status epilepticus), exhausting the brain's glucose and oxygen reserves and causing permanent neuron damage within 30–60 minutes."}
6. {'what': 'Vital signs (blood pressure, pulse, oxygen saturation) stay normal for hours to days, hiding the danger inside the skull.', 'why': 'Blood pressure, heart rate, and oxygen level measured on a finger probe can look completely fine even as brain cells are dying. This is the dangerous window when caregivers or family might underestimate how sick the person really is—always trust worsening confusion, new weakness, or repeated seizures over reassuring vital signs.'}

7. {'what': 'The crash point: status epilepticus (a seizure that will not stop) (seizures that will not stop), herniation (brain tissue squeezes down through the skull opening), coma, or death.', 'why': 'Once intracranial pressure is too high or seizures exhaust the brain's energy stores, compensation fails completely. Brain tissue herniates (gets pushed out of normal position and crushes the brainstem), blood flow stops, breathing stops, and the person loses consciousness or dies. Untreated HSV encephalitis kills more than 70 out of 100 people. Even with treatment started late (after 48–72 hours), many survivors have permanent memory loss, language problems, personality changes, or paralysis.'}]

## Domino effect

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1. A virus—usually herpes simplex type 1 (HSV-1)—reactivates from a nerve cluster near the face, or a new virus enters the bloodstream and crosses the blood-brain barrier into brain tissue. — HSV-1 lives dormant in the trigeminal ganglion (a cluster of nerve cells near your cheekbone) after a childhood cold sore. Stress, illness, or a weakened immune system lets the virus wake up, travel along nerve fibers, and invade the temporal lobes (the parts of the brain near your ears that handle memory and emotion). Other viruses—like West Nile virus from a mosquito bite, enteroviruses from contaminated water, or varicella-zoster from reactivated chickenpox—reach the brain through the bloodstream by slipping past or breaking through the blood-brain barrier.
2. The virus (or autoimmune antibodies) attacks neurons, especially in the temporal lobes, causing those brain cells to swell and die. — HSV-1 loves temporal lobe neurons—those cells control recent memory, emotion, and language. When the virus copies itself inside those neurons, it kills them directly. Dead and dying neurons leak their contents, triggering inflammation. Autoimmune antibodies (like anti-NMDA receptor antibodies) stick to receptors on neurons across the whole brain, blocking normal signals and causing widespread confusion, hallucinations, and abnormal movements.
3. The immune system floods the area with white blood cells, antibodies, and inflammatory chemicals (cytokines), adding even more swelling inside the rigid skull. — Immune cells are trying to kill the virus or calm the mistaken attack, but their arrival and the chemicals they release (like interleukin-6 and tumor tissue death (necrosis) factor) make blood vessels leaky. Fluid leaks into brain tissue, the tissue swells, and because the skull is bone and cannot expand, pressure inside the skull (intracranial pressure) rises.
4. Swollen, irritated neurons misfire, sending chaotic electrical signals—this is a seizure. You see shaking, jerking, staring spells, or loss of consciousness. — Healthy neurons fire electrical signals in organized, rhythmic patterns. Damaged, swollen neurons fire all at once in a chaotic storm—this misfiring spreads across the brain and causes a seizure. Seizures drain the brain's glucose (sugar) and oxygen, damaging more cells and making confusion worse.

5. Rising pressure inside the skull squeezes blood vessels, cutting oxygen delivery to brain tissue. If untreated, brain tissue starts to die (infarct) or herniate (shift out of place). — The skull is a closed box—any swelling inside has nowhere to go, so it squeezes the soft brain against the hard bone. High intracranial pressure flattens blood vessels like stepping on a garden hose, stopping blood flow and starving neurons of oxygen. If pressure keeps rising, brain tissue gets pushed downward through the foramen magnum (the opening at the skull base), crushing the brainstem (which controls breathing and heart rate)—this is called herniation, and it causes coma and death within hours.
6. You see fever (often 102–104°F / 39–40°C), severe headache (from stretched brain coverings called meninges), confusion or bizarre behavior (from damaged temporal and frontal lobes), weakness on one side (if one brain hemisphere is more affected), and seizures. — Each symptom maps directly to inflamed or dying brain tissue. Fever comes from the immune fight. Headache comes from swollen meninges (the coverings around the brain) and rising pressure. Confusion, memory loss, and bizarre behavior (saying strange things, acting paranoid, forgetting loved ones) come from damaged temporal lobes. Weakness or paralysis on one side comes from damaged motor areas in the opposite brain hemisphere. Seizures come from misfiring neurons.
7. Without immediate antiviral treatment (acyclovir for HSV) or immune therapy (corticosteroids, intravenous immunoglobulin, or plasmapheresis for autoimmune encephalitis), brain damage becomes permanent—or the person dies. — Acyclovir stops HSV-1 from copying its DNA, halting further neuron destruction. Immune therapies (steroids like methylprednisolone, IVIG, or plasmapheresis to filter out antibodies) calm the body's attack on its own brain. Started within the first 48–72 hours, these treatments stop the domino chain and let surviving neurons recover. Delayed treatment leaves dead brain tissue that cannot regenerate—causing permanent memory loss, language problems, personality changes, paralysis, or death. Current guidelines (IDSA, AAN) say to start acyclovir empirically (before test results come back) in anyone with suspected encephalitis because HSV encephalitis is the most treatable cause and delays are deadly.
8. Even with treatment, some people are left with lasting memory trouble, personality changes, movement problems, or seizures that need lifelong medicine. — Neurons that died during the infection do not grow back. The temporal lobes (which handle memory, emotion, and language) are often hardest hit by HSV-1, so survivors may forget recent events, struggle to learn new things, lose emotional control, or speak in a flat, slow way. Scar tissue (gliosis) forms in place of dead neurons and can keep triggering abnormal electrical signals—causing epilepsy (repeated seizures) that requires daily antiseizure medicine (like levetiracetam or lamotrigine) for years or life.

## Symptoms · what the patient feels, and why

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- **Fever:** The body raises its temperature to fight the virus or germ attacking the brain. Immune cells release chemicals called cytokines (messengers that sound the alarm) that tell the hypothalamus (the brain's thermostat, deep in the center of your brain) to turn up the heat.
- **Headache:** The meninges (the three thin layers wrapping the brain and spinal cord) and blood vessels swell because of inflammation. Swelling presses on pain-sensing nerves around the brain, triggering a deep, throbbing ache.
- **Confusion or change in behavior:** The infection damages neurons (brain cells that send messages) in the cerebral cortex (the outer layer that controls thinking, memory, and personality). When those cells stop working right, the person can't think clearly or act like themselves.
- **Seizures:** Inflamed brain tissue becomes irritable and sends out chaotic electrical signals, like short circuits. These wild bursts of activity spread through the cortex and cause muscles to shake or jerk, or the person to lose awareness and stare.
- **Weakness or trouble moving one side of the body:** Swelling or cell damage hits the motor cortex (the strip of brain near the top that sends 'move' signals to muscles) or the corticospinal tract (the highway carrying those signals down to the spinal cord). When those pathways break, muscles on one side of the body can't get the command.
- **Trouble speaking or understanding words:** Inflammation in language centers like Broca's area (front left brain, for forming words) or Wernicke's area (back left brain, for understanding words) disrupts the circuits that turn thoughts into speech or decode the meaning of sounds.
- **Stiff neck:** The meninges (layers wrapping the brain and spinal cord) are inflamed and irritated. Bending the neck stretches them and hurts, so neck muscles reflexively tighten to protect the area.
- **Sensitivity to light (photophobia):** Inflamed meninges and brain tissue make nerve pathways extra sensitive. Bright light triggers pain signals along the trigeminal nerve (the main nerve carrying sensation from the face and eyes) that normally wouldn't bother you.
- **Sleepiness or difficulty waking up:** Infection disrupts the reticular activating system (a network in the brainstem that keeps you awake and alert). Widespread inflammation slows down communication between brain cells, so the person drifts into sleep and is hard to rouse.
- **Hallucinations or seeing or hearing things that aren't there:** Inflammation in the temporal lobes (side parts of the brain that process sights, sounds, and memories) scrambles signals. The brain misreads its own activity as real sights or sounds, creating vivid false experiences.

## Focused exam

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- High fever (over 101°F) with stiff neck: When the brain or the layers covering it (the meninges) swell from infection, bending the neck forward stretches that inflamed tissue and causes sharp pain, so the muscles lock up to protect it. A stiff neck plus high fever means something serious is happening inside the skull—infection or dangerous swelling pressing on the brain itself.
- New confusion, strange talk, or personality change that appeared over hours to days: The virus—most often herpes simplex virus (HSV), the same family that causes cold sores—attacks the parts of the brain that control thinking, memory, and behavior (especially the temporal lobes on the sides of the brain). When those areas swell and misfire, the person stops acting like themselves. This tells you the infection is inside the brain tissue itself, not just the covering around it.
- Seizure or shaking that the person cannot control: A swollen, inflamed brain sends out chaotic electrical signals—like a short circuit in a wire. Seizures mean the inflammation is severe enough to disrupt the brain's normal electrical activity. In encephalitis, seizures are common and can be the very first clue that brain tissue is under attack.
- One-sided weakness or trouble speaking clearly: Swelling from the infection can press on specific areas of the brain that control movement or speech. When one side of the body is weak or words come out wrong, it tells you which part of the brain is inflamed. HSV encephalitis often hits the temporal lobe, which sits close to areas that control language and movement on one side, causing these focused symptoms.
- Decreased alertness—hard to wake up, eyes closed most of the time, slow to respond: When the brain swells, it can squeeze the brainstem (the stalk at the base of the brain that controls wakefulness, breathing, and heart rate). A person who is harder and harder to wake is at risk of the brain shutting down completely. This is a sign that time is running out and the brain is in immediate danger.
- Memory loss or forgetting recent events, sometimes with strange emotional outbursts: The temporal lobe—where memories are stored and emotions are processed—is the favorite hiding spot for HSV. When HSV wakes up from its dormant state and attacks this area, the person loses the ability to form new memories or recall recent ones, and emotions can swing wildly. This finding is a strong clue pointing specifically to HSV encephalitis.

## Diagnostics · every test answers a question

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- Lumbar puncture (spinal tap) with cerebrospinal fluid (CSF) analysis—cell count, protein, glucose, Gram stain, and culture → Is there inflammation in the fluid around the brain and spinal cord, and is it caused by a virus or bacteria?

- CSF PCR (polymerase chain reaction) for herpes simplex virus (HSV-1 and HSV-2) → Is HSV—the most common and treatable cause of viral encephalitis in the United States—present in the spinal fluid?
- Brain MRI with and without contrast (or head CT if MRI is not available quickly) → Is there swelling, abnormal signal, or bleeding in the brain, and where exactly is it located?
- Electroencephalogram (EEG)—recording of brain electrical activity → Is the brain showing abnormal electrical patterns or ongoing seizure activity that is not visible on the outside?
- Blood tests: complete blood count (CBC), comprehensive metabolic panel (CMP), and blood cultures → Is the body fighting an infection, and are the kidneys and liver still working well enough to handle medications?
- CSF testing for autoimmune antibodies (anti-NMDA receptor, anti-LGI1, anti-CASPR2, anti-GAD65, others) if viral tests are negative or clinical picture suggests autoimmune encephalitis → Is the person's own immune system attacking brain cells instead of a virus being the cause?
- CSF opening pressure measured during lumbar puncture → Is the pressure inside the skull dangerously high, which can squeeze the brain?

## Treatment logic

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- IV acyclovir 10 mg/kg every 8 hours (or 30 mg/kg/day divided into three doses), started immediately even before test results return → Acyclovir blocks the enzyme HSV needs to copy its genetic material (DNA polymerase), stopping the virus from spreading to more brain cells. Starting it within hours of suspecting encephalitis cuts the risk of death or permanent brain damage in half. Every hour of delay allows more neurons to die—HSV encephalitis has over 70% mortality without treatment, but under 20% with early acyclovir.
- Anti-seizure medication—lorazepam 0.1 mg/kg IV (up to 4 mg per dose) for active seizures; levetiracetam 1000–1500 mg IV load (then 500–1000 mg every 12 hours) or fosphenytoin 15–20 mg phenytoin equivalents (PE) per kg IV load for seizure prevention → Lorazepam boosts GABA (the brain's main calming messenger), stopping the chaotic electrical storm of a seizure within minutes. Levetiracetam or fosphenytoin keeps the brain's electrical threshold high, preventing new seizures while the inflammation is treated. Stopping seizures protects neurons from exhaustion, oxygen starvation, and death.
- IV methylprednisolone 1 gram daily for 3–5 days or IV immunoglobulin (IVIG) 2 g/kg total dose divided over 2–5 days, if autoimmune encephalitis is suspected or confirmed → Steroids shut down the immune system's attack on brain tissue by blocking inflammatory signals (cytokines like interleukin-1 and TNF-alpha). IVIG floods the bloodstream with normal antibodies that distract and neutralize the harmful autoantibodies attacking the brain. Both reduce brain swelling from the inside and stop further damage when the cause is autoimmune, not infectious.

- Mannitol 0.25–1 g/kg IV bolus over 15–30 minutes or hypertonic saline (3% NaCl) 250 mL IV bolus to reduce intracranial pressure if signs of brain herniation appear (blown pupil, posturing, sudden decreased consciousness) → These solutions pull water out of swollen brain tissue and into the blood vessels through osmosis (water moving toward higher salt concentration), lowering the pressure inside the skull. This buys time by preventing the brain from being squeezed down through the base of the skull (herniation), which cuts off blood flow to the brainstem and causes death within minutes to hours.
- Supportive care in the ICU—mechanical ventilation if needed to protect the airway, fever control with acetaminophen 15 mg/kg every 4–6 hours (max 4 grams per day in adults) or cooling blanket, head of bed elevated 30 degrees, and hourly neurologic checks → Lowering fever reduces the brain's oxygen and energy demand when it is already struggling. Elevating the head helps blood and cerebrospinal fluid drain away from the brain through the jugular veins, reducing pressure. Mechanical ventilation ensures oxygen reaches the brain even if the person cannot breathe well on their own or is too drowsy to protect their airway from choking. Close monitoring catches any sudden worsening (like new seizures, blown pupil, or signs of herniation) within minutes, not hours.

## Medications

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### Acyclovir (IV) · Antiviral (nucleoside analog)

Acyclovir tricks the herpes virus into using it as a building block when the virus tries to copy its DNA (the instruction manual inside the virus). Once acyclovir gets inside that copying machine, it jams it shut so the virus can't make more of itself. The virus dies out, and your immune system can catch up and clear what's left.

1. Acyclovir enters infected brain cells through the bloodstream.
2. Viral thymidine kinase (an enzyme the virus carries) activates acyclovir by adding phosphate groups to it.
3. The activated form looks like a normal DNA building block, so the virus's DNA polymerase (the enzyme that strings DNA together) grabs it.
4. Once acyclovir is added to the growing DNA chain, the chain can't grow anymore—it's stuck.
5. The virus stops making new copies and dies.

**SAFETY WATCH**

Kidney damage: The drug can form crystals in the kidney tubes if you're dehydrated. Give plenty of IV fluids and watch kidney function tests (creatinine, blood urea nitrogen) and urine output daily. · Nervous system effects: Rarely causes confusion, tremors, hallucinations, or seizures, especially in people with kidney problems or at very high doses. · Infusion site irritation: IV acyclovir is harsh on veins and can cause pain or inflammation. Give it slowly over one hour through a large vein or a central line, and flush well with saline.

**Ganciclovir (IV) or Foscarnet (IV) · Antiviral (nucleoside analog or pyrophosphate analog)**

These drugs stop cytomegalovirus (CMV) from copying its DNA. Ganciclovir works like acyclovir—it tricks the virus into using it as a fake DNA piece, then jams the copying machine. Foscarnet skips that trick and directly blocks the virus's DNA polymerase (the enzyme that copies DNA). Both stop CMV from multiplying in the brain.

1. Ganciclovir or foscarnet enters infected cells through the blood.
2. Ganciclovir is activated by viral enzymes (viral kinases), then blocks DNA polymerase. Foscarnet blocks DNA polymerase directly without needing activation.
3. The virus can't finish copying its DNA.
4. The virus stops multiplying and dies.

**SAFETY WATCH**

Ganciclovir: Bone marrow suppression—it lowers white blood cells, red blood cells, and platelets. Check complete blood counts twice a week. Low white cells can make infections worse. · Foscarnet: Kidney damage and electrolyte chaos—calcium, magnesium, phosphate, and potassium can all drop dangerously. Check labs (metabolic panel with these minerals) at least twice a week. Can also cause painful ulcers on the genitals. · Both need lower doses if kidneys aren't working well—adjust based on creatinine clearance.

**Dexamethasone (IV or oral) · Corticosteroid (anti-inflammatory)**

Dexamethasone turns down the immune system's alarm bells. In some kinds of encephalitis—like autoimmune or post-infectious types—your own immune cells attack brain tissue and cause swelling. Dexamethasone tells those immune cells to calm down and stop releasing inflammatory chemicals (cytokines like TNF-alpha and interleukins). This lowers brain pressure and protects brain cells from collateral damage.

1. Dexamethasone enters immune cells and binds to glucocorticoid receptors inside them.

2. It turns off genes that make inflammatory chemicals (cytokines like TNF-alpha and IL-1, and prostaglandins).
3. It also stabilizes blood vessel walls so they leak less fluid into brain tissue.
4. Brain swelling goes down, and immune attack slows.

**SAFETY WATCH**

Can worsen infections by suppressing immune defenses—only use when the benefit outweighs the risk, and make sure infection-specific treatment (antiviral, antibiotic) is started first. · Raises blood sugar—check glucose levels daily, especially in people with diabetes. May need insulin temporarily. · Can cause stomach ulcers, mood changes (agitation, depression, psychosis), high blood pressure, and bone weakening with long-term use (more than a few weeks). · Taper the dose slowly when stopping—sudden stop can crash your body's stress response (adrenal insufficiency), causing dangerous low blood pressure and weakness.

**IVIG (Intravenous Immunoglobulin) · Immunomodulator (antibody replacement and immune regulation)**

IVIG is a mixture of antibodies collected from thousands of healthy blood donors. When your own immune system is mistakenly attacking your brain (autoimmune encephalitis), IVIG floods your body with normal antibodies that calm down the rogue immune cells. It also blocks harmful autoantibodies from sticking to brain cell receptors (like NMDA receptors or VGKC) and helps clear those bad antibodies faster.

1. IVIG antibodies are infused into the bloodstream.
2. They bind to receptors on immune cells (Fc receptors) and turn down their attack signals.
3. They compete with harmful autoantibodies for binding spots on brain cells, blocking them from causing damage.
4. They speed up the breakdown and removal of harmful autoantibodies through the reticuloendothelial system (the body's cleanup crew in the liver and spleen).
5. Inflammation and autoimmune attack decrease.

**SAFETY WATCH**

Infusion reactions: Headache, chills, fever, nausea, back pain during or right after infusion. Slow the infusion rate and give acetaminophen or diphenhydramine if this happens. Pre-medicate patients with a history of reactions. · Blood clots: Rare but serious—risk is higher in people with heart disease, stroke history, thick blood (polycythemia), or those who are immobile. Watch for leg swelling, chest pain, or sudden shortness of breath. · Kidney damage: Especially with sucrose-containing IVIG products. Use sucrose-free products in people with existing kidney disease. Monitor creatinine before and after. · Aseptic meningitis: Can cause headache, stiff neck, fever, and nausea that mimic worsening encephalitis. Usually starts within 24 hours of infusion and resolves in a few days.

**Levetiracetam (Keppra) or Phenytoin (Dilantin) · Antiepileptic (anti-seizure medication)**

These drugs calm overexcited brain cells that are firing out of control and causing seizures. Levetiracetam works by binding to the SV2A protein on nerve terminals, which controls how much neurotransmitter (chemical signal) gets released. When it blocks this protein, cells can't fire as wildly. Phenytoin blocks voltage-gated sodium channels—the doors that let electrical signals rush through a neuron—so cells can't fire rapidly over and over.

1. Levetiracetam binds to the SV2A protein on nerve endings, reducing release of excitatory neurotransmitters like glutamate.
2. Phenytoin blocks voltage-gated sodium channels, stopping rapid-fire electrical signals from traveling down the neuron.
3. Neurons slow their firing rate.
4. Seizures stop or happen less often.

**SAFETY WATCH**

Levetiracetam: Mood and behavior changes—irritability, aggression, anxiety, depression, and rarely suicidal thoughts. Watch closely, especially in the first few weeks. If severe, switch to a different medication. · Phenytoin: Many side effects—gum overgrowth, drowsiness, unsteady walking (ataxia), double vision, and rash. Some rashes are dangerous, like Stevens-Johnson syndrome (painful blisters and peeling skin). Stop immediately if rash appears. Check phenytoin blood levels regularly to keep them in the safe zone. Interacts with many other drugs by speeding up or slowing down liver enzymes. · Both can cause dizziness and sleepiness, especially at the start or with dose increases.

## **Mannitol (IV) or Hypertonic Saline (3% NaCl IV) · Osmotic diuretic (mannitol) / Hyperosmolar agent (hypertonic saline)**

When the brain swells inside the rigid skull, pressure builds up and can crush brain tissue against bone. Mannitol and hypertonic saline pull water out of swollen brain tissue and into the blood vessels, like a sponge drawing water. This shrinks the swelling and lowers the intracranial pressure (ICP), buying time for other treatments—antiviral, anti-inflammatory, or surgery—to work.

1. Mannitol or hypertonic saline is infused into a vein.
2. Because they have more dissolved particles (higher osmolarity) than the fluid in swollen brain tissue, water flows from brain tissue into the blood to balance the concentration.
3. The kidneys filter this extra water out as urine.
4. Brain swelling decreases, and intracranial pressure drops—usually within 15 to 30 minutes.

### **SAFETY WATCH**

Kidney damage: Both can overload the kidneys, especially with repeated doses. Monitor urine output (should stay above 0.5 mL/kg/hour), creatinine, and blood urea nitrogen daily.

- Electrolyte imbalances: Sodium, potassium, chloride, and osmolarity can swing dangerously. Check a basic metabolic panel and serum osmolarity every 6 to 12 hours during treatment.
- Fluid overload: Hypertonic saline increases blood volume and can worsen heart failure or cause fluid in the lungs. Use carefully in people with weak hearts or lung disease.
- Rebound swelling: If used too long or too often, the brain tissue adapts to the high osmolarity. When the drug wears off, water rushes back in and swelling can return worse than before. Limit use to acute crises.

## **Red flags**

- Seizures or repeated jerking movements
- Cannot stay awake or is very hard to wake up
- Sudden weakness or numbness on one side of the body
- Severe confusion or aggressive, strange behavior that is brand new
- Trouble breathing or very slow, irregular breathing

## Nursing priorities

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1. Check airway, breathing, and oxygen saturation every 15 minutes until stable; keep oxygen saturation above 94 percent with supplemental oxygen — Encephalitis can damage the brainstem (the part that controls automatic breathing), and swelling inside the hard skull pushes brain tissue downward into the breathing-control centers, causing slow or stopped breathing
2. Perform and document a full neurological check every hour: Glasgow Coma Scale score, pupil size and reaction to light, arm and leg strength on both sides, and ability to follow commands — The brain swells quickly inside the rigid skull, and rising intracranial pressure (pressure inside the skull) will show up first as drowsiness, unequal pupils, or new weakness; catching these changes early lets the team give medicines or surgery to save brain tissue
3. Start IV acyclovir within 30 minutes of the order and give every 8 hours on time; hang each dose over 1 hour and flush the line with at least 100 mL normal saline after each infusion — Herpes simplex virus kills brain cells every hour treatment is delayed; acyclovir stops the virus from copying itself, but it crystallizes in the kidney tubules and causes kidney failure if we push it too fast or do not flush with extra fluid
4. Place the patient on continuous seizure precautions: padded side rails up, suction at bedside, IV access secure, and lorazepam 4 mg drawn up and ready; watch for subtle seizures like lip smacking, eye twitching, or staring spells — Inflamed brain tissue has a low seizure threshold (it fires off abnormal electrical activity easily), and ongoing seizures burn huge amounts of glucose and oxygen, killing more brain cells and causing permanent damage if they last more than 5 minutes
5. Keep the head of the bed elevated 30 degrees, keep the neck straight and midline, and avoid tight cervical collars or neck flexion — Elevating the head lets venous blood (blood returning from the brain) drain downward through the jugular veins using gravity, which lowers intracranial pressure; twisting or bending the neck kinks those veins and traps blood inside the skull
6. Maintain a quiet, dimly lit room; limit visitors to one at a time; cluster care to allow 90-minute rest periods; avoid sudden loud noises or bright overhead lights — Overstimulation—noise, light, or too much activity—raises metabolic demand in already-injured brain cells and can trigger seizures or agitation, which both increase intracranial pressure and oxygen consumption
7. Monitor strict intake and output every hour; alert the provider immediately if urine output drops below 30 mL per hour or if urine becomes dark or cloudy — Acyclovir crystallizes in the renal tubules (the tiny kidney filters) and plugs them, causing acute kidney injury; keeping urine flowing fast washes out crystals before they form stones, and dark urine or low output means crystals are already blocking the tubules

8. Check temperature every 2 hours and treat any fever above 38.3°C (101°F) promptly with acetaminophen 650 mg oral or rectal; use a cooling blanket if fever does not drop within 30 minutes — Fever increases the brain's metabolic rate by 10 percent for every 1°C rise in temperature, so the swollen brain needs even more oxygen and glucose that the damaged blood vessels cannot deliver; this mismatch kills more neurons

## Sources

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- IDSA Clinical Practice Guideline for Encephalitis 2008
- American Academy of Neurology Autoimmune Encephalitis Guidelines 2016
- CDC Arboviral Encephalitis
- Cochrane Systematic Reviews

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