

Myasthenia Gravis

Myasthenia gravis means your immune system attacks the docking stations where nerve messages land on muscle — so muscles get weaker the more you use them, then bounce back with rest.

THE ONE-LINE TRUTH

The immune system makes antibodies that block or destroy acetylcholine receptors at the neuromuscular junction (the tiny gap where a nerve ending talks to a muscle fiber), so the nerve's 'contract now' signal cannot get through.

The chain — how it unfolds

1. Autoantibodies (anti-AChR, anti-MuSK, or anti-LRP4) attach to acetylcholine receptors or the proteins that organize them at the neuromuscular junction. — why: The immune system mistakenly flags these receptors as foreign invaders (the trigger is often a thymus gland abnormality — about 10–15 % of myasthenia gravis patients have a thymoma [thymus tumor], and 70 % have thymic hyperplasia [an overgrown thymus]; the thymus teaches immune cells what to attack, and when it is abnormal it can train antibodies to attack self-proteins like acetylcholine receptors).
2. Antibodies block acetylcholine binding, cross-link receptors for internalization, and activate complement to destroy the motor endplate, so the number of working receptors drops. — why: Fewer receptors means each nerve impulse releases the same amount of acetylcholine but fewer molecules find a landing spot, so the endplate potential (the electrical bump that starts muscle contraction) is smaller and closer to the threshold for failure.
3. The first muscle contraction works fairly well because the remaining receptors are rested and ready, but repeated contractions (looking side to side, chewing, holding your arms up) rapidly deplete the small acetylcholine reserve in the nerve terminal and exhaust the limited receptor pool. — why: Each contraction uses up some acetylcholine and temporarily desensitizes some receptors; normally the safety margin is huge, but in myasthenia gravis the margin is paper-thin, so the third or fifth contraction may fail to generate enough endplate potential to fire the muscle.

4. Eye muscles (the extraocular muscles that move the eyeball, and the levator palpebrae that lifts the eyelid) fail first, causing a drooping eyelid (ptosis) (droopy eyelid, often worse at the end of the day or after reading) and diplopia (double vision because the two eyes no longer aim together). — why: Eye muscles are tiny, fire constantly to track and focus, and have the smallest neuromuscular safety margin in the body — they run on a lean receptor budget even when healthy, so any receptor loss shows up as weakness immediately. About 50 % of patients present with purely ocular symptoms, and 85 % have eye involvement at some point.
5. Bulbar muscles (the muscles of the face, throat, and tongue) weaken next, so speech becomes nasal or slurred (dysarthria, especially for long words or after talking for a while), chewing tires the jaw (you may need to prop your jaw with your hand halfway through a meal), and swallowing becomes unsafe (dysphagia, with risk of choking or aspiration because food or liquid slips into the airway). — why: Bulbar muscles are also small, work continuously (you swallow every few minutes even at rest, and talking requires fast, coordinated firing), and have less reserve than big limb muscles, so they hit the receptor floor early in the disease.
6. Proximal limb muscles (shoulders, hips) and neck extensors weaken, making it hard to lift arms overhead (combing hair, reaching a high shelf), climb stairs, stand from a chair, or hold the head up (the head may drop forward after sitting upright for a while). — why: These large muscles have more receptors and a bigger safety margin than eye or bulbar muscles, so they fail later — but once the disease is moderate or severe, even they cannot maintain force during sustained or repeated effort.
7. The diaphragm (the dome-shaped muscle under the lungs that does 70–80 % of the work of breathing) and the intercostal muscles (between the ribs) lose strength, so the patient cannot pull in a deep breath, vital capacity falls, and carbon dioxide starts to build up in the blood (hypercapnia). — why: Respiratory muscles are working every second and have no chance to rest, so when their receptor count drops below the critical threshold they simply cannot generate enough negative pressure to inflate the lungs — this is myasthenic crisis, the life-threatening emergency of myasthenia gravis, seen in about 15–20 % of patients at some point and requiring mechanical ventilation until treatment (plasmapheresis, intravenous immunoglobulin, or high-dose steroids) can reduce the antibody load and restore receptor function.
8. After rest (a nap, a night's sleep, or even just closing the eyes for a few minutes), strength partially returns because rested nerve terminals have rebuilt their acetylcholine stores and rested receptors have recovered from desensitization — but the underlying receptor shortage remains, so the fatigue pattern repeats with the next round of activity. — why: Fluctuating, fatigable weakness that improves with rest and worsens with repetitive use is the clinical signature of myasthenia gravis and distinguishes it from most other causes of weakness (which are usually constant or progressive rather than use-dependent).

Spot it — what you see, and why

- Drooping eyelid (ptosis) that gets worse when you look up for a long time: Acetylcholine receptors (the docking spots where nerve signals tell muscles to move) on the eyelid muscles are blocked by your own antibodies, so the signal fades quickly and the lid droops more and more as you use it.
- Double vision (diplopia) that comes and goes: The tiny muscles that move your eyes get weaker as you use them because antibodies block the acetylcholine receptors, so the eyes can't stay lined up and you see two images instead of one.
- Drooping or weak face muscles, especially when you chew, smile, or talk a lot: Face and jaw muscles depend on acetylcholine to fire, and when antibodies jam those receptors, the muscles tire out fast—your smile may fade or your jaw may droop mid-meal.
- Trouble swallowing (dysphagia) or slurred speech that gets worse as you talk: The muscles in your throat and voice box (bulbar muscles) use acetylcholine receptors to move; when antibodies block them, these muscles weaken with use, making words slur and food harder to push down.
- Arm or leg weakness that improves with rest and worsens with repeated movement: Antibodies block acetylcholine receptors on limb muscles, so the nerve signal gets weaker each time you lift or move—rest lets a few receptors recover, but the next round of movement fatigues them again.
- Trouble breathing or feeling short of breath, especially when lying flat or after activity: The diaphragm and chest-wall muscles (the muscles that pump air in and out) rely on acetylcholine; when antibodies block enough receptors, those muscles can't move air well, and you feel breathless or may stop breathing (myasthenic crisis).

Red flags — act now

- Trouble breathing, very short of breath, or can't take a deep breath (may mean the diaphragm is failing—myasthenic crisis—and you need emergency care right away)
- Choking often, coughing every time you swallow, or food or liquid going down the wrong pipe (aspiration risk—food can get into the lungs and cause pneumonia)
- Sudden big jump in weakness after starting a new medicine, after surgery, or during an infection (these can trigger a dangerous flare called a crisis)

Treat it — in this order

1. Pyridostigmine (acetylcholinesterase inhibitor), 30–60 mg by mouth every 4–6 hours → Blocks acetylcholinesterase (the enzyme that chops up acetylcholine in the synapse), so each molecule of acetylcholine stays around longer and gets more chances to bind to the few open receptors. This buys back some strength by stretching the signal. Weakness improves within 30 minutes to 2 hours.
2. Corticosteroids (prednisone 0.75–1 mg/kg/day, then taper) to suppress the immune system → Quiets the overactive immune system so it makes fewer antibodies against acetylcholine receptors and stops destroying them. Over weeks to months, more receptors survive and muscle strength improves. This treats the root cause.
3. Steroid-sparing immunosuppressants (azathioprine 2–3 mg/kg/day, mycophenolate 1000 mg twice daily, or rituximab for refractory cases) → Suppresses the immune cells (B cells and T cells) that make the anti-AChR or anti-MuSK antibodies, reducing antibody production and receptor destruction. Allows you to lower or stop steroids and avoid their side effects. Takes 6 to 12 months to reach full effect.
4. Thymectomy (surgical removal of the thymus gland) → The thymus (a small gland behind the breastbone) is where the immune system is trained; in myasthenia gravis, it often harbors the B cells making anti-AChR antibodies or contains a thymoma tumor that drives the autoimmune attack. Removing it reduces the antibody source and improves long-term remission rates, especially in AChR-positive patients under 60 years old.
5. Intravenous immunoglobulin (IVIG, 2 g/kg over 2–5 days) during myasthenic crisis or severe flare-up (exacerbation) → Floods the bloodstream with pooled antibodies from thousands of donors; these neutral antibodies bind to and block the receptors on immune cells (Fc receptors) that would otherwise help destroy acetylcholine receptors, and they dilute and clear the harmful anti-AChR antibodies. Strength improves within 3 to 7 days.

Your top priorities at the bedside

1. Assess respiratory effort every two to four hours: measure vital capacity (how much air the lungs can hold), watch for shallow breathing, use of neck muscles to breathe, and inability to cough or clear secretions — why: Myasthenic crisis causes respiratory muscle failure which is the number one cause of death; early detection lets us get the patient on a breathing machine before full respiratory arrest happens
2. Keep suction equipment and bag-valve mask at bedside; ensure rapid ICU transfer plan is ready — why: Respiratory failure can happen fast in myasthenic crisis; having emergency airway equipment immediately available saves minutes that prevent brain damage from low oxygen

3. Monitor swallowing carefully before every meal; keep patient upright at ninety degrees during and thirty minutes after eating; have patient take small bites and sips — why: Bulbar muscle weakness (throat and mouth weakness) causes aspiration (food or liquid going into lungs instead of stomach) which leads to aspiration pneumonia and worsens respiratory status