

Multisystem Inflammatory Syndrome in Children

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THE STORY IN ONE SENTENCE

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“Multisystem Inflammatory Syndrome in Children (MIS-C)”

Normal anatomy — the body's job

After any infection, the immune system has a two-part job: destroy the invader, then turn off the attack and clean up the mess. Special immune cells called regulatory T cells (Tregs) act like referees, telling the fighter cells to stand down once the virus is cleared. At the same time, the blood vessels stay calm and sealed tight, the heart pumps steadily, and the belly and other organs go back to their usual work. This shutdown phase is called immune resolution — everything returns to quiet and ready.

BODY'S JOB

The immune system's normal job after an infection is to recognize 'all clear,' stop making inflammatory chemicals (cytokines like IL-6, IL-1, and TNF-alpha — messengers that ramp up inflammation), pull back the attack cells, and let damaged tissue heal. The blood vessels relax, inflammation drops, and organs go back to normal. Think of it like turning off the fire alarm and sending the firefighters home once the fire is out.

1. COVID-19 virus enters the body and immune cells — T cells (squad leaders), B cells (antibody makers), and macrophages (cleanup crew) — swarm to fight it.
2. Once the virus is cleared, regulatory T cells (Tregs, the referees) release calming signals like IL-10 and TGF-beta (chemicals that say 'stop fighting') that tell the attack cells to quit making inflammatory chemicals.

3. Cytokine levels — IL-6 (an inflammation booster), TNF-alpha (another alarm signal), and IL-1 (a fever trigger) — drop back to normal. Blood vessels seal up, and tissues begin to repair.
4. The heart, blood vessels, gut, kidneys, and skin return to steady-state work with no leftover inflammation.

What breaks

In MIS-C, the immune system never gets the 'all clear' signal. Even though the COVID virus is long gone — usually 2 to 6 weeks earlier — the regulatory T cells (Tregs, the referees that tell the immune system to calm down) fail to shut down the attack. Instead, the immune system keeps making huge amounts of inflammatory chemicals (cytokines) as if the virus were still there. These chemicals flood the bloodstream and attack the child's own tissues — especially the lining of blood vessels (the endothelium, the thin inner coat of every blood vessel), the heart muscle (myocardium, the muscular walls that squeeze blood out), and the coronary arteries (the small arteries that feed the heart muscle itself). This runaway inflammation is why so many organs get hit at once.

CLINICAL TERM

Post-infectious hyperinflammatory syndrome with immune dysregulation. The upstream break is failure of immune resolution — regulatory T-cell (Treg) dysfunction allows unchecked cytokine storm (especially IL-6, IL-1 beta, and TNF-alpha) and complement activation (a cascade of immune proteins that amplifies inflammation). The downstream signs you see at the bedside are multisystem: shock (vasoplegic, often warm with high cardiac output early, then cold cardiogenic as myocarditis sets in), myocardial dysfunction (weakened heart muscle), coronary artery dilation or aneurysm, gastrointestinal inflammation, dermatologic and mucocutaneous findings (red eyes called conjunctivitis, rash, and changes in the lips and mouth), and acute kidney injury. All findings trace back to endothelial injury (damage to blood vessel linings) and cytokine-driven inflammation.

How the body compensates

The body tries to protect vital organs by ramping up heart rate, redistributing blood flow, and triggering fever to fight what it thinks is still an infection. Early on, kids can look deceptively stable — warm skin, normal or even high cardiac output (the heart pumping hard and fast) — because the heart is working overtime and blood vessels are wide open (vasodilated, widened to let more blood through). This warm shock phase hides how sick they really are. As the heart muscle weakens from inflammation (myocarditis, swelling and damage to the heart muscle) and fluid leaks everywhere (capillary leak, where blood vessels become porous like a sponge), compensation fails: blood pressure crashes, the heart can't pump enough (cardiogenic shock,

when the pump is too weak to push blood out), and organs start shutting down. The crash point to watch for is shock — especially cold shock with poor blood flow (perfusion) (cold, pale, or mottled skin, weak pulses, confusion) — and coronary artery complications. Once the heart tips into failure, the window to reverse damage narrows fast.

1. The body raises heart rate (tachycardia, a fast heartbeat) and dilates blood vessels (widens them) to try to keep oxygen delivery up even as inflammation leaks fluid out of the bloodstream and into tissues.
2. Fever stays high — often 38.0°C (100.4°F) or higher for 24 hours or more — as the hypothalamus (the brain's thermostat, a small region at the base of the brain) resets upward in response to cytokines (IL-1 and IL-6, chemicals that tell the brain to raise body temperature), trying to 'burn out' what it thinks is still an infection.
3. The heart pumps harder and faster (hyperdynamic phase, where cardiac output is high) to compensate for low blood pressure — skin may feel warm, pulses bounding (strong and forceful) — masking the true severity. This is called warm or vasodilatory shock (shock caused by blood vessels opening too wide and fluid leaking out, even though the heart is still pumping well).
4. As myocardial inflammation worsens, the heart muscle weakens — depressed ejection fraction (the percentage of blood squeezed out each beat drops, normal is 55–70%, in MIS-C it can fall to 30–40% or lower), elevated BNP or NT-proBNP (blood markers that rise when the heart is stretched and struggling), and elevated troponin (a protein that leaks from dying heart muscle cells). The heart can no longer keep up — cardiac output drops, blood pressure falls, and blood flow (perfusion) to organs fails. This is cold or cardiogenic shock (shock caused by a weak pump, with cold, clammy skin, weak pulses, and confusion).
5. The kidneys respond to low blood flow (perfusion) (not enough blood flow) by holding onto salt and water (the renin-angiotensin-aldosterone system, or RAAS, kicks in to try to boost blood volume) — urine output drops (oliguria, less than 0.5 mL/kg/hour), and creatinine rises (a waste product that builds up when the kidneys aren't filtering well). This worsens fluid overload and pulmonary edema (fluid flooding the lungs) (fluid backs up into the lungs, making breathing hard).
6. The liver and gut, starved of blood flow, leak enzymes — AST and ALT (liver enzymes) rise, showing liver cell damage — and cause worsening belly pain, nausea, vomiting, and diarrhea. Some children have such severe abdominal pain they are mistaken for having appendicitis or bowel obstruction.

7. The crash point is shock requiring inotropic support — medicines like epinephrine (adrenaline, which makes the heart squeeze harder and raises blood pressure) or milrinone (a drug that strengthens the heart's squeeze and relaxes blood vessels) — and/or coronary artery aneurysm rupture (the bulge bursts, cutting off blood to the heart) or clot formation (thrombosis) (a clot forms inside the aneurysm, blocking flow). Once the heart decompensates (tips into failure) or coronaries are damaged, morbidity (severe complications) and mortality (death) spike.

Domino effect

1. COVID-19 clears, but the immune system never shuts down — regulatory T cells (Tregs, the specialized cells that tell the immune system to stand down) fail and cytokines (IL-6, IL-1 beta, TNF-alpha — powerful alarm chemicals) flood the bloodstream. — The virus is gone, but the immune alarm stays on. Without the normal 'all clear' signal from Tregs, inflammatory chemicals keep pouring out as if the threat is still present, priming every organ for attack.
2. Cytokines attack the endothelium (the thin inner lining of every blood vessel, like the coating inside a pipe), causing widespread vascular inflammation and capillary leak (fluid seeps out of vessels into surrounding tissue). — The lining of every blood vessel swells and becomes porous like a leaky sponge — fluid seeps out into tissues, blood pressure drops, and clotting factors (proteins in the blood that form clots) get activated, setting up for shock and dangerous clots.
3. The heart muscle (myocardium, the thick muscular walls of the heart) becomes inflamed (myocarditis, inflammation of the heart muscle), weakening its pump and causing chest pain, elevated troponin (a blood marker of heart muscle damage), and falling ejection fraction (the percentage of blood pumped out each beat drops). — Inflammatory cells — T cells and macrophages — invade the heart muscle, damaging the myocytes (the cells that contract to squeeze blood out with each beat). The heart struggles to keep up, and pump failure looms.
4. The coronary arteries (the small arteries that wrap around the heart and feed it oxygen and nutrients) dilate (widen abnormally) and risk forming aneurysms (permanent balloon-like weak spots in the artery wall). — Inflammation weakens the walls of the coronary arteries, causing them to stretch and bulge — aneurysms can clot off (thrombosis, where a blood clot blocks the artery) or rupture (burst), starving the heart muscle of oxygen and causing a heart attack.

5. Shock develops: first warm shock (high heart rate, wide-open vessels, warm skin, strong pulses) then cold shock (weak heart, low output, cold clammy skin, weak pulses, organ failure). — Early, the body compensates by revving the heart (tachycardia) and dilating vessels (vasodilation) to keep blood moving despite leaky pipes — but as the heart weakens from myocarditis and fluid leaks everywhere (capillary leak), compensation breaks and blood pressure crashes into life-threatening shock.
6. Organs begin to fail: kidneys (rising creatinine, low urine output called low urine output (oliguria)), liver (elevated AST and ALT enzymes), gut (severe pain, bloody diarrhea), and brain (confusion, headache, irritability). — With poor blood flow (hypoperfusion) and ongoing inflammation, every organ is starved of oxygen and nutrients while being bathed in toxic cytokines — cells start dying, and multi-organ failure accelerates.
7. Without treatment — IVIG (intravenous immunoglobulin, a mix of antibodies that neutralizes cytokines and calms the immune system), steroids (strong anti-inflammatory drugs like methylprednisolone that shut down cytokine production), and supportive care (fluids, pressors like norepinephrine to raise blood pressure, inotropes like milrinone to strengthen the heart) — the cytokine storm and cardiac damage spiral toward irreversible shock, coronary clot formation (thrombosis) (clots in the heart arteries), or death. — The body's own attempt to fight an enemy that isn't there becomes the disease itself — you must shut down the hyperinflammation with immune-calming drugs and support the heart and circulation before permanent organ damage or death occurs.
8. With prompt treatment, most children recover fully, though some need long-term cardiology follow-up for coronary artery changes (monitoring for late clotting, narrowing (stenosis), or persistent aneurysms). — Catching MIS-C early and hitting the inflammation hard allows the immune system to reset, the heart to heal, and the blood vessels to recover — but any coronary aneurysms that formed need monitoring with echocardiograms (ultrasound of the heart) for months to years to watch for late clotting or narrowing that could cause a heart attack down the road.

Symptoms · what the patient feels, and why

- Fever lasting several days (usually 3 or more): Two to six weeks after fighting off COVID, the immune system gets confused and releases a huge wave of inflammation signals called cytokines (chemical messengers that turn on the body's defense system) — these signals crank up the body's thermostat in the hypothalamus (the brain's temperature control center) to make heat, creating a stubborn fever that will not break.
- Belly pain, throwing up, or diarrhea: The cytokine storm inflames the lining of the stomach and intestines (the mucosa) — the swollen tissue slows down digestion, traps gas and fluid, and irritates the nerve endings that trigger cramping, nausea, and urgent, loose stools.

- Rash, very red and cracked lips, and a bright red bumpy tongue (strawberry tongue): Inflammation damages the tiny blood vessels (capillaries) just under the skin, leaking fluid and red cells that show up as patches of rash; at the same time, the mucous membranes in the mouth swell, making the tongue puffy with big, red taste bumps (papillae) and causing lips to crack and redden.
- Red, bloodshot eyes without any gunk or yellow discharge: The clear membrane covering the white of the eye (the conjunctiva) becomes inflamed from the immune overreaction — the tiny blood vessels there swell and shine through as red streaks, but because there is no real infection, no bacteria or viruses are present to make pus or sticky discharge.
- Swollen, puffy hands or feet: Inflammation weakens the walls of small blood vessels in the hands and feet, allowing fluid from the blood to leak out into the surrounding tissue (edema) — this extra fluid pools under the skin and puffs up the fingers, palms, toes, and soles.
- Swollen lymph nodes in the neck: Lymph nodes are tiny bean-shaped filters packed with immune cells — when the immune system is on overdrive, the nodes fill with extra white blood cells trying to fight the inflammation, swelling into tender lumps you can feel under the jaw or along the neck.
- Fast heartbeat or chest pain: The heart muscle itself (the myocardium) or the thin sac around it (the pericardium) becomes inflamed and swollen — the irritated, stiff heart cannot pump smoothly, so it speeds up to try to move enough blood, and the inflamed tissue sends sharp or aching pain signals to the chest.
- Trouble breathing, very fast breathing, or shortness of breath: Inflammation in the lung tissue reduces oxygen exchange, or the weakened heart cannot pump blood forward efficiently so fluid backs up into the lungs (pulmonary swelling (edema)) — either way, oxygen levels drop and the brain tells the lungs to speed up to pull in more air.
- Extreme tiredness, confusion, or difficulty waking up: Inflamed, leaky blood vessels cause blood pressure to drop (hypotension), so less oxygen-rich blood reaches the brain — without enough oxygen and glucose fuel, the brain's nerve cells slow down, leading to confusion, heavy drowsiness, or trouble staying alert.

Focused exam

- Fever lasting 4 or more days, often high ($\geq 38.0^{\circ}\text{C}$ or $\geq 100.4^{\circ}\text{F}$): After fighting off COVID-19, the immune system sometimes gets stuck in overdrive mode. The virus is gone, but the immune cells keep pumping out inflammatory signals (cytokines like IL-1, IL-6, and TNF-alpha—chemicals that tell the body to heat up and fight). That relentless chemical storm shows up first as fever that won't quit, signaling the inflammation is spreading through the whole body.

- Rash on the trunk, arms, or legs—sometimes flat and red like measles, sometimes blotchy or sunburn-like: The runaway inflammation attacks the endothelium (the thin layer of cells lining all blood vessels). When those cells swell and leak, fluid seeps into the skin, causing a rash. This tells you the problem is not just one organ—it is spreading everywhere through the bloodstream.
- Swollen, red hands and feet; skin may peel days later: Inflammation damages the capillaries (the tiniest blood vessels) in the hands and feet, making them leak fluid into the surrounding tissue. The tissue puffs up and turns red. This is a hallmark of Kawasaki-like inflammation and points to the same hyperinflammation pathway at work in Multisystem Inflammatory Syndrome in Children.
- Red, cracked lips; bright red, bumpy tongue (strawberry tongue); red eyes without pus: The mucous membranes (the moist lining of the mouth and eyes) are packed with blood vessels. When cytokines inflame those vessels, they swell and turn red, making lips crack and dry out and the tongue look like a strawberry. Red eyes without pus (conjunctivitis) confirm the inflammation is hitting multiple body surfaces at once, not an infection.
- Belly pain, vomiting, or diarrhea: The gut has its own rich network of blood vessels in the intestinal wall. When inflammation damages those vessels, the intestines can't absorb nutrients or move food properly, causing pain, nausea, and diarrhea. Gut symptoms in Multisystem Inflammatory Syndrome in Children mean the inflammation has reached the digestive system too.
- Chest pain, shortness of breath, rapid heart rate, or signs of shock (pale or mottled skin, weak pulse, low blood pressure, cool hands and feet): The myocardium (heart muscle) and the coronary arteries (the vessels that feed the heart oxygen and nutrients) can become inflamed and swollen. When that happens, the heart struggles to pump blood, oxygen delivery to the whole body drops, and the child can slide into shock. This is the most dangerous complication of Multisystem Inflammatory Syndrome in Children and demands immediate intensive care.

Diagnostics · every test answers a question

- C-reactive protein (CRP) and red blood cell (erythrocyte) sedimentation rate (ESR) → How severe is the inflammation in the body right now?
- Complete blood count (CBC) with differential → Are the white blood cells, red blood cells, and platelets responding to the inflammation?
- Troponin and B-type natriuretic peptide (BNP or NT-proBNP) → Is the heart muscle damaged or struggling to pump?
- Echocardiogram (heart ultrasound) → Are the heart chambers pumping normally, and are the coronary arteries swollen?
- D-dimer and fibrinogen → Is the blood forming clots or breaking them down too fast?

- SARS-CoV-2 PCR (nasal swab) or antibody test (IgG, IgM) → Is there current or recent COVID-19 infection?
- Albumin and ferritin → Is the inflammation so severe that it is draining the body's protein stores and activating iron-storage systems?
- Procalcitonin → Is this inflammation from a bacterial infection or from the immune system misfiring?

Treatment logic

- Intravenous immunoglobulin (IVIG), typically 2 g/kg as a single infusion over 8–12 hours → Floods the bloodstream with ready-made antibodies pooled from thousands of healthy donors. These antibodies neutralize the runaway inflammatory signals (cytokines like IL-1, IL-6, TNF-alpha) and block the Fc receptors on immune cells (macrophages, neutrophils) that keep pumping out more inflammation. This calms the hyperinflammation, reduces fever, and protects blood vessels and organs from further damage.
- Corticosteroids (methylprednisolone 1–2 mg/kg per day IV, or equivalent dose of dexamethasone or prednisolone) → Shuts down the genes inside immune cells (T cells, macrophages) that code for inflammatory cytokines (IL-1, IL-6, TNF-alpha). Steroids bind to receptors in the nucleus of the cell and block the DNA from making more inflammatory proteins. This stops the immune cells from pumping out more signals, reduces swelling in blood vessel walls (the endothelium) and organs, and lets the heart, lungs, and gut recover function.
- Aspirin (anti-inflammatory dose 30–50 mg/kg per day divided into 4 doses in the acute phase, then low-dose 3–5 mg/kg per day once daily for antiplatelet effect) → Blocks cyclooxygenase (COX-1 and COX-2) enzymes inside cells, which stops the body from making prostaglandins (chemicals that drive inflammation, fever, and pain) and thromboxane (a chemical that makes platelets sticky and clump together). High-dose aspirin reduces vessel inflammation and fever. Low-dose aspirin prevents clots from forming in inflamed or swollen coronary arteries.
- Supportive care in the intensive care unit: continuous cardiorespiratory monitoring, oxygen, IV fluid boluses to maintain blood pressure, and sometimes inotropes (medicines like milrinone, epinephrine, or dobutamine to help the heart squeeze) or mechanical ventilation → Keeps oxygen flowing to the brain, kidneys, and other vital organs while the immune system calms down. IV fluid boluses (10–20 mL/kg of normal saline or lactated Ringer's) fill the blood vessels to support blood pressure if the child is in shock. Inotropes help a struggling heart pump harder by making the muscle contract more forcefully or relaxing the vessels so the heart doesn't have to push as hard. Mechanical ventilation takes over breathing if the lungs are too inflamed or full of fluid to work on their own.

- Serial echocardiograms and cardiac biomarkers (troponin, BNP or NT-proBNP) monitoring—initially at diagnosis, then at 1–2 weeks and 4–6 weeks → Detects early signs of myocarditis (heart muscle inflammation), weak pumping (low ejection fraction), or swelling in the coronary arteries (aneurysms defined as z-score ≥ 2.5). Catching these changes early lets the care team escalate therapy—add stronger immunosuppression (like the IL-1 blocker anakinra or IL-6 blocker tocilizumab) or start anticoagulation—before the heart fails or a clot blocks a coronary artery.
- Anticoagulation (low-molecular-weight heparin subcutaneously, or aspirin if milder risk) if coronary aneurysms (z-score ≥ 2.5) or severe hypercoagulable state (very high D-dimer, low platelets, low fibrinogen suggesting consumption) → Low-molecular-weight heparin (enoxaparin, dosed by weight) blocks factor Xa in the clotting cascade, stopping new clots from forming. Aspirin prevents platelets from clumping together. Both reduce the risk that a clot will form inside a swollen or damaged coronary artery and cause a heart attack (myocardial tissue death from blocked blood flow (infarction)) by blocking blood flow to the heart muscle.
- Escalation to biologic immunotherapy (anakinra, an IL-1 receptor blocker, or tocilizumab, an IL-6 receptor blocker) if the child does not respond to IVIG and steroids within 24–48 hours or has refractory shock → Anakinra blocks the receptor for interleukin-1 (IL-1), one of the key cytokines driving the inflammatory storm. Tocilizumab blocks the receptor for interleukin-6 (IL-6), another major inflammatory signal. By shutting down these specific pathways, biologics can break the cytokine loop when first-line therapy is not enough, allowing fever, shock, and organ inflammation to improve.

Medications

Intravenous Immunoglobulin (IVIG) · Immune modulator (antibody infusion)

IVIG is a liquid packed with healthy antibodies collected from thousands of blood donors. When we give it through an IV, those antibodies flood into the child's bloodstream and calm down the runaway immune attack. They grab onto and block the harmful antibodies the child's own immune system is making, turn down the alarm signals that tell white blood cells to attack, and help reset the immune system so it stops attacking the body's own blood vessels and organs.

1. Healthy donor antibodies enter the bloodstream through the IV line.
2. These antibodies attach to and neutralize the harmful antibodies the child is making against their own tissues.
3. The donor antibodies also bind to immune cells (macrophages, the cleanup crews, and B cells, the antibody factories) and signal them to slow down their attack.
4. Inflammation markers like cytokines (chemical alarm signals such as IL-6 and TNF-alpha) drop because the immune system gets the message to stand down.

5. Blood vessel walls begin to heal as the immune attack on them weakens and the swelling goes down.

SAFETY WATCH

Allergic reactions during the infusion (rash, fever, chills, headache) — nurses watch closely during and right after the infusion and can slow it down or give medicine to ease symptoms. · Headache (sometimes severe) in the hours or days after — this happens because the extra fluid and antibodies can raise pressure slightly around the brain and irritate the protective layers (the meninges). · Blood clots (rare but serious) — IVIG can make blood stickier, so doctors watch for warning signs like leg pain, swelling, chest pain, or trouble breathing. · Kidney stress (rare) — some IVIG products contain sugar (sucrose or maltose) that can hurt the kidneys if they are already weak, so doctors choose the right type and watch urine output and kidney blood tests. · Aseptic meningitis (sterile inflammation of the layers around the brain, rare) — causes severe headache, stiff neck, sensitivity to light, nausea, and vomiting a day or two after IVIG; it is not an infection but irritation from the antibodies. · Red blood cell destruction (Hemolysis) (breakdown of red blood cells, rare) — watch for dark urine, yellowing skin, or dropping red blood cell counts in the days after IVIG, especially if the child's blood type does not perfectly match the donor antibodies.

Methylprednisolone or Dexamethasone (corticosteroids) · Corticosteroid (immune suppressor and anti-inflammatory)

Steroids are powerful medicines that dial down inflammation all over the body. They work by slipping into immune cells and turning off the genes that make inflammatory chemicals (cytokines like TNF-alpha, IL-1, and IL-6). Think of it like flipping the 'off' switch inside the cells that are making the firestorm. This helps stop the immune attack on the heart, blood vessels, gut, and other organs so they can start to heal.

1. The steroid molecule (methylprednisolone or dexamethasone) enters immune cells.
2. Inside the cell, it binds to a docking site called the glucocorticoid receptor in the cytoplasm (the cell's inner gel).
3. The steroid-receptor pair moves into the nucleus (the cell's control center where DNA lives).
4. It attaches to DNA and turns off the genes that make cytokines (TNF-alpha, IL-1, IL-6, and others) and other inflammatory signals.
5. The cell stops churning out inflammation chemicals, so the attack on blood vessels and organs slows down and eventually stops.
6. Swelling drops, fever falls, blood vessels stop leaking, and organs begin to recover and heal.

SAFETY WATCH

High blood sugar (hyperglycemia) — steroids make cells resist insulin (the hormone that moves sugar out of blood and into cells), so blood sugar can spike; doctors check blood sugar regularly, especially in children with diabetes or obesity. · Increased infection risk — steroids dampen the whole immune system, making it harder to fight off new bacteria, viruses, or fungi, so watch for new fevers, cough, pain, or other signs of infection even while on treatment. · Mood and behavior changes — irritability, trouble sleeping, anxiety, restlessness, or (rarely) confusion, hallucinations, or extreme mood swings. · High blood pressure (hypertension) — steroids make the kidneys hold onto salt and water, raising blood volume and pressure. · Stomach irritation — can cause belly pain, nausea, or (rarely) ulcers or bleeding in the stomach lining, especially when combined with aspirin or other NSAIDs. · Bone weakening (osteoporosis with long-term use) — not usually a problem in the short courses (days to weeks) used for MIS-C, but worth knowing if treatment extends. · Masks other infections — because steroids hide fever and inflammation, a new bacterial or fungal infection might not show the usual warning signs like high fever or severe pain, so doctors stay vigilant. · Adrenal suppression (if used for weeks) — the body's own adrenal glands (the small glands above the kidneys that make natural steroids like cortisol) can slow down or stop making cortisol, so doctors taper the dose slowly rather than stopping suddenly.

Aspirin (low-dose or anti-inflammatory dose) · Antiplatelet agent and anti-inflammatory (NSAID)

Aspirin has two jobs in MIS-C. First, it keeps platelets (the tiny blood cell fragments that form clots) from sticking together, which lowers the risk of dangerous clots forming in inflamed blood vessels, especially the coronary arteries (the vessels that feed the heart muscle). Second, at higher doses, aspirin blocks an enzyme called cyclooxygenase (COX) inside cells, which stops the cells from making prostaglandins (chemicals that cause pain, fever, and swelling). This helps calm inflammation and bring down fever.

1. Aspirin enters the bloodstream after the child swallows the pill or liquid.
2. It permanently blocks the COX-1 enzyme inside platelets, so they can no longer make thromboxane A2 (a chemical signal that tells platelets to clump together).
3. Platelets stay slippery and do not stick together as easily, so dangerous clots are less likely to form in inflamed or damaged coronary arteries.
4. At the same time, aspirin blocks COX enzymes in other cells throughout the body, stopping them from making prostaglandins.
5. Less prostaglandin means less pain signal sent to the brain, less fever (because prostaglandins raise the brain's temperature set-point), and less swelling in tissues.

SAFETY WATCH

Bleeding risk — because aspirin makes platelets less sticky, any cuts, scrapes, or injuries bleed longer than usual; watch for nosebleeds, easy bruising, tiny red spots on the skin (petechiae), blood in stool (black or red poop), or blood in urine (pink or red pee). · Stomach irritation (gastritis) — aspirin can hurt the stomach lining, causing pain, nausea, heartburn, or (rarely) ulcers or bleeding; giving it with food or milk helps protect the stomach. · Reye syndrome (rare but serious) — a dangerous condition that damages the liver and brain, seen mostly when aspirin is given to children with certain viral infections like influenza (flu) or varicella (chickenpox). In MIS-C, the benefits of aspirin usually outweigh this small risk, but doctors watch liver blood tests (AST, ALT) and mental status (alertness, confusion) closely, especially in younger children. · Allergic reactions — rash, hives, wheezing, trouble breathing, or swelling of the face or throat (rare but urgent if it happens). · Ringing in the ears (tinnitus) or hearing changes — a sign the dose might be too high, especially at anti-inflammatory doses; let the care team know right away. · Do not give aspirin at the same time as live-virus vaccines (like varicella or MMR) without checking with the care team, because of the Reye syndrome risk if a vaccine virus is circulating.

Anakinra (IL-1 receptor antagonist) · Interleukin-1 (IL-1) blocker (biologic immune modulator)

Anakinra blocks interleukin-1 (IL-1), one of the most powerful alarm chemicals the immune system makes. IL-1 is like a megaphone telling the body to ramp up inflammation, fever, and tissue damage. Anakinra works by sitting on the receptors (the docking sites on cells) where IL-1 usually lands, so the real IL-1 cannot get through and deliver its inflammatory message. Think of it like plugging the lock so the alarm key cannot turn it. This helps calm the runaway inflammation in children with very severe MIS-C who are not improving enough with IVIG and steroids alone.

1. Anakinra is injected under the skin (subcutaneous) or given through an IV and enters the bloodstream.
2. It travels to cells throughout the body and attaches to IL-1 receptors on the surface of immune cells and blood vessel cells.
3. By blocking the receptor, anakinra prevents the real IL-1 (made by overactive immune cells) from landing and turning on inflammation genes inside the cell.
4. Without IL-1's signal, the cell does not make more cytokines (like IL-6 and TNF-alpha), does not call more white blood cells to the area, and does not ramp up fever or tissue damage.
5. Inflammation cools down, fever drops, blood vessel damage slows, and organs start to recover.

SAFETY WATCH

Infection risk — anakinra dampens a key part of the immune defense, making it harder to fight bacteria, fungi, and some viruses; watch for new fever, cough, pain, redness, or pus. · Injection site reactions — redness, swelling, itching, or pain where the shot goes in (common with subcutaneous injections, usually mild). · Low white blood cell count (neutropenia, rare) — doctors check blood counts to make sure infection-fighting cells do not drop too low. · Allergic reactions — rash, hives, trouble breathing, or swelling (rare but stop the medicine and get help right away if it happens). · Liver enzyme changes (rare) — doctors monitor liver blood tests. · Do not give live vaccines while on anakinra without checking with the care team.

Infliximab or Tocilizumab (biologic cytokine blockers) · Monoclonal antibody (biologic immune modulator) — Infliximab blocks TNF-alpha; Tocilizumab blocks IL-6

These are targeted biologic medicines used in severe or treatment-resistant MIS-C. Infliximab grabs onto TNF-alpha (tumor tissue death (necrosis) factor alpha), a powerful inflammatory alarm chemical, and stops it from landing on cells and turning on inflammation. Tocilizumab blocks the receptor for IL-6 (interleukin-6), another major inflammation driver that is often sky-high in MIS-C. By blocking these specific cytokines, the medicines shut down key pathways that drive the runaway immune attack, helping the body calm down when IVIG and steroids are not enough.

1. The biologic antibody is given through an IV and enters the bloodstream.
2. Infliximab binds directly to TNF-alpha molecules floating in the blood and tissue, neutralizing them so they cannot attach to cells and trigger inflammation.
3. Tocilizumab attaches to the IL-6 receptor on the surface of cells, blocking IL-6 from landing and activating inflammation genes inside the cell.
4. With TNF-alpha or IL-6 blocked, the cell does not make more inflammatory chemicals, does not recruit more attack cells, and does not keep damaging tissue.
5. Inflammation markers (like CRP and ferritin) drop, fever goes down, blood vessel swelling decreases, and organ function improves.

SAFETY WATCH

Serious infection risk — blocking TNF-alpha or IL-6 makes it much harder to fight bacteria (especially tuberculosis and other hidden infections), fungi, and some viruses; doctors screen for TB and hepatitis before starting and watch closely for any new infections. · Infusion reactions — fever, chills, rash, low blood pressure, or trouble breathing during or right after the IV (more common with infliximab); nurses watch closely and can slow the infusion or give medicine to ease symptoms. · Liver enzyme changes — both medicines can raise liver blood tests; doctors monitor AST, ALT, and bilirubin. · Low white blood cell or platelet counts (rare) — doctors check blood counts regularly. · Heart failure worsening (mostly a concern with infliximab in adults with existing heart failure, less common in children, but doctors monitor heart function). · Reactivation of latent infections like tuberculosis or hepatitis B — screening and monitoring are key. · Allergic reactions (rare) — rash, hives, severe swelling, or anaphylaxis. · Do not give live vaccines while on these medicines without talking to the care team.

Red flags

- Chest pain, trouble breathing, or very fast breathing — the heart muscle or lungs may be severely inflamed and struggling to work, risking heart failure or dangerous drops in oxygen.
- Confusion, extreme drowsiness, or difficulty waking the child — blood pressure may be dangerously low, starving the brain of oxygen and signaling possible shock.
- Severe belly pain that does not go away — inflammation may be causing dangerous swelling, fluid buildup in the abdomen, or even damage to organs like the pancreas or liver.
- Pale, cold, or blotchy skin with a weak, racing pulse — signs that blood pressure has dropped so low the body is going into shock and cannot deliver blood to vital organs.
- Little or no urine output for many hours — the kidneys are not getting enough blood flow and may be starting to fail (acute kidney injury).

Nursing priorities

1. Place child on continuous cardiac monitor and pulse oximeter, measure blood pressure every 1 to 2 hours — MIS-C causes myocarditis (heart muscle inflammation) and can quickly lead to arrhythmias (irregular heartbeat), low cardiac output (weak heart pumping), and shock (dangerously low blood pressure). Early detection allows immediate treatment before cardiac arrest.

2. Establish large-bore IV access and monitor strict intake and output every hour — Children with MIS-C often need rapid fluid resuscitation (giving IV fluids quickly) for shock, plus IVIG (intravenous immunoglobulin) infusions. Tracking fluid balance prevents overload that worsens heart failure while ensuring adequate kidney blood flow (perfusion) (blood flow to kidneys).
3. Assess for signs of shock: cold hands and feet, delayed capillary refill over 3 seconds, weak pulses, low urine output under 1 mL/kg/hour — MIS-C causes vasodilatory shock (blood vessels relax too much) and cardiogenic shock (heart too weak to pump). Catching early shock allows vasopressor (blood pressure medicine) support before organ damage occurs.
4. Monitor respiratory status including work of breathing, oxygen saturation, and lung sounds every 2 to 4 hours — Inflammation causes fluid to leak into lungs creating pulmonary edema (fluid flooding the lungs) (lung swelling) and ARDS (acute respiratory distress syndrome, severe lung injury). Early detection guides oxygen therapy, diuretic (water pill) use, and prevents respiratory failure.
5. Draw and monitor cardiac biomarkers including troponin (heart enzyme), BNP (brain natriuretic peptide, heart stress hormone), and inflammatory markers like CRP (C-reactive protein) and ferritin as ordered — Troponin shows active heart muscle damage. BNP shows how hard the heart is working. Rising levels indicate worsening cardiac function requiring treatment escalation. CRP and ferritin track inflammation response to IVIG and steroids.
6. Perform complete skin assessment and document rash location, eye redness, mouth changes, and swelling of hands or feet — Mucocutaneous findings (skin and mucous membrane changes) help confirm MIS-C diagnosis versus sepsis (infection in bloodstream) or toxic shock syndrome. Tracking changes shows treatment response and rules out drug reactions.
7. Assess neurological status including level of consciousness, pupil response, and behavior changes every 2 to 4 hours — Brain poor blood flow (hypoperfusion) (not enough blood flow to brain) from shock causes altered mental status. Some children develop aseptic meningitis (brain lining inflammation without bacteria). Changes signal need for brain imaging or shock treatment intensification.
8. Administer aspirin with food or milk and monitor for bleeding signs including gums, stool, and bruising — High-dose aspirin prevents platelet clumping (blood cells sticking together) to reduce coronary artery clot formation (thrombosis) (blood clots in heart arteries) risk but increases bleeding risk. Gastric protection (stomach protection) prevents ulcers. Monitoring catches complications early.

Sources

- CDC MIS-C case definition and clinical guidance
- American Academy of Pediatrics (AAP) MIS-C interim guidance

- WHO preliminary case definition for multisystem inflammatory syndrome in children
- American College of Rheumatology MIS-C clinical guidance

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