

Microangiopathic Hemolytic Anemia (MAHA)

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THE STORY IN ONE SENTENCE

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“Microangiopathic destroying red blood cells (hemolytic) anemia happens when red blood cells get torn apart while traveling through damaged or blocked tiny blood vessels. This releases hemoglobin into the bloodstream and causes anemia, yellowing of the skin and eyes (jaundice), and organ damage. Common causes include TTP, HUS, DIC, and severe high blood pressure.”

Normal anatomy — the body's job

Red blood cells (erythrocytes) are flexible disk-shaped cells that carry oxygen from the lungs to all body tissues. They flow smoothly through arteries, capillaries (the tiniest blood vessels), and veins without breaking. The inner lining of blood vessels (endothelium) is smooth and releases chemicals that prevent clots from forming. Red blood cells live about 120 days before being removed by the spleen.

BODY'S JOB

Red blood cells are like soft rubber water balloons traveling through a network of pipes—they squeeze and bend to fit through narrow spaces, then pop back into shape without breaking.

1. Red blood cells are made in bone marrow and released into the bloodstream as flexible biconcave disks.
2. They travel through large arteries that branch into smaller arterioles.
3. Cells squeeze through capillaries only 5 to 10 micrometers wide (smaller than the cell itself).

4. Smooth endothelial cells lining the vessels produce nitric oxide and prostacyclin to prevent clotting.
5. Red cells deliver oxygen to tissues and pick up carbon dioxide waste.
6. After 120 days, old red cells are removed by the spleen and recycled.

What breaks

In MAHA, something damages the lining of small blood vessels or causes fibrin strands (tiny protein threads) to form clots inside them. When red blood cells try to squeeze through, the sharp edges slice them into pieces called schistocytes (fragmented red cells). The cells break open, spilling hemoglobin into the blood and causing anemia and organ damage.

CLINICAL TERM

Endothelial injury (damage to vessel lining) or intravascular fibrin deposition (clot protein strands inside vessels) creates physical obstacles in capillaries and arterioles. Red blood cells (Erythrocytes) (red blood cells) undergo mechanical fragmentation (physical tearing) as they pass through narrowed or obstructed microvessels, producing schistocytes (helmet cells, triangular fragments) on blood smear. This intravascular red blood cell destruction (hemolysis) (red cell destruction inside vessels) releases free hemoglobin, lactate dehydrogenase (LDH), and causes consumption of haptoglobin (a protein that binds free hemoglobin).

How the body compensates

The bone marrow responds to anemia by increasing red blood cell production, releasing reticulocytes (young red cells) into the bloodstream. The kidneys produce more erythropoietin (a hormone that stimulates red cell production), and the liver works to clear free hemoglobin and bilirubin (a yellow breakdown product). However, if red blood cell destruction (hemolysis) continues faster than the marrow can replace cells, severe anemia develops.

1. {'step': 'Kidney detection of low oxygen', 'detail': 'Kidneys sense decreased oxygen delivery from anemia and release erythropoietin hormone into the blood.'}
2. {'step': 'Bone marrow stimulation', 'detail': 'Erythropoietin signals bone marrow to speed up red blood cell production and release reticulocytes early.'}
3. {'step': 'Reticulocytosis', 'detail': 'Young red cells (reticulocytes) appear in blood within 3 to 5 days, seen as polychromasia (blue-tinged cells) on blood smear.'}
4. {'step': 'Haptoglobin binding', 'detail': 'Haptoglobin protein binds free hemoglobin released from broken red cells to prevent kidney damage, but stores become depleted quickly.'}

5. {'step': 'Hemoglobin breakdown', 'detail': 'The liver converts free hemoglobin into unconjugated bilirubin, causing yellowing of the skin and eyes (jaundice) (yellowing) and dark urine from hemoglobinuria (hemoglobin in urine).'}
6. {'step': 'Spleen activation', 'detail': 'The spleen removes damaged red cells and schistocytes, but becomes overwhelmed if red blood cell destruction (hemolysis) is severe or ongoing.'}

Domino effect

1. Endothelial injury or intravascular clot formation begins in microvessels — Triggering cause (Shiga toxin, ADAMTS13 deficiency, DIC, malignant high blood pressure (hypertension), or cancer) damages vessel walls or activates clotting.
2. Fibrin strands and platelet microthrombi form mesh-like networks in capillaries — Damaged endothelium exposes tissue factor and von Willebrand factor, triggering localized clotting and platelet aggregation.
3. Red blood cells fragment into schistocytes as they pass through narrowed vessels — Physical shearing forces exceed membrane strength, creating helmet cells, triangular fragments, and cell rupture.
4. Intravascular red blood cell destruction (hemolysis) releases free hemoglobin, LDH, and depletes haptoglobin — Broken red cells spill their contents into plasma, overwhelming the body's ability to bind and clear hemoglobin.
5. Anemia worsens as red cell destruction exceeds bone marrow production — Ongoing red blood cell destruction (hemolysis) consumes red cells faster than reticulocytes can replace them, dropping hemoglobin to 6 to 8 g/dL or lower.
6. Tissue low oxygen (hypoxia) develops as oxygen delivery falls — Fewer functional red cells combined with blocked microvessels reduces oxygen reaching brain, kidneys, heart, and other organs.
7. Organ starved blood flow (ischemia) and tissue death from blocked blood flow (infarction) occur from combined anemia and microvascular blockage (occlusion) — Brain (stroke, confusion), kidneys (acute kidney injury), heart (ischemia, arrhythmias), and gut (ischemia) sustain damage from clots and low oxygen.
8. Multi-organ failure and death if untreated — Without treatment (plasmapheresis for TTP, supportive care for HUS, treating DIC cause, controlling high blood pressure (hypertension)), progressive starved blood flow (ischemia) leads to renal failure, neurologic injury, cardiac arrest, or fatal bleeding.

Symptoms · what the patient feels, and why

- Dark or tea-colored urine: Hemoglobin (oxygen-carrying protein from broken red blood cells) passes through kidneys into urine when cells rupture in small vessels
- Pale skin and mucous membranes: Anemia (low red blood cell count) reduces hemoglobin available to give skin its pink color
- Fatigue and weakness: Fewer red blood cells deliver less oxygen to muscles and organs, forcing body to work harder for basic tasks
- Shortness of breath with mild activity: Reduced oxygen delivery from anemia forces faster breathing to compensate for decreased oxygen-carrying capacity
- Yellowing of skin or eyes (jaundice): Bilirubin (yellow breakdown product of hemoglobin) accumulates when red blood cells are destroyed faster than liver can process the waste
- Pinpoint bleeding spots (Petechiae) or purple bleeding blotches (purpura) (small red or purple spots on skin): Low platelets (blood-clotting cells) from consumption in microthrombi (tiny clots) allow small bleeds under skin
- Confusion or altered mental status: Microthrombi block blood flow in brain capillaries or severe anemia reduces oxygen to brain tissue
- Decreased urine output: Microthrombi damage kidney glomeruli (tiny filters) and hemoglobin clogs kidney tubules, reducing filtration

Focused exam

- Blood pressure measurement in both arms: Malignant high blood pressure (hypertension) (>180/120) directly injures endothelial cells lining small vessels, causing MAHA; requires immediate treatment to prevent stroke and kidney failure
- Neurologic examination including mental status, speech, focal weakness, and gait: TTP causes brain microthrombi in 40-60% of cases, producing confusion, stroke symptoms, or seizures; neurologic deficits predict higher mortality
- Skin and mucous membrane inspection for pinpoint bleeding spots (petechiae), purple bleeding blotches (purpura), yellowing of the skin and eyes (jaundice), and pale skin (pallor): Pinpoint bleeding spots (Petechiae) and purple bleeding blotches (purpura) indicate severe a low platelet count (thrombocytopenia) (low platelets); yellowing of the skin and eyes (jaundice) shows red blood cell destruction (hemolysis); pale skin (pallor) reflects anemia severity
- Abdominal examination for tenderness, an enlarged liver and spleen (hepatosplenomegaly), and fluid buildup in the belly (ascites): Right upper quadrant tenderness suggests HELLP syndrome; an enlarged spleen (splenomegaly) may indicate alternative causes like lymphoma or autoimmune red blood cell destruction (hemolysis)

- Cardiac listening with a stethoscope (auscultation) for murmurs and mechanical valve sounds: New or changing murmurs indicate valve dysfunction causing shear stress on red blood cells; helps identify mechanical red blood cell destruction (hemolysis) as the cause
- Volume status assessment including jugular venous pressure, lung sounds, and swelling (edema): Fluid overload from acute kidney injury requires diuretic adjustment; dehydration from diarrhea in HUS needs careful rehydration to protect kidneys

Diagnostics · every test answers a question

- Peripheral blood smear microscopy → Are schistocytes (fragmented red blood cells) present, confirming mechanical destruction in small vessels?
- Complete blood count with differential → How severe is the anemia and a low platelet count (thrombocytopenia), and are other cell lines affected?
- Lactate dehydrogenase (LDH) → Is there biochemical evidence of red blood cell breakdown releasing intracellular enzymes?
- Haptoglobin level → Is free hemoglobin in plasma being consumed by this scavenger protein?
- ADAMTS13 activity and inhibitor assay → Is severe deficiency of this von Willebrand factor-cleaving enzyme causing TTP?
- Creatinine and blood urea nitrogen → How severely are the kidneys damaged by microthrombi and hemoglobin toxicity?
- Shiga toxin stool testing or culture for E. coli O157:H7 → Is bacterial infection with Shiga toxin the trigger for HUS?
- Direct antiglobulin test (Coombs test) → Is immune-mediated red blood cell destruction (hemolysis) (antibodies coating red blood cells) the cause instead of mechanical destruction?

Treatment logic

- Plasma exchange (plasmapheresis) → Removes ADAMTS13 autoantibodies and replenishes functional enzyme in TTP; reduces mortality from 90% to 10-20% when started immediately
- Packed red blood cell transfusion → Improves oxygen delivery when hemoglobin drops below 7 g/dL or patient has chest pain, severe shortness of breath, or altered mental status from anemia
- Supportive care with IV fluids and electrolyte monitoring → Prevents dehydration-induced kidney damage in HUS; corrects electrolyte imbalances (hyperkalemia, metabolic acidosis (acid building up in the blood)) from kidney injury; maintains adequate blood flow (perfusion)

- Delivery of fetus and placenta in pregnancy-related MAHA → Removes the trigger for HELLP syndrome and severe preeclampsia; usually resolves red blood cell destruction (hemolysis) and a low platelet count (thrombocytopenia) within 48-72 hours postpartum
- Blood pressure control to target <140/90 in malignant high blood pressure (hypertension) → Reduces shear stress on vessel walls and stops endothelial injury that triggers microthrombi; allows vessel healing over days to weeks
- Avoidance of platelet transfusion in TTP unless life-threatening bleeding → Prevents adding fuel to microthrombi formation; observational data suggest platelet transfusion may increase thrombotic complications in TTP

Medications

caplacizumab · Anti-von Willebrand factor nanobody (monoclonal antibody fragment)

Caplacizumab is a tiny antibody piece that blocks von Willebrand factor (a sticky protein) from attaching to platelets. When von Willebrand factor cannot grab platelets, it stops forming the abnormal clumps in small blood vessels that destroy red blood cells. This drug works immediately while plasma exchange removes the autoantibodies causing TTP.

1. Caplacizumab binds to the A1 domain of ultra-large von Willebrand factor multimers in plasma
2. Binding blocks the site where von Willebrand factor normally attaches to platelet GPIb receptors
3. Platelets cannot stick to von Willebrand factor or each other to form microthrombi
4. Existing microthrombi stop growing and red blood cells pass through vessels without fragmenting
5. Platelet count rises quickly (often within 3 days) as consumption in clots decreases

SAFETY WATCH

Bleeding risk increases, especially mucosal bleeding (nosebleeds, gum bleeding); hold for major surgery · Continue for 30 days after stopping plasma exchange to prevent early relapse · Monitor platelet count; rebound a low platelet count (thrombocytopenia) can occur after stopping · Contraindicated in inherited TTP (congenital ADAMTS13 deficiency) where it offers no proven benefit

rituximab · Anti-CD20 monoclonal antibody (B-cell depleting immunosuppressant)

Rituximab finds and kills the B-cells (white blood cells) that make autoantibodies against the ADAMTS13 enzyme in acquired TTP. By removing these antibody-producing cells, the drug stops new autoantibodies from forming and allows normal ADAMTS13 levels to return. Effects begin in days but peak benefit takes weeks as existing antibodies clear.

1. Rituximab binds to CD20 protein on surface of mature B-cells and some pre-B cells
2. Immune system recognizes antibody-coated B-cells as targets for destruction
3. Complement cascade and natural killer cells destroy marked B-cells within hours to days
4. Production of new ADAMTS13 autoantibodies stops as antibody-making cells disappear
5. ADAMTS13 enzyme levels gradually rise over 2-4 weeks as autoantibody levels fall

SAFETY WATCH

Infusion reactions common (fever, chills, rash); premedicate with acetaminophen and antihistamine · Severe immunosuppression lasting 6-12 months increases infection risk; avoid live vaccines · Progressive multifocal leukoencephalopathy (rare fatal brain infection) reported; watch for new neurologic symptoms · Reactivation of hepatitis B can occur; screen for hepatitis before starting

prednisone or methylprednisolone · Corticosteroid immunosuppressant

Corticosteroids reduce production of autoantibodies against ADAMTS13 by suppressing B-cell and T-cell activity. They also decrease inflammation in small blood vessels damaged by microthrombi. Steroids are added to plasma exchange and rituximab to speed remission and reduce relapse risk in acquired TTP.

1. Corticosteroid enters immune cells and binds to intracellular glucocorticoid receptors
2. Receptor-steroid complex moves into cell nucleus and alters gene transcription
3. Production of inflammatory cytokines (IL-2, IL-6, TNF-alpha) decreases
4. B-cell activation and proliferation slow, reducing autoantibody synthesis
5. Endothelial cell inflammation decreases, stabilizing vessel walls

SAFETY WATCH

High blood sugar (Hyperglycemia) common; monitor blood sugar closely in diabetic patients · Infection risk increases with prolonged use; watch for fever or unusual symptoms · Taper slowly over weeks to months to prevent adrenal insufficiency · Gastritis and peptic ulcers possible; consider proton pump inhibitor if risk factors present

eculizumab or ravulizumab · Anti-C5 complement inhibitor (monoclonal antibody)

These drugs block the C5 protein in the complement system (part of immune defense). Atypical HUS happens when complement attacks the body's own blood vessel lining. By stopping C5 from splitting into C5a and C5b, the drug prevents the membrane attack complex from punching holes in endothelial cells that trigger microthrombi formation.

1. Eculizumab or ravulizumab binds to complement protein C5 in bloodstream
2. Binding prevents C5 convertase enzyme from cleaving C5 into C5a and C5b fragments
3. Without C5b, the membrane attack complex (C5b-9) cannot form on cell surfaces
4. Endothelial cells are protected from complement-mediated lysis and injury
5. Microthrombi formation decreases as endothelial damage and platelet activation stop

SAFETY WATCH

Meningococcal infection risk markedly increased; vaccinate at least 2 weeks before starting or give antibiotics if urgent · Revaccinate every 3-5 years against meningococcus while on therapy · Monitor for breakthrough red blood cell destruction (hemolysis) if drug levels drop or C5 polymorphisms present · Extremely expensive; requires long-term or lifelong therapy in most atypical HUS cases

folic acid supplementation · Water-soluble B vitamin (folate)

Folic acid is needed to make new red blood cells in bone marrow. When red blood cell destruction (hemolysis) destroys red blood cells rapidly, the body uses up folate stores trying to replace them. Supplementing 1 mg daily prevents folate deficiency that would make anemia worse by impairing red blood cell production.

1. Folic acid is absorbed in small intestine and converted to active tetrahydrofolate
2. Tetrahydrofolate provides one-carbon units needed for purine and thymidine synthesis
3. DNA synthesis proceeds normally in rapidly dividing erythroid cells
4. Red blood cell production (erythropoiesis) keeps pace with destroying red blood cells (hemolytic) destruction
5. Reticulocyte count (young red blood cells) remains appropriately elevated

SAFETY WATCH

High doses can mask vitamin B12 deficiency; check B12 if macrocytic anemia present · Generally very safe with minimal side effects at 1 mg daily dose · Needs continued supplementation as long as red blood cell destruction (hemolysis) persists

renal replacement therapy (hemodialysis or peritoneal dialysis) · Non-pharmacologic intervention for kidney failure

When microthrombi destroy enough kidney glomeruli, waste products (creatinine, urea) and excess fluid accumulate because kidneys cannot filter blood. Dialysis temporarily replaces this filtering function by removing toxins and fluid across an artificial membrane. In HUS, 50-70% of children need temporary dialysis, though most recover kidney function within weeks.

1. Blood flows across semipermeable membrane with dialysate solution on other side
2. Concentration gradient causes urea, creatinine, and excess potassium to move into dialysate
3. Ultrafiltration removes excess body water to control blood pressure and prevent pulmonary edema (fluid flooding the lungs)
4. Bicarbonate diffuses from dialysate into blood to correct metabolic acidosis (acid building up in the blood)
5. Cleaned blood returns to body until next treatment session (typically 3 times weekly if hemodialysis)

SAFETY WATCH

Vascular access complications (bleeding, infection, clotting) in hemodialysis · Low blood pressure (Hypotension) during rapid fluid removal requires careful monitoring · Peritonitis risk with peritoneal dialysis requires sterile technique · Most patients with STEC-HUS recover kidney function and stop dialysis within 2-4 weeks

Red flags

- Platelet count below 30,000/microL with confusion or neurologic changes suggests TTP requiring immediate plasma exchange
- Hemoglobin below 7 g/dL with chest pain or severe shortness of breath needs urgent transfusion
- Creatinine rising despite fluids with decreased urine output indicates acute kidney injury needing nephrology consultation
- New pinpoint bleeding spots (petechiae) or purple bleeding blotches (purpura) with any mucosal bleeding requires platelet count check and hematology evaluation within hours

Nursing priorities

1. Monitor for signs of organ damage from microthrombi (tiny blood clots) — MAHA causes small clots in tiny blood vessels that block blood flow to the brain, kidneys, and heart. Early detection of stroke symptoms, decreased urine output, or chest pain allows rapid intervention.
2. Assess for bleeding tendencies despite low platelet count — The destruction of platelets (blood-clotting cells) in small vessels causes a low platelet count (thrombocytopenia) (low platelet count). Patients may bruise easily, have pinpoint bleeding spots (petechiae) (tiny red spots), or bleed from gums or nose.
3. Evaluate neurologic status every 2-4 hours — Brain microthrombi cause fluctuating confusion, headache, vision changes, or seizures in thrombotic thrombocytopenic purple bleeding blotches (purpura) (TTP) and other MAHA causes. Subtle changes require urgent provider notification.
4. Protect patient from falls and injury — Anemia (low red blood cell count) causes weakness and dizziness, while neurologic changes impair judgment and coordination. Bleeding risk from low platelets makes injuries more dangerous.
5. Monitor urine output and color hourly — Red blood cell destruction (Hemolysis) (red blood cell destruction) releases hemoglobin (the oxygen-carrying protein) that damages kidneys and turns urine dark brown or red. Acute kidney injury develops in 50% of severe MAHA cases.
6. Prepare for urgent plasmapheresis (plasma exchange) in TTP — TTP is fatal in 90% of untreated cases but survival exceeds 80% with prompt plasmapheresis. Large-bore IV access and coordination with apheresis (blood-filtering) teams saves lives.
7. Hold all antiplatelet and anticoagulant medications until provider review — Aspirin, heparin, and warfarin worsen bleeding in a low platelet count (thrombocytopenia). However, the underlying cause (like disseminated intravascular coagulation) may eventually require anticoagulation, so provider decision is essential.
8. Educate family about disease severity and need for ICU monitoring — MAHA can deteriorate rapidly with multi-organ failure. Families need preparation for intensive interventions like dialysis (artificial kidney filtering), mechanical ventilation (breathing machine), or plasmapheresis.

Sources

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