

TTP and HUS

TTP and HUS both cause broken red blood cells and low platelets from tiny clots in small vessels—TTP needs plasma exchange immediately.

THE ONE-LINE TRUTH

Tiny clots form throughout small blood vessels, shredding red blood cells and using up platelets.

The chain — how it unfolds

1. ADAMTS13 enzyme is absent or blocked (TTP), or vessel lining is injured by toxin or complement (HUS). — why: In TTP, autoantibodies destroy ADAMTS13 or a person is born without the gene to make it. In typical HUS, Shiga toxin from *E. coli* binds to and kills endothelial cells in the kidneys. In atypical HUS, mutations let complement proteins attack the body's own vessel walls. This is the single upstream break.
2. Giant vWF tangles trap platelets (TTP) or damaged vessel walls activate platelets (HUS), forming microthrombi in small vessels throughout the body. — why: Without ADAMTS13 cutting vWF, ultra-large multimers stay sticky and spontaneously bind platelets. In HUS, injured endothelium exposes clotting triggers. Either way, platelets clump into tiny clots that clog capillaries.
3. Platelet count drops (thrombocytopenia) and red blood cells are shredded (microangiopathic destroying red blood cells (hemolytic) anemia with schistocytes). — why: Platelets are consumed faster than the marrow can make them. Red cells are physically torn apart as they are forced through narrowed, clot-filled vessels, releasing hemoglobin and leaving schistocyte fragments visible on the blood smear.
4. Hemoglobin spills into the blood; LDH, indirect bilirubin, and free hemoglobin rise while haptoglobin drops to zero. — why: Broken red cells dump their contents—hemoglobin and LDH—into the plasma. The liver cannot make haptoglobin (the hemoglobin-binding protein) fast enough to clear it. Bilirubin rises as the liver processes dead red cell debris.

5. Brain and kidneys are hit hardest in TTP; kidneys are the main target in HUS. — why: TTP microthrombi clog small vessels everywhere, but the brain (causing confusion, seizures, stroke) and kidneys (causing acute kidney injury) are especially vulnerable because their capillaries are dense and sensitive to low oxygen. HUS targets the glomeruli (kidney filters) preferentially because Shiga toxin or complement binds most strongly there, leading to acute renal failure, proteinuria, and blood in the urine (hematuria).
6. Organs starved of oxygen begin to fail: confusion, stroke, or coma (brain); acute kidney injury with rising creatinine and low urine output (kidneys); chest pain or arrhythmia (heart). — why: Microthrombi block blood flow, so tissues downstream get too little oxygen (ischemia). Brain cells die or misfire, causing neurologic symptoms. Kidney tubules and glomeruli cannot filter waste or regulate fluid. Heart muscle may become blood-starved (ischemic), triggering arrhythmias or tissue death from blocked blood flow (infarction).
7. Without treatment, multi-organ failure, irreversible brain damage, or death occurs; with prompt plasma exchange (TTP) or supportive care and complement blockade (atypical HUS), most patients survive. — why: TTP is >90% fatal without plasma exchange, which removes autoantibodies and replaces ADAMTS13. Plasma exchange reverses the clotting cascade within days. Typical HUS (Shiga toxin) is managed with fluids and dialysis; most children recover. Atypical HUS requires eculizumab (a complement blocker) to stop vessel attack. Early recognition and treatment prevent permanent organ damage.

Spot it — what you see, and why

- Broken red blood cells (schistocytes) on the blood smear: Tiny blood clots made of sticky platelets form throughout small vessels, and red blood cells slam into these clots at high speed and shatter into pieces (like a bug hitting a windshield). These broken fragments are called schistocytes.
- Very low platelet count (thrombocytopenia): Platelets clump together abnormally inside small blood vessels all over the body, using them up faster than the bone marrow can replace them, so the number in the bloodstream drops sharply.
- Low haptoglobin and high LDH in the blood: Haptoglobin is a protein that mops up free hemoglobin (the oxygen-carrying part of red blood cells). When lots of red cells break open, haptoglobin gets used up and drops low. LDH (an enzyme normally inside cells) spills out when cells break, so it rises high in the blood.
- Dark or tea-colored urine: When red blood cells break apart, hemoglobin is released into the bloodstream; the kidneys filter it out and dump it into the urine, turning the urine dark brown or red (hemoglobinuria).
- Sudden confusion, trouble speaking, or weakness on one side of the body: Tiny clots block blood vessels in the brain, starving patches of brain tissue of oxygen (ischemia). This can cause stroke-like symptoms or altered mental status as brain cells stop working properly.

- Sharp drop in urine output or swelling in the legs and face: Clots jam the tiny filters (glomeruli) in the kidneys, damaging them so they cannot clean the blood or make urine normally. Fluid and waste build up in the body (acute kidney injury).

Red flags — act now

- New confusion, slurred speech, or one-sided weakness (signs of stroke or brain bleeding)
- Urine output drops sharply or stops completely (acute kidney failure)
- Platelet count falls dangerously low (often below 20,000) with active bleeding (nosebleeds, bleeding gums, or bruises that spread quickly)
- Severe chest pain or trouble breathing (possible heart or lung clots)
- Seizures or sudden loss of consciousness

Treat it — in this order

1. Plasma exchange (plasmapheresis or therapeutic plasma exchange, TPE) started within hours → Removes the giant sticky von Willebrand factor clumps (ultra-large vWF multimers) and the antibodies attacking ADAMTS13 from the blood. Replaces them with fresh frozen plasma that contains working ADAMTS13 enzyme. This stops platelets from sticking together, breaks the clotting cycle, and saves the brain and kidneys. Without plasma exchange, TTP kills over 90 percent of patients; with it, survival jumps to over 80 percent.
2. High-dose corticosteroids (methylprednisolone 1 to 2 mg per kg per day IV, or prednisone 1 mg per kg per day by mouth) → Quiets the immune system so it stops making antibodies that attack ADAMTS13 in acquired TTP. Reduces inflammation in the blood vessel lining in atypical HUS. This slows the destruction of red cells, platelets, and blood vessel walls, and helps the body stop the disease process.
3. Rituximab (anti-CD20 monoclonal antibody, 375 mg per square meter IV once a week for 4 weeks) → Kills the B cells (a type of white blood cell) that are making antibodies against ADAMTS13. This stops the source of the immune attack in acquired TTP. Studies show rituximab cuts the relapse rate in half and helps more patients go into remission. It is now standard first-line treatment along with plasma exchange and steroids.
4. Caplacizumab (anti-von Willebrand factor nanobody, 10 mg IV once, then 10 mg subcutaneous daily) → Blocks the sticky part of von Willebrand factor so it cannot grab platelets and build clots, even while the giant clumps are still in the blood. This speeds up platelet recovery, reduces the number of plasma exchange sessions needed, and cuts the risk of death and major complications during the acute phase. FDA approved in 2019 for TTP.

5. Eculizumab (complement C5 inhibitor, 900 mg IV weekly for 4 weeks, then 1,200 mg every 2 weeks) for atypical HUS → Blocks the complement cascade (part of the immune system) at the C5 step. In atypical (non-Shiga-toxin) HUS, a broken complement system attacks the lining of blood vessels. Eculizumab stops this attack, protects the kidney filters (glomeruli), and prevents further damage. Studies show it restores kidney function and prevents relapse in most patients with atypical HUS.

Your top priorities at the bedside

1. Monitor neurological status every 2 hours using Glasgow Coma Scale and check for new confusion, headache, vision changes, or seizure activity — why: Tiny clots in brain blood vessels cause stroke-like symptoms and seizures in TTP. Brain injury can progress rapidly, and any change in mental status signals worsening disease that needs immediate plasma exchange or increased treatment intensity.
2. Measure strict intake and output every hour and notify provider immediately if urine output drops below 0.5 mL per kg per hour — why: The kidneys are damaged by broken red blood cell pieces clogging tiny kidney filters (glomeruli). Dropping urine output signals acute kidney injury that may require urgent dialysis to remove waste products and prevent dangerous potassium levels.
3. Hold all platelet transfusions unless approved by hematology and the patient has life-threatening bleeding — why: Giving platelets when the patient is making tiny clots everywhere provides more fuel for clotting and can worsen organ damage. Platelets are being consumed in the disease process, not truly low from bone marrow failure, so transfusion is dangerous.