

Autoimmune Hemolytic Anemia

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THE STORY IN ONE SENTENCE

The immune system mistakes the patient's own red blood cells for foreign invaders and destroys them faster than the bone marrow can replace them.

“Autoimmune destroying red blood cells (hemolytic) anemia is a condition where the body's immune system attacks and destroys its own red blood cells. This causes anemia (low red blood cell count) because the bone marrow cannot make new red cells fast enough to replace the ones being destroyed.”

Normal anatomy — the body's job

Red blood cells (erythrocytes) are made in the bone marrow and live about 120 days in the bloodstream, carrying oxygen from the lungs to all body tissues. The immune system normally recognizes self-antigens (protein markers on your own cells) and does not attack them. Old or damaged red cells are gently removed by the spleen and liver, and the iron from hemoglobin (the oxygen-carrying protein inside red cells) is recycled to make new cells.

BODY'S JOB

Think of red blood cells like delivery trucks that carry oxygen packages to every house in a city, making round trips for about four months before they retire; meanwhile, the immune system acts like a security force that checks ID badges and only stops trucks with foreign or expired tags, letting all properly marked trucks pass safely.

1. Bone marrow produces millions of new red blood cells every second, filling them with hemoglobin to carry oxygen
2. Mature red cells enter the bloodstream and circulate through arteries and veins for approximately 120 days
3. Immune system continuously checks cell surface markers (antigens) and recognizes red cells as 'self' so it does not attack them
4. Red cells pick up oxygen in the lungs and deliver it to tissues throughout the body

5. As red cells age, they develop surface changes that signal they are old and ready for removal
6. Spleen and liver gently remove old red cells, recycle the iron, and bone marrow uses that iron to make new red cells

What breaks

In autoimmune destroying red blood cells (hemolytic) anemia, the immune system loses its ability to recognize red blood cells as 'self' and starts making antibodies against them. These antibodies attach to the red cell surface like sticky tags, marking them for destruction. The spleen and liver then destroy these tagged red cells much faster than normal—sometimes within hours instead of months—causing severe anemia because the bone marrow cannot keep up with the rapid loss.

CLINICAL TERM

The patient develops autoantibodies (antibodies directed against their own tissues) that bind to red blood cell membrane antigens, typically targeting Rh proteins or other surface markers. IgG antibodies (immunoglobulin G, the most common antibody type) coat the red cells in warm autoimmune destroying red blood cells (hemolytic) anemia, while IgM antibodies (immunoglobulin M, a larger antibody) activate complement (a cascade of immune proteins that punch holes in cells) in cold agglutinin disease. Extravascular red blood cell destruction (hemolysis) (red cell destruction outside blood vessels) occurs primarily in the spleen, or intravascular red blood cell destruction (destruction inside blood vessels) happens when complement directly ruptures the cell membrane.

How the body compensates

The bone marrow immediately increases red blood cell production up to six to eight times normal, releasing immature red cells called reticulocytes (young red blood cells still containing RNA) into the bloodstream. The kidneys sense low oxygen delivery and produce more erythropoietin (EPO, a hormone that stimulates red cell production), further driving the marrow response, but this compensation fails when red blood cell destruction (hemolysis) (red cell destruction) outpaces production.

1. {'step': 'Tissue low oxygen (hypoxia) detection', 'detail': 'When red cell numbers drop, tissues receive less oxygen; kidney sensors detect this low oxygen state within hours'}
2. {'step': 'Erythropoietin release', 'detail': 'Kidneys release EPO into the bloodstream, signaling the bone marrow to urgently increase red blood cell production'}

3. {'step': 'Bone marrow expansion', 'detail': 'Marrow ramps up erythropoiesis (red blood cell production) by expanding the erythroid (red cell-forming) compartment and shortening maturation time'}
4. {'step': 'Early release of reticulocytes', 'detail': 'Marrow releases reticulocytes (immature red cells that are larger and still contain RNA) into circulation before they fully mature, causing elevated reticulocyte count on lab tests'}
5. {'step': 'Cardiovascular compensation', 'detail': 'Heart rate increases and cardiac output rises to circulate the remaining red cells faster, attempting to deliver adequate oxygen despite fewer cells'}
6. {'step': 'Increased 2,3-DPG production', 'detail': 'Red cells increase 2,3-diphosphoglycerate (2,3-DPG, a molecule that helps hemoglobin release oxygen) so each remaining red cell delivers more oxygen to tissues'}

Domino effect

1. Autoantibody formation and red cell coating — Immune system produces antibodies against red blood cell surface antigens, coating the cells and marking them for destruction within hours to days instead of the normal 120-day lifespan
2. Accelerated extravascular red blood cell destruction (hemolysis) in spleen — Splenic macrophages rapidly remove antibody-coated red cells, causing unconjugated hyperbilirubinemia (elevated indirect bilirubin from hemoglobin breakdown) and depleting red cell mass faster than bone marrow can replace it
3. Progressive anemia despite compensatory erythropoiesis — Hemoglobin drops because red cell destruction outpaces production; reticulocyte count rises as bone marrow works overtime, but patient becomes increasingly anemic with fatigue, pale skin (pallor), and trouble breathing (dyspnea) (shortness of breath)
4. Tissue low oxygen (hypoxia) and organ dysfunction — Low hemoglobin means inadequate oxygen delivery to heart, brain, and kidneys; patient develops a fast heart rate (tachycardia) (fast heart rate), confusion, angina (chest pain), and decreased urine output as organs suffer
5. Cardiovascular strain and high-output state — Heart pumps harder and faster to compensate for low oxygen-carrying capacity, increasing myocardial oxygen demand and risking heart failure, especially in patients with pre-existing cardiac disease
6. Severe intravascular red blood cell destruction (hemolysis) with complement activation — In severe cases or cold agglutinin disease, complement proteins punch holes in red cells inside blood vessels, releasing free hemoglobin into plasma, which is toxic to kidneys and causes hemoglobinuria (dark urine from hemoglobin)

7. Acute kidney injury from hemoglobin precipitation — Free hemoglobin filtered by kidneys precipitates in renal tubules, causing acute tubular tissue death (necrosis), rising creatinine, and potentially requiring dialysis if not corrected rapidly
8. Life-threatening anemic crisis and multi-organ failure — Severe untreated red blood cell destruction (hemolysis) drops hemoglobin to critically low levels (sometimes below 4-5 g/dL), causing cardiovascular collapse, lactic acidosis (acid from oxygen-starved tissues) (buildup of lactic acid from oxygen-starved tissues), altered mental status, and death without urgent transfusion and immunosuppressive therapy

Symptoms · what the patient feels, and why

- Fatigue and weakness: Low hemoglobin (oxygen-carrying protein in red blood cells) means less oxygen reaches muscles and brain because antibodies destroy red blood cells faster than the bone marrow can make new ones
- Pale skin and mucous membranes: Decreased number of circulating red blood cells reduces the pink color normally seen in skin, gums, and inside the eyelids
- Yellowing of the skin and eyes (Jaundice) (yellow skin and eyes): When red blood cells break apart, hemoglobin releases bilirubin (a yellow pigment) faster than the liver can process it, causing yellow discoloration
- Dark urine: Hemoglobin and bilirubin spill into urine when red blood cells are destroyed in large numbers, turning urine tea-colored or cola-colored
- Shortness of breath with exertion: Low red blood cell count means less oxygen delivery to tissues, so the body tries to compensate by breathing faster during activity
- Chest pain or rapid heartbeat: The heart pumps faster and harder to deliver enough oxygen when hemoglobin is low, increasing cardiac workload and oxygen demand
- Fever: Immune system activation and massive red blood cell destruction release inflammatory cytokines (chemical messengers) that reset the body's temperature control center
- Abdominal fullness or left upper quadrant pain: The spleen enlarges (splenomegaly) as it traps and destroys antibody-coated red blood cells, stretching the capsule around the spleen

Focused exam

- Scleral yellowing of the eyes (icterus) (yellow discoloration of the white part of the eyes): Indicates elevated indirect bilirubin from red blood cell breakdown, confirming red blood cell destruction (hemolysis) as the cause of anemia rather than bleeding or bone marrow failure

- An enlarged spleen (Splenomegaly) (enlarged spleen) on left upper abdomen examining by touch (palpation): The spleen traps antibody-coated red blood cells and becomes enlarged in about 50 to 60 percent of autoimmune destroying red blood cells (hemolytic) anemia cases, also suggesting possible underlying lymphoma
- A fast heart rate (Tachycardia) (heart rate above 100 beats per minute) and flow murmur: Rapid heart rate and turbulent blood flow sounds indicate the cardiovascular system is compensating for low oxygen-carrying capacity, signaling moderate to severe anemia
- An enlarged liver (Hepatomegaly) (enlarged liver) on right upper abdomen examining by touch (palpation): Liver enlargement combined with an enlarged spleen (splenomegaly) raises concern for underlying lymphoproliferative disease or indicates increased bilirubin processing workload
- Swollen lymph nodes (Lymphadenopathy) (swollen lymph nodes) in neck, armpits, or groin: Enlarged lymph nodes suggest underlying lymphoma or chronic lymphocytic leukemia, which causes secondary autoimmune destroying red blood cells (hemolytic) anemia in 10 to 15 percent of cases
- Mental status changes, confusion, or altered level of consciousness: Brain low oxygen (hypoxia) (low oxygen) from severe anemia indicates hemoglobin is critically low and immediate transfusion is needed to prevent permanent neurologic damage

Diagnostics · every test answers a question

- Complete blood count with differential and reticulocyte count → Is the patient anemic, and is the bone marrow responding by making new red blood cells?
- Direct antiglobulin test (DAT or Coombs test) → Are antibodies or complement proteins coating the patient's red blood cells?
- Indirect bilirubin and lactate dehydrogenase (LDH) → Is there biochemical evidence of red blood cell breakdown?
- Haptoglobin → Is free hemoglobin being released into the bloodstream from destroyed red blood cells?
- Peripheral blood smear → What do the red blood cells look like under the microscope?
- Cold agglutinin titer → Are cold-reactive antibodies present that destroy red blood cells at low temperatures?
- Flow cytometry for paroxysmal nocturnal hemoglobinuria (PNH) and lymphoproliferative disorders → Is there an underlying blood cancer or a different cause of red blood cell destruction (hemolysis) mimicking autoimmune destroying red blood cells (hemolytic) anemia?
- Serum protein electrophoresis and immunofixation → Is there a monoclonal protein suggesting an underlying plasma cell or lymphoid disorder?

Treatment logic

- Corticosteroids (prednisone or methylprednisolone) → Suppresses the immune system's production of antibodies against red blood cells and reduces removal of antibody-coated cells by the spleen, raising hemoglobin in 70 to 85 percent of warm autoimmune destroying red blood cells (hemolytic) anemia patients within 1 to 3 weeks
- Packed red blood cell transfusion → Immediately increases oxygen-carrying capacity and prevents organ damage from severe low oxygen (hypoxia) when hemoglobin drops below 7 g/dL or patient has chest pain, confusion, or severe shortness of breath
- Rituximab (anti-CD20 monoclonal antibody) → Destroys B-lymphocytes (cells that make antibodies) and achieves remission in 80 to 90 percent of patients with warm autoimmune destroying red blood cells (hemolytic) anemia who fail steroids or relapse after steroid taper
- Splenectomy (surgical removal of the spleen) → Eliminates the major site where antibody-coated red blood cells are trapped and destroyed, producing long-term remission in 60 to 70 percent of warm autoimmune destroying red blood cells (hemolytic) anemia patients who do not respond to steroids and rituximab
- Cold avoidance measures and warming strategies → Prevents activation of cold-reactive antibodies in cold agglutinin disease by keeping body and extremities warm, reducing red blood cell destruction (hemolysis) episodes triggered by temperature below 30 degrees Celsius
- Folic acid supplementation (1 mg daily) → Supports increased red blood cell production by the bone marrow during chronic red blood cell destruction (hemolysis) because folate (a B-vitamin) is consumed rapidly when the marrow makes extra reticulocytes

Medications

Prednisone · Corticosteroid (glucocorticoid)

Prednisone is a steroid hormone that turns down the immune system's attack on red blood cells. It stops immune cells from making antibodies and reduces the spleen's ability to trap and destroy antibody-coated red blood cells. The drug enters immune cells and changes which genes are turned on or off, reducing inflammation and antibody production throughout the body.

1. Prednisone enters B-lymphocytes (antibody-making white blood cells) and binds to glucocorticoid receptors inside the cell
2. The receptor-drug complex moves into the cell nucleus and attaches to DNA, turning off genes that make antibodies and inflammatory proteins
3. B-cells reduce production of IgG antibodies that target red blood cell surface proteins

4. Macrophages in the spleen become less able to recognize and engulf antibody-coated red blood cells through their Fc receptors
5. Red blood cell survival increases from days to weeks as fewer cells are removed from circulation

SAFETY WATCH

Monitor blood glucose weekly because steroids raise blood sugar and can trigger diabetes · Give pneumonia vaccine and check for tuberculosis before starting because immune suppression increases infection risk · Taper dose slowly over 3 to 6 months to prevent adrenal crisis when the body's own cortisol production has been suppressed · Watch for mood changes, insomnia, weight gain, high blood pressure, and bone thinning with long-term use

Rituximab · Monoclonal antibody (anti-CD20 immunotherapy)

Rituximab is a laboratory-made antibody that locks onto CD20 proteins found on the surface of B-lymphocytes. Once rituximab attaches, it marks these B-cells for destruction by the immune system. Since B-cells are the cells that make the harmful antibodies against red blood cells, removing B-cells stops new antibody production and allows red blood cell counts to recover over several weeks.

1. Rituximab binds tightly to CD20 proteins on the outer membrane of mature B-lymphocytes
2. The bound rituximab activates complement proteins in blood, which punch holes in the B-cell membrane (complement-mediated cytotoxicity)
3. Natural killer cells recognize the rituximab-coated B-cells and release toxic granules that kill them (antibody-dependent cellular cytotoxicity)
4. Macrophages engulf and digest the rituximab-marked B-cells (antibody-dependent phagocytosis)
5. Over 1 to 2 weeks, B-cell counts drop to near zero, antibody production against red blood cells stops, and hemoglobin begins to rise

SAFETY WATCH

Premedicate with acetaminophen and antihistamine to prevent infusion reactions like fever, chills, and low blood pressure during the IV infusion · Screen for hepatitis B before treatment because rituximab can reactivate dormant hepatitis B virus, causing severe liver damage · Monitor for infections during the 6 to 12 months after treatment when B-cell counts are low and antibody production is reduced · Rare progressive multifocal leukoencephalopathy (PML, a fatal brain infection) can occur months after rituximab in severely immunosuppressed patients

Folic acid · Vitamin (water-soluble B-vitamin)

Folic acid is a B-vitamin that bone marrow cells need to make DNA for new red blood cells. During red blood cell destruction (hemolysis), the marrow tries to replace destroyed red blood cells by making reticulocytes very quickly. This uses up folate stores faster than diet can replace them. Supplemental folic acid keeps the marrow supplied with this essential building block so red blood cell production does not slow down from folate deficiency.

1. Folic acid is absorbed in the small intestine and converted to tetrahydrofolate (the active form) by enzymes in intestinal cells and liver
2. Tetrahydrofolate enters bone marrow erythroblasts (red blood cell precursors) that are dividing rapidly to replace destroyed red blood cells
3. Inside the nucleus, tetrahydrofolate donates carbon atoms needed to build thymidine, one of the four DNA building blocks
4. With adequate folate, erythroblasts can complete DNA synthesis and divide normally to produce reticulocytes
5. Reticulocyte production stays high to compensate for ongoing red blood cell destruction (hemolysis) without developing megaloblastic changes (enlarged abnormal cells from folate deficiency)

SAFETY WATCH

Check vitamin B12 level before starting folic acid because giving folate alone can mask B12 deficiency symptoms while allowing nerve damage to progress · Standard 1 mg daily dose is safe with no significant side effects or drug interactions in most patients

Packed red blood cell transfusion · Blood product (cellular therapy)

Packed red blood cell transfusion provides millions of functional red blood cells from a healthy donor directly into the patient's bloodstream. Each unit of packed cells contains about 200 mL of concentrated red blood cells that immediately increase the hemoglobin level by about 1 g/dL in adults. This quickly restores oxygen-carrying capacity to prevent organ damage while other treatments have time to work. The transfused cells will eventually be destroyed by the patient's antibodies, but they provide a critical bridge during severe anemia.

1. Donor red blood cells are carefully cross-matched to find blood that reacts least with the patient's antibodies
2. Packed red blood cells are infused through IV over 2 to 4 hours, mixing with the patient's own blood
3. The transfused hemoglobin immediately begins carrying oxygen from lungs to tissues, relieving low oxygen (hypoxia) symptoms

4. Oxygen delivery to heart, brain, kidneys, and other organs increases within hours, reducing compensatory a fast heart rate (tachycardia) and shortness of breath
5. The patient's antibodies will gradually destroy transfused cells over days to weeks, but hemoglobin stays higher than pre-transfusion levels during this time

SAFETY WATCH

Extensive cross-matching is needed because patient antibodies may react with donor red blood cells, causing severe transfusion reactions · Monitor closely during infusion for signs of destroying red blood cells (hemolytic) transfusion reaction (fever, back pain, dark urine, shock) which can be life-threatening · Use white blood cell (leukocyte)-reduced blood to minimize feverish (febrile) reactions and consider washed red blood cells if patient has had severe allergic reactions · Reserve transfusion for hemoglobin below 7 g/dL or symptomatic anemia with chest pain, confusion, or severe trouble breathing (dyspnea) because transfusion carries risks

Immunoglobulin (IVIG, intravenous immune globulin) · Immunomodulator (pooled human antibody preparation)

IVIG is a mixture of antibodies collected from thousands of healthy blood donors. When given at high doses, these normal antibodies temporarily block the receptors on spleen and liver cells that grab and destroy antibody-coated red blood cells. IVIG also contains anti-idiotypic antibodies that neutralize the harmful anti-red blood cell antibodies. This provides a rapid but temporary increase in hemoglobin, buying time for other treatments to take effect.

1. High-dose IVIG saturates Fc receptors on macrophages in the spleen and liver, blocking their ability to bind antibody-coated red blood cells
2. Normal antibodies in IVIG compete with pathologic antibodies for binding sites on red blood cells, reducing the density of harmful antibodies on each cell
3. Anti-idiotypic antibodies in IVIG directly neutralize some of the patient's anti-red blood cell antibodies
4. Splenic destruction of red blood cells slows within 24 to 72 hours, allowing hemoglobin to stabilize or rise
5. Effect lasts only 2 to 4 weeks as IVIG antibodies are cleared from circulation and Fc receptors become available again

SAFETY WATCH

Infuse slowly and monitor for headache, fever, and aseptic meningitis which occur in 5 to 10 percent of patients within 24 hours · Risk of clot formation (thrombosis) (blood clots) in elderly patients and those with cardiovascular disease because IVIG increases blood viscosity · Check IgA level before first dose because patients with IgA deficiency can have severe anaphylactic reactions to trace IgA in IVIG preparations · Rare destroying red blood cells (hemolytic) reactions can occur if IVIG contains antibodies against recipient red blood cell antigens

Mycophenolate mofetil · Immunosuppressant (purine synthesis inhibitor)

Mycophenolate blocks a key enzyme that B-lymphocytes need to make DNA and multiply. B-cells depend heavily on this enzyme pathway, while most other body cells have an alternate route for DNA building blocks. By selectively slowing B-cell division, mycophenolate reduces the population of antibody-producing cells. This steroid-sparing agent helps maintain remission in autoimmune destroying red blood cells (hemolytic) anemia while allowing prednisone dose to be lowered, avoiding long-term steroid complications.

1. Mycophenolate is converted to mycophenolic acid, which blocks inosine monophosphate dehydrogenase (IMPDH), an enzyme that makes guanosine for DNA
2. B-lymphocytes, which rely heavily on the IMPDH pathway, cannot make enough guanosine nucleotides to support rapid cell division
3. Activated B-cells attempting to proliferate and make antibodies undergo cell cycle arrest and die
4. Over weeks to months, the pool of antibody-secreting B-cells shrinks, reducing production of anti-red blood cell antibodies
5. Red blood cell survival improves as antibody levels decline, allowing hemoglobin to stabilize at higher levels

SAFETY WATCH

Monitor complete blood count monthly because mycophenolate can cause a low white blood cell count (leukopenia) (low white blood cells) and increase infection risk · Gastrointestinal side effects (diarrhea, nausea, abdominal pain) occur in 30 to 40 percent of patients and may require dose reduction · Absolute contraindication in pregnancy due to high risk of miscarriage and birth defects; women must use two forms of contraception · Check for latent infections before starting and avoid live vaccines during treatment due to immunosuppression

Red flags

- Hemoglobin below 7 g/dL with chest pain, confusion, or severe shortness of breath at rest requiring immediate transfusion
- New swollen lymph nodes (lymphadenopathy) or an enlarged spleen (splenomegaly) suggesting underlying lymphoma or chronic lymphocytic leukemia driving the red blood cell destruction (hemolysis)
- Drug-induced destroying red blood cells (hemolytic) anemia with continued exposure to the causative medication
- Cold agglutinin disease with distal starved blood flow (ischemia) (blue fingers or toes) from red blood cell agglutination blocking small vessels

Nursing priorities

1. Monitor for signs of acute red blood cell destruction (hemolysis) and severe anemia — Autoimmune destroying red blood cells (hemolytic) anemia (AIHA, a condition where the immune system destroys red blood cells) can cause rapid drops in hemoglobin leading to low oxygen (hypoxia) (low oxygen), heart failure, and shock requiring immediate intervention.
2. Assess respiratory status and oxygen saturation continuously — Severe anemia reduces oxygen-carrying capacity of the blood, so patients may develop trouble breathing (dyspnea) (shortness of breath), fast breathing (tachypnea) (rapid breathing), and low oxygen in the blood (hypoxemia) (low blood oxygen) requiring supplemental oxygen.
3. Monitor vital signs for hemodynamic instability — Acute red blood cell destruction (hemolysis) causes a fast heart rate (tachycardia) (fast heart rate), low blood pressure (hypotension) (low blood pressure), and signs of shock as the body tries to compensate for decreased oxygen delivery to tissues.
4. Observe for yellowing of the skin and eyes (jaundice) and dark urine indicating active red blood cell destruction (hemolysis) — Red blood cell destruction (Hemolysis) releases bilirubin (yellow breakdown product of hemoglobin) causing yellowing of the skin and eyes (jaundice) and hemoglobinuria (hemoglobin in urine) making urine tea-colored, which helps track disease activity.
5. Administer corticosteroids as ordered and monitor for side effects — Corticosteroids like prednisone are first-line treatment to suppress the autoimmune response destroying red blood cells, but nurses must watch for high blood sugar (hyperglycemia) (high blood sugar), infection risk, and mood changes.

6. Prepare for and monitor blood transfusions if hemoglobin is critically low — Patients with hemoglobin below 7 g/dL or symptomatic anemia may need packed red blood cells, but crossmatching can be difficult due to antibodies, and transfusions may trigger more red blood cell destruction (hemolysis).
7. Educate patient to avoid cold exposure in cold agglutinin disease — Cold-type AIHA is triggered by cold temperatures activating antibodies, so patients must keep extremities warm, avoid cold drinks, and stay in warm environments to prevent destroying red blood cells (hemolytic) episodes.
8. Monitor laboratory values including hemoglobin, reticulocyte count, and bilirubin — Serial labs track treatment response: rising hemoglobin and falling bilirubin show improvement, while high reticulocytes (young red blood cells) indicate the bone marrow is responding to anemia.

Sources

- American Society of Hematology (ASH) 2022 guidelines for the diagnosis and management of autoimmune hemolytic anemia
- British Society for Haematology 2017 guidelines on the diagnosis and management of warm and cold autoimmune haemolytic anaemias
- UpToDate: Diagnosis and treatment of warm autoimmune hemolytic anemia (2023)
- Blood (journal): Consensus recommendations for the diagnosis and treatment of autoimmune hemolytic anemia (Hill et al., 2023)

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