Hemolytic Anemia

Confirm hemolysis, then split it with the DAT · Immune and non-immune are managed nothing alike

DAT SPLITS IT
immune vs non-immune

CONFIRM IT IS HEMOLYSIS *four tests, and the film alongside them*

THE SCREEN

Raised LDH, raised unconjugated bilirubin, low or absent haptoglobin, and a high reticulocyte count. Haptoglobin is the most useful single test and falls first in intravascular hemolysis. A raised reticulocyte count confirms the marrow is responding appropriately.

INTRAVASCULAR OR EXTRAVASCULAR

Intravascular destroys cells in the circulation: **hemoglobinemia, hemoglobinuria and undetectable haptoglobin**, with red or black urine that is **dipstick-positive for blood but shows no red cells**. **Extravascular** removal by the spleen and liver is commoner, gentler, and gives splenomegaly and jaundice.

ALWAYS SEND THE FILM

The film frequently gives the diagnosis outright. Spherocytes mean autoimmune hemolysis or hereditary spherocytosis · **schistocytes** mean a microangiopathy · **bite and blister cells** mean oxidative damage as in G6PD deficiency · **sickle cells, target cells or parasites** speak for themselves.

THEN SEND THE DAT *the single test that divides the differential*

Result	What it means and what follows
DAT positive	**Immune-mediated hemolysis.** The laboratory will report whether the coating is **IgG, complement (C3d), or both**, and that pattern points directly to the subtype. Always ask for it rather than accepting "positive" alone.
Warm autoimmune (IgG)	**The commonest immune type. Spherocytes**, extravascular destruction, often splenomegaly. **Corticosteroids are first-line**, with **rituximab** next and splenectomy later. **Look for a cause**: lymphoproliferative disease, lupus, drugs, and infection. Add **folate**, since high red cell turnover consumes it.
Cold agglutinin (C3d, IgM)	**Managed completely differently. Keep the patient warm**, including warming intravenous fluids and blood. **Steroids and splenectomy are largely ineffective** here, so the reflex from warm disease is wrong. **Rituximab-based therapy** is used. Classically follows ***Mycoplasma*** **or EBV**, or reflects an underlying lymphoproliferative disorder.
Drug-induced	**Review every recent drug** — cephalosporins, penicillins, NSAIDs and others. **Stopping the drug is the treatment**, and recovery follows within weeks.
DAT negative	**Non-immune hemolysis** — go to the causes below. Note the DAT can be **falsely negative** in low-level or IgA-mediated disease, so a convincing clinical picture warrants discussion with hematology rather than abandoning the diagnosis.

DAT-NEGATIVE CAUSES *mechanical, inherited, acquired and infective*

Group	Detail
Microangiopathy	**Schistocytes with thrombocytopenia is an emergency. TTP** needs plasma exchange within hours and **platelet transfusion is contraindicated**; also consider **hemolytic uremic syndrome, DIC, malignant hypertension, HELLP and mechanical valve hemolysis**. Check a coagulation screen: it is **normal in TTP and deranged in DIC**.
Enzyme defects	**G6PD deficiency** — episodic hemolysis triggered by **oxidant drugs (including primaquine, nitrofurantoin, dapsone and rasburicase), fava beans and infection**. **Test after the episode**: assaying during a crisis can read falsely normal because the deficient cells have already been destroyed.
Membrane defects	**Hereditary spherocytosis** — family history, splenomegaly, pigment gallstones, spherocytes with a **negative DAT**, which is what separates it from warm autoimmune disease.
Hemoglobinopathy	**Sickle cell disease and thalassemia.** Confirm with **hemoglobin electrophoresis or HPLC**, and check the ethnic and family background.
Acquired clonal	**Paroxysmal nocturnal hemoglobinuria** — suspect with **intravascular hemolysis, cytopenias and unusual-site thrombosis** such as hepatic or cerebral veins. **Diagnosed by flow cytometry**, not by the historical urine tests, and specifically treatable with complement inhibition.
Infection and toxins	**Malaria and babesiosis** — take a travel history and request thick and thin films urgently. Also **Clostridium sepsis, snake venom, copper in Wilson's disease**, and severe burns.

MANAGING IT *while the cause is being established*

1. **Take the diagnostic samples before transfusing** — DAT, film, haptoglobin, LDH, reticulocytes, and a hemolysis screen. Transfusion obscures all of them, and in immune hemolysis it also complicates crossmatching.
2. **Transfuse for symptoms and physiology, not the number.** In warm autoimmune hemolysis **crossmatching may be difficult or impossible**, but **do not withhold blood from a patient who is compromised** — discuss urgently with the transfusion laboratory and give the best-matched units available. In **cold agglutinin disease use a blood warmer**.
3. **Give folic acid** in any sustained hemolysis; ongoing high turnover exhausts stores and can produce a superimposed megaloblastic crisis.
4. **Look for the underlying disease, not just the mechanism.** Send **autoimmune serology, immunoglobulins and electrophoresis, viral serology including HIV and hepatitis, and imaging or flow cytometry for lymphoproliferative disease**. In an older patient, new warm autoimmune hemolysis is a lymphoma until shown otherwise.
5. **Watch for the complications of chronic hemolysis: pigment gallstones, iron overload if repeatedly transfused, aplastic crisis with parvovirus B19**, leg ulcers, and **thrombosis**, which is markedly increased in PNH and in severe immune hemolysis. **Vaccinate before any planned splenectomy.**

PEARLS & PITFALLS

- **Send the DAT and the film before the first unit.** They split the entire differential and transfusion obscures both.
- **Schistocytes with a low platelet count is TTP until excluded** — plasma exchange within hours, and no platelet transfusion.
- **Cold agglutinin disease is not treated like warm disease.** Keep the patient warm; steroids and splenectomy largely do not work.
- **Test for G6PD after the crisis.** During hemolysis the deficient cells are gone and the assay reads falsely normal.
- **Spherocytes with a negative DAT** point to hereditary spherocytosis rather than autoimmune hemolysis.
- **New warm autoimmune hemolysis in an older patient warrants a search for lymphoma**, not just a course of prednisolone.

References: BSH guidelines on the management of autoimmune hemolytic anemia · international consensus on the diagnosis and treatment of cold agglutinin disease · BSH guidance on the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria · G6PD deficiency drug safety lists.

Educational aid; verify against local hematology and transfusion protocol and patient factors.

roundsrx.com
roundsrx Infographic Series · #143