



Anemia — The Workup

Two numbers open the whole differential · And take the sample *before* you transfuse

MCV + RETICS

size, then marrow response

START WITH TWO NUMBERS *cell size sorts the causes; the reticulocyte count sorts the mechanism*

THE MCV

Microcytic, normocytic or macrocytic narrows the list immediately. **A normal MCV does not exclude a deficiency** — combined iron and B12 deficiency produces a normal average with a **wide red cell distribution width and a dimorphic film**, which is why the RDW and the film matter alongside it.

THE RETICULOCYTE COUNT

Is the marrow responding? **High retics** mean the marrow is working and red cells are being **lost or destroyed** — bleeding or hemolysis. **Low or normal retics** in the face of anemia mean **underproduction**: deficiency, chronic disease, renal failure or marrow disease.

SEND IT BEFORE TRANSFUSING

Take iron studies, B12, folate and a hemolysis screen before the first unit, and ideally before starting iron. Transfusion and treatment obscure every one of these results for weeks, and the patient then gets investigated twice. **Always look at the film yourself.**

MICROCYTIC *iron deficiency until proven otherwise — and then find the bleeding*

Cause	How to confirm and what to do
Iron deficiency	Ferritin below 30 µg/L is essentially diagnostic. But ferritin is an acute phase reactant , so a normal value does not exclude deficiency: with inflammation, chronic kidney disease or heart failure use a higher cutoff around 100 , and support it with a transferrin saturation below 20% .
Then ask why	Iron deficiency is a symptom, not a diagnosis. In men and postmenopausal women it is gastrointestinal blood loss until proven otherwise and warrants upper and lower endoscopy , plus celiac serology . Do not simply prescribe iron and discharge — a missed right-sided colon cancer presents exactly like this.
Thalassemia trait	Microcytosis out of proportion to the anemia, with a normal or high red cell count and normal iron studies. Lifelong and familial, so old blood counts are diagnostic gold. Confirm with hemoglobin electrophoresis , and do not iron-load someone who is not deficient.
Anemia of chronic disease	Usually normocytic but can become microcytic . Low serum iron with a low or normal transferrin and a normal or raised ferritin. Treat the underlying inflammation; iron alone will not fix it.
Rarer	Sideroblastic anemia (alcohol, isoniazid, lead, myelodysplasia) and lead poisoning with basophilic stippling on the film.

MACROCYTIC AND NORMOCYTIC *the retic count splits the normocytic group in two*

Group	Causes and the action point
Macrocytic — megaloblastic	B12 or folate deficiency , with hypersegmented neutrophils on the film. Always check and replace B12 before folate : giving folate alone to a B12-deficient patient can precipitate or worsen subacute combined degeneration of the cord , which is irreversible. Use methylmalonic acid for borderline B12 levels.
Macrocytic — other	Alcohol and liver disease, hypothyroidism, myelodysplasia , and drugs such as methotrexate, hydroxyurea, azathioprine and antiretrovirals. Reticulocytosis itself raises the MCV , so a macrocytosis with high retics may simply be brisk hemolysis or recovery from bleeding.
Normocytic, low retics	Anemia of chronic disease, chronic kidney disease (erythropoietin deficiency), early or mixed deficiency , endocrine failure, and marrow infiltration or failure . Other cytopenias, blasts or a leukoerythroblastic film mean hematology and a marrow examination , not another iron course.
Normocytic, high retics	Bleeding or hemolysis. Acute blood loss does not drop the hemoglobin immediately — it falls as the plasma volume is restored, so a normal hemoglobin early in a bleed is falsely reassuring . If there is no obvious bleeding, screen for hemolysis.

IS IT HEMOLYSIS? *four tests, then split immune from non-immune*

- 1 **Screen with the quartet: raised LDH, raised unconjugated bilirubin, low or absent haptoglobin, and a raised reticulocyte count.** Haptoglobin is the most useful single test when intravascular hemolysis is suspected.
- 2 **Send a direct antiglobulin test. Positive means immune hemolysis** — autoimmune (warm or cold), drug-induced, or a transfusion reaction. **Negative points to a non-immune cause**: microangiopathy, membrane or enzyme defects, hemoglobinopathy, infection or a mechanical valve.
- 3 **Look at the film urgently for schistocytes.** Fragments with thrombocytopenia is a **hematological emergency** — consider **TTP, hemolytic uremic syndrome and DIC**. TTP needs plasma exchange within hours, and **platelet transfusion is contraindicated**. Spherocytes suggest autoimmune hemolysis or hereditary spherocytosis; bite cells suggest G6PD deficiency.
- 4 **Take a drug and travel history.** Recent antibiotics, a new oxidant drug in G6PD deficiency, or malaria after travel. Check **G6PD after the acute episode** — testing during a crisis can be falsely normal because the deficient cells have already been destroyed.

TREAT AND TRANSFUSE SENSIBLY *the hemoglobin is not the indication on its own*

REPLACING IRON

Oral iron is first-line and is **better absorbed on alternate days** than several times daily, because each dose raises hepcidin and blocks the next. **Expect a reticulocyte rise within a week and a hemoglobin rise of about 1 g/dL every 2 to 3 weeks**; failure to respond means non-adherence, ongoing bleeding, malabsorption or the wrong diagnosis. **Continue for 3 months after normalization** to refill stores. Use **intravenous iron** for intolerance, malabsorption, chronic kidney disease, heart failure or when the need is urgent.

WHEN TO TRANSFUSE

A restrictive threshold of around 7 g/dL suits most stable inpatients, with about **8 g/dL where there is cardiovascular disease**. **Transfuse for symptoms and hemodynamics, not for a number**, and **give one unit then reassess**. In chronic deficiency anemia the patient has usually compensated and needs the deficiency corrected, not blood. **Never transfuse before the diagnostic samples are taken.**

PEARLS & PITFALLS

- **Send iron studies, B12 and folate before the first unit.** Transfusing first costs weeks of diagnostic clarity.
- **Iron deficiency in a man or postmenopausal woman means endoscopy.** Prescribing iron without investigating is how cancers get missed.
- **A normal ferritin does not exclude iron deficiency** when there is inflammation — check the transferrin saturation.
- **Replace B12 before folate.** Folate alone can precipitate irreversible cord degeneration.
- **Schistocytes with a low platelet count is an emergency** — think TTP, and do not give platelets.
- **A normal hemoglobin early in acute bleeding is meaningless.** It falls only once the plasma volume is replaced.

References: BSH guidelines on the laboratory diagnosis and management of iron deficiency · BSH guidelines on the diagnosis and treatment of cobalamin and folate disorders · AABB red blood cell transfusion thresholds and storage guidance · KDIGO anemia in chronic kidney disease.

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

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