MEDLAB BASICS · STUDY SHEET

Red Cell Morphology and the Anemias

Size, color, shape and inclusions on the smear, anemia by MCV with the tests that sort it, hemoglobin variants and thalassemias, hemolytic anemias and erythrocytosis

33 sources + more detail

medlabbasics.com/sheets/lab-rbc-morphology.html

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1 Size and color

FINDING	WHAT IT LOOKS LIKE	INDEX	SEEN IN
Normocytic, normochromic	Normal size, with a pale center and an even rim of hemoglobin	MCV 76–100 fL (ASCP)	Normal; acute blood loss, chronic disease, marrow failure, many hemolytic anemias
Microcytes	Small cells	MCV below 76 fL	Iron deficiency, thalassemia, sideroblastic anemia, some anemia of inflammation
Oval macrocytes	Large, egg-shaped cells	MCV above 100 fL	Megaloblastic anemia (B12, folate), myelodysplasia, hydroxyurea
Round macrocytes	Large, round cells	MCV above 100 fL	Liver disease, alcohol use, reticulocytosis
Hypochromia	Wider pale center with a thin rim of hemoglobin	Low MCH and MCHC	Iron deficiency, thalassemia, sideroblastic anemia
Hyperchromic-looking cells	No central pallor (spherocytes, sickle cells)	MCHC may rise above 36 g/dL	Hereditary spherocytosis, immune hemolysis, burns
Polychromasia	Slightly large cells with a blue-gray tint (residual RNA)	Reticulocytes raised	Hemolysis, bleeding, response to iron, B12 or folate
Anisocytosis	Cells of many sizes	RDW above 14.5%	Iron deficiency, megaloblastic anemia, mixed deficiency, transfusion

EXAM TIP A normal MCV with a high RDW can hide two disorders at once, for example iron and folate deficiency together. The smear shows both small and large cells.

2 Shape changes (poikilocytes)

CELL (OTHER NAME)	WHAT IT LOOKS LIKE	SEEN IN
Target cell (codocyte)	Thin cell with a dot of hemoglobin in the middle of the pale zone, like a bullseye	Hb C, Hb SC, Hb E, thalassemias, liver disease (cholestasis), after splenectomy; iron deficiency
Sickle cell (drepanocyte)	Crescent or sickle with pointed ends; irreversibly sickled cells keep the shape when oxygenated	Hb SS, Hb SC, Hb S-beta thalassemia (not sickle trait)
Spherocyte	Small, round, dense cell with no central pallor	Hereditary spherocytosis, warm autoimmune hemolysis, ABO HDFN, burns
Schistocyte (helmet cell, triangle, keratocyte)	Fragment of a red cell with sharp corners or straight edges	Microangiopathic hemolysis: DIC, TTP, HUS, HELLP, mechanical heart valves; severe burns
Teardrop cell (dacrocyte)	Cell drawn out into one tail	Primary myelofibrosis, marrow infiltration (myelophthisis), thalassemia, megaloblastic anemia
Burr cell (echinocyte, crenated cell)	Short, even projections spaced all round the edge; central pallor kept	Artifact (old sample, slow drying, poor fixation); uremia; pyruvate kinase deficiency
Acanthocyte (spur cell)	Dense cell with a few irregular, thorn-like spicules of different lengths, unevenly spaced; no central pallor	Severe liver disease (spur cell anemia), abetalipoproteinemia, McLeod phenotype, neuroacanthocytosis
Stomatocyte	Pale area is a slit or mouth instead of a circle	Artifact, alcohol use, liver disease, hereditary stomatocytosis, Rh null
Elliptocyte or ovalocyte	Oval to cigar or pencil shape	Hereditary elliptocytosis; severe iron deficiency (pencil and cigar cells); oval macrocytes in megaloblastic anemia
Bite cell (degmacyte)	Cell with a bite taken from the edge (where the spleen removed a Heinz body)	G6PD deficiency in hemolysis, oxidant drugs, unstable hemoglobins
Blister cell	Hemoglobin pushed to one side, leaving an empty blister at the edge	G6PD deficiency, oxidant injury

EXAM TIP Burr cell versus acanthocyte: burr cells have many short, even scallops all round and keep central pallor; acanthocytes have a few irregular spikes of uneven length and look dense. Burr cells in only one part of the slide are usually a drying artifact.

SAFETY Schistocytes with a falling platelet count suggest a thrombotic microangiopathy (TTP, HUS) or DIC. Report them promptly and tell the provider.

3 Inclusions

INCLUSION	WHAT IT LOOKS LIKE	MADE OF	STAIN THAT SHOWS IT	SEEN IN
Howell-Jolly body	One (sometimes two) round, dark purple dot near the edge	DNA (nuclear remnant)	Wright-Giemsa	After splenectomy, functional asplenia (sickle cell disease), megaloblastic anemia
Basophilic stippling	Many fine or coarse blue dots spread through the cell	Precipitated ribosomal RNA	Wright-Giemsa	Lead poisoning (coarse), thalassemia, sideroblastic and megaloblastic anemia, unstable Hb, pyrimidine 5'-nucleotidase deficiency
Pappenheimer bodies (siderotic granules)	Small purple granules	Iron	Wright-Giemsa (purple); Prussian blue (blue), which confirms iron	Sideroblastic anemia and other iron-utilization disorders
Heinz bodies	Not visible on Wright stain; round inclusions at the membrane on a supravital stain	Denatured, precipitated hemoglobin	Supravital stain (for example brilliant cresyl blue)	G6PD deficiency under oxidant stress, unstable hemoglobins
Hb H inclusions	Many fine, evenly spread dots: a golf ball	Precipitated Hb H (beta-chain tetramers)	Supravital stain after incubation	Hb H disease (alpha-thalassemia, 3 genes missing)
Cabot ring	Thin ring-shaped strand in a polychromatic cell	Nuclear or spindle remnant (debated)	Wright-Giemsa	Megaloblastic anemia, lead poisoning, severe thalassemia, myelofibrosis, after splenectomy

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3 Inclusions CONTINUED

INCLUSION	WHAT IT LOOKS LIKE	MADE OF	STAIN THAT SHOWS IT	SEEN IN
Reticulum (reticulocyte)	Blue network or strands	Ribosomal RNA	Supravital stain; polychromatic on Wright stain	Marrow response
Intracellular parasites	Rings, trophozoites, schizonts or gametocytes inside red cells	Plasmodium or Babesia	Giemsa or Wright, thick and thin films	Malaria, babesiosis (see the mycobacteria, fungi, parasites and viruses page)

EXAM TIP Pappenheimer bodies and basophilic stippling both look like blue-purple dots on Wright stain. Only Pappenheimer bodies turn blue with Prussian blue, because they are iron; stippling is RNA.

4 Rouleaux versus agglutination

	ROULEAUX	AGGLUTINATION
Appearance	Cells stacked like coins in rows	Irregular clumps with no order
Background	Often blue (high protein)	Usually normal
Cause	Raised plasma proteins: monoclonal protein (myeloma, Waldenström), high fibrinogen	Antibody: cold agglutinin (IgM), also Waldenström
Effect on CBC	ESR high; blood bank: false agglutination (pseudoagglutination)	Falsely low RBC and Hct, falsely high MCV and MCHC
How to tell	Saline replacement disperses rouleaux	Persists in saline; warming the sample to 37 °C disperses a cold agglutinin

5 Anemia by MCV

MCV	MAIN CAUSES	TESTS THAT SORT THEM
Microcytic (below 76 fL)	Iron deficiency, thalassemia, anemia of chronic inflammation, sideroblastic anemia (including lead)	Ferritin, iron, TIBC, transferrin saturation; RDW and RBC count; hemoglobin electrophoresis or HPLC; smear for stippling; lead level; Prussian blue on marrow
Normocytic (76–100 fL), retic high	Hemolysis, acute bleeding (after a few days)	Haptoglobin, LD, indirect bilirubin, DAT, smear (spherocytes, schistocytes, bite cells, sickle cells), G6PD, PNH flow
Normocytic, retic low	Anemia of chronic disease or kidney disease, marrow failure or infiltration, early iron deficiency, very early bleeding	Creatinine, ferritin and iron studies, smear (teardrops, nRBCs, blasts), marrow examination
Macrocytic (above 100 fL), megaloblastic	Vitamin B12 deficiency, folate deficiency, antifolate drugs	B12, folate, methylmalonic acid, homocysteine, intrinsic factor antibodies; smear: oval macrocytes, hypersegmented neutrophils
Macrocytic, non-megaloblastic	Alcohol, liver disease, reticulocytosis, myelodysplasia, hypothyroidism, drugs (zidovudine, hydroxyurea)	Liver tests, reticulocyte count, TSH, round macrocytes and target cells on the smear, marrow if MDS is suspected

6 Microcytic patterns

TEST	IRON DEFICIENCY	CHRONIC INFLAMMATION	THALASSEMIA TRAIT	SIDEROBLASTIC
Serum iron	Low	Low or normal	Normal (may be high)	High
TIBC (transferrin)	High	Low or normal	Normal	Normal
Transferrin saturation	Low (under 15%)	Low or normal	Normal	High (over 50%)
Ferritin	Low (under 30 ng/mL; under 100 with inflammation)	High (over 100 ng/mL)	Normal or high	High (over 400 ng/mL)
RDW	High	Normal or slightly high	Usually normal	High (two populations)
RBC count	Low	Low	Normal or high for the Hb	Low
Marrow iron	Absent	Present	Present	Increased; ringed sideroblasts
Key confirmatory test	Ferritin	Ferritin with clinical inflammation	Hb A2 above about 3.5% (beta); DNA testing (alpha)	Prussian blue stain of marrow; lead level

EXAM TIP Ferritin is an acute-phase protein. A low ferritin proves iron deficiency; a normal ferritin in an inflamed patient does not rule it out.

7 Hemolysis markers

MARKER	IN HEMOLYSIS	NOTES
Reticulocytes	High (ASCP range 0.5–2.5%; 20–115 × 10^3/µL)	Low despite hemolysis: marrow suppression, infection, kidney disease
Haptoglobin	Low (ASCP 30–200 mg/dL, 0.3–2.0 g/L)	Falls in liver disease; rises with inflammation, which can hide hemolysis
LD	High	Also high in ineffective erythropoiesis (B12 deficiency) and tissue injury
Indirect (unconjugated) bilirubin	High	Also high with a resolving hematoma and in Gilbert syndrome
Urine	Hemoglobinuria (red-brown, dipstick blood positive, no RBCs on microscopy); hemosiderin later	Both point to intravascular hemolysis
Plasma	Free hemoglobin turns plasma red-brown	Myoglobin does not color plasma
DAT	Positive in immune hemolysis	Negative in hereditary spherocytosis, G6PD, MAHA, PNH

EXAM TIP Most hemolysis is extravascular (spleen and liver): spherocytes, high bilirubin, little free hemoglobin. Intravascular hemolysis (ABO incompatibility, MAHA, PNH, PCH) adds hemoglobinemia, hemoglobinuria, hemosiderinuria and a haptoglobin near zero.

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