MAYO CLINIC LABORATORIES

Test Definition: RETB

Reticulocyte Profile, Blood

Overview

Useful For

Assessing erythropoietic bone marrow activity in anemia and other hematologic conditions

Assessment of acute iron deficiency

Monitoring early response to iron therapy or erythropoiesis-stimulating agents

Early monitoring of therapy for nutritional anemias (eg, megaloblastic, iron deficiency) where immature reticulocyte fraction precedes reticulocyte count increase by several days

Monitoring therapeutic efficacy of erythropoietin treatment

Monitoring early engraftment after bone marrow transplantation

Method Name

Flow Cytometry

NY State Available

Yes

Specimen

Specimen Type

Whole Blood EDTA

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions: Send whole blood specimen in original tube. **Do not aliquot.**

Forms

If not ordering electronically, complete, print, and send a Benign Hematology Test Request (T755) with the specimen.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject

Gross lipemia	OK
Gross icterus	OK
Clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole Blood EDTA	Refrigerated (preferred)	48 hours	
	Ambient	24 hours	

Clinical & Interpretive

Clinical Information

Reticulocytes are immature erythrocytes (red blood cells: RBC) that have been released into the peripheral blood from the bone marrow after extrusion of their nucleus. The reticulocyte contains residual polyribosomes used in the formation of hemoglobin in the developing erythrocyte.

Iron deficiency suppresses hemoglobin synthesis.(1) Iron indices that rely on measurement of mature RBC may not accurately reflect acute iron status due to their long (approximately 120 days) lifespan.

Reticulocytes are differentiated from erythroblasts (RBC containing a nucleus made in the bone marrow) after hemoglobin synthesis is complete and enucleation (extrusion of the nucleus). The reticulocyte is released from the bone marrow into peripheral circulation to complete maturation through loss of its reticulum (RNA and protein visible with staining) over the course of 1 to 2 days becoming mature RBC. Ultimately, hemoglobin content in reticulocytes is more reflective of real-time hemoglobin synthesis, provided there is not an underlying hematopoietic disorder preventing the production of reticulocytes.

Reticulocyte hemoglobin may be particularly useful to evaluate iron deficiency in patients with chronic kidney disease who are on hemodialysis and receiving erythropoietin or other erythropoiesis-stimulating agents, as they are prone to chronic inflammatory states that complicate traditional iron evaluations. Studies report reticulocyte hemoglobin concentrations below 29 to 32 pg in this population have areas under the receiver-operating curve (ROC area) of 0.74-0.95 for diagnosing iron deficiency compared to low serum ferritin (ROC area range: 0.53 to 0.63) or transferrin saturation (ROC area range: 0.56 to 0.76).(2)

Iron deficiency in childhood is common yet critical to recognize early and treat. Guidelines recommend using hemoglobin in combination with either ferritin and C-reactive protein or reticulocyte hemoglobin. The advantage of using reticulocyte hemoglobin is its lower cost and does not require additional blood volume to be collected when combined with complete blood cell count testing.

Reticulocyte hemoglobin is also used to evaluate response to treatment for iron deficiency, which is one of the earliest markers of response to oral iron treatment (48 hour) in children with severe iron deficiency anemia. Measurement within 7 days from the start of oral iron is predictive of reaching reference value of hemoglobin at day 30 (3) and has been used to improve iron sufficiency rates in neonatal intensive care unit populations.(4)

Other patient populations that may benefit from reticulocyte hemoglobin measurement include those with anemia of chronic disease, postpartum, and blood donors.(2)

The reticulocyte is released from the bone marrow into peripheral circulation to complete maturation through loss of its reticulum (RNA and protein measured via fluorescence) over the course of 1 to 2 days becoming mature RBC. The immature reticulocyte fraction measures reticulocyte maturity through quantitation of fluorescence intensity. The most intense signal corresponds to the most immature reticulocytes containing the greatest amount of reticulin. When present in highest proportion of total reticulocytes can be the earliest indicator of beginning erythropoiesis.

Reference Values

% RETICULOCYTES
1-3 days: 3.47-5.40%
4 days-4 weeks: 1.06-2.37%
5 weeks-7 weeks: 2.12-3.47%
8 weeks-5 months: 1.55-2.70%
6 months-23 months: 0.99-1.82%
24 months-5 years: 0.82-1.45%
6-11 years: 0.98-1.94%
12-17 years: 0.90-1.49%
Adults: 0.60-2.71%

ABSOLUTE RETICULOCYTES
1-3 days: 147.5-216.4 x 10(9)/L
4 days-4 weeks: 51.3-110.4 x 10(9)/L
5 weeks-7 weeks: 51.8-77.9 x 10(9)/L
8 weeks-5 months: 48.2-88.2 x 10(9)/L
6 months-23 months: 43.5-111.1 x 10(9)/L
24 months-5 years: 36.4-68.0 x 10(9)/L
6-11 years: 42.4-70.2 x 10(9)/L
12-17 years: 41.6-65.1 x 10(9)/L
Adults: 30.4-110.9 x 10(9)/L

IMMATURE RETICULOCYTE FRACTION (IRF)
1-3 days: 30.5-35.1%
4 days-4 weeks: 14.5-24.6%
5 weeks-2 months: 19.1-28.9%
3-5 months: 13.4-23.3%
6 months-<2 years: 11.4-25.8%
2-<6 years: 8.4-21.7%
6-<12 years: 8.9-24.1%
12-<18 years: 9.0-18.7%
> or = 18 years:
Female:3.0-15.9%
Male: 2.3-13.4%

RETICULOCYTE HEMOGLOBIN
Males:
1 day-5 months: 27.6-38.7 pg
6 months-<2 years: 28.7-35.7 pg
2-<6 years: 27.7-37.8 pg
6-<12 years: 32.4-37.6 pg
12-<18 years: 30.0-37.6 pg
Adults: 30.0-37.6 pg

Females:
1 day-5 months: 29.2-37.5 pg
6 months-<2 years: 30.1-35.7 pg
2-<6 years: 29.3-37.3 pg
6-<12 years: 30.4-39.7 pg
12-<18 years: 30.0-37.6 pg
Adults: 30.0-37.6 pg

RED BLOOD CELL COUNT (RBC)
Males:
0-14 days: 4.10-5.55 x 10(12)/L
15 days-4 weeks: 3.16-4.63 x 10(12)/L
5 weeks-7 weeks: 3.02-4.22 x 10(12)/L
8 weeks-5 months: 3.43-4.80 x 10(12)/L
6 months-23 months: 4.03-5.07 x 10(12)/L
24 months-35 months: 3.89-4.97 x 10(12)/L
3-5 years: 4.00-5.10 x 10(12)/L
6-10 years: 4.10-5.20 x 10(12)/L
11-14 years: 4.20-5.30 x 10(12)/L
15-17 years: 4.30-5.70 x 10(12)/L
Adults: 4.35-5.65 x 10(12)/L

Females:
0-14 days: 4.12-5.74 x 10(12)/L
15 days-4 weeks: 3.32-4.80 x 10(12)/L
5 weeks-7 weeks: 2.93-3.87 x 10(12)/L
8 weeks-5 months: 3.45-4.75 x 10(12)/L
6 months-23 months: 3.97-5.01 x 10(12)/L
24 months-35 months: 3.84-4.92 x 10(12)/L
3-5 years: 4.00-5.10 x 10(12)/L
6-10 years: 4.10-5.20 x 10(12)/L
11-14 years: 4.10-5.10 x 10(12)/L
15-17 years: 3.80-5.00 x 10(12)/L
Adults: 3.92-5.13 x 10(12)/L

Interpretation

Reticulocyte Quantitation:
The reticulocyte count is a measure of the number of red blood cells delivered by the bone marrow. It is elevated with active erythropoiesis such as regeneration and is decreased in hypoplastic or deficiency conditions such as vitamin B12 deficiency.

Reticulocyte Hemoglobin:
Decreased values are suggestive of acute iron deficiency.
Increasing values following treatment with iron or erythropoiesis-stimulating agents suggest early response to therapy.

Immature Reticulocyte Fraction:
Immature reticulocyte fraction (IRF) is interpreted in conjunction with the reticulocyte count. It provides similar information as the traditional reticulocyte production index, which was a value calculated from the reticulocyte percentage and hematocrit.

An increase in both total reticulocytes and IRF is associated with erythropoiesis in conditions, such as acquired hemolytic anemias, or the loss of blood.(5)

A decrease in both IRF and absolute reticulocyte count is associated with reduced marrow production.(5)

An increased IRF associated with reduced or normal reticulocyte count is associated with acute infections, myelodysplastic syndromes, or dyserythropoietic anemias.(5)

Cautions

Reticulocyte counts must be carefully correlated with other clinical and laboratory findings.

Clotted specimens yield unreliable results and are unacceptable for analysis.

Reticulocyte hemoglobin concentration is decreased in thalassemia syndromes and other microcytic anemias resulting from congenital hemoglobin diseases.

A pronounced decrease in reticulocyte hemoglobin greater than 25 pg has a high degree of accuracy for detecting alpha or beta thalassemia.(6)

Reticulocyte hemoglobin values should be interpreted in the context of the patient's overall erythrocyte physiology, including knowledge of recent blood transfusions, iron therapy, vitamin B12 or folate deficiency, chemotherapy, and the results of hemoglobin analysis.

Clinical Reference

1. Chabot-Richards DS, Zhang QY, George TI. Automated hematology. In: Rifai N, Horvath AR, Wittwer CT, eds. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics; 6th ed. 2018:1734-1734
2. Ogawa C, Tsuchiya K, Maeda Kl. Reticulocyte hemoglobin content. Clinica Chimica Acta. 2020;504:138-145
3. Parodi E, Romano F, Ramenghi U. How we use reticulocyte parameters in workup and management of pediatric hematologic diseases. Front Pediatr. 2020;8:588617
4. Morton SU, Yuen JC, Feldman HA, et al. Screening with reticulocyte hemoglobin increased iron sufficiency among NICU patients. Pediatr Qual Saf. 2020;5(2):e258. doi:10.1097/pq9.0000000000000258
5. Buttarello M. Laboratory diagnosis of anemia: are the old and new red cell parameters useful in classification and

treatment, how? Int Jn Lab Hematol. 2016;38 Suppl 1:123-132
6. Saboor M. Discrimination of iron deficiency, alpha and beta thalassemia on the basis of red cell distribution width and reticulocyte indices. Clin Lab. 2021;67(6):10.7754
7. Morkis IV, Farias M, Scotti L. Determination of reference ranges for immature platelet and reticulocyte fractions and reticulocyte hemoglobin equivalent. Rev Bras Hematol Hemoter. 2016;3 8(4):310-313
8. Soldin J, Brugnara C, Wong EC. Pediatric Reference Intervals. 5th ed. AACC Press; 2005

Performance

Method Description

The Sysmex XN reticulocyte analysis is based on flow cytometry method using a semiconductor laser. A two-dimensional scattergram is plotted, with the X-axis representing the intensity of the side fluorescent light, and the Y-axis representing the intensity of the forward scattered light. This scattergram displays groups of reticulocytes, mature red blood cells, and platelets.

The scattergram is divided into three reticulocyte (RET) zones based on the intensity of the fluorescent light, and the ratio of the reticulocytes in each zone to the total number of reticulocytes is calculated.

The immature reticulocyte fraction (IRF) is obtained as a ratio of reticulocytes count in the area with strong fluorescent light intensity in the RET scattergram (IRF zone), to the total reticulocytes count.

RET-He (reticulocyte hemoglobin equivalent) is a unique parameter developed by Sysmex that is derived using the reticulocyte scattered light signals and a proprietary Sysmex calculation equation.(Instruction manual: Automated Hematology Analyzer XN series [XN-9000/XN-9100] North American Edition, Code No. BF691913 en-am. Sysmex Corp; rev: 09/2022)

PDF Report

No

Day(s) Performed

Monday through Sunday

Report Available

1 day

Specimen Retention Time

3 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

85046

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
RETB	Reticulocyte Profile, B	50262-5

Result ID	Test Result Name	Result LOINC® Value
RBC	Erythrocytes	789-8
PRTIC	Reticulocytes, B	17849-1
ARTIC	Absolute Reticulocyte	60474-4
IRF1	Immature Retic Fraction	33516-6
RETHB	Reticulocyte Hemoglobin	71694-4