Reticulocyte Hemoglobin Content (CHr)

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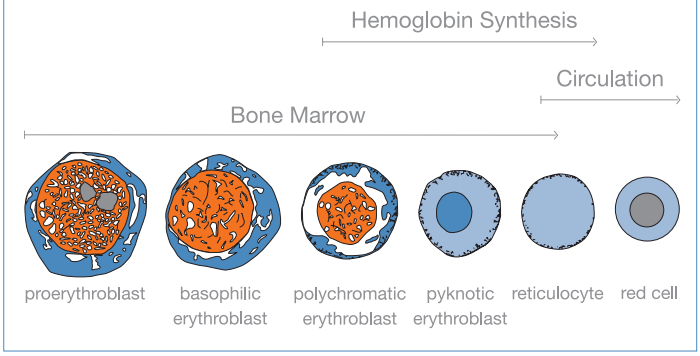
A Test for Diagnosing Iron Deficiency

- CHr measures the hemoglobin content of reticulocytes (immature red blood cells).
- CHr is an early, direct measurement of available iron for erythropoiesis (red blood cell production).
- CHr is reported to have greater sensitivity and specificity for diagnosing iron deficiency than traditional iron measurements.[1, 2]

Reticulocyte hemoglobin content (CHr) measures the amount of hemoglobin in reticulocytes. Reticulocytes are the most immature red blood cells found in circulation in the body. They exist in circulation for only a day or two before becoming fully mature red blood cells. The stages of red blood cell maturation are shown in Figure 1.

Measurement of the reticulocyte hemoglobin content provides a snapshot of the iron directly available for hemoglobin synthesis and is an early indicator of the body's iron status.

Figure 1. The Stages of Red Blood Cell Maturation[3]



Relevance in Kidney Disease

Effective management of anemia in dialysis patients is enhanced by close monitoring of iron status or treatment of iron deficiency.

Patients may become iron deficient due to bleeding, hemodialysis treatment related blood loss and poor nutrition.[4] After treatment with erythropoietin (EPO), available iron may be depleted and some patients may develop functional iron deficiency. This is a state in which tissue iron stores are adequate (or even excessive) while hemoglobin synthesis is limited by an inability of the iron transport system to mobilize stored iron at a rate adequate to keep up with the demand.[5]

Recognizing functional iron deficiency is important because patients with this condition will have a sub-optimal response to EPO therapy, requiring a higher dose to achieve equivalent hemoglobin levels.[6] Providing additional (IV) iron for these patients may enhance their response, thus potentially reducing their EPO requirement. Providing iron to patients who are not functionally iron deficient and will not benefit from the additional iron only increases the risk for iron overload and its associated comorbidities.[7]

The most common tests used to assess iron status are transferrin saturation (calculated from the serum iron and iron binding capacity) and ferritin. These tests may sometimes be difficult to interpret in dialysis patients. Both ferritin and transferrin saturation may be affected by factors that are unrelated to iron status such as infection and inflammation.[8]

CHr is less affected by inflammation, than transferrin saturation and ferritin. Both transferrin saturation and ferritin tests provide indirect information regarding the amount of iron available in the bone marrow for erythropoiesis.

The CHr test provides an early, direct measurement of the available iron utilized in red blood cell production.

As a direct measurement of iron in red blood cells, CHr has greater sensitivity and specificity for diagnosing iron deficiency than traditional iron measurements. Fishbane reported that patients with CHr values less than 26 pg are iron deficient and these patients' reticulocyte counts are likely to increase in response to an IV bolus of iron dextran.[1] At a level of 26 pg, CHr has a sensitivity of 100% and a specificity of 80% in diagnosing iron deficiency. In contrast, transferrin saturation values of less than 20% and ferritin values of less than 100 ng/mL had sensitivities of 57.1% and 71.4%, respectively. In similar studies, Mittman et al. demonstrated comparable, if less dramatic, results using CHr < 28 pg as a reference point, but with a lower sensitivity and specificity than Fishbane reported.[2] Sixty percent (60%) of the patients in this study who had desirable values for ferritin and transferrin saturation demonstrated substantial increases in CHr following iron dextran infusion. This would indicate that these patients were in fact functionally iron deficient despite having "normal" values for the traditional iron measures.

The reticulocyte count is an important adjunct to the CHr measurement. While reticulocytes indicate the adequacy of red blood cell production as a response to EPO, the CHr level indicates actual red blood cell hemoglobin content. If iron stores are low, any reticulocytes produced may have low hemoglobin content (hypochromia).

Test Methodology

The test methodology used to measure CHr is flow cytometry. The cellular hemoglobin content of the reticulocytes is measured on a per cell basis by dual angle light scatter and the mean is reported as the CHr.

Specimen Collection

Refer to your laboratory's Reference Guide or Directory of Services. In general, 2 mL of whole blood in a lavender top tube is required. Specimens should be collected and handled carefully, especially when collecting from a central venous catheter.

To ensure accurate results:

- Obtain samples before the initiation of dialysis.
- Avoid contaminating blood with heparin or saline.
- Use luer adapter to collect specimen directly into lavender top tube – avoid using syringes.
- Be sure to mix samples by gently inverting 5 times after collection.
- Refrigerate specimens promptly while awaiting shipment. Do not freeze.

Interpretation of Results

The normal limits for CHr are: 24.5 – 31.8 pg. Values of less than 26 pg may be indicative of iron deficiency in dialysis patients.

Factors Which May Influence CHr

- Changes in EPO dose[1]
- Administration of IV iron[2]
- Infection and/or inflammation[9, 10]

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