

Reticulocyte Haemoglobin equivalent

Ret-He Parameter



Anaemia is one of the most common symptoms of many diseases and one of the most underestimated RBC disorders. The mean intracellular haemoglobin content of erythrocytes (MCH) is an all-inclusive measure of both the availability of iron over the preceding 90-120 days. The haemoglobin and haematocrit are also relatively static parameters and may change too slowly to be useful as primary indicators of the rate of erythropoiesis or cellular iron status. Iron store estimates do not provide an assessment of the availability of iron for introduction into erythrocyte haemoglobin. This leads to the concept of ***‘functional iron deficiency’*** a phenomenon seen in anaemia of chronic disease (ACD).

By directly measuring the mean haemoglobin content of reticulocytes (reticulocyte haemoglobin equivalent -Ret-He), early stages of iron deficiency may be identified, at a time that other traditional biochemical markers and other red cell parameters are non-informative. The Ret-He is a direct assessment of the incorporation of iron into erythrocyte haemoglobin and thus a direct estimate of the functional availability of iron into the erythron. Whilst a reticulocyte count provides a ***‘quantity’*** measurement of erythropoiesis in the marrow, the Ret-He indicates cell haemoglobinization and thus reflects the ***‘quality’*** of the newly produced reticulocytes. The use of both parameters provides a complete picture of the patient’s erythropoietic status.

The Ret-He when used with other RBC indices and biochemical markers can provide additional information to assist with earlier detection, differential diagnosis and management of iron deficiency. The Ret-He may also be able to gauge a patient’s response to iron therapy in days rather than weeks using more traditional methods (haemoglobin concentration may only see a significant change after 2-3 weeks).

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**Guidelines:**

Wayne Thomas D, Hinchliffe Rod F, Briggs C, Macdougall I, Littlewood T, Cavill I. (2013) Guideline for the laboratory diagnosis of functional iron deficiency. *British Journal of Haematology,* **161**, 639-648

**Summary of recommendations**

* Mean cell volume (MCV) and mean cell haemoglobin (MCH) values are useful at diagnosis and in assessing trends over periods of weeks or months. They have NO use in assessing acute changes in iron availability secondary to therapy with erythropoiesis-stimulating agents (ESAs). (1B)
* A reticulocyte haemoglobin equivalent (Ret-He) value <25 pg is suggestive of classical iron deficiency and may also predict functional iron deficiency in those receiving ESA therapy. (1B)
* The serum ferritin assay is essential in the assessment and management of patients with all forms of iron-restricted erythropoiesis (IRE) including functional iron deficiency (1B)
* Serum ferritin values <12 ng/mL indicate absent iron stores. (1A)
* The serum ferritin concentration is not useful in predicting ESA responsiveness in cancer-related anaemia.(1A)
* The measurement of serum erythropoietin concentration in the setting of anaemia has limited value in the diagnosis of functional iron deficiency.(1A)

***In managing anaemia in chronic kidney disease***

* A Ret-He value <30.6 pg appears to have the best predictive value for likelihood of response to intravenous iron therapy in chronic kidney disease (CKD) patients on haemodialysis. (1B)
* A serum ferritin concentration <100 ng/mL in non-dialysed patients or <200 ng/mL in chronic haemodialysis patients is associated with a HIGH LIKELIHOOD of iron deficiency and a potentially good response intravenous iron therapy. (1A). Values above the suggested cut-offs given above should therefore NOT be used to guide iron therapy.
* In isolation, the transferrin saturation is NOT recommended as a predictor of responsiveness to intravenous iron therapy in patients with CKD.(1A)
* Transferrin saturation may be used to monitor response to ESA and/or iron deficiency in CKD. When used with either the serum ferritin concentration or Ret-He it may be useful in the diagnosis of functional iron deficiency. (1A)

***In addition,***

National Institute for Health and Clinical Excellence (NICE) guidelines (NICE 2015) advise against the use of serum ferritin and transferrin saturation alone (unless thalassaemia or thalassaemia trait is present) to assess need for iron replacement in CKD patients. The Ret-He has improved clinical utility and should be used if available (NICE 2015). For CKD patients on treatment with ESA, iron supplementation should routinely be offered to patients to keep their Ret-He >29 pg, or transferrin saturation >20% unless their serum ferritin is >800 ng/mL, with markers checked every 1-3 months in patients on haemodialysis, or every 3 months in patients who are pre-dialysis or on peritoneal dialysis.

**References**

Wayne Thomas D, Hinchliffe Rod F, Briggs C, Macdougall I, Littlewood T, Cavill I. (2013) Guideline for the laboratory diagnosis of functional iron deficiency. *British Journal of Haematology,* **161**, 639-648

Cullis J, Fitzsimons E, Griffiths W, Tsochatzis E, Wayne Thomas D. Investigation and management of a raised serum ferritin (2018). *British Journal of Haematology,* **181**, 331-340

Chronic kidney disease: managing anaemia (2015). NICE guidelines (NG8)

Reticulocyte Haemoglobin Content (RET-He): A parameter with well-established clinical value (2013). Sysmex America White Paper

The importance of reticulocyte detection (2016). Sysmex Educational Enhancement and Development (SEED Haematology)

**For any further information please discuss with haematology laboratory (Ex.4728) or haematology clinical staff**

Royal United Hospitals Bath NHS Foundation Trust  
Combe Park, Bath BA1 3NG  
01225 428331 [www.ruh.nhs.uk](http://www.ruh.nhs.uk)