ANEMIA DISEASE MANAGEMENT:
SCIENTIFIC EVIDENCE FOR A
COMPREHENSIVE DIAGNOSTIC MENU.
Anemia is a prevalent disease affecting children, young adults, pregnant women, cancer patients and the elderly. Anemia has been recognized by the World Health Organization as an important disease leading to significant health care burden.¹

Anemia represents a diagnostic challenge due to the complexity of its etiology. Anemia is defined as a lower-than-normal hemoglobin level, or a reduced red blood cell count. Nevertheless, in order to identify the underlying cause of anemia, and subsequently an accurate diagnosis, a good interpretation of clinical symptoms, combined with the information provided by several laboratory tests, is required. This may involve various clinical disciplines such as hematology, chemistry and immunodiagnostics.

Beckman Coulter provides a complete menu of immunoassays to support the diagnosis of anemia. The excellent analytical and clinical performances of the Access anemia panel of assays are demonstrated in the peer-reviewed publications presented in this document.

Iron Deficiency Anemia (IDA)

Robust, routine haematology reference ranges for healthy adults
› Accurate, reliable laboratory reference ranges are essential for effective clinical evaluation and monitoring.
› These results represent an extensive study to establish robust reference ranges in healthy adults.
› This study establishes reference ranges for Beckman Coulter Access Ferritin, Vitamin B12 and Folate assays from blood samples that were obtained from 250 healthy donors.

Automated immunoassay methods for ferritin: recovery studies to assess traceability to an international standard
› This article investigates the performance of various assays relative to their calibration to the international standard (IS).
› The data presented in this study shows the benefit of standardization against the 3rd IS 94/572, in order to avoid assay drift that may result in poor sensitivity and specificity in the diagnosis of iron status.
› Standardization to the 3rd IS 94/572 ensures compliance with the European Union In-Vitro Diagnostic Directive which requires traceability of assay calibrators to reference materials of a higher order.
› The Access Ferritin assay is traceable to the 3nd IS 94/572.

Serum transferrin receptor and its ratio to serum ferritin in the diagnosis of iron deficiency
› The objective of the study was to evaluate the diagnostic efficiency of laboratory tests, including soluble serum transferrin receptor (sTfR) measurements, in the diagnosis of iron deficiency anemia (IDA).
› sTfR measurement thus provided a reliable diagnosis of iron deficiency anemia (AUC ROC 0.98).
› Calculation of the ratio sTfR/log ferritin (sTfR-F Index), a way of combining sTfR and ferritin, provided an outstanding parameter for the identification of patients with depleted iron stores (AUC ROC 1.00).
› In anemic patients, sTfR measurement is a valuable noninvasive tool for the diagnosis of iron depletion, and offers an attractive alternative to more conventional laboratory tests in the detection of depleted iron stores.
Anemia of Chronic Disease (ACD)

**SOLUBLE TRANSFERRIN RECEPTOR (sTfR)**

**Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: A prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index**


- This multicenter prospective study demonstrates a significant clinical benefit of using sTfR and the sTfR/log ferritin index for the differential diagnosis of IDA and ACD.
- Use of sTfR and the sTfR/log ferritin index improves detection of IDA from 41% (ferritin alone) to 92% (ferritin, sTfR and the sTfR/log ferritin index), identifying combined IDA + ACD.
- This study establishes a clinically validated decision point for the Access sTfR assay and the derived sTfR/log ferritin index.

**Transfusion suppresses erythropoiesis and increases hepcidin in adult patients with β-thalassemia major: A longitudinal study**


- This study explored the relationship between transfusion and iron overload due to regulation of hepcidin hormone in β-thalassemic patients.
- Pre- and post-transfusion levels of hemoglobin, hepcidin, ferritin, erythropoietin (EPO), growth differentiation factor-15 (GDF-15) and sTfR were determined in relation with erythropoiesis and iron metabolism.
- Monitoring of EPO, sTfR and GDF-15 could have a potentially valuable clinical role in the future in quantitatively and qualitatively evaluating erythropoiesis and thus optimizing transfusion dosing.

**INTERLEUKIN 6 (IL-6)**

**Role of Interleukin-6 in the Anemia of Chronic Disease**


- This article reviews the published evidence supporting the involvement of interleukin-6 in the pathophysiology of anemia of chronic disease.
- Interleukin-6 is a multifunctional cytokine that regulates the hepatic acute-phase response, the immune response, inflammation and hematopoiesis.
- Interleukin-6 appears to be the central mediator of anemia of chronic disease in a range of inflammatory diseases, including end-stage renal disease and rheumatoid arthritis.
Vitamin Deficiency Anemia

**VITAMIN B12**

Comparison of isotopic and immunoenzymatic methods for folate and vitamin B12 determination


- This article compares the analytical performance of the manual isotopic assays with the Beckman Coulter Access fully-automated assays.
- The results presented in this publication indicate a very good correlation of the automated assay with the manual isotopic assays with excellent intra- and inter-assay variability ranging from 5 to 9%.
- The automated Access Vitamin B12 and Folate assays appear to be good alternatives to replace the radio-immunoassays.

**INTRINSIC FACTOR ANTIBODY (IFAb)**

Development and validation of an automated chemiluminometric immunoassay for human intrinsic factor


- Intrinsic factor is essential for the absorption of vitamin B12. The presence of intrinsic factor autoantibody can reduce the absorption of vitamin B12 leading to pernicious anemia.
- Although a negative IFAb test does not rule out pernicious anemia, a positive IFAb test, in combination with macrocytic red blood cells and low vitamin B12 levels, confirm the diagnosis of pernicious anemia.
- This article describes the development and the validation of the automated Access Intrinsic Factor Ab assay.

**FOLATE**

The development and role of international biological reference materials in the diagnosis of anaemia


- Accurate diagnosis of anemia is dependent on reliable diagnostic tests and reference ranges, which in turn are dependent on effective standardization.
- This review article demonstrates the benefit of standardization to improve method comparability.
- The Beckman Coulter Access Folate assay is traceable to the World Health Organization (WHO) International Standard 03/178 to ensure optimal accuracy of patient diagnosis.
Anemia of Cancer

**SOLUBLE TRANSFERRIN RECEPTOR (sTfR)**

**Prediction of the responsiveness to treatment with erythropoiesis-stimulating factors: A prospective clinical study in patients with solid tumors**

› Human recombinant erythropoietin (rHuEPO) is used as an erythropoiesis stimulating agent to treat anemia related to cancer chemotherapy. Only half of the patients respond to the rHuEPO treatment.
› This article demonstrates that the determination of sTfR two weeks after treatment, combined with the hemoglobin level four weeks after treatment, can predict the long term response to rHuEPO treatment in cancer patients.

**The soluble transferrin receptor reflects tumor load in chronic lymphocytic leukemia**

› The results presented in this article indicated that sTfR serum concentration directly reflects the tumor burden in chronic lymphocytic leukemia.
› Patients with normal sTfR had a small tumor load and no abdominal involvement.
› sTfR values and sTfR Index decrease, or even normalize, after successful treatment.
› Therefore, sTfR may be of clinical value in monitoring disease activity, response to treatment and disease progression.

**Soluble transferrin receptor and depth of bone marrow suppression following high dose chemotherapy**

› The serum level of sTfR was shown to correlate with erythropoietic activity.
› This article explores the role of sTfR determination to reflect the level or the duration of myelosuppression in patients receiving high-dose chemotherapy.
› The authors conclude that sTfR may be helpful in predicting the degree of bone marrow suppression in patients receiving intensive chemotherapy.
Anemia of Renal Failure

**ERYTHROPOIETIN (EPO)**

**Associations between changes in hemoglobin and administered erythropoiesis-stimulating agent and survival in hemodialysis patients**


- Erythropoiesis-stimulating agents (ESA) including human recombinant erythropoietin (rHuEPO) have been proposed to treat anemia related to renal failure and chronic kidney disease (CKD).
- This article demonstrates that an increase in hemoglobin levels following ESA treatment in patients with advanced CKD is associated with a lower risk of death.
- These results illustrate the importance of anemia management in patients with renal failure in order to limit the rate of cardiovascular events and improve survival.

**SOLUBLE TRANSFERRIN RECEPTOR (sTfR)**

**Pumping iron: revisiting risks, benefits and strategies in treatment of iron deficiency in end-stage renal disease**


- Iron deficiency is a common cause of anemia in patients with end-stage renal disease (ESRD).
- Intravenous iron administration, especially in those requiring treatment with erythropoiesis stimulating agents (ESA) is an essential component of the management of anemia in ESRD patients. However, iron can promote oxidative stress, cause endothelial dysfunction, inflammation and tissue injury, and has a potential to cause progression of both CKD and cardiovascular disease.
- This review article discusses the benefits and risks associated with i.v. iron and the practical aspects of iron administration that can minimize the complications related to iron therapy in ESRD.
- The determination of sTfR serum levels is mentioned for the assessment of iron store in patients with CKD.
PARTNERING TO MOVE YOUR LAB FORWARD

Laboratories around the world rely on Beckman Coulter’s promise of quality, integrity and innovation. Our total laboratory solutions deliver accurate information, for medical research breakthroughs, clinical trials, laboratory diagnostics and point-of-care testing. A partnership with Beckman Coulter extends far beyond our products. With proven expertise in analyzing laboratory test processes, we collaborate with you to understand your requirements and create flexible solutions that meet your evolving needs.

The foundation of patient care starts with the lab, and we are committed in our partnership with you to keep it moving forward.

IMMUNODIAGNOSTIC ASSAYS FOR DIAGNOSIS OF ANEMIA

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