



Clinical Approach To Hemoglobin Levels With Diagnostic Application Of Blood Indices (Mcv, Mch, Mchc)

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Abstract:

Hemoglobin (Hb) abnormalities are commonly encountered in medical practice and represent a gateway to diagnosing a wide spectrum of clinical disorders. Understanding deviations in Hb levels—either elevated or decreased—requires a meticulous and methodical clinical approach. This article focuses on providing a comprehensive, stepwise diagnostic strategy for evaluating abnormal hemoglobin values, with an emphasis on interpreting red cell indices such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Diagnostic algorithms and decision trees are presented as clinical flowcharts to aid real-time diagnosis and enhance physician decision-making.

Keywords: Hemoglobin, Anemia, Polycythemia, MCV, MCH, MCHC, Diagnostic Algorithm, Clinical Decision Tree, CBC Reading, CBC interpretation, High Hb(Hemoglobin), Low Hb.

1. Introduction:

Blood is a vital connective tissue responsible for the transportation of essential elements such as oxygen, nutrients, hormones, and metabolic waste throughout the body. Among its cellular components, red blood cells (RBCs) play a crucial role in maintaining physiological homeostasis, primarily through their oxygen-carrying capacity, which is attributed to a specialized iron-containing protein known as **hemoglobin**. **Hemoglobin** is a complex metalloprotein composed of four globin chains—two alpha and two beta chains in adults (HbA)—each with an embedded heme group that contains a central iron ion (Fe^{2+}). This structure enables hemoglobin to reversibly bind with oxygen, facilitating its transport from the alveoli of the lungs to the tissues and the return transport of carbon dioxide and hydrogen ions. Hemoglobin also serves as an important buffer system, contributing to the regulation of blood pH.

The synthesis of hemoglobin is tightly regulated and occurs within the erythroid precursors in the bone marrow, requiring adequate supplies of iron, vitamin B6, vitamin B12, and folate. Any disruption in this process—whether due to nutritional deficiencies, genetic disorders (such as thalassemia or sickle cell disease), chronic inflammation, or bone marrow failure—can lead to defective hemoglobin production or function, ultimately

manifesting as anemia. The physiological concentration of hemoglobin varies by age, sex, and altitude. In adults, normal ranges typically fall between 13.5–17.5 g/dL for males and 12.0–15.5 g/dL for females. Even slight deviations from these ranges can indicate underlying pathology and should prompt further diagnostic evaluation.

Anemia, a common hematological condition, is defined by a reduction in the total number of red blood cells or a decrease in hemoglobin concentration below the normal reference range for age and sex. This condition compromises the oxygen-carrying capacity of blood, resulting in tissue hypoxia and a wide spectrum of clinical symptoms, including fatigue, pallor, dyspnea, and tachycardia. Anemia is not a disease per se, but rather a manifestation of various underlying causes, such as nutritional deficiencies (iron, vitamin B12, folic acid), chronic diseases, bone marrow failure, or blood loss. Understanding the structure and function of hemoglobin, as well as the pathophysiological basis of anemia, is essential for clinical evaluation, diagnosis, and therapeutic decision-making in both general and specialized medical practice.

Hemoglobin concentration is a crucial parameter measured routinely in the complete blood count (CBC) and is a fundamental marker of the oxygen-carrying capacity of blood. Abnormal hemoglobin levels—either elevated or decreased—often indicate underlying disease processes ranging from benign nutritional deficiencies to complex hematological malignancies. The red blood cell indices—MCV, MCH, and MCHC—serve as vital tools for differential diagnosis and provide insights into red blood cell morphology and function. Because of the broad spectrum of possible causes, a structured and algorithmic approach is essential for an accurate and efficient clinical diagnosis. This review aims to provide a detailed diagnostic algorithm for clinicians, supported by data from standard hematology and physiology references.

2. Materials and Methods:

This article is based on a comprehensive review of primary textbooks, peer-reviewed journals and algorithmic framework based on integrative insights drawn from authoritative sources including Harrison's Principles of Internal Medicine (21st Edition), ABC of CBC by D.P. Lokwani, Essentials of Medical Physiology by Sembulingam (25th Edition), and Williams Hematology. Additional reference materials such as laboratory handbooks and clinical manuals were incorporated. A diagnostic framework was developed using a pathophysiological and algorithmic approach, reinforced by flowcharts for enhanced clinical utility.

3. Results and Discussion:

3.1 Diagnostic Approach to High Hemoglobin / Polycythemia

Polycythemia is classified into two main categories: relative and absolute i.e. A) Relative (hemoconcentration due to decrease in plasma volume leading to an apparent increase in Hb concentration without an actual rise in red cell mass) commonly caused by dehydration (of any cause), stress, or diuretic use. B) Absolute (true increase in red cell mass). Absolute polycythemia is further classified into primary (e.g., Polycythemia Vera) and secondary causes (e.g., hypoxia, tumors producing erythropoietin).

Stepwise Clinical Algorithm:

Step 1: Verification of Elevated Hb and Exclusion of Laboratory Error

- Define elevated Hb: >17.5 g/dL in men, >15.5 g/dL in women.
- Confirm findings with a repeat CBC and review hydration status, altitude exposure, smoking, or stress-related causes.¹⁻⁵
- Evaluate blood smear to identify signs of increased RBC mass.

Step 2: Assessment of Plasma Volume and Relative Polycythemia

- Evaluate for signs of hemoconcentration (vomiting, diarrhea, excessive diuretic use).
- In suspected cases, measure plasma volume or hematocrit/plasma ratio.

Step 3: Distinguish Absolute Polycythemia

- Confirm RBC mass using nuclear red cell mass study (if available).
- Proceed with erythropoietin (EPO) level measurement.

Step 4: Serum Erythropoietin (EPO) Levels

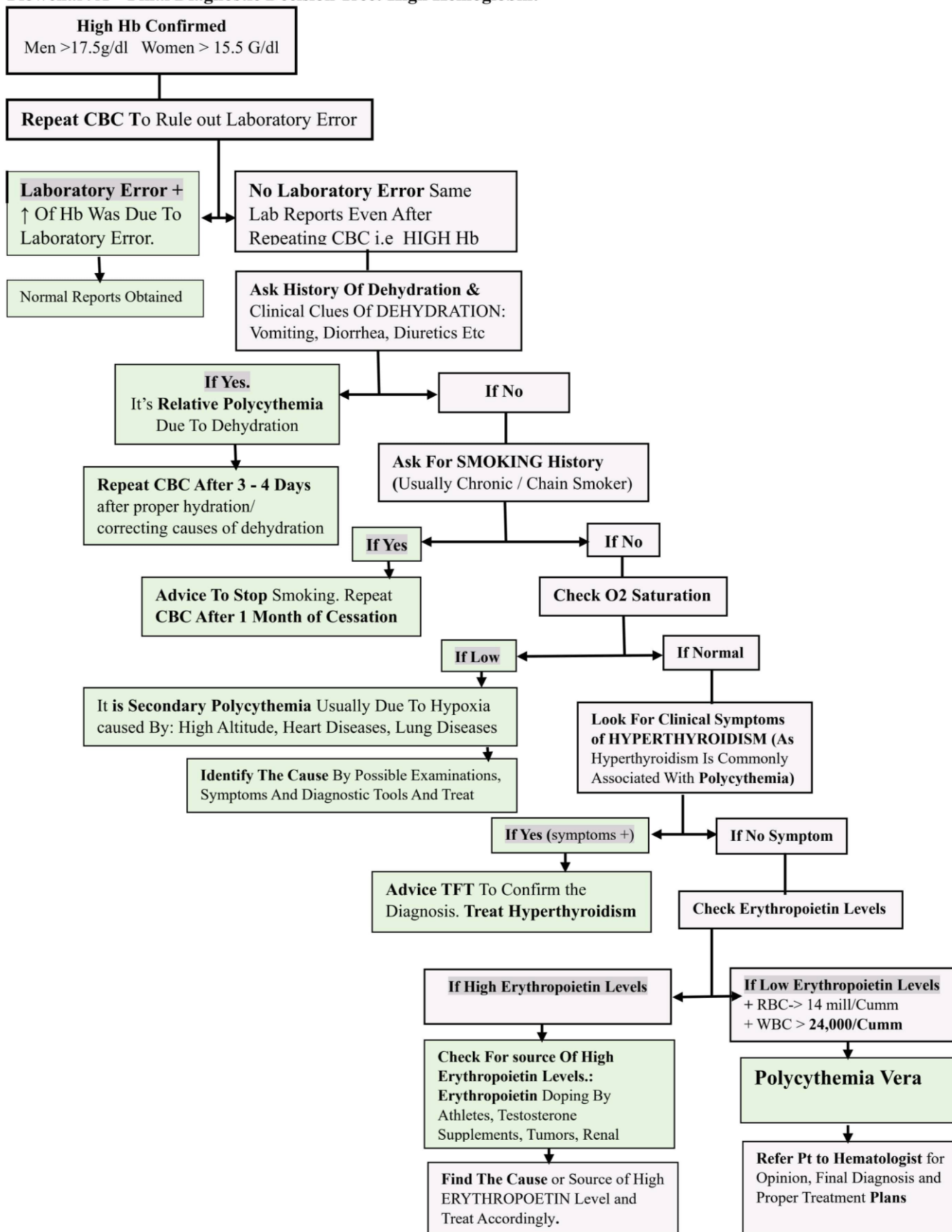
- **Low EPO** suggests Polycythemia Vera (PV) → Check for JAK2 mutation (present in ~95%).²
- **Normal/High EPO** indicates secondary polycythemia:
 - **Hypoxia-related:** chronic lung disease, obstructive sleep apnea, cyanotic heart disease.
 - **Ectopic EPO production:** renal cell carcinoma, hepatocellular carcinoma.

Step 5: Ancillary Tests and Confirmatory Diagnostics

- ABG, pulse oximetry, and carboxyhemoglobin in smokers, suspected CO exposure and to detect hypoxemia in lung disease or obstructive sleep apnea.
- Imaging: Chest X-ray or CT chest/abdomen, renal USG.
- Bone marrow biopsy if myeloproliferative disorder suspected.

Step 6: Clinical Features and Red Flag Symptoms

- **Polycythemia Vera:** Aquagenic pruritus, erythromelalgia, splenomegaly, thrombosis.
- **Secondary polycythemia:** Dyspnea, cyanosis, or systemic symptoms indicative of malignancy or endocrine abnormalities

Figure 1: Flowchart A – Final Diagnostic Decision Tree: High Hemoglobin⁸**Flowchart A – Final Diagnostic Decision Tree: High Hemoglobin:**

3.2 Diagnostic Approach to Low Hemoglobin / Anemia

Anemia is defined as Hb <13.0 g/dL in men and <12.0 g/dL in women. ³ the first step in anemia evaluation involves classifying it using red cell size i.e. known through one of the CBC parameters MCV, and further refined using MCH and MCHC. A meticulous analysis of these indices helps clinicians distinguish between various etiologies of anemia, ranging from nutritional deficiencies to hemolytic and marrow disorders.

Stepwise Clinical Algorithm:

Step 1: Classify Anemia by MCV

- **Microcytic (<80 fL):** Iron deficiency anemia (IDA), thalassemia, lead poisoning, anemia of chronic disease (ACD) in later stages.
- **Normocytic (80–100 fL):** Acute blood loss, ACD Anemia of chronic disease, chronic kidney disease (CKD), marrow suppression, early hemolysis.
- **Macrocytic (>100 fL):** Vitamin B12/folate deficiency, alcoholism, hypothyroidism, liver disease, myelodysplastic syndrome.

Step 2: Evaluate MCH and MCHC

- **Low MCH/MCHC:** Hypochromic RBCs—supportive of IDA, thalassemia.
- **Normal MCH/MCHC:** Normochromic anemia—ACD, CKD or early marrow failure.
- **High MCHC:** Hereditary Spherocytosis, autoimmune hemolysis (cold agglutinin disease).

Step 3: Confirm with Peripheral Smear and Reticulocyte Count

- Microcytic with target cells → thalassemia
- Microcytic with anisopoikilocytosis → iron deficiency anemia
- Macrocytic with Oval macrocytes, hypersegmented neutrophils → B12/folate deficiency
- Normocytic with reticulocytosis → hemolysis or acute blood loss
- Normocytic with low retic count → anemia of chronic disease

Step 4: Focused Diagnostic Work-up on Suspected Etiology:

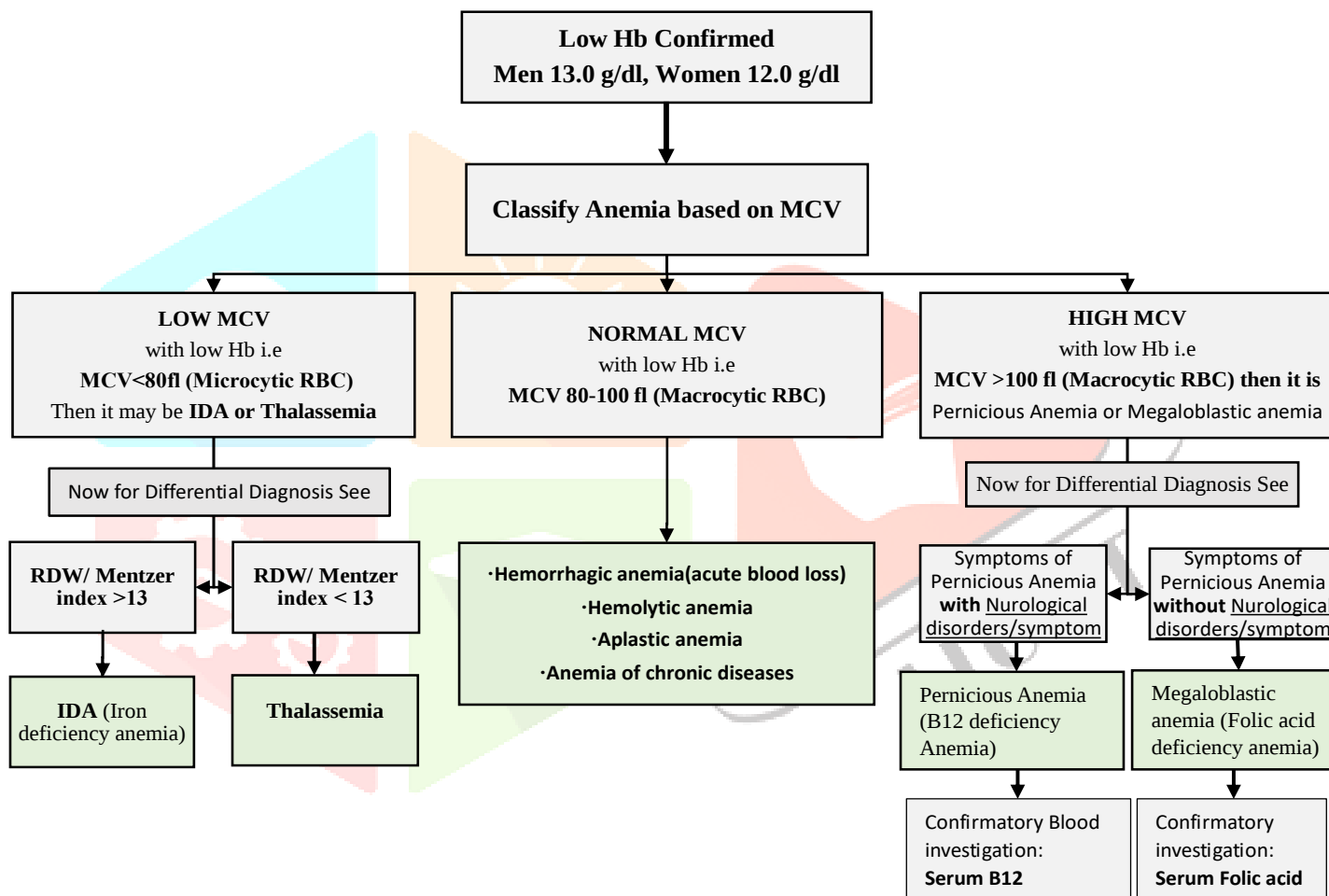
- **Iron studies:** if microcytosis- IDA = Serum ferritin (↓), TIBC (↑), serum iron (↓); if normocytosis ACD = Serum ferritin (Normal/↑), TIBC (↓), serum iron (↓).³
- **Vitamin assays:** if -macrocytosis Serum B12 and folate.
- **Kidney, liver, thyroid function tests:** To uncover systemic contributors.
- **Hemoglobin electrophoresis:** Essential for diagnosing thalassemia and sickle cell disease.
- **Bone marrow biopsy:** Required in pancytopenia, macrocytosis, unexplained anemia, suspected aplastic anemia, or myelodysplasia

Diagnostic Table – Red Cell Indices Interpretation

MCV MCH MCHC Interpretation

Low	Low	Low	IDA, Thalassemia
Norm	Norm	Norm	ACD, CKD, early Hemolysis
High	High	Norm	B12/Folate Deficiency, Liver Disease
Norm	Norm	High	Hereditary Spherocytosis, Cold Agglutinin

Flowchart B – Final Diagnostic Decision Tree: Low Hemoglobin:



4. Conclusion:

Understanding hemoglobin abnormalities requires a nuanced, algorithmic approach that incorporates red cell indices, clinical symptoms, and targeted investigations. MCV, MCH, and MCHC provide immediate diagnostic direction when interpreting CBC results. Decision trees and flowcharts significantly enhance clinician efficiency in differentiating between primary and secondary polycythemia and among types of anemia. This structured method allows for timely interventions and better patient outcomes.

5. References:

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Figures:

Figure 1: Flowchart A – Final Diagnostic Decision Tree: High Hemoglobin

Figure 2: Flowchart B – Final Diagnostic Decision Tree: Low Hemoglobin

