



CLINICAL LABORATORY TESTING:

BLOOD CHEMISTRY

& CBC ANALYSIS

FROM A FUNCTIONAL MEDICINE PERSPECTIVE

Part 2 of 8 Hematology

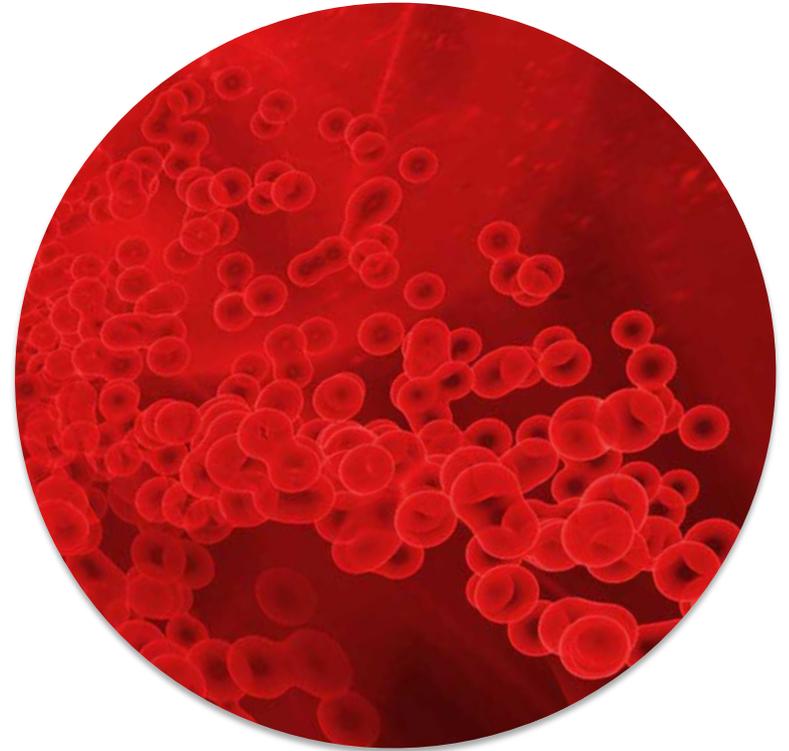
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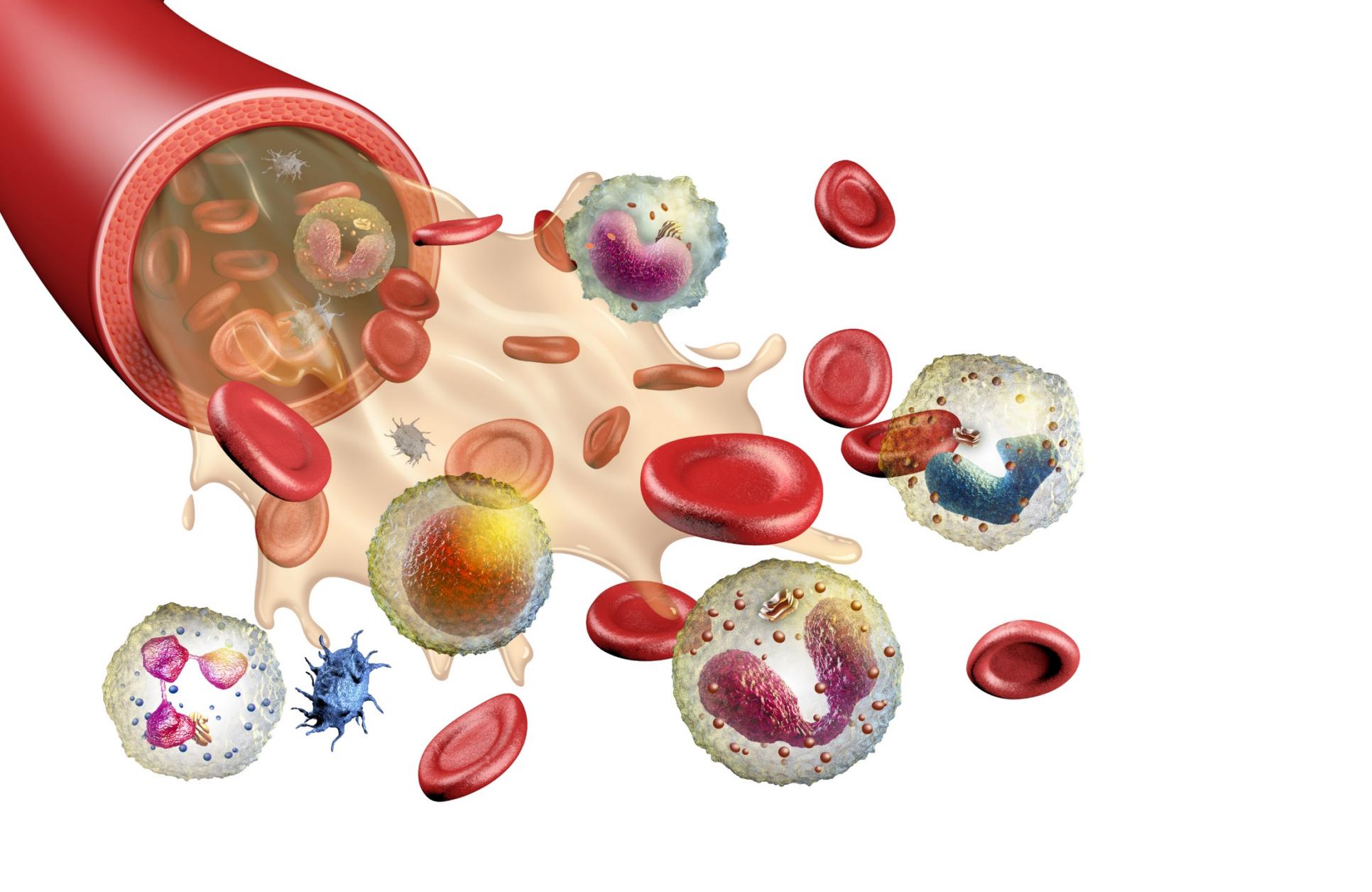


Hematology: Blood Composition and Life Span of Blood Cells

Composition of Blood

Blood is specialized fluid tissue that is composed of both cellular and non-cellular tissue. Its function is to serve as a transport system that allows for various substances to be circulated within the body. The amount of blood in the average adult is about 5 liters with a specific gravity between 1.055 – 1.065 and a narrow pH range between 7.3 – 7.4





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& CBC ANALYSIS
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Life Span of Blood Cells

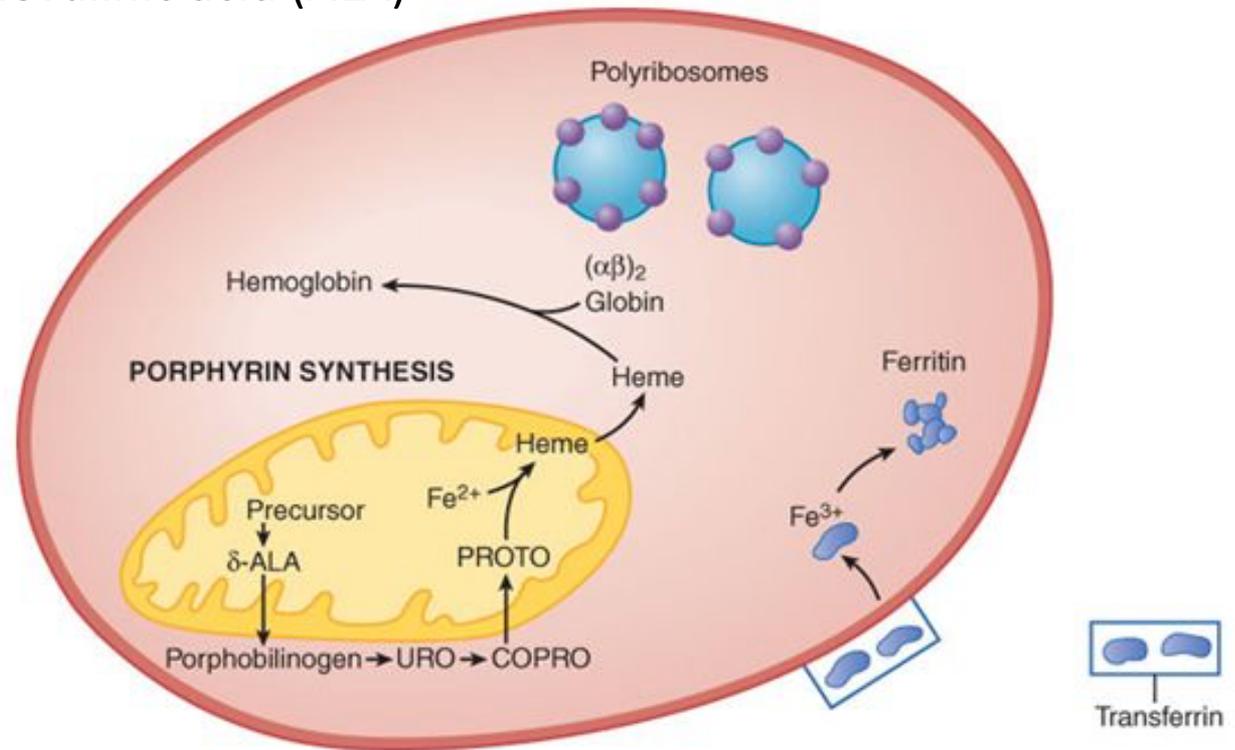
Cell type	Average Normal Life Span
Red Blood Cells	120 days
Granulocytes	4 to 8 hours in circulation + 4 to 5 days in tissue
Monocytes	10 to 20 hours in circulation (Macrophages can live for several months if not used)
Lymphocytes	Weeks to months
Platelets	Replaced every 10 days

Hemoglobin Synthesis

- The production of blood cells requires a significant amount of energy expenditure.
- Hematopoiesis is maintained at optimal levels **only** when an adequate amount of high-quality protein is consumed and optimal proportions of fatty acids are present.
- The hemoglobin combines with oxygen, loosely and reversibly. The hemoglobin molecule transports oxygen to the peripheral tissue capillaries, then releases it.
- Synthesis of hemoglobin begins in the pro-erythroblasts and continues into the reticulocyte stage of the red blood cell formation.

Hemoglobin Synthesis

Hemoglobin synthesis begins in the mitochondria where succinyl-CoA, formed in the Krebs cycle, binds with the amino acid glycine to form 5-aminolevulinic acid (ALA)



Hemoglobin Synthesis

- Understanding the synthesis of hemoglobin, the inherited enzyme defects that block its formation, and the impact of environmental toxins on hemoglobin formation is of vital importance for the integrative medicine clinician.
- Substances such as heavy metals, pharmaceuticals, metabolic disturbances, and host environmental toxins such as pesticides, herbicides, and industrial and manufacturing by-products block heme synthesis, which eventually leads to an anemia state.

Nutrients Required

Vitamin B6 (pyridoxine)

- Multiple forms of vitamin B6: active form of vitamin B6 is pyridoxal-5'-phosphate (PLP or P-5-P).
- Involvement in more than 100 enzymes that are involved mainly in protein and amino acid metabolism.
- Cofactor for decarboxylases, aminotransferases, racemases, and dehydrogenases.
- **Liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) require B6 as a coenzyme.**
- PLP is a coenzyme for the enzyme aminolevulinate synthase, which involved in the synthesis of heme. **A deficiency of vitamin B6 can decrease hemoglobin synthesis leading to hypochromic microcytic anemia.**

Nutrients Required (continued)

Vitamin B12 (Cobalamin) and Folate

- Deficiencies of the two related vitamins, folic acid and vitamin B12, cause megaloblastic anemia (abnormally large red blood cell precursors and larger than normal red cells (macrocytic cells) in the peripheral blood. The abnormalities in cell morphology arise due to impaired production of 5, 10-methylene-tetrahydrofolate (MTHF), an essential nutrient for DNA synthesis.
- **Vitamin B12 and folate depletion occur long before changes can be seen in red blood cell morphology.**

Nutrients Required (continued)

Pantothenic acid (B5)

- A precursor to coenzyme A (CoA): essential for the metabolism of carbohydrates, the metabolism of lipids and proteins.
- Pantothenic acid, along with thiamine pyrophosphate (B1), lipoic acid, flavin adenine dinucleotide (B2), and nicotinamide adenine dinucleotide (B3), is a part of **the pyruvate dehydrogenase complex** (PDC) that converts pyruvate to acetyl-CoA. The acetyl-CoA then enters the citric acid cycle for energy metabolism.
- In lipid metabolism, CoA is important in the synthesis of cholesterol, bile salts, ketone bodies, fatty acids, and steroid hormones. **It also appears the pantothenic acid is required for the synthesis of heme.**

Nutrients Required (continued)

Vitamin C (Ascorbic acid)

- Reducing agent (antioxidant) to maintain the iron and copper atoms in the reduced state.
- Antioxidant for many reactive oxygen species such as hydroxyl radical, hydroperoxyl radical, superoxide radical, alkoxyl radical and peroxy radical.
- The anemia of scurvy is due to in part to the depletion of the folate pool.
Vitamin C appears to reduce the rate of oxidation of 10-formyl-tetrahydrofolate; thereby keeping the folate metabolic pool replete.

Nutrients Required (continued)

Copper (Cu)

- Required for over 30 metalloproteins involved in oxidation-reduction reactions; neurotransmitter, energy, myelin and bone/connective tissue production, immune function, and hematopoiesis.
- Low serum copper can contribute to cytopenia or bone marrow failure. The most frequently used biomarkers of copper status are plasma or serum copper and serum ceruloplasmin levels. RBC copper may be useful as a marker of copper status.

Nutrients Required (continued)

Iron (Fe)

- **Hemoglobin contains about 70% of total-body iron.** Another 3.9% found in myoglobin and in mitochondrial proteins involved in energy metabolism and respiration such as cytochromes, catalase, peroxidase and metallo-flavoprotein enzymes.
- Iron is in the center of the heme molecule and enables oxygen transport to tissues; transitional storage of oxygen in tissues; and transport of electrons through the respiratory chain via the cytochromes.
- The thyroid enzyme involved in the production of thyroid hormones, thyroid peroxidase, is a heme-dependent enzyme.

Amino Acids

Amino acids are critical for virtually every function in the body. Aside from their involvement in protein synthesis, amino acids are an integral part of neurotransmitters, hormones, and detoxification. In addition, certain amino acids are precursors of the heme molecule, nucleotides and cell membranes.

The amino acid glycine is used in the formation of heme (porphyrins).

The Complete Blood Count

- Measures the concentration of the white blood cells, red blood cells and platelets.
- It provides a substantial amount of information that assists in the diagnosis and treatment of numerous conditions such as: anemia, infections, cancer of the blood cells, inflammation, environmental toxin exposure, renal disease (decreased erythropoietin), liver disease, autoimmune disease and nutrient deficiencies.

Components

- white blood cell count with differential
- red blood cell count
- hemoglobin (HGB)
- hematocrit (HCT)
- mean corpuscular volume (MCV)
- mean corpuscular hemoglobin (MCH)
- mean corpuscular hemoglobin concentration (MCHC)
- red blood cell distribution width (RDW)
- platelet count, and mean platelet volume.

Collectively, MCV, MCH and MCHC are known as the red blood cell indices, which assist in the diagnosis of several types of anemia.

Additional CBC Analytes

- Reticulocyte count: underutilized test that is can assess erythropoietic activity. Used to evaluate a patient's responsiveness to vitamin therapy, follow the progress of bone marrow transplant, or assess the impact of chemotherapy on hematopoietic function.
- The RBC blood smear is used to evaluated abnormally shaped RBCs and assess for RBC inclusions.

Red Blood Cell Count (erythrocyte count)

- The average life span: about **120 days**.
- **No nucleus:** cannot synthesize proteins for cellular repair.
- The RBCs possess systems capable of preventing oxidative stress to the hemoglobin molecule.
- **Low membrane concentration of vitamin E in erythrocytes will shorten their life span and contributing to anemia.**

Indications and Use:

- Evaluate for anemia
- Support other hematologic test for diagnosing anemia
- Serial testing in patients with blood loss
- Assess for other conditions, such as polycythemia
- Provide data for calculating RBC indices

Red Blood Cell Count (erythrocyte count)

Gender	Age	Reference Range Cells/uL	SI Units Cells/L	Optimal Range Cells/uL
Male	>18 y	$4.5 - 5.9 \times 10^6$	$4.5 - 5.9 \times 10^{12}$	$4.2 - 4.90 \times 10^6$
Female	>18 y	$4.1 - 5.1 \times 10^6$	$4.1 - 5.1 \times 10^{12}$	$3.9 - 4.50 \times 10^6$

Increased RBCs

- Polycythemia vera (primary polycythemia). Secondary polycythemia (erythrocytosis)
- Chronic obstructive pulmonary disease (COPD)
- Significant dehydration
- Hemoglobinopathies
- Medications: anabolic steroids, erythropoietin, gentamicin, methyldopa
- High altitudes

Decreased RBCs

- Various types of anemia (aplastic, anemia of chronic disease, iron-deficiency, megaloblastic, pernicious, sickle cell, thalassemia, malabsorption (celiac disease), and hemolytic anemia)
- Blood loss (bleeding; GI, NSAIDs, menstruation)

Hemoglobin (Hgb, Hb)

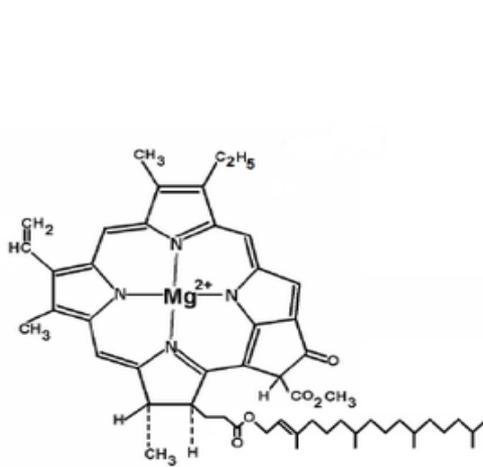
- Transport mechanism oxygen and carbon dioxide
- Hemoglobin value is the amount of this metalloporphyrin-protein contained in a given volume of blood.
- Hemoglobin consists of heme (iron surrounded by protoporphyrin) and globulin (alpha and beta polypeptide chains).
- Abnormalities in **globulin structure** are called hemoglobinopathies (e.g. sickle cell disease, hemoglobin C disease. Some diseases are caused by abnormalities in **globulin synthesis**, such as thalassemia

Heme Biosynthesis

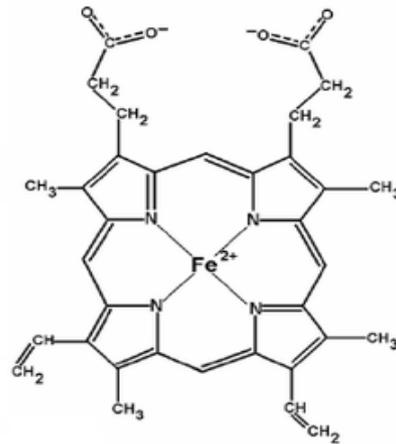
- Hemoglobin synthesis starts and ends in the mitochondrial matrix, however enzymes located in the cytosol perform the ring-forming and decarboxylation steps.
- The intermediate structures along the pathway are called porphyrinogens.
- **Heme is required at the active sites of oxygen-binding, oxygen-utilizing and oxidizing systems, hemoglobin (and myoglobin), cytochromes, and mitochondrial electron carriers.**

The final phase of metal incorporation inserts iron, cobalt or magnesium into the protoporphyrin ring to produce **heme**, **cobalamin** and, in plants, **chlorophyll**, respectively.

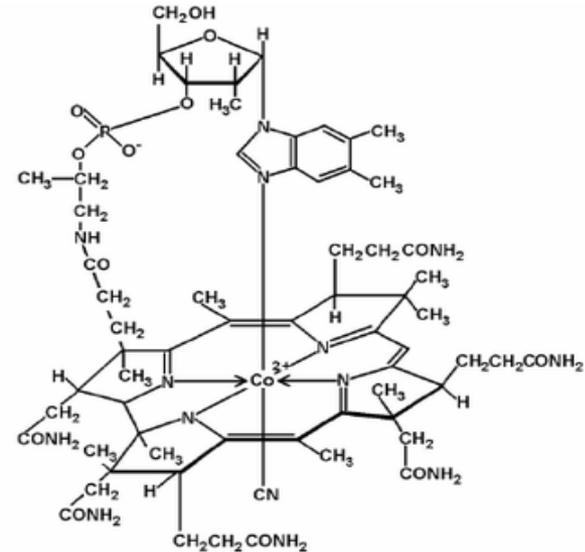
These complex organometallic structures are sometimes called the pigments of life.



Chlorophyll



Heme group



Cyanocobalamin
(Vitamin B12)

Porphyria

- **Inherited enzyme defects** that can occur at specific location along the pathway.
- **Metabolic disorders** (e.g. diabetes, disturbances in iron metabolism, and hematologic disease), environmental toxins (esp. heavy metals), and certain disease states (e.g. infectious disease, liver diseases, and malignancies) are conditions that can cause **acquired porphyria**.

Hemoglobin (Hgb, Hb)

Gender	Age	Reference Range g/dL	SI Units mmol/L	Optimal Range g/dL
Male	Adult	14 – 17.5	8.7 – 11.2	14.0 – 15.0
Female	Adult	12.3 – 15.3	7.4 – 9.9	13.5 – 14.5

Increased Hemoglobin

Dehydration

Polycythemia vera

COPD/Emphysema

Smoking

High altitude

Congenital heart disease

Decreased Hemoglobin

Anemia

Hemorrhage

Digestive disorders

(e.g. malabsorption, IBD, IBS)

Hemoglobinopathy

Renal disease

(reduced erythropoietin)

Bone marrow

failure/Cancer

Dietary deficiency

(e.g. iron, B12, B6, folate, copper,
vitamin C)

Chronic illnesses

(e.g. RA, lupus, sarcoidosis)

Hematocrit (Hct)

The hematocrit (packed cell volume) is the percentage of the total blood volume that is composed of RBCs. It is used as an indirect measurement of RBC number and volume.

Gender	Age	Reference Range %	SI Units (Proportion of 1)	Optimal Range %
Male	Adult	42 – 50	0.42 – 0.50	40.0 – 48.0
Female	Adult	36 – 45	0.36 – 0.45	37.0 – 44.0

Increased Hematocrit – same as Increased Hemoglobin

Decreased Hematocrit – same as Decreased Hemoglobin

RBC Indices - MCV, MCHC, MCH and RDW

The RBC indices: classification of anemias.

Mean Corpuscular Volume (MVC) and red blood cell distribution width (RDW):
RBC size

Mean Corpuscular Hemoglobin (MCH): average amount (weight) of hemoglobin
in the RBC

Mean Corpuscular Hemoglobin Concentration (MCHC): average percentage of
hemoglobin in the RBC

RBC size is categorized by the following terms: normocytic, microcytic, and macrocytic.

Hemoglobin content is categorized by the following term: normochromic, hypochromic and hyperchromic.

RBC Indices - Mean Corpuscular Volume (MCV)

Most clinically useful of the indices

Macrocytic: large RBC – B12/Folate deficiency

Normocytic: normal size

Microcytic: small RBC – abnormal synthesis of hemoglobin – iron deficiency anemia

Hyperglycemia can cause macrocytosis: increased osmotic expansion

$$\text{MCV} = \frac{\text{Hematocrit (\%)} \times 10}{\text{RBC count}}$$

RBC Indices - Mean Corpuscular Hemoglobin (MCH)

Individuals **with iron deficiency or thalassemia** who are unable to synthesize normal amounts of hemoglobin have a significantly reduced MCH value.

$$\text{MCH} = \frac{\text{Hemoglobin (g/dL)} \times 10}{\text{Total RBC count}}$$

RBC Indices - Mean Corpuscular Hemoglobin Concentration (MCHC)

MCHC is calculated by dividing the hemoglobin times 100 by the hematocrit. Iron deficiency is the only anemia in which the MCHC is routinely low, although it can also be decreased in other disorders of Hgb synthesis.

MCHC can be falsely elevated in hyperlipidemia.

$$\text{MCHC} = \frac{\text{Hemoglobin (g/dL)} \times 100}{\text{Hematocrit \%}}$$

RBC Indices - Red Blood Cell Distribution (RDW)

RDW is an indication of the variation in RBC size (anisocytosis- unequal RBC size).

RDW is calculated by lab instrumentation using the MCV and RBC values.

Used primarily with other tests to differentiate iron deficiency anemia from thalassemias.

RDW increases in macrocytic anemias and in early iron deficiency, often before other tests show signs of this kind of anemia.

Increased valued of RDW suggest the presents of a mixed population of cells (anisocytosis).

RBC Indices

Analyte	Age	Reference Range	Optimal Range
MCV	Adult	80 – 96 fL/cell	85.00 – 92.00 fL/cell
MCHC	Adult	33.4 – 35.5 g/dL or 33.4 – 35.5 %	32 – 35 %
MCH	Adult	27 – 34 pg	27 – 31.9 pg
RDW	Adult	11.5 – 15.5 %	11.70 – 13.00



Increased MCV

Vitamin B12/folate deficiency

Hypochlorhydria

Poor nutrition

Chemotherapy

Chronic liver disease

Alcoholism

Hypothyroidism

Decreased MCV

Iron deficiency

Thalassemia

Anemia of chronic illness

Increased MCHC

Spherocytosis

Intravascular hemolysis

Decreased MCHC

Iron deficiency anemia

Thalassemia

Heavy metal toxicity

Increased MCH

Macrocytic anemias

Vitamin B12/folate deficiency

Decreased MCH

Iron deficiency

Blood loss

Heavy metal toxicity

Increased RDW

Iron deficiency anemia

Vitamin B12/folate deficiency

Hemoglobinopathies

(fragmentation increases RDW)

Reticulocyte Count and Reticulocyte Production Index

Reticulocyte: immature nonnucleated red blood cell that contains some ribosomal ribonucleic acid in the cytoplasm that can be identified under the microscope on the peripheral blood smear

Determining the production and development of red blood cells, and bone marrow function.

Small number of reticulocytes is considered normal.

Essential component of the CBC and plays a prominent role in initially classifying many anemias.

Reticulocyte Count

Pivotal decision-making test when deciding whether the anemia is **hyperproliferative anemia** or **hypoproliferative anemia**.

Useful in determining whether or not the bone marrow is responding to the anemia.

When anemia develops, the bone marrow should respond with an increase in the reticulocyte count in an effort to maintain the hemoglobin level.

The absence of an increase in reticulocyte count reflects an inability of the bone marrow to compensate for the anemia

Reticulocyte Count

The retic count is calculated as a percentage of the total red blood cell count, and must be viewed in relationship to the RBC count. (false elevation – anemia)

In states of anemia, the reticulocyte percentage is not a true reflection of reticulocyte production.

In order to use the reticulocyte count as a measure of red blood cell production, the count needs to be correct for both changes in hematocrit (RBC count) and the effect of erythropoietin on reticulocyte release from the marrow.

The first correction involves adjusting the reticulocyte count for the degree of anemia

$$\text{Reticulocyte \%}_{\text{corrected}} = \text{reticulocyte \%}_{\text{reported}} \times \left(\frac{\text{patient's hematocrit}}{\text{normal hematocrit}} \right)$$

A **normal or low reticulocyte count in a patient with anemia** indicates that the marrow response to the anemia by way of production of RBCs is inadequate and perhaps is contributing to or is the cause of the anemia (**aplastic anemia, iron deficiency, vitamin B12 deficiency, depleted iron stores**).

An elevated reticulocyte count found in patients with a normal hemogram indicates increased RBC production compensating for an ongoing loss of RBCs (**hemolysis or hemorrhage**).

To obtain the true index of marrow production in a **severely anemic patient**, a second correction must be made if marrow reticulocytes have entered circulation in response to high levels of erythropoietin.

The **second calculation** is called the reticulocyte production index (RPI).

$$\text{RPI} = \frac{\text{Reticulocyte \% corrected}}{\text{Correction Factor}}$$

Patient's Hematocrit

Correction Factor

40-45

1.0

35-39

1.5

25-34

2.0

15-24

2.5

<15

3.0



RPI of less than < 2 (hypoproliferative)

Inadequate bone marrow response:

- iron deficiency anemia
- vitamin B12/folate deficiency
- chronic disease
- aplastic anemia
- myeloproliferative disease

Note: The second correction may not be accurate in the case of anemia caused by chronic disease due to the suppression of erythropoietin.

RPI of greater than > 2 (hyperproliferative)

Bone marrow is responding appropriately for the degree of anemia.

- Anemia of acute blood loss
- Hemolysis
- response to treatment

Elevated levels of bilirubin (indirect) and lactic dehydrogenase (LDH, esp. LDH1) are seen in cases of hemolysis.

Indications and Use of the Retic Count:

- Evaluate erythropoietic activity (bone marrow responds to anemia)
- To help distinguish between hypoproliferative and hyperproliferative anemias
- To assist with the assessment of blood loss
- Monitor response to therapy of various anemias

Gender	Age	Reference Range
M/F	Infant	0.5 – 3.1 % of RBCs
M/F	Adult and child	0.5 – 2.0 % of RBCs

Increased Retic Count

- Microscopic internal bleeding
- Hemolytic
- Hemorrhage (3 to 4 days later)
- In response to treatment of iron deficiency anemia, pernicious anemia and folic acid deficiency.
- Oxidative stress (free radical pathology)
- Heavy metal toxicity
- Kidney disease (e.g. tumor) with increased erythropoietin production

Decreased Retic Count

- Pernicious anemia/folic acid deficiency
- Iron deficiency anemia
- Aplastic anemia
- Adrenocortical Hypofunction
- Anterior Pituitary Hypofunction
- Radiation therapy
- Malignancy
- Chronic diseases
- Kidney disease with decreased erythropoietin production
- Cirrhosis of the liver

White Blood Cell Count

- Fight infection and react against foreign bodies or tissue
- Acute and chronic diabetic complications are correlated with an elevated WBC count; elevated WBC count, even within the normal range, is associated with both macro- and microvascular complications of type 2 diabetes
- Higher WBC counts may be associated with the development of retinopathy, albuminuria, and peripheral vascular disease

White Blood Cell Count

Age	Reference Range Cells/uL	SI Units Cells/L	Optimal Range Cells/uL
Adult	4.4 – 11.3 x 10 ³	4.4 – 11.3 x 10 ⁹	5.3 – 7.5 x 10 ³

Increased WBC count (leukocytosis)

Infection: viral, bacterial
Inflammation
Neoplastic disorder
Trauma
Tissue necrosis
Dehydration
Thyroid storm
Steroid use: glucocorticoids stimulate WBC production
Stress

Decreased WBC count (Leukopenia)

Autoimmune disease
Overwhelming infections
Chronic infections
Nutritional deficiencies (e.g. B12, iron)
Bone marrow failure
Malabsorption
Drug toxicity

White Blood Cell Count

Cell Type	RR* %	OR %	Absolute Count**	Description
Neutrophils	45 – 73	40-60	1000-7800/uL	<p>Primary function: phagocytosis</p> <p>Immature cells: Band/stab cells</p> <p>More immature = shift to the left</p> <p>More immature: ongoing acute infection</p> <p>Most common granulocyte</p>
Basophils	0-1	0-1	0 – 200/uL	<p>Phagocytosis of antigen-antibody complexes</p> <p>Contains: heparin, histamine, serotonin</p>
Eosinophils	0-4	0-3	0 – 450 uL	Phagocytosis of antigen-antibody complexes
Lymphocytes	20-40	24-39	1000-4800/uL	<p>T cells: thymus cells</p> <p>B cells: antibody production</p> <p>Natural Killer cells: NK cells</p>
Monocytes	2-8	0-9	200 – 1000/uL	Phagocytic: remove necrotic debris and microorganisms

Abnormal Diff and Absolute Count: Potential Etiologies

Cell Type	% Increased	% Decreased	AC* ↑Threshold Cells/uL	AC ↓Threshold Cells/uL
Neutrophils	<p>Neutrophilia</p> <p>Acute suppurative infection</p> <p>Physical/emotional stress</p> <p>Myelocytic leukemia</p> <p>Cushing syndrome</p> <p>Inflammatory disorders (e.g. RA, thyroiditis)</p> <p>Metabolic disorders (e.g. gout, ketoacidosis, eclampsia)</p>	<p>Neutropenia</p> <p>Aplastic anemia</p> <p>Dietary deficiency</p> <p>Overwhelming bacterial infection</p> <p>Viral infection</p> <p>Radiation Therapy</p> <p>Chemotherapy</p>	<p>> 12,000</p> <p>Acute bacterial infection</p> <p>Trauma</p> <p>Myocardial infarction</p> <p>Chronic bacterial infection</p> <p>Sickle cell crises</p> <p>Epinephrine</p> <p>Lithium</p> <p>Glucocorticosteroids</p>	<p>< 1500</p> <p>Radiation exposure</p> <p>Vitamin B₁₂ or folate deficiency</p> <p>Pertussis</p> <p>Salmonellosis</p>

Cell Type	% Increased	% Decreased	AC* ↑Threshold Cells/uL	AC ↓Threshold Cells/uL
Basophils	Basophilia Myeloproliferative disease Leukemia	Basopenia Acute allergic reaction Hyperthyroidism Stress reaction	> 300 Chronic inflammation Leukemia	

Cell Type	% Increased	% Decreased	AC* ↑Threshold Cells/uL	AC ↓Threshold Cells/uL
Eosinophils	<p>Eosinophilia</p> <p>Parasitic infection</p> <p>Allergic reactions (food/heavy metal**)</p> <p>Eczema</p> <p>Leukemia</p> <p>Autoimmune diseases</p> <p>Oxidative stress</p>	<p>Eosinopenia</p> <p>Increased adrenosteriod production</p>	<p>> 300</p> <p>Allergic disorder/asthma</p> <p>Parasitic infections</p> <p>Leukemia</p> <p>Medications</p> <p>ACE inhibitors</p> <p>Antibiotics</p> <p>Allergic reaction to drugs</p>	<p>< 50</p> <p>Acute infection</p>

Cell Type	% Increased	% Decreased	AC* ↑Threshold Cells/uL	AC ↓Threshold Cells/uL
Lymphocytes	Lymphocytosis Chronic bacterial infection Viral infection Lymphocytic leukemia Multiple myeloma Radiation Infectious mononucleosis Infectious hepatitis	Lymphocytopenia Leukemia Immunodeficiency Lupus Radiation therapy Drug therapy	> 4000 Infectious mononucleosis Viral infections Tuberculosis Syphilis Lymphoma	< 1000 HIV type 1 Radiation exposure Glucocorticosteroids Lymphoma (Hodgkin's) Aplastic anemia



Cell Type	% Increased	% Decreased	AC* ↑Threshold Cells/uL	AC ↓Threshold Cells/uL
Monocytes	<p>Monocytosis</p> <p>Chronic inflammatory disorders</p> <p>Viral infections (e.g. mono)</p> <p>Tuberculosis</p> <p>Chronic ulcerative colitis</p> <p>Parasites</p>	<p>Monocytopenia</p> <p>Aplastic anemia</p> <p>Hairy cell leukemia</p> <p>Drug therapy: prednisone</p> <p>Long-term chronic inflammation</p>	<p>> 800</p> <p>Recovery state of acute bacterial infection</p> <p>Protozoal or rickettsia infection</p> <p>Endocarditis</p> <p>Leukemia/lymphoma</p>	

Platelet (Thrombocytes) and Mean Platelet Volume

Platelets are non-nucleated, disk shaped structure, 1-5 micron in diameter.

Megakaryocyte production and maturation are promoted by the hormone thrombopoietin

Their main role is to maintain vascular integrity (blood clotting)

Play a role in the pathological process of the formation of arterial thrombi

Affected by numerous factors such as medications, vitamins foods, spices, and systemic conditions, including chronic renal disease and hematological diseases such as myeloproliferative and lymphoproliferative disease, dysproteinemias, and the presence of antiplatelet

Platelet (Thrombocytes)

Age	Reference Range Count/ uL or count/mm ³	SI Units (___ x 10 ⁹ /L)	Optimal Range Count/uL
Adult	150,000 – 450,000	0.42 – 0.50	150,000 – 400,000

Platelet antibody testing can help differentiate between immune and non-immune thrombocytopenia (low platelet count).

Increased Thrombocythemia

(thrombocytosis, elevated platelet count)

- Acute hemorrhage
- Severe trauma
- Malignancies - about 50% of patients with unexpected thrombocytosis are found to have a malignancy
- After splenectomy
- Infections
- Chronic inflammatory disorders (e.g. rheumatoid arthritis, pancreatitis)
- Stress
- Cirrhosis
- Magnesium deficiency (Generalized stimulation of bone in response to anemia may cause thrombocytosis and leukocytosis as a consequence of increased demand for RBCs imparted by a deficiency in magnesium)

Thrombocytopenia

Mucosal and/cutaneous bleeding is the most common clinical consequence of thrombocytopenia; however, patients with only modest decreases in platelet counts may be asymptomatic.

Decreased Production: Any disease/condition that affects bone marrow production such as viral infections, toxic chemical, heavy metals, oxidative stress, chemotherapy, and heavy alcohol consumption.

Increased platelet consumption: Any disease/condition that causes an increase in platelet destruction such as, pregnancy, idiopathic thrombocytopenic purpura, autoimmune diseases (e.g. lupus, RA), hemolytic uremic syndrome, disseminated intravascular coagulation and thrombotic thrombocytopenia purpura

Hyperthyroidism and hypothyroidism

Medications

MPV: Reference and Optimal Range: 7 – 11fL

Mean platelet volume (MPV) is generally used to assess disturbances in platelet production.

In general, lower platelet counts are common with higher platelet volumes, as an inverse relationship exists between the platelet count and MPV.

Elevated MPV with thrombocytopenia suggests the production of platelets is intact.

Normal or lower MPV with thrombocytopenia suggest a problem with platelet production.

Increased MPV	Diabetes mellitus Hereditary Hyperthyroidism Immune thrombocytopenic purpura Myocardial infarction Pregnancy-induced hypertension Renal failure Respiratory disease Sepsis
Decreased MPV	HIV infection Chemotherapy Hypersplenism Hypothyroidism Marrow aplasia Reactive thrombocytosis

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Next lesson: Part 3 of 8
**Clinical Laboratory Medicine:
Liver, Gallbladder and Pancreas**