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An Overview of Red Blood Cell Properties and Functions

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Haematopoiesis, the process of forming blood cells, changes dynamically throughout life. It starts in the yolk sac and moves to the liver around the sixth week, where it produces small erythrocytes. After three months of foetal development, haemoglobin converts into foetal myoglobin, and the spleen becomes a new site for haematopoiesis. Blood-forming cells begin to colonise the medullary chambers of all bones in the fourth month, and this process continues until the child is four years old. Except for the axial skeleton, peripheral bone cavities become hematopoietically dormant when they fill with adipose tissue during adulthood. In some pathological situations, the liver and spleen may re-establish hematopoietic sites. The article discusses RBCs' unique structure, including their biconcave form, lack of a nucleus, and excess haemoglobin, which gives them their distinctive red colour. The article provides a detailed explanation of RBCs' role in oxygen transport, emphasising

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the importance of haemoglobin in binding and releasing oxygen. The article also discusses the role of RBCs in overall health, such as preventing anaemia and other blood disorders. The article also discusses several medical diseases that can impact red blood cells, such as sickle cell anaemia and thalassemia. Overall, this article gives a thorough summary of RBC structure, function, and importance.

Keywords: Hemoglobin; fetal; hematopoiesis; blood; spleen; erythrocyte; cells.

1. INTRODUCTION

Red blood cells are essential components of blood that give vertebrate blood its characteristic red colour. They also help transport oxygen from the lungs to various tissues. In the human body, mature red blood cells have a small, spherical, and biconcave shape, and they are flexible enough to change shape during their journey through narrow blood vessels. A membrane of proteins and lipids encloses these cells and lacks a nucleus [1]. They contain haemoglobin, a protein responsible for oxygen binding, which gives them their crimson colour. Red blood cells play a crucial role in the circulatory system by conveying oxygen from the lungs to the body tissues and transporting carbon dioxide from the tissues back to the lungs for excretion. This function is essential for cellular metabolism since oxygen is necessary for tissue oxygenation, and carbon dioxide is a metabolic waste product [2,3].

Vertebrates developed red blood cells to concentrate oxygen-carrying pigments within them, enhancing gas exchange efficiency. In mammalian red cells, the absence of a nucleus is a further adaptation that minimizes oxygen requirements for cellular metabolism while maximizing the release of oxygen into the tissues [3,4]. The biconcave shape of these cells facilitates a constant rate of oxygen exchange over the largest possible surface area. Red blood cells in the bone marrow undergo a complicated development process. They start as the hemocytoblast, a multipotential cell in the mesenchyme, and become the erythroblast and reticulocyte [1,5]. The cell fills up with haemoglobin during this process while losing its nucleus and mitochondria. Fully mature red cells have an average lifespan of 100–120 days, and an adult human body typically contains around 5.2 million red cells per cubic millimetre of blood. While red blood cells usually have a round shape, a minority may assume an oval form in normal individuals, and certain hereditary conditions or diseases may lead to abnormal shapes such as oval cells in pernicious anaemia, crescent-shaped cells in sickle cell anaemia, or cells with thorny projections in acanthocytosis [5-7]. The number of red cells and the haemoglobin concentration can vary among individuals and in different conditions, with higher counts observed, for instance, in individuals living at high altitudes or those with polycythaemia. Notably, the red cell count is elevated at birth, decreases shortly after, and gradually rises to adult levels during puberty. Red blood cells are essential components of blood that give vertebrate blood its characteristic red color. They also help transport oxygen from the lungs to various tissues. In the human body, mature red blood cells have a small, spherical, and biconcave shape, and they are flexible enough to change shape during their journey through narrow blood vessels. A membrane of proteins and lipids encloses these cells and lacks a nucleus. They contain haemoglobin, a protein responsible for oxygen binding, which gives them their crimson colour. Red blood cells play a crucial role in the circulatory system by conveying oxygen from the lungs to the body tissues and transporting carbon dioxide from the tissues back to the lungs for excretion. This function is essential for cellular metabolism since oxygen is necessary for tissue oxygenation, and carbon dioxide is a metabolic waste product. Vertebrates developed red blood cells to concentrate oxygen-carrying pigments within them, enhancing gas exchange efficiency with haemoglobin. In mammalian red cells, the absence of a nucleus is a further adaptation that minimizes oxygen requirements for cellular metabolism while maximizing the release of oxygen into the tissues. The biconcave shape of these cells facilitates a constant rate of oxygen exchange over the largest possible surface area [7,8].

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an adult human body typically contains around 5.2 million red cells per cubic millimetre of blood. While red blood cells usually have a round shape, a minority may assume an oval form in normal individuals, and certain hereditary conditions or diseases may lead to abnormal shapes such as oval cells in pandemic anaemia, crescent-shaped cells in sickle cell anaemia, or cells with thorny projections in acanthocytosis. The number of red cells and the haemoglobin concentration can vary among individuals and in different conditions, with higher counts observed, for instance, in individuals living at high altitudes or those with polycythaemia. Notably, the red cell count is elevated at birth, decreases shortly after, and gradually rises to adult levels during puberty [5,7-10].

Red blood cell structure: Red blood cells (RBCs) are unique in their biconcave form, which provides a high surface area for efficient gas exchange. They lack a nucleus, maximizing the space for hemoglobin, the protein responsible for oxygen transport. The RBCs' flexible membrane allows them to change shape as they travel through tight capillaries, and their cytoskeleton provides structural support and flexibility. The red color of RBCs comes from the high hemoglobin concentration in their cytoplasm. RBCs have a lifespan of around 120 days, after which the spleen and liver remove damaged or aging cells, and their components are recycled [1,5,11]. The RBCs' small diameter, approximately 7-8 micrometers, allows them to pass through thin capillaries easily. The cell membrane contains several proteins, including glycophorin, that maintain the cell's structural integrity and play a role in the hemoglobin classification process. Beyond oxygen transport, RBCs have several other crucial functions. They facilitate the removal of carbon dioxide, maintain pH balance in the blood, modulate blood viscosity, act as blood type beacons, and perform emerging functions such as immune regulation, nitric oxide signaling, and scavenging for free radicals [12,13]. These versatile cells are essential for maintaining overall health and well-being. Erythrocytes are cells produced in the bone marrow and have a lifespan of roughly one hundred twenty days. Their principal function, in conjunction with that of hemoglobin, is to transport oxygen from the lungs to all of the tissues in the body and to transport carbon dioxide, which is a by-product of metabolism, to the lungs so that it can be exhaled [11-13].

Standard values for red blood cells (RBCs) [14,15]: Here's a rewritten version of the information you provided, focusing on a clear and concise presentation of RBC standard values:

Hemoglobin (Hb):

- Men: 13.0 - 17.0 g/dL
- Women: 12.0 - 16.0 g/dL
- Newborns: 13.5 - 19.5 g/dL

Hematocrit (Hct):

- Men: 40 - 54%
- Women: 35 - 47%

Red Blood Cell Count (RBC):

- 4.3 - 5.7 x 10^12/L

Red Blood Cell Indices:

- Mean Corpuscular Volume (MCV): 78 - 98 fl
- Mean Corpuscular Hemoglobin (MCH): 26 - 33 pg
- Mean Corpuscular Hemoglobin Concentration (MCHC): 30 - 35 g/dL

Table 1. RBC normal values in humans across different life spans

Life Stage	RBC Count (x10^12/L)	Hemoglobin (g/dL)	Hematocrit (%)	Reference
Newborn (0-7 days)	4.5-6.5	17-21	45-55	[1]
Infant (1-12 months)	4.0-5.5	11-13	35-45	[4]
Child (1-5 years)	4.0-5.0	11-13	35-45	[11]
Child (6-12 years)	4.0-5.0	12-16	35-45	[4]
Adolescent (13-19 years)	4.2-5.4	12-16	37-47	[1]
Adult Male (20-64 years)	4.6-6.2	14-18	41-53	[4,11]
Adult Female (20-64 years)	4.2-5.4	12-16	37-47	[11]
Adult Male (>65 years)	4.0-5.5	13-17	36-46	[11]
Adult Female (>65 years)	3.7-4.9	11-15	34-44	[11]

RBC diseases: Inborn errors and chromosome abnormalities: Red blood cell (RBC) diseases encompass a wide range of conditions that affect red blood cells' production, function, or lifespan. Inborn errors of metabolism cause some of these diseases, while others involve chromosome number or structure abnormalities [15-24].

Inborn errors:

- **Enzymes:** Mutations in genes encoding enzymes crucial for red blood cell production or function can lead to various diseases. Examples include:
  - **Thalassemia**: Mutations affect globin genes, producing insufficient hemoglobin [17].
  - **G6PD deficiency**: Deficiency of the glucose-6-phosphate dehydrogenase enzyme causes red blood cell damage under certain triggers [20].
  - **Pyruvate kinase deficiency:** This enzyme deficiency affects energy metabolism in red blood cells, leading to anemia [21].
- **Membrane defects:** Mutations in genes encoding proteins that make up the red blood cell membrane can cause fragility and hemolysis (premature breakdown). Examples include:
  - **Spherocytosis:** Defective membrane proteins lead to a spherical shape, making them susceptible to destruction by the spleen.
  - **Elliptocytosis:** Abnormal oval-shaped red blood cells are vulnerable to hemolysis [24].

Chromosome abnormalities:

- **Numerical abnormalities:** An extra or missing chromosome can affect red blood cell production. Examples include**:**
  - **Trisomy 21 (Down syndrome):** Individuals have an extra copy of chromosome 21, which can lead to mild anemia [25].
  - **Turner syndrome:** Females are missing one X chromosome, which can cause microcytic anemia (small red blood cells) [24].
- **Structural abnormalities:** Deletions, translocations, or inversions in chromosomes can disrupt gene expression and lead to red blood cell disorders [25-28].
- **Examples include:**
  - **Cri du chat syndrome:** Deleting part of chromosome 5 can cause severe anemia and other developmental problems [27,28].
  - **Diamond-blackfan anemia:** Deletions or mutations in specific genes on chromosomes 13 or 20 cause this type of anemia [27].

Table 2. Diseases of the red blood cells: Inborn errors and chromosome abnormalities

Inborn Error	Gene Chromosome Number	RBC Occurrence	References
Alpha-thalassemia	HBA1 (16p13.3)	Reduced hemoglobin production, microcytic anemia	[17]
Beta-thalassemia	HBB (11p15.5)	Reduced beta-globin synthesis, anemia, ineffective erythropoiesis	[18]
Sickle Cell Disease	HBB (11p15.5)	Point mutation in beta-globin, sickle-shaped RBCs, hemolytic anemia	[19]
G6PD Deficiency	G6PD (Xq28)	X-linked recessive, decreased NADPH production in RBCs, hemolytic anemia after oxidative stress.	[20]
Pyruvate Kinase Deficiency	PKLR (15q22.31)	Autosomal recessive, impaired glycolysis in RBCs, hemolytic anemia	[21]
Hereditary Spherocytosis	Multiple genes (ANK1, SPTA1, etc.)	Diverse mutations affecting membrane proteins, spherocytic RBCs, hemolytic anemia	[22]
Enzyme Deficiencies (e.g., Glucose-6-phosphate isomerase deficiency)	Various genes	Impair specific metabolic pathways in RBCs, hemolytic anemia	[23]
Porphyrias	Multiple genes (e.g., PPOX, ALAD)	Defects in heme synthesis, accumulation of porphyrins, neurological and skin symptoms	[8]

Erythrocytes go through a life cycle: Erythrocytes, also known as red blood cells, have three stages: creation, maturation, and destruction. Hematopoiesis is the process that takes place in the red bone marrow, and erythropoiesis is a sub-process that produces erythroid stem cells. The hormone erythropoietin triggers this process. The cells go through several phases of differentiation, such as erythroblasts, proerythroblasts, and reticulocytes, before becoming mature red blood cells. This continuous cycle ensures a steady supply of erythrocytes, essential for optimal body function [4,5].

Classification of red blood cells: Red blood cells (RBCs) are classified into different types and subtypes based on various characteristics, primarily their surface antigens. The two major blood group systems that classify red blood cells are the ABO system and the Rh system [4,29,30].

ABO system:

1. Type A: Individuals with A-type blood have A antigens on the surface of their red blood cells and anti-B antibodies in their plasma.
2. Type B: Individuals with B-type blood have B antigens on the surface of their red blood cells and anti-A antibodies in their plasma.
3. Type AB: Individuals with AB-type blood have both A and B antigens on the surface of their red blood cells and no anti-A or anti-B antibodies in their plasma.
4. Type O: Individuals with O-type blood have no A or B antigens on the surface of their red blood cells but have both anti-A and anti-B antibodies in their plasma [4,29,30].

Rh system:

1. Rh-positive (Rh+): Individuals with Rh-positive blood have the Rh antigen (also known as the D antigen) on the surface of their red blood cells [4,29,30].
2. Rh-negative (Rh-): Individuals with Rh-negative blood lack the Rh antigen on the surface of their red blood cells [4,29,30].

Subtypes and minor blood group systems: Besides the ABO and Rh systems, there are numerous other minor blood group systems, each characterized by specific antigens. Examples include the Kell system, Duffy system, Kidd system, and Lewis system, among others. These minor blood group systems contribute to the diversity of blood types and are essential in blood transfusions and organ transplantation [4,29,30].

The classification of anemia: Anemia is characterized by a decrease in red blood cells (RBCs) or a reduction in the blood's hemoglobin. The classification of anemia is often based on various factors, including the size of red blood cells, the underlying cause, and the specific characteristics of the condition. Here are the standard classifications of anemia [4,31]:

1. **Based on red blood cell size (Mean corpuscular volume - MCV):**

- **Microcytic Anemia:** Characterized by small-sized red blood cells.
- Common causes include iron deficiency, thalassemia, and certain chronic diseases [32,33].
- **Macrocytic Anemia:** Characterized by larger-than-normal red blood cells.
- Common causes include vitamin B12 deficiency, folate deficiency, and certain medications [34,35].

2. **Based on hemoglobin content (Mean corpuscular hemoglobin - MCH):**

- **Hypochromic anemia:** Characterized by low hemoglobin content in red blood cells.
- Typically associated with iron deficiency anemia [34,36].

3. **Based on red blood cell shape and appearance:**

- **Normocytic anemia:** Characterized by normal-sized red blood cells.
- Common causes include chronic diseases, kidney disease, and some types of anemia of chronic inflammation [34].

4. **Based on underlying cause:**

- **Iron-deficiency anemia:** Caused by insufficient iron, leading to decreased hemoglobin production.
- **Vitamin deficiency anemia results from deficiencies in vitamin B12 or folate,** essential for red blood cell production.
- **Hemolytic anemias:** Result from increased destruction of red blood cells, either due to intrinsic factors (such as genetic disorders)

or extrinsic factors (such as autoimmune reactions).

- **Anemia of chronic disease:** Associated with chronic inflammatory conditions, infections, or other long-term illnesses.
- **Aplastic anemia:** Characterized by a decrease in red blood cells due to bone marrow dysfunction [34-37].

5. Hereditary and genetic anemias:

- **Sickle cell anemia:** Caused by a genetic mutation leading to abnormal hemoglobin structure.
- **Thalassemia:** Genetic disorders affecting the production of hemoglobin [17,18].

6. Acute vs. chronic anemia:

- **Acute anemia:** Rapid onset of anemia, often due to sudden blood loss.
- **Chronic anemia:** Develops gradually over time and may be associated with long-term conditions [4,17,18].

A lack of iron causes anemia: Iron deficiency anemia is the most prevalent type of nutritional deficit experienced by people worldwide. The reason for iron deficiency can vary in different age ranges and different population groupings. Worm infestation is the most common cause of iron deficiency anemia in children suffering from the condition in India [4,11,38, 39].

Iron deficiency anemia is defined as the following: The World Health Organization describes Iron deficiency anemia as having a hemoglobin level that is lower than 14g/DL for adult men, 12g/DL for adult women who are not pregnant, and 11g/DL for pregnant women [4].

Presenting clinical signs: Iron deficiency anemia is not an illness in and of itself but a symptom of a more severe condition. Patients have symptoms such as weariness, pallor, and a diminished capacity for physical activity. The patients exhibit symptoms as soon as the hemoglobin level falls below seven g/dl. Koilonychias, characterized by flattened fingernails resembling spoons and fissures in the angle of the mouth, are signs of severe iron shortage. A painful tongue that has undergone papillary atrophy, which causes the tongue to become smooth, is another common sign[4,16-21].

2. RESEARCH CONDUCTED IN THE LABORATORY

The hemoglobin: Microcytic and hypochromic RBCs are found in low peripheral blood smears (about eight g/dL or lower). Hypochromia is characterized by a whiteness that is greater than one-third. There is a correlation between the severity of anemia and the number of microcytes. RBCs may take the form of rings in really severe cases [4,11].

Iron in serum: In patients with iron deficiency anemia, serum iron levels are lower. A serum iron reading of 50-150 micrograms per deciliter is expected [4,39,40].

(TIBC) stands for total iron binding capacity: Regarding typical humans, the total iron binding capability of transferrin ranges from 300 to 600 micrograms per deciliter. In cases of iron-deficient anemia, the amount of transferrin that is accessible for binding is increased since there is less iron available. The iron binding capacity (TIBC) is increased due to this [41].

Medical care: The treatment typically consists of oral medication for three months. In addition, intramuscular, intravenous, and oral iron may be administered to patients who cannot tolerate these forms of iron. Anaphylaxis, on the other hand, is always an issue. It is possible to help a packed red cell transfusion to tide over the immediate crisis. The number of reticulocytes is used to evaluate how well the treatment works [41-44].

3. THE ANEMIA OF MEGALOBLASTIC

One of the primary reasons for megaloblastic anemia is a disruption in the production of DNA. Because of this, the development of the nuclear structure is behind that of the cytoplasmic structure. Because of this, the nucleus is significantly more extensive and more immature than the cytoplasm.

Megaloblastic anemia can be caused by vitamin B12 (cyanocobalamin) deficiency or folic acid. This is because DNA synthesis is dependent on both of these nutrients.

A deficiency in DNA synthesis is responsible for the delayed development of the nucleus and aberrant mitotic activity. The nucleus is, therefore, quite big and has open chromatin. The maturation of the nucleus occurs at a later stage than the maturation of the cytoplasm (a process known as asynchronous maturation) [41-44].

Thalassemia (T): Anemias caused by alpha or beta-globin synthesis genetic defects are referred to as thalassemia syndromes. These syndromes exist in a variety of different categories. Neither the alpha nor the beta chains are present or only partially present.

Two distinct forms of thalassemia are as follows: To begin, beta thalassemia. An insufficient amount of the beta chain of hemoglobin is being synthesized and produced. Alpha Thalassemia is the case. Inadequate production of the alpha chain of hemoglobin is the defining characteristic of this condition [41-44].

The study of epidemiology: Thalassemia is a disease that is prevalent in the countries of the Mediterranean region and can be found in the Middle East, Pakistan, and India, as well as in Southeast Asia. There is a good chance that it arrived in India during the Western invasion.

T-cell beta-thalassemia: An entire or partial impairment in the production of the beta-globin chain of hemoglobin is the defining characteristic of B-thalassemia, even though the beta chain maintains its normal structural integrity. However, there is no sign of impairment in the alpha-chain synthesis. In synthesizing the beta-globin chain, the degree of anemia is determined by the amount of deficiency present [41-44].

4. PATHOGENESIS AND ALTERATIONS IN GENETIC MAKEUP

As explained earlier, beta-thalassemia is caused by a full or partial deficit in beta-globin production. Specifically, the mutation in the Beta gene is responsible for this impairment in the production of beta-globin chains. In a heterozygous situation, which occurs when one normal gene is present, the synthesis of normal beta-globin only results in mild anemia; otherwise, the individual is asymptomatic on multiple occasions. All these disorders are referred to as beta-thalassemia benign or beta-thalassemia trait respective [45]. They do not need any cure. However, when patients are homozygous for the beta-globin gene, they are diagnosed with thalassemia major, characterized by severe anemia ranging from three to six grams per deciliter.

There are biochemical shifts:

- There is a rise in bilirubin (unconjugated)
- Urobilinogen, which is found in urine

A general image of the blood: A well-made peripheral blood smear is probably the most critical laboratory test. This is because it allows for the estimation of approximately the numbers of each of the three cellular elements, the study of the morphology of these elements, the observation of blood parasites, and the investigation of the body's reaction to various disease processes. When examining a blood smear, it is essential to consider all the cellular components [46,47,48], even though many believe the term "blood picture" refers solely to describing the red blood cells. About 7.2 micrometers is the diameter of a red blood cell that is considered normal. Even with an average blood film, there will be a tiny fluctuation in size. Because the average variation is similar to the standard variation, we do not comment on it. Both anisocytosis and poikilocytosis are terms that can be used to describe the changes in the RBCs. A significant number of microcytic hypochromic RBCs are visible. It is the target cells that are the distinguishing trait. These red blood cells have a predominantly dark color in the center (as a result of the core collection of hemoglobin), whereas the portions surrounding them are lighter in color [41-44].

Clinician's evaluation of pallor: The cranial bone exhibits radiations perpendicular to the X-ray's direction. A frontal bossing style is present. A thinning of the cortex and a fracture can be seen in long bones. On account of additional medullary hematopoiesis, hepatosplenomegaly is seen. The destruction of erythrocytes also occurs in the spleen, another body organ [4].

One of the causes of jaundice is hemolysis: Alpha-thalassemia Alpha-thalassemia is characterized by decreased synthesis of the Alpha-globin chain, mainly caused by deleting the Alpha-globin gene. Alpha-thalassaemia is most typically observed in Asian adults [17-21].

Deliverer of silence: One Alpha gene is deleted, while the other three are expected. These patients have no symptoms at all. There is a loss of one Alpha gene. Consequently, the decrease in the Alpha-globin chain is exceedingly minimal and complex to detect. Alpha-thalassaemia trait is an asymptomatic illness identical to Beta-thalassaemia minor (trait). Thalassemia trait was named after the disease [41-44].

Anemia: Detection and therapeutic approaches: Anemia, a prevalent hematologic disorder, is characterized by a deficiency in red blood cell (RBC) count, hemoglobin level, or

hematocrit. This deficiency impairs the blood's oxygen-carrying capacity, leading to symptoms like fatigue, dyspnea, pallor, and dizziness [1, 2,49].

Etiological landscape:

- Iron Deficiency: The most common culprit, often stemming from inadequate dietary intake, blood loss (menstrual, gastrointestinal), or impaired iron absorption [3].
- Vitamin B12/Folate Deficiencies: Crucial for erythropoiesis, these deficiencies can arise from dietary insufficiency, malabsorption, or medications [4,5].
- Bone Marrow Disorders: Leukemias, aplastic anemia, and myelofibrosis disrupt RBC production within the bone marrow [6].
- Chronic Diseases: Kidney, liver, and autoimmune diseases can contribute to anemia through diverse mechanisms [7,8].
- Inherited Conditions: Sickle cell anemia and thalassemias are prime genetic disorders affecting RBC production or function [9,10].

Diagnostic strategies:

- Clinical Evaluation: A thorough history and physical examination by a healthcare professional are essential, exploring symptoms, risk factors, and family history [11].
- Laboratory Investigations: Complete blood count (CBC) remains the cornerstone for assessing RBC count, hemoglobin level, and hematocrit. Further tests, like iron studies, vitamin B12/folate levels, and bone marrow aspirates, may be necessary for specific diagnoses [12].

Therapeutic interventions:

- Iron Supplementation: Oral or intravenous iron supplements are the mainstay for iron-deficiency anemia [13].
- Vitamin B12/Folate Replacement: Injections or oral supplements address respective deficiencies [14, 15].
- Blood Transfusions: In severe cases or patients with underlying conditions, transfusions may be required to improve oxygen delivery [16].
- Disease-Specific Therapies: Addressing the underlying condition, like treating chronic diseases or managing bone marrow disorders, is crucial for long-term management [17,18].
- Nutritional Counseling: A balanced diet rich in iron, vitamin B12, and folate can prevent or manage anemia [19,49].

5. CONCLUSION

Red blood cells (RBCs) have evolved beyond their traditional role of carrying oxygen to become essential circulatory system components. Their unique characteristics, such as their biconcave shape, flexible membrane, and hemoglobin concentration, make them perform gas exchange. These incredible cells originate in the bone marrow and play a crucial role in maintaining overall health by controlling blood viscosity and pH balance. RBCs are more than just red dots; they are diverse and active cells that perform an essential symphony of oxygen, carbon dioxide, and cellular health. Understanding the complexities of their roles and the consequences of dysfunction is crucial for maintaining good health and treating a wide range of blood disorders.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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