

The Curious Case of the Sphered Blood Cells: Unveiling Hereditary Spherocytosis

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Abstract

Hereditary spherocytosis (HS) is an inherited blood disorder that disrupts the shape and flexibility of red blood cells (RBCs) due to genetic mutations. These abnormal, sphere-shaped RBCs, called spherocytes, are prematurely destroyed in the spleen, leading to hemolytic anemia. Symptoms range from mild fatigue to chronic weakness and shortness of breath. While incurable, Hereditary spherocytosis can be effectively managed. Regular monitoring, folic acid supplementation, and in severe cases, splenectomy (surgical removal of the spleen) can improve quality of life for affected individuals. Consulting a healthcare professional is essential for diagnosis and creating personalized treatment plans. Hereditary spherocytosis presents a complex picture with diverse symptoms and management strategies. Understanding the underlying mechanisms, potential symptoms, and available treatment options empowers both individuals and healthcare professionals to navigate this condition effectively and achieve a better quality of life. Consulting a healthcare professional for individualized diagnosis and treatment remains paramount for those living with Hereditary spherocytosis.

Keywords: Spherocyte, RBC, Symptoms, Splenectomy, Disorder.

INTRODUCTION

Spherocytes are abnormal red blood cells that have lost their characteristic biconcave shape and become spheres. On a blood smear, these cells appear smaller and stain darker due to their increased thickness. Additionally, they lack the central pale area typically seen in healthy red blood cells. In a wet preparation, unlike normal red blood cells which rotate like discs, spherocytes tend to roll in the fluid. The presence of a significant number of spherocytes in the blood is a definite sign of abnormality. These abnormal cells can be found in two main conditions: hereditary spherocytosis and some immune hemolytic anemia. Hereditary spherocytosis (HS) is a complex, inherited blood disorder characterized by abnormal red blood cell shape and function. This can lead to a variety of symptoms, including fatigue, shortness of breath, and an enlarged spleen. While there is no cure, Hereditary spherocytosis can be effectively managed with regular monitoring, medication, and sometimes, surgery. Understanding the

disease process, potential complications, and available treatment options empowers both individuals and healthcare professionals to make informed decisions and improve quality of life for those affected [1–5]. Hemolytic anemia is a disorder where the body's supply of healthy red blood cells is reduced due to the early breakdown of red blood cells brought on by this anomaly. One mutated gene copy from one parent (autosomal dominant inheritance) or from both parents (autosomal recessive inheritance) can cause hereditary spherocytosis. There is a wide range in the severity of symptoms; some people have no obvious problems, while others have gallstones, an enlarged spleen, pale skin, weariness, and jaundice (a

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yellowing caused by an accumulation of bilirubin). Hereditary spherocytosis now has no known cure, however there are a number of treatments that can help control symptoms and enhance quality of life. These include blood transfusions for severe anemia, splenectomy—a surgical removal of the spleen—for mild instances, and folic acid administration to promote the synthesis of red blood cells. Hereditary spherocytosis can be managed well and monitored by a doctor on a regular basis. Complications can be avoided and symptoms can be greatly improved with early diagnosis and adequate treatment. But it's important to speak with a healthcare provider for precise diagnosis, tailored guidance, and available treatment options.

WHAT ARE RED BLOOD CELLS (RBCS)

Red blood cells (RBCs), also known as erythrocytes, are the unsung heroes of our internal transportation system [6]. These tiny, disc-shaped cells hold a critical responsibility – delivering life-giving oxygen to every nook and cranny of the body [Figure 1]. Their efficiency in this task is intricately linked to their unique biconcave shape. Imagine a journey – oxygen molecules inhaled through the lungs need to reach trillions of cells across the body [7]. RBCs act as the oxygen taxis, carrying this precious cargo. Inside each RBC lies the magic: haemoglobin, an iron-rich protein with a remarkable ability to bind with oxygen. Haemoglobin acts like a sponge, soaking up oxygen in the lungs where there's a high concentration. Now comes the importance of the biconcave shape. Unlike a perfect sphere, the biconcave disc has a flattened, indented centre on both sides. This seemingly simple design offers several advantages:

Increased Surface Area

Compared to a sphere with the same volume, the biconcave disc has a larger surface area [8–10]. Think of it like a flattened ball compared to a perfectly round one. The increased surface area provides more space for haemoglobin molecules to be embedded within the RBC membrane. This translates to a greater capacity for oxygen carriage – more oxygen molecules can hitch a ride on each RBC.

Enhanced Diffusion

Oxygen needs to get from the RBC into the surrounding tissues. The biconcave shape facilitates this diffusion process. The shorter distance between the haemoglobin molecules in the centre of the disc and the outer membrane allows for a faster release of oxygen to tissues. Imagine a thin sheet of paper compared to a thick book – information (oxygen) can travel more readily through the thinner barrier.

Flexibility for Tight Spaces

Our circulatory system is a vast network, with tiny capillaries reaching every corner of the body. These capillaries are much narrower than RBCs [11–12]. The biconcave shape grants RBCs remarkable flexibility. As they squeeze through these narrow passages, the indentations allow them to deform and fold in momentarily, enabling them to navigate the intricate maze of blood vessels without getting stuck. A rigid sphere, on the other hand, would struggle to manoeuvre through these tight spaces, potentially disrupting oxygen delivery to vital tissues. In essence, the biconcave shape is an ingenious evolutionary adaptation that optimizes oxygen transport. It maximizes oxygen-carrying capacity, facilitates efficient diffusion, and ensures smooth passage through the body's intricate network of blood vessels. Without this remarkable design, our cells wouldn't receive the vital oxygen they need to function, leading to fatigue, organ damage, and potentially life-threatening consequences.

UNDERSTANDING HEREDITARY SPHEROCYTOSIS

Hereditary spherocytosis is an inherited blood disorder affecting the shape and lifespan of red blood cells. Unlike their characteristic disc-like form, red blood cells in this condition become abnormally spherical, resembling spheres. These atypical red blood cells, termed spherocytes, are more fragile and susceptible to premature breakdown, leading to a condition called hemolytic anaemia [13]. Hemolytic anemia signifies a deficiency in the number of circulating red blood cells, impacting the body's ability to efficiently deliver oxygen to tissues. This disorder arises from genetic mutations affecting proteins

crucial for maintaining the structural integrity and flexibility of the red blood cell membrane. These proteins act like a scaffold, providing the red blood cell with its distinctive shape and allowing it to navigate the narrow blood vessels throughout the body. In hereditary spherocytosis, the defective proteins compromise the membrane's strength, making the spherocytes vulnerable to destruction in the spleen, an organ responsible for filtering blood [14–15]. The severity of symptoms associated with hereditary spherocytosis varies significantly between individuals. Some individuals experience mild or even no noticeable symptoms, while others may exhibit chronic fatigue, weakness, and pale skin due to the underlying anemia. Additionally, the breakdown of excessive red blood cells releases a yellowish pigment called bilirubin, which can cause jaundice, a condition characterized by the yellowing of the skin and eyes. An enlarged spleen (splenomegaly) is another potential consequence of hereditary spherocytosis, as the spleen becomes overworked in attempting to remove the damaged spherocytes. The inheritance pattern of hereditary spherocytosis can be either autosomal dominant or autosomal recessive. In the dominant form, inheriting a single mutated gene copy from either parent is sufficient for the condition to manifest. Conversely, recessive inheritance necessitates inheriting two copies of the mutated gene, one from each parent. Management of hereditary spherocytosis primarily focuses on alleviating symptoms and preventing complications. Depending on the severity, treatment options may include folic acid supplementation to stimulate red blood cell production, medications to suppress excessive spleen activity, and, in extreme cases, splenectomy, a surgical procedure to remove the spleen. Understanding hereditary spherocytosis empowers individuals and healthcare professionals to identify, manage, and potentially mitigate the impact of this inherited blood disorder. Early diagnosis and proper management can significantly improve the quality of life for individuals affected by this condition.

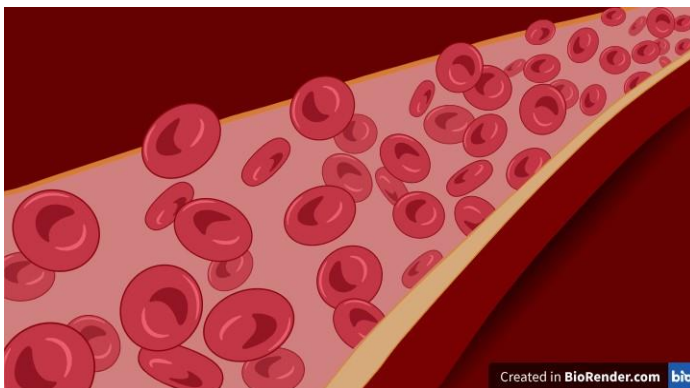


Figure 1. Red Blood cells (RBCs) a Biconcave Discs.

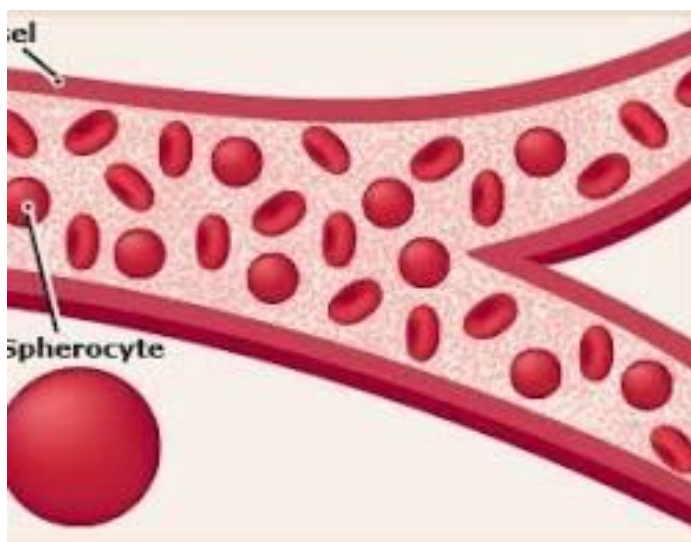


Figure 2. Spherocytosis blood Cells.

SYMPTOMS AND COMPLICATIONS

Hereditary spherocytosis, an inherited blood disorder, manifests through a spectrum of symptoms and potential complications stemming from its impact on red blood cells. These atypical, sphere-shaped red blood cells, termed spherocytes, are more fragile and prone to premature destruction, leading to *hemolytic anemia*. This deficiency in red blood cells hinders the body's capacity to deliver oxygen effectively, resulting in various symptoms [Figure 2].

Chronic fatigue and weakness are prevalent features, often accompanied by pale skin due to the reduced number of red blood cells carrying oxygen. The breakdown of excessive spherocytosis releases bilirubin, a yellowish pigment, causing jaundice, a condition manifesting as yellowing of the skin and eyes.

Enlargement of the spleen (splenomegaly) is another potential consequence. The spleen, responsible for filtering blood, becomes overburdened as it attempts to remove the damaged spherocytosis. This can lead to abdominal discomfort and a sense of fullness in the upper left abdomen. The severity of these symptoms varies considerably. Some individuals experience only mild fatigue, while others may face more debilitating symptoms that significantly impact their daily lives. Additionally, certain factors, such as infections, can exacerbate symptoms and trigger aplastic crisis, a temporary but severe decrease in red blood cell production. Beyond the immediate symptoms, hereditary spherocytosis carries potential for long-term complications. Gallstones are a frequent occurrence, as the elevated bilirubin levels can solidify and form stones in the gallbladder. In severe cases, individuals may experience growth delays during childhood and adolescence due to impaired oxygen delivery to tissues. While there is no cure for hereditary spherocytosis, effective management strategies can significantly improve the quality of life for individuals affected by the condition. These strategies focus on alleviating symptoms and preventing complications [16–18].

Depending on the severity, treatment options may include:

- *Folic acid supplementation*: To stimulate red blood cell production.
- *Medications*: to suppress excessive spleen activity and reduce the rate of red blood cell destruction.
- *Splenectomy*: a surgical procedure to remove the spleen, considered in severe cases or when other therapies prove inadequate.

Understanding the spectrum of symptoms and potential complications associated with hereditary spherocytosis empowers individuals and healthcare professionals to make informed decisions regarding management and treatment options. Early diagnosis and appropriate intervention can significantly improve prognosis and ensure individuals affected by this condition can lead fulfilling lives.

DIAGNOSIS

Hereditary spherocytosis, an inherited blood disorder characterized by abnormally shaped red blood cells (spherocytes), necessitates a multi-pronged approach for accurate diagnosis. This involves *clinical evaluation*, *family history assessment*, and a series of *laboratory tests* working in conjunction to paint a clear picture of the underlying condition.

Clinical evaluation forms the initial step. Healthcare providers will inquire about the presence of symptoms such as chronic fatigue, weakness, jaundice, pale skin, and abdominal discomfort. The physical examination may reveal an enlarged spleen (splenomegaly) in some individuals.

Family history holds immense significance. A positive family history of individuals with similar symptoms or a confirmed diagnosis of hereditary spherocytosis strengthens the suspicion of the condition.

Following these initial assessments, several *laboratory tests* play a crucial role in confirming the diagnosis. A *complete blood count (CBC)* reveals a *decrease in red blood cell count (anemia)*, while an *increase in reticulocytes*, immature red blood cells, signifies the body's attempt to compensate for the ongoing destruction.

Peripheral blood smear examination directly visualizes the presence of spherocytes under a microscope. This test is essential for identifying the characteristic misshapen red blood cells.

Several specialized tests further aid in confirming the diagnosis and assessing the severity of the condition. These include:

- *Osmotic fragility test*: This test evaluates the sensitivity of red blood cells to hypotonic solutions. Spherocytes, due to their abnormal shape and membrane weakness, are more susceptible to rupturing in these solutions, indicating the presence of hereditary spherocytosis.
- *Flow cytometry*: This advanced test can detect abnormalities in specific red blood cell membrane proteins, potentially aiding in identifying the specific type of hereditary spherocytosis and guiding further management decisions.
- *Genetic testing*: While not routinely performed in all cases, genetic testing can definitively identify the specific gene mutation responsible for the condition, especially when the diagnosis remains unclear.

Combining the information gleaned from clinical evaluation, family history, and laboratory tests allows healthcare providers to make an accurate diagnosis of hereditary spherocytosis. Early diagnosis paves the way for timely intervention and appropriate management strategies, ultimately improving the quality of life for individuals affected by this condition. While there is no definitive cure for hereditary spherocytosis, an inherited blood disorder characterized by abnormally shaped red blood cells (spherocytes), effective management strategies can significantly improve the quality of life for individuals affected by the condition. The chosen treatment approach depends on the severity of symptoms and a comprehensive evaluation by a healthcare professional. For mild cases with minimal or no symptoms, watchful waiting may be the recommended course of action. Regular monitoring of blood counts and spleen size allows healthcare providers to track the condition and intervene if necessary. Folic acid supplementation is typically recommended for all individuals with hereditary spherocytosis to support red blood cell production. In moderate to severe cases, where symptoms significantly impact daily life or complications arise, a more proactive approach may be required. Medications can help manage the condition by suppressing excessive activity of the spleen, the organ responsible for filtering blood and often responsible for destroying spherocytes. These medications, known as immunosuppressants, aim to reduce the rate of red blood cell destruction and alleviate symptoms.

Splenectomy, the surgical removal of the spleen, is considered a definitive treatment option in severe cases. This option is typically reserved for individuals experiencing debilitating symptoms, frequent transfusions, or complications such as severe growth delays in children. While splenectomy eliminates the primary site of spherocyte destruction, it also compromises the immune system's ability to fight certain infections. Therefore, individuals who undergo splenectomy require lifelong vaccination and antibiotic prophylaxis, preventive measures to minimize the risk of infections.

Emerging therapies are currently being explored for managing hereditary spherocytosis. These include gene therapy, which aims to correct the underlying genetic defect, and investigational medications targeting specific pathways involved in red blood cell destruction. The decision regarding the most appropriate treatment option for an individual with hereditary spherocytosis is a personalized one, taking into account the severity of symptoms, potential risks and benefits of each approach, and the individual's overall health and preferences. Open dialogue and collaboration between healthcare professionals and individuals affected by the condition are crucial in navigating the treatment journey and achieving positive outcomes.

LIVING WITH HEREDITARY SPHEROCYTOSIS

Living with hereditary spherocytosis, an inherited blood disorder characterized by abnormally shaped red blood cells (spherocytes), can present unique challenges for individuals and their families. While the condition can manifest in a spectrum of ways, understanding its implications and developing effective coping mechanisms can empower individuals to lead fulfilling and active lives. One of the primary challenges lies in managing the symptoms. Individuals may experience fatigue, weakness, and pale skin due to the underlying anemia. Monitoring energy levels and adapting daily activities accordingly can be crucial. Additionally, managing other potential symptoms, such as jaundice and abdominal discomfort, through dietary adjustments or medications, can improve overall well-being.

Maintaining regular communication with healthcare professionals is vital for individuals with hereditary spherocytosis. Attending scheduled appointments, undergoing necessary tests, and adhering to prescribed medications or treatment plans are instrumental in managing the condition effectively.

Psychological well-being also deserves attention. Living with a chronic condition can be emotionally taxing. Joining support groups, connecting with other individuals facing similar experiences, and seeking professional help if needed can provide invaluable emotional support and a sense of community.

Maintaining a healthy lifestyle is vital for individuals with hereditary spherocytosis. Eating a balanced diet, getting regular exercise, and prioritizing adequate sleep all contribute to overall health and can help manage symptoms effectively. Additionally, avoiding strenuous activities or sports that may increase the risk of spleen injury can be crucial, particularly for individuals who have not undergone splenectomy.

Education and awareness are key to navigating life with hereditary spherocytosis. Educating family members, friends, and educators about the condition can foster understanding and support. Additionally, staying informed about the latest advancements in research and potential new treatment options empowers individuals to advocate for themselves and participate actively in their healthcare decisions. Living with hereditary spherocytosis requires adjustment, commitment, and resilience. By adopting a proactive approach to symptom management, maintaining open communication with healthcare professionals, and prioritizing overall well-being, individuals can effectively manage this condition and lead fulfilling lives.

Recent and Ongoing Research on Hereditary Spherocytosis (HS)

Hereditary spherocytosis (HS) research is actively exploring new avenues to improve diagnosis, treatment, and understanding of the disease. Here's a summary of some key areas:

Enhanced Diagnostics

- *Next-generation osmotic fragility test (NG-OGE)*: This innovative test provides a more sensitive and specific way to diagnose HS compared to traditional methods. It utilizes advanced technology to analyse red blood cell behaviour under varying salt concentrations, making it a valuable tool for accurate diagnosis.
- *Multi-gene panel testing*: This approach allows for a more comprehensive diagnosis by examining multiple genes associated with HS. This can help identify milder or atypical forms of the disease, leading to better management strategies.

Gene Therapy as a Potential Cure

Researchers are actively exploring gene therapy as a potential cure for HS. This involves introducing healthy copies of the mutated gene into red blood cell precursors. Early studies in animals have shown promising results, and clinical trials in humans are underway. This approach holds the potential to offer a permanent solution for HS patients.

Finding Alternatives to Splenectomy

Splenectomy, the surgical removal of the spleen, is a traditional treatment option for severe HS cases. However, it leaves patients vulnerable to infections. Research is ongoing to develop alternative therapies, such as targeted medications, to avoid the need for splenectomy. These alternatives aim to improve patient outcomes and quality of life by reducing the risk of post-surgical complications.

Personalized Medicine for Customized Treatment

Researchers are investigating ways to use individual patient data, including genetic information and other factors, to predict the disease course and personalize treatment plans. This approach allows for tailoring treatment strategies to each patient's specific needs and potentially identifying those who might benefit from less invasive interventions. This personalized approach aims to optimize treatment outcomes and improve patient well-being.

CONCLUSION

Hereditary spherocytosis, an inherited red blood cell disorder characterized by abnormally shaped "spherocytes," presents a spectrum of challenges. While there is currently no cure, effective management strategies coupled with ongoing research offer a hopeful outlook for individuals living with the condition. The current standard of care involves monitoring symptoms, regular check-ups with healthcare professionals, and supportive measures like folic acid supplementation. In moderate to severe cases, medications to suppress spleen activity and, in extreme scenarios, splenectomy may be considered. These interventions effectively manage symptoms, improve quality of life, and, in most cases, allow individuals to lead fulfilling lives. However, the future of hereditary spherocytosis holds exciting possibilities. Gene therapy offers the potential for a definitive cure by correcting the underlying genetic defect. Early research shows promising results, but further development and refinement are needed before widespread application. Another area of active research is the development of targeted drug therapies. These medications aim to specifically inhibit the pathways involved in spherocyte destruction, offering a potential alternative to traditional therapies like splenectomy and potentially minimizing side effects. Furthermore, advancements in advanced diagnostics may lead to earlier and more accurate diagnosis. This includes novel genetic testing methods and non-invasive imaging techniques, allowing for quicker intervention and improved long-term outcomes. Personalized medicine approaches are also being explored, aiming to tailor treatment plans to the specific needs and variations of the disease seen in individual patients. This individualization has the potential to further enhance the efficacy of management strategies. Hereditary spherocytosis presents challenges, but the current standard of care allows for effective symptom management and a good quality of life for most individuals. Looking ahead, ongoing research avenues like gene therapy, targeted drug therapies, advanced diagnostics, and personalized medicine offer a beacon of hope for a future with improved treatment options and potentially even a cure. By embracing the journey and actively participating in research advancements, individuals with hereditary spherocytosis can contribute to a brighter future for themselves and others affected by this condition.

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