Paroxysmal Nocturnal Hemoglobinuria (PNH)

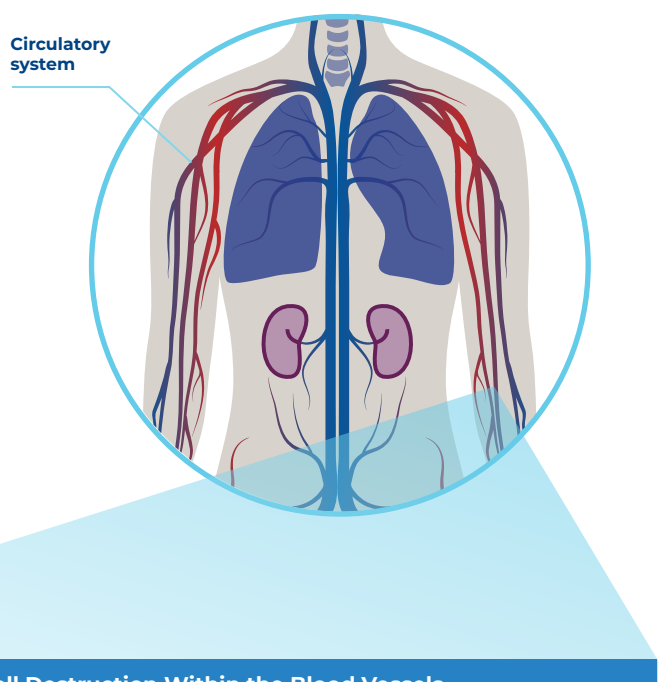
ALEXION
AstraZeneca Rare Disease

WHAT IS PNH?

Paroxysmal nocturnal hemoglobinuria (PNH) is a **rare, chronic, progressive, and potentially life-threatening blood disorder.**

PNH is characterized by **red blood cell (RBC) destruction** within blood vessels (also known as **intravascular hemolysis**, or IVH) and **white blood cell and platelet activation**, which may lead to blood clots (thrombosis).

PNH is caused by an **acquired genetic mutation** (not inherited) that may happen any time after birth and results in the **production of abnormal blood cells** that are **missing important protective blood cell surface proteins**. These missing proteins enable the complement system to 'attack' and **destroy or activate these abnormal blood cells**.[1-3]



PNH is estimated to affect approximately **16-20 people per million worldwide**.[4]

PNH can occur in **children and adults** at any age; the average age of diagnosis is in the **early 30s**.[5]

PNH affects both **men and women** and people of **every racial and ethnic group**.[5]

Living with PNH can be debilitating, and signs and symptoms may include[1,6,7]

- **Blood clots (thrombosis)**
- **Abdominal pain**
- **Difficulty swallowing**
- **Erectile dysfunction**
- **Shortness of breath**
- **Excessive fatigue**
- **Anemia**
- **Dark-colored urine (hemoglobinuria)**

PNH can lead to **thrombosis**, which can occur in blood vessels throughout the body, and/or damage to other vital organs, such as **kidneys and lungs**. This can result in an overall **impaired quality of life** and **potentially premature death**.[8,9]

HOW IS PNH DIAGNOSED AND MONITORED?

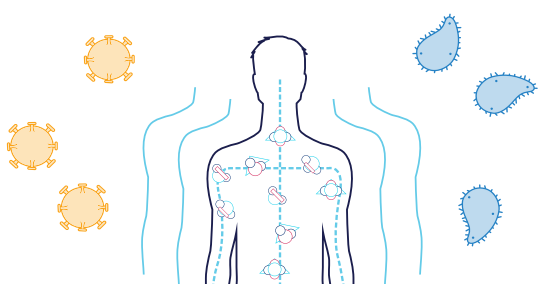
Diverse symptoms and varied clinical presentation can delay diagnosis by up to **10 years**.[8]

PNH can be **diagnosed from a simple blood test** (high-sensitivity flow cytometry), which can detect and count PNH blood cells.[10]

Another type of blood test is used to **monitor ongoing PNH disease activity**. This test measures lactate dehydrogenase (LDH), an enzyme that is released from red blood cells during IVH.

Monitoring LDH regularly is a very important part of managing PNH. If high levels of LDH are present, it means that many red blood cells have been destroyed within blood vessels. This has been shown to correlate with complications, such as thrombosis and early mortality.

THE COMPLEMENT SYSTEM



The complement system is a part of the immune system and is **essential to the body's defense against infection**.[13]

When the system is **thrown out of balance**, or dysregulated, these proteins can **trigger a dangerous, uncontrolled cascade of reactions** that attack cells and tissues resulting in **harmful inflammation** and the **destruction of healthy cells**.[14]

WHAT ROLE DOES COMPLEMENT INHIBITION PLAY IN TREATING PNH?

In PNH, **immediate, complete and sustained terminal complement inhibition** (by blocking the C5 protein) is the proven standard of care to **prevent the destruction of PNH red cells and activation of PNH white cells and platelets**. This helps reduce symptoms and complications and improve survival, transforming the lives of those impacted by PNH.

Alexion's leadership in complement inhibition has set the course for the continued study and development of innovative treatments for certain rare complement-mediated diseases, including PNH.

WHAT TREATMENT APPROACH IS BEING STUDIED BY ALEXION?

In addition to developing the **first approved therapy for PNH**, Alexion aims to uncover new innovations and **provide additional treatment options** for those impacted by this devastating disease. Alexion is conducting **ongoing clinical trials** in PNH to investigate the safety and efficacy of blocking **Factor D**, another complement system protein, as well as **new treatment delivery choices**.

We continue to **advance the understanding of PNH** and accelerate the **development of innovative life-changing therapies**.

References:

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