Take control of PNH

To protect patient privacy, patient names and some identifying details have been removed, and photos are for illustration only.

Stay informed and play an active role

Find out how inside

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"If anything, living with PNH has made me appreciate my time even more and given me more drive to focus on the things that I love to do."

- Patient diagnosed
at 24 years old

To protect patient privacy, patient names and some identifying details have been removed, and photos are for illustration only.

PNH is a serious disease, but you can manage it

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and serious disease that can cause severe effects, such as blood clots, damage to your body's organs, heart attack, or stroke. If you had it and didn't know it, you might have felt unwell or tired all the time without understanding why. Now that you've gotten the diagnosis, you might be feeling a little scared or overwhelmed. But understanding more about the disease is essential to successfully managing the disease. And with the right tools and support, you can take control.

You might have a lot of questions about the disease, such as:

- What is PNH and what causes it?
- What are the symptoms?
- How can I find help?
- Where can I find out more?

This brochure will answer those questions and give you some additional insights into PNH that will help you play an active role in your disease management. Learning about PNH, keeping track of how the disease is affecting you, and working with your doctor to design a management plan that works for you can help you take control of PNH.

What is PNH?

PNH is:

- A serious disease in which an important part of your blood—the red blood cells—are destroyed. This destruction is called hemolysis
- An acquired disease, which means you were not born with it and it is not inherited, but rather, PNH develops in some people over time
- Progressive, which means it can get worse over time, increasing your risk of major health problems
- Chronic, which means it is a long-term illness

Hemolysis is the main cause of the major health problems in people with PNH.

What does PNH mean?

P

paroxysmal

"sudden, from time to time"

N

nocturnal

"at nighttime"

H

hemoglobinuria

"hemoglobin in the urine"

Hemoglobin is the reddish brown material found inside your red blood cells that carries oxygen throughout your body. When red blood cells break apart—because of hemolysis in PNH—hemoglobin leaves the inside of the cell and becomes free. Free hemoglobin is harmful, and it can build up and lead to serious health problems, such as blood clots, damage to your body's organs (such as the kidneys), heart attack, or stroke.

Who gets PNH?

Anyone can get PNH:

- Males and females
- People of all races
- People of any age; however, most diagnoses happen in the early 30s

Once PNH occurs, it remains for life in most patients:

- PNH is not hereditary—you cannot give it to your children
- PNH is not contagious—you cannot "catch" it or pass it to other people

PNH comes with a wide range of signs and symptoms that are often similar to other diseases. As a result, everyone experiences PNH differently, and a PNH diagnosis can be delayed by years.

It was originally believed that PNH sometimes occurred during the night, occasionally causing dark urine. We now know that PNH is always present and hemolysis is always happening—not just at night and not from time to time—even if you cannot see or feel it. PNH does not always cause dark urine, although most people with PNH will experience it at some point.

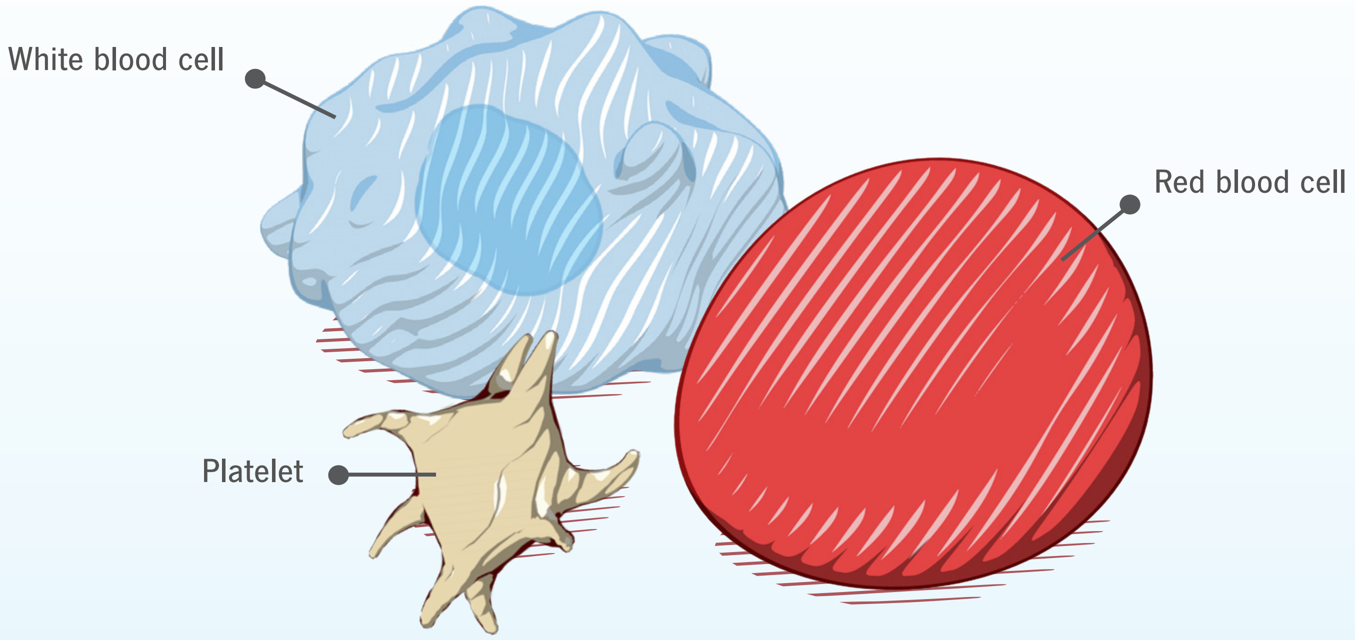
If you have any questions about what PNH is, speak with your doctor and visit PNHSource.com for further information.

Blood and PNH

Understanding blood basics

Your blood is living tissue made up of liquid and solids. The liquid part, called plasma, is made of water, salts, sugar, fat, and protein. Over half of your blood is plasma. The solid part of your blood contains:

- **Red blood cells:** cells that make up almost all of the solid part of your blood. They are filled with hemoglobin, which delivers oxygen to all body tissues and organs and helps in the removal of waste products (such as carbon dioxide) from the body
- **White blood cells:** cells that make up a much smaller number of cells in the blood. They help your immune system fight disease and infection
- **Platelets:** small pieces of cells that cluster together to form a blood clot and stop or control bleeding



Blood cells are made by stem cells in the bone marrow. Stem cells are a special type of cell in the body that are able to develop into many different types of cells (for example, blood cells, skin cells, etc.).

Stem cells can develop into red blood cells, white blood cells, and platelets. These cells can then divide and create new cells that are identical copies. Through this process, your body can continue to make new cells throughout your life.

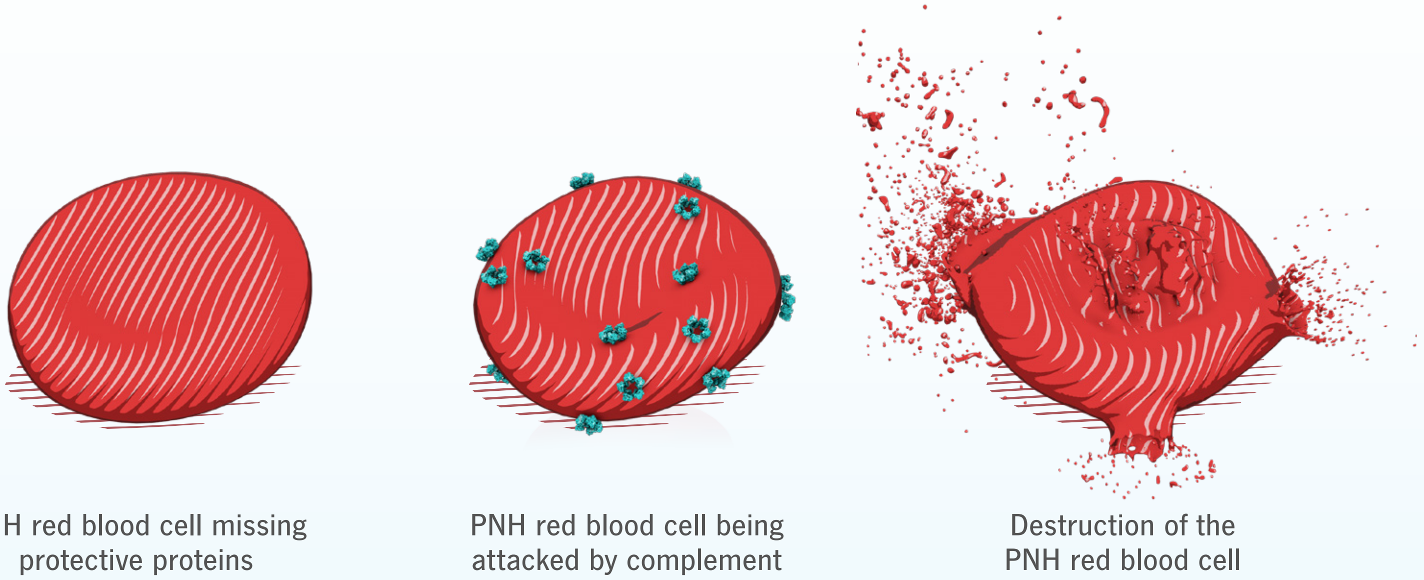
When blood cells are functional, they leave the bone marrow and enter your bloodstream to mature further and perform the specific job they are made for.

What causes PNH?

In PNH, a change, or mutation, occurs in the stem cells of the bone marrow. This stem cell change causes the lifelong production of abnormal cells that are missing protective proteins on their surface.

Without the protective proteins, red blood cells are destroyed by a part of your body's natural defenses, the complement system.

The complement system is a group of proteins in the blood that work as a normal part of your immune system by helping white blood cells fight infection. These proteins are always active on a low level, but if they sense an infection, a virus, or an invading abnormal cell, they become more active and start to attack these abnormal cells.



PNH red blood cell missing protective proteins

PNH red blood cell being attacked by complement

Destruction of the PNH red blood cell

The meaning of clone size

Clone size refers to the percentage (or number) of blood cells that are affected by PNH. Not all of your blood cells are missing protective proteins. A test called high-sensitivity flow cytometry can measure how many cells have protective proteins and how many do not. The percentage that do not have protective proteins is called your PNH clone size.

When your doctor measures clone size, they look at both red and white blood cells. The number of white blood cell clones is the "true" clone size because white blood cells are not destroyed by complement whereas the red blood cells are. The difference in the two clone sizes helps to estimate the amount of hemolysis going on within your body and is a good estimate of the number of red blood cells that have been destroyed.

Your PNH clone size may sometimes go up or down. Even with a small clone size, you can have PNH-related health problems. And in some people, it can increase over time, which may make their PNH symptoms worse. This is why it is important to follow your clone size over time. There are recommendations about how often your doctor should test, but your doctor may test more frequently. Speak with your doctor about testing for PNH clone size.

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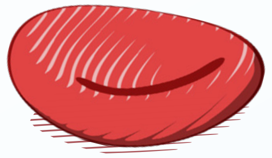
Understanding hemolysis

What is hemolysis?

When complement destroys red blood cells in PNH, this destruction is known as hemolysis.



Hemo - blood

Lysis - breakdown or destruction of the cell

Ongoing hemolysis is the root cause of the signs, symptoms, and serious health problems of PNH. If you have PNH, hemolysis happens constantly and sometimes at high rates.

Why is hemolysis so bad?

When a red blood cell is destroyed during hemolysis, some of the contents release into the bloodstream, including hemoglobin. When hemoglobin is inside the red blood cell, it helps to carry oxygen throughout your body. But, when hemoglobin is outside the cell, it can be harmful for your body. Even if you can't see or feel hemolysis, you can still have serious health problems, including:

- Blood clots
- Kidney failure
- Stroke
- Heart attack
- Damage to organs such as your liver, brain, and lungs

How will I know hemolysis is happening?

You cannot see or feel hemolysis, which makes it tough to manage. The results of it can often affect the way you feel and live your life.

Hemolysis can make you feel very tired and weak. It might affect your ability to walk short distances, work regular hours at your job, make it to doctors' appointments, or even attend family functions. Hemolysis can lead to many other symptoms, including:

- Difficulty swallowing
- Abdominal, chest, and/or back pain
- Shortness of breath
- Dark-colored urine
- Impaired quality of life
- Erectile dysfunction

The hemolysis that happens in PNH may cause you to develop anemia. Anemia can cause you to feel fatigued; however, the fatigue that patients with PNH experience is often worse than would be expected from the amount of anemia they have. This is because hemolysis itself is actually the main cause of fatigue in patients with PNH.

Anemia - a condition in which your body does not have enough hemoglobin. With anemia, you may have fewer whole red blood cells

Enzyme - a type of protein that helps reactions/processes happen in the body

The importance of LDH

To find out how much hemolysis is actually happening, your physician will measure and track your lactate dehydrogenase (LDH).

LDH is an enzyme found inside red blood cells. Because it is released during hemolysis, your LDH level can show how much hemolysis is happening in your body. If you have high levels of it in your bloodstream, it means a lot of your red blood cells have been destroyed. Your doctor can check for LDH through a simple blood test. Testing your LDH regularly is an important part of monitoring and managing PNH.

Serious health problems of PNH are caused by ongoing hemolysis, and reducing it is key to managing PNH. Speak with your doctor about your management options.

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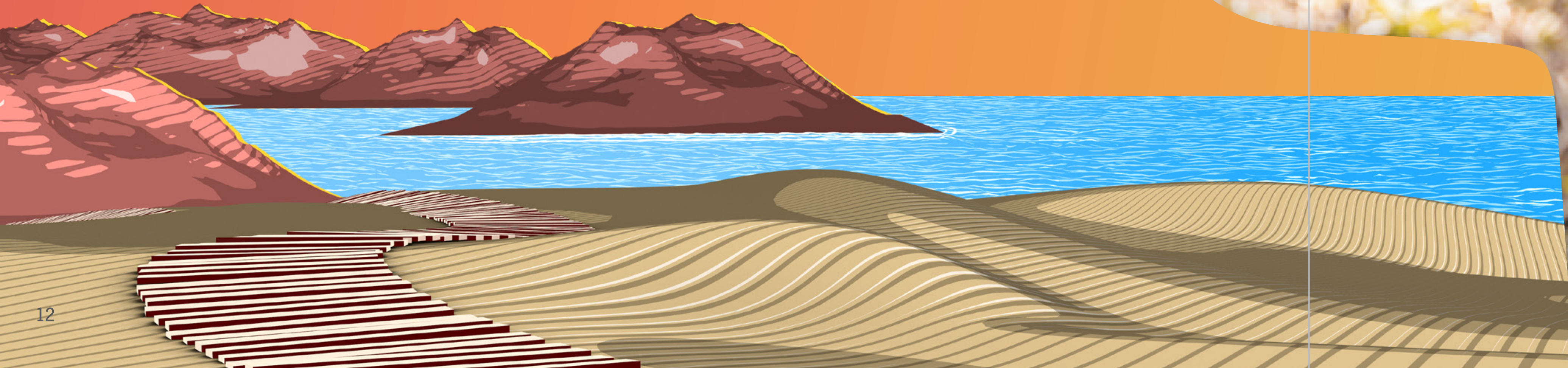
Know what you're dealing with

Signs and symptoms of PNH include a wide range of unpredictable and potentially life-threatening complications. It is a serious and progressive disease that can get worse over time, putting you at risk for serious health problems, even when you feel fine. Make sure to speak to your doctor.



Serious health risks of PNH

The signs and symptoms of PNH can be silent and unpredictable. They affect everyone differently and can change over time. Even when you can't see or feel symptoms, you can still be at risk for serious health problems. PNH can lead to a range of serious conditions.

Blood clots

Normal blood clotting begins when there is an injury to a blood vessel. Platelets that circulate in the blood clump together to stop bleeding.

In PNH, clotting begins without injury. The destruction of red blood cells releases the contents of those cells, or hemoglobin, into the bloodstream. Hemoglobin can cause reactions that activate platelets, which cause clots.

Blood clots can block veins and arteries and lead to heart attack, stroke, and organ damage, as well as other problems. Clots are the main cause of death in people with PNH. Research has shown that if you've already had a blood clot, you are at a higher risk of having another one.

Hemolysis increases your risk of having a blood clot. With PNH, blood clots can:

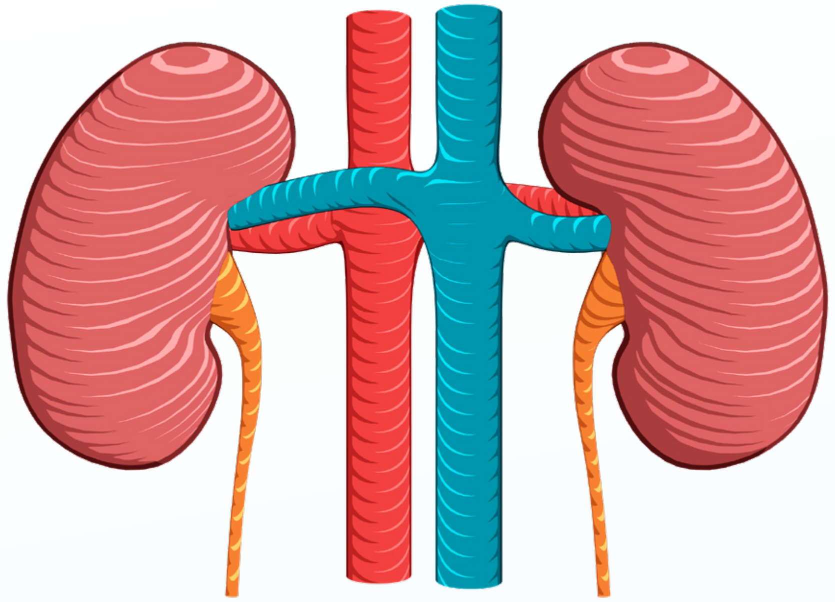
- Occur at any time
- Be potentially life-threatening—even the first time you experience one
- Occur anywhere in your body

Clone size (the percentage of blood cells affected by PNH) doesn't predict your risk of clotting. Patients with small clone sizes can still develop blood clots that can lead to more serious and life-threatening health problems.

Sometimes patients are put on medicines, often referred to as blood thinners, to try and prevent blood clots. In some patients with PNH, blood thinners may not prevent all blood clots from forming because they don't stop the hemolysis that is always happening.

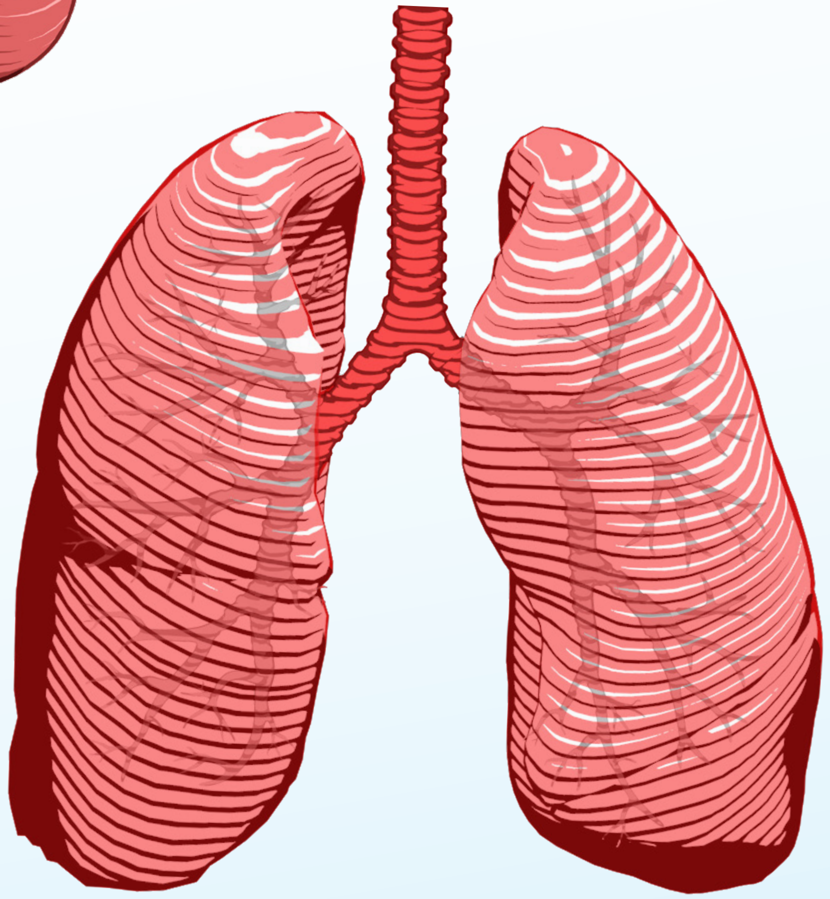
Speak with your doctor about the risks associated with blood clots.

With PNH, you can be at risk for serious health problems even if you feel fine. Be aware of how you're feeling, and if something changes, let your doctor know.



Kidney damage

Almost two-thirds of people with PNH have chronic kidney disease. It is a life-threatening condition that can lead to kidney failure, which means your kidneys stop working.



Lung problems

Almost half of patients with PNH have signs of lung problems. Symptoms can include shortness of breath and other serious health problems.

Pulmonary hypertension

Pulmonary hypertension is high blood pressure in the arteries that deliver blood to the lungs. This means that blood has a hard time getting to the lungs, causing your heart to pump harder.

Fatigue

Hemolysis prevents oxygen from getting to parts of your body. This can make you feel weak and tired to the point where everyday activities become a struggle.

You don't have to accept feeling sick

When you deal with PNH every day, you may learn to cope with your symptoms over time. Changes in how you are feeling can be so gradual that you don't even notice them. That is why it's important to track your signs and symptoms, so you can tell if they're getting worse over time. Speak with your doctor about management options—you shouldn't have to feel like being sick is normal. Common signs and symptoms of PNH are:

- Difficulty swallowing
- Lung problems
  (such as shortness of breath and pulmonary hypertension)
- Abdominal, chest, and/or back pain
- Kidney disease
- Dark-colored urine
- Erectile dysfunction
- Blood clots
- Anemia
- Fatigue/impaired quality of life

The signs and symptoms of PNH are like an iceberg—some symptoms are noticeable but many go unnoticed and may be damaging

Symptoms you may see or feel:

Fatigue

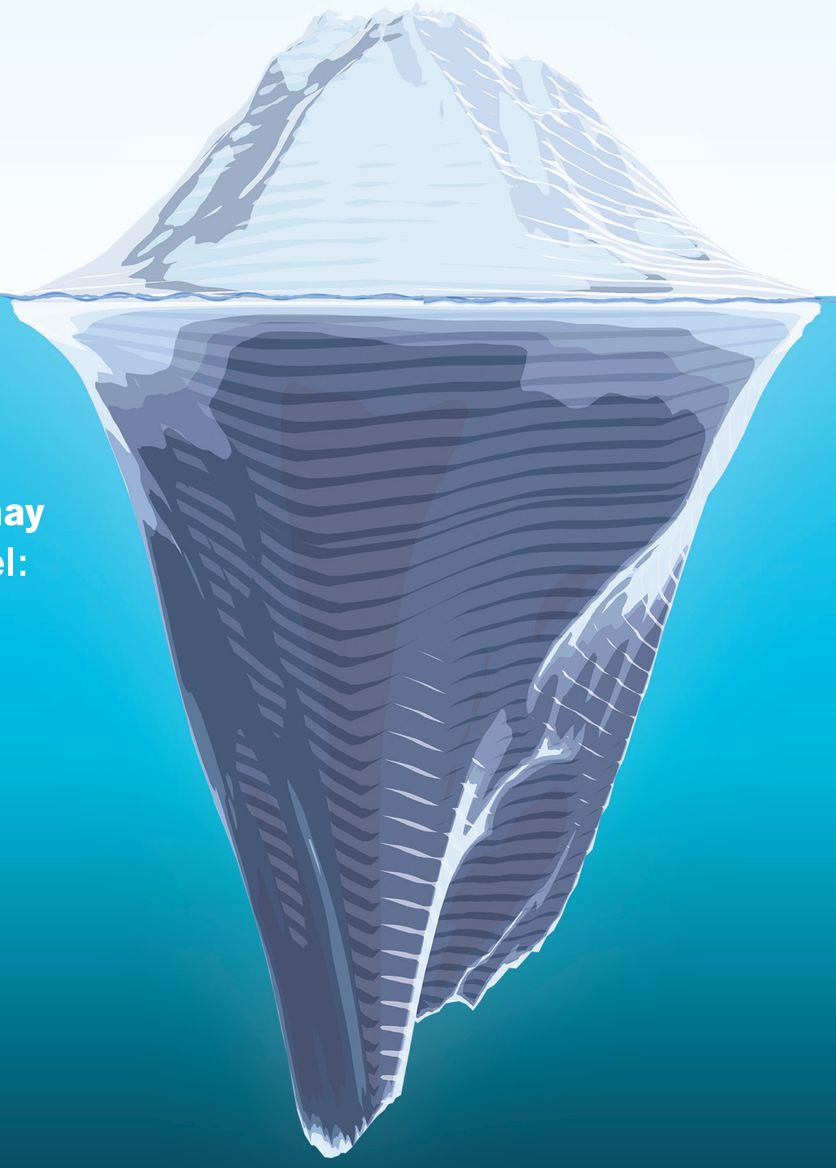
- Tiredness
- Difficulty performing daily activities
- Trouble concentrating
- Weakness

Pain

- Stomach pain
- Chest pain
- Back pain

Other symptoms

- Dark-colored urine
- Shortness of breath
- Difficulty swallowing
- Erectile dysfunction



Consequences you may not always see or feel:

- Blood clots
- Kidney disease
- Stroke
- Heart attack
- Damage to your organs

You can do something about it

Even if you can't see or feel it, it's important to take an active role in managing PNH and to regularly monitor your signs and symptoms. Keep track of how you feel, your symptoms, and your labs to stay informed of how PNH is progressing. And always stay in close contact with your doctor to make sure your management strategy is working.

Take an active role in managing your PNH

Keep track of your symptoms regularly

When you live with PNH, your symptoms may get worse over time and have an effect on your life and the things you are able to do each day. These changes may be small and gradual enough that you don't notice them right away. Over time, these changes may become a part of your life to the point that you may forget what life was like before PNH and accept your current lifestyle as "normal."

It's important to create a record of your symptoms and ability to do everyday activities and to track changes in your lifestyle over the course of your disease. Tracking changes in your lifestyle and sharing them with your doctor and other members of your healthcare team are ways you can help manage your disease.

Record your symptoms of PNH, bring the record to your medical appointments, and discuss them with your healthcare team.
Signs and symptoms to track include:

General signs and symptoms	Pain	Fatigue
• Dark-colored urine • Shortness of breath • Difficulty swallowing • Erectile dysfunction	• Abdominal pain • Chest pain • Back pain	• Tiredness • Difficulty performing daily activities • Trouble concentrating • Weakness

Track your symptoms and your lab results: they're key to managing PNH successfully. Find helpful tools for tracking at PNHSource.com by clicking on Patient Resources or contacting OneSource™ at 1-888-765-4747.

Know your lab results

To regularly monitor your PNH, your doctor might order some of these lab tests:

Complete blood count to measure the amounts of the different parts of your blood

- **Red blood cells:** a type of blood cell that contains a protein called hemoglobin, which carries oxygen to your body tissues
- **White blood cells:** cells of the immune system that are involved in protecting your body against both infectious disease and foreign invaders
- **Platelets:** the smallest of the blood cells, whose function is to help the blood clot and control or stop bleeding
- **Reticulocytes:** slightly immature red blood cells that have recently left the bone marrow. Measuring them can indicate whether you are making red blood cells in the bone marrow at an appropriate rate. When red blood cells are destroyed—through hemolysis in PNH—the reticulocyte number should go up as your body makes more red blood cells to replace them. Some people with PNH may have other problems with their bone marrow, and their reticulocytes may not go up like they should

Blood chemistry to measure the chemical balance of your blood

- **Lactate dehydrogenase (LDH):** an enzyme released from red blood cells when they are destroyed by hemolysis. The level of LDH in the blood can show how much hemolysis is happening
- **Haptoglobin:** a substance normally found in your blood. Haptoglobin attaches to free hemoglobin in your blood and takes it to the liver to be recycled. When there is hemolysis, the free hemoglobin rises and the haptoglobin level falls, so low haptoglobin shows that hemolysis is happening
- **Creatinine:** a waste product in the blood that shows how well your kidneys are working
- **Estimated glomerular filtration rate (eGFR):** an indicator calculated using your creatinine level and a formula that takes into account things like your age, weight, and sex. This shows how well your kidneys are working by estimating how much blood is filtered by your kidneys

Clone size to measure the percentage of PNH cells in your blood

- **High-sensitivity flow cytometry:** a test that measures the number of red and white blood cells affected by PNH in a small sample of blood taken from your arm. This is the standard test for confirming whether or not you have PNH and is used to monitor your PNH over time

These are just some tests that your doctor might order. There may be other tests too. You should speak to your doctor about what these tests mean and what results are considered a healthy range and keep track of your numbers.

Communicating with your doctor

Now that you've been tracking how you feel, make sure your doctor is too. Discuss regular PNH monitoring if your doctor isn't already providing it. Be sure to share all of your symptoms with your doctor. Even a small change or a minor symptom could be important.

- At every visit, tell your doctor about the symptoms you are experiencing, even if you don't think they're related to PNH
- Tell your doctor when the symptoms started and how often they happen
- Show your doctor where on your body you feel your symptoms
- Describe how bad your symptoms get
- If symptoms suddenly get worse, tell your doctor. Let your doctor know if you are sick or stressed when it happens

Discuss your lab results with your doctor

- Make sure you understand the meaning of all your lab results
- Stay informed about how much hemolysis (indicated by LDH levels) is happening in your body and what that means for you
- Find out your clone size and if it has gone up or down

At times, you may be feeling better, but your lab results won't show improvement. The reverse of this can also happen.

No single sign, symptom, or lab result defines PNH. This is why it is important to keep a close watch on all your signs, symptoms, and important lab results. It's the best way for you and your doctor to understand the full story of what's going on with your PNH.

Ask questions

It is also important for you to understand how PNH is affecting you. If you're not sure you are understanding your lab results, ask questions such as:

- I would like a copy of my lab test results. Would you please help me understand them?
- Are my results normal?
- What does it mean if my results are above/below normal?
- Is there anything I can do to get them within a normal range?

You should also ask questions that help you manage living with PNH, such as:

- What can I do to feel less tired?
- What can I do to help reduce the health risks of PNH?
- Can my disease get worse over time?
- What are my options for managing PNH?

These are just some of the questions you might want to ask. For more information on questions to ask your doctor, visit **PNHSource.com** and click on **Patient Resources**.

You can also contact OneSource™ at 1-888-765-4747 and speak to a Patient Navigator to learn more about PNH and receive free one-on-one support as you manage the disease.

Ask your doctor

for regular monitoring of your signs, symptoms, and lab results. It is important for you to know how PNH is affecting you.

Diagnosed with PNH and aplastic anemia or myelodysplastic syndrome

Differences between aplastic anemia/myelodysplastic syndrome and PNH

Some patients are diagnosed with aplastic anemia or myelodysplastic syndrome (MDS) as well as PNH. Like PNH, aplastic anemia and MDS are also bone marrow failure disorders.

“Aplastic” means that bone marrow can’t produce new blood cells properly. As a result, patients with aplastic anemia have fewer red blood cells, white blood cells, and platelets. MDS is a condition in which there’s a problem with the way bone marrow makes blood cells.

Unlike PNH, which is a disease of **red blood cell destruction**, aplastic anemia and MDS are diseases that affect the **production** of blood cells in the bone marrow. In these conditions, the bone marrow is not making enough cells. As a result, there are fewer than normal red blood cells circulating in the body.

In patients with aplastic anemia or MDS, fewer blood cells are produced and in PNH, the red blood cells that are produced are missing protective proteins and are subject to intravascular hemolysis.

PNH is managed separately and differently than aplastic anemia or MDS

If you have aplastic anemia or MDS as well as PNH, ask your doctor about the options available to you for managing those conditions in addition to your PNH.

Get the support you need along the way.

Patient support from OneSource™

If you have PNH, you are not alone

It is natural to think you are alone when you are diagnosed with PNH because it is a rare disease. Communicating with others who have had similar experiences and who understand can make a difference.

With a phone call or click of a button, OneSource is available at no cost to people living with PNH. You’ll get one-on-one education and personalized support, every step of the way, as you manage your PNH.

OneSource is a complimentary, personalized support program offered by Alexion and staffed by Alexion Patient Navigators, Patient Liaisons, and Patient Education Managers, all of whom have extensive knowledge of PNH and can assist you every step of the way. They are ready to provide needed support and resources—wherever you may be in your PNH journey.

OneSource is a place to ask questions and find answers. Connect with a Patient Navigator, with no obligations, by calling 1-888-765-4747 or by visiting **AlexionOneSource.com**.

Call 1-888-765-4747 or visit AlexionOneSource.com

Work closely with those who support you

Open lines of communication can make the difference.

Your healthcare team

Together, you and your doctor and nurses can develop a plan to manage PNH and watch your progress. Your healthcare team can also provide you with information about PNH. Ask them any questions you might have about the disease.

Your loved ones

PNH can take a lot out of you, so it's important to ask friends and family for support when you need it. Be sure to let them know what PNH is and how you're feeling day to day. That way, they'll know when they need to reach out to lend a hand.

Your PNH community

PNH is a rare disease, but that makes those who have it that much closer. Connect with others with PNH to help you learn about, cope with, and manage the disease. The next page lists some organizations that offer information, advice, and support.

Patient viewpoints

Learn about PNH from actual patients as they share their personal experiences. To see how others live and cope with the disease, visit **PNHSource.com**.

Stay informed, stay connected, and learn from others

PNHSource:

This site provides complete information about PNH and helpful tools to manage the disease, all in one place. **PNHSource.com**

OneSource™:

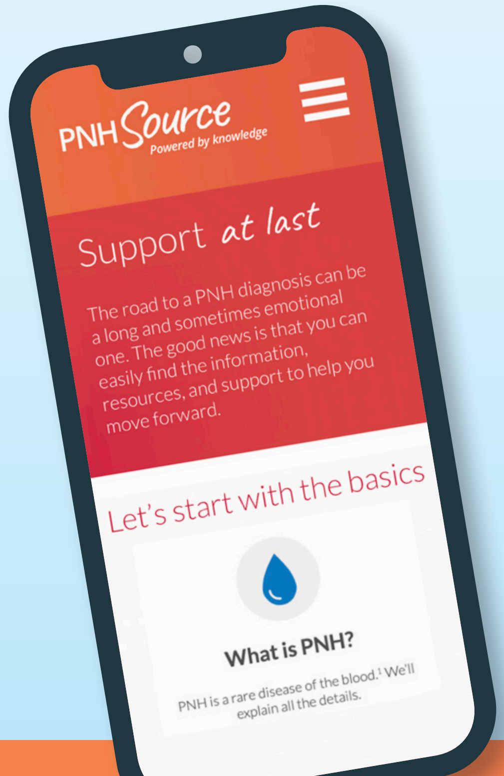
Patient Navigators from Alexion can help answer questions about PNH and provide personal support for people living with PNH and their caregivers. Call **1-888-765-4747**, or visit **AlexionOneSource.com**.

The Aplastic Anemia and MDS International Foundation:

This nonprofit site is a resource for assistance, advocacy, and support for patients living with aplastic anemia, myelodysplastic syndromes, and PNH. **aamds.org**

Living With PNH Facebook Page:

The purpose of the Living With PNH Facebook page is to raise awareness of PNH and build an active community of patients, caregivers, and advocates to learn together and share their experiences living with the disease. **facebook.com/LivingWithPNH**



PNHSource Powered by knowledge

Support at last

The road to a PNH diagnosis can be a long and sometimes emotional one. The good news is that you can easily find the information, resources, and support to help you move forward.

Let's start with the basics

What is PNH?

PNH is a rare disease of the blood.[1] We'll explain all the details.

Finding tools to actively manage PNH

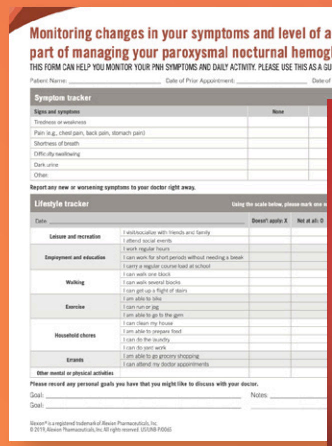
Actively managing PNH can go a long way, and there are tracking tools to help you do it.

Go to **PNHSource.com** and click on **Patient Resources**.

There, you can download **trackers** to monitor your symptoms and lab results—including your LDH—over time. You can also find helpful tools for speaking with your doctor about your signs and symptoms.

Take your trackers with you on every visit and discuss your results with your doctor. If you notice your symptoms getting worse, don't wait until your next visit. Contact your doctor right away.

Resources and tools:



Monitoring changes in your symptoms and level of activity is an important part of managing your paroxysmal nocturnal hemoglobinuria (PNH)

THIS FORM CAN HELP YOU MONITOR YOUR PNH SYMPTOMS AND DAILY ACTIVITY. PLEASE USE THIS AS A GUIDE WHEN SPEAKING WITH YOUR DOCTOR.

Patient Name: ______ Date of Prior Appointment: ______ Date of Next Appointment: ______

Symptom tracker

Signs and symptoms	None
Tiredness or weakness	
Pain (e.g., chest pain, back pain, stomach pain)	
Shortness of breath	
Difficulty swallowing	
Dark urine	
Other:	

Report any new or worsening symptoms to your doctor right away.

Lifestyle tracker Using the scale below, please mark one

Date:		Doesn't apply: X	Not at all: 0
Leisure and recreation	I visit/socialize with friends and family		
	I attend social events		
Employment and education	I work regular hours		
	I can work for short periods without needing a break		
	I carry a regular course load at school		
Walking	I can walk one block		
	I can walk several blocks		
	I can get up a flight of stairs		
Exercise	I am able to bike		
	I can run or jog		
	I am able to go to the gym		
Household chores	I can clean my house		
	I am able to prepare food		
	I can do the laundry		
	I can do yard work		
Errands	I am able to go grocery shopping		
	I can attend my doctor appointments		
Other mental or physical activities			

Please record any personal goals you have that you might like to discuss with your doctor.

Goal: ______ Notes: ______

Goal: ______

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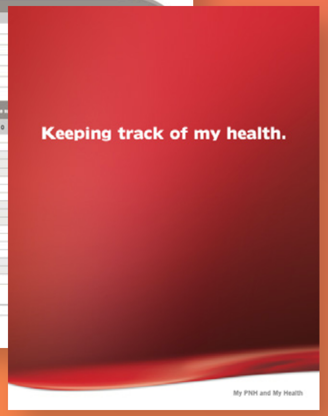
Symptoms/ LDH Tracker Tool



Keeping track of my health.

My PNH and My Health

PNH Tracker Tool

Frequently asked questions

Here are some answers to questions that patients with PNH frequently ask. You might have the same questions too.

Will my children or spouse get PNH? Can they catch it from me?

PNH is an acquired disease, which means it's not hereditary and it cannot be passed on to your children. PNH is not a contagious disease and cannot be transmitted to other people.

How did I get PNH? Was I born with it?

PNH is an acquired disease, which means it's not inherited. It results from changes/mutations in your DNA that occur after you are born. It is not known why some people develop it over time and others don't.

What is LDH and why is it important?

LDH stands for lactate dehydrogenase, which is an enzyme found inside red blood cells. LDH is released when red blood cells are destroyed. This means that the amount of LDH released into your bloodstream can show how much hemolysis is happening in your body. Testing your LDH regularly is an important part of managing PNH.

What is a clone? What does that mean?

A clone refers to the percentage (or number) of blood cells (red blood cells or white blood cells) that are affected by PNH and do not have the protective surface proteins. Only the red blood cells that are affected by PNH are destroyed by the complement system and contribute to the signs and symptoms of PNH.

I have a small clone size. Does this mean that I am not at risk for the serious health problems of PNH?

In PNH, clone size can increase or decrease over time. Even with a small clone size, you can have PNH-related health complications.

Can PNH go away? Can it get worse?

There is a very small possibility that you could recover from PNH but it is unlikely. PNH is a progressive disease and can get worse over time. Consistently work with your doctor to track and manage the disease.

What is aplastic anemia? What is myelodysplastic syndrome (MDS)?

Aplastic anemia and MDS are disorders of the bone marrow. Bone marrow is the soft tissue found at the center of the large bones in your body. The bone marrow makes the cells that form your blood. In aplastic anemia and MDS, the bone marrow does not make enough new blood cells.

Notes

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ALEXION®
AstraZeneca Rare Disease