TAKE CONTROL OF PNH

Stay informed and play an active role

FIND OUT HOW INSIDE
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 to 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 always happening

Hemolysis is the main cause of the major health problems in patients with PNH.
What does PNH mean?

P — paroxysmal “sudden, from time to time”
N — nocturnal “at nighttime”
H — hemoglobinuria “hemoglobin in the urine” (see box on right)

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.

Who gets PNH?

People from all walks of life get PNH:
- Men and women
- People of all races
- People of any age, although the average age at diagnosis is 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

PNH comes with a wide range of signs and symptoms that are often similar to other diseases. As a result, everyone experiences PNH differently, making it tough to diagnose.

Hemoglobin is the reddish brown material found inside your red blood cells that carries oxygen through 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.

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 (RBCs):** 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 (WBCs):** make up a much smaller number of cells in the blood. They help your immune system fight disease and infection.
- **Platelets:** are small pieces of cells whose function is to help the blood form clots and control or stop bleeding.

Blood cells are made by “master cells,” called stem cells, and are made mostly in the bone marrow. Bone marrow is the soft tissue in the center of the large bones of the body, such as the femur (upper leg bone).

Stem cells will mature into red blood cells, white blood cells, and platelets, and can divide to make new cells that are identical copies. Through this process, you can continue to make new cells throughout your life.

When the mature blood cells are fully formed and functional, they leave the bone marrow and enter your bloodstream to perform the specific job for which they are made.
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 (see box on right).

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.

The meaning of clone size

Clone size refers to the percentage (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 the clone size is measured, both red and white blood cells are looked at. The white blood cells show your true clone size because they are not destroyed by complement like the red blood cells. The difference between the white blood cell clone size and the red blood cell clone size can show how much red blood cell destruction is happening.

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—every 6 months to 1 year—but your doctor may test more frequently. Speak with him or her about testing for PNH.
What is hemolysis?
When complement destroys red blood cells in PNH, this destruction is known as hemolysis.

Hemo — blood
Lysis — breaking apart of cells
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 red blood cells burst, they release hemoglobin into the bloodstream. Hemoglobin is good for the body when it’s inside your red blood cells. When it’s outside, it is very dangerous and can harm your body in many ways. Even if you can’t see or feel hemolysis, you can still have serious health problems. These health problems can include:

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

Understanding hemolysis

Serious health problems of PNH are caused by ongoing hemolysis and reducing it is key to managing PNH. Speak with your doctor about the best way to do this.
What are the effects of PNH?

How will I know hemolysis is happening?

You cannot see or feel hemolysis, which makes it tough to manage. The results of it often can 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
- Stomach 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 (see box on right). 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.

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 (see box on right) 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 managing PNH.
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 into the bloodstream. Those contents can cause reactions that activate platelets, which causes clots.

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
- Can be life-threatening—even the first time you experience one
- Can 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 ways to reduce your risk of blood clots.
Kidney damage:
Almost 2/3 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. Lung problems can be caused by pulmonary hypertension (see box on right). Symptoms can include shortness of breath and other serious health problems.

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.

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.

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. This will help you manage PNH in the best way possible.
When you deal with PNH every day, over time you may learn to cope with your symptoms. 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**

- Difficulty swallowing
- Lung problems (such as shortness of breath and pulmonary hypertension)
- Stomach pain
- Kidney disease
- Dark-colored urine
- Erectile dysfunction
- Blood clots
- Anemia
- Fatigue/Impaired quality of life
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What are signs and symptoms of PNH?

Fatigue:
• Tiredness
• Difficulty performing daily activities
• Trouble concentrating
• Dizziness
• Weakness

Pain:
• Stomach pain
• Leg pain or swelling
• Chest pain
• Back pain

Other signs and symptoms:
• Dark-colored urine
• Shortness of breath
• Difficulty swallowing
• Yellowing of the skin and/or eyes
• Erectile dysfunction

PNH is just like an iceberg — what you can’t see or feel can cause the most damage

Blood clots
Kidney disease
Damage to your organs
Stroke
Heart attack

Consequences you may not always see or feel
Take an active role in managing your PNH

Keep track of your signs and symptoms regularly

When you live with PNH every day, the symptoms you feel may worsen over time and change the way you live. Changes in your lifestyle may be so gradual that you may not even notice them. You forget what your life was like before PNH and come to accept your current lifestyle as “normal.”

It’s important to create a record of your signs and 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 signs and symptoms of PNH, bring the record to your medical appointments, and discuss them with your healthcare team. Signs and symptoms to track include:

<table>
<thead>
<tr>
<th>General signs and symptoms</th>
<th>Pain</th>
<th>Fatigue</th>
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<tbody>
<tr>
<td>Dark-colored urine</td>
<td>Stomach pain</td>
<td>Tiredness</td>
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<td>Shortness of breath</td>
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<td>Yellowing of the skin and/or eyes</td>
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<td>Weakness</td>
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Know your lab results

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

**Complete blood count (CBC)** to measure the amounts of the different parts of your blood

- **Red blood cells (RBCs)**
- **White blood cells (WBCs)**
- **Platelets**: The smallest of the blood cells, whose function is to help the blood clot and control or stop bleeding
- **Reticulocytes**: These are slightly immature red blood cells that have recently left the bone marrow. Measuring them can tell 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 amount of enzyme/waste product in 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**: This substance is 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
- **eGFR**: The estimated glomerular filtration rate (eGFR) is calculated using your creatinine level and a formula that takes into account things like your age, weight, and gender. This shows how well your kidneys are working by estimating how much blood passes through the glomeruli each minute

**Clone size** to measure the percentage of PNH cells

- **High-sensitivity flow cytometry**: This test 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 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 can be others. 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 him or her know if you are sick or stressed when it happens

Discuss your lab results with your doctor

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

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

No one 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 labs. It’s the best way for you and your doctor to understand the full story of what’s going on with your PNH.

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 Printable Brochures or contacting OneSource™ at 1.888.765.4747.
Ask questions

It is also important for you to understand how PNH is affecting you, so ask questions if you’re not sure you understand your lab results:

• 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 questions you might want to ask. For more information on questions to ask your doctor, visit PNHSource.com and click on Printable Brochures.

You can also contact OneSource at 1.888.765.4747 and speak to a Nurse Case Manager to learn more about PNH and to receive free one-to-one support as you manage the disease.

If you have any questions about PNH or options for managing the disease, be sure to speak with your doctor.
Diagnosed with PNH and aplastic anemia or myelodysplastic syndrome

**Differences between aplastic anemia/MDS and PNH**

Some patients are diagnosed with aplastic anemia (AA) 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 AA or MDS as well as PNH, fewer blood cells are produced and the red blood cells that are produced are missing protective proteins and are subject to hemolysis.

**PNH is managed separately and differently than AA or MDS**

If you have AA or MDS as well as PNH, ask your doctor about the options available to you for managing those conditions in addition to your PNH.
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-to-one education and personalized support, every step of the way, as you manage your PNH.

A Nurse Case Manager from OneSource can help answer questions about PNH, provide support for people living with PNH and their caregivers, and keep you connected with a supportive community. If you would like a Nurse Case Manager from OneSource to put you in touch with other people like you who are living with PNH, just ask.

OneSource is a place to ask questions and find answers. Connect with a Nurse Case Manager, with no obligations, by calling 1.888.765.4747 or visiting PNHSource.com and clicking on Patient Resources/Patient Support from OneSource.

PNH is often found along with aplastic anemia, while only a small percentage of patients with PNH have MDS.

Get the support you need along the way.
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 confront 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:** Complete information about PNH and helpful tools to manage the disease, all in one resource. [PNHSource.com](http://PNHSource.com)

**OneSource™:** Nurse Case Managers 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 [PNHSource.com](http://PNHSource.com) and click on Patient Resources, then Patient Support From OneSource. You can also e-mail OneSource by going to PNHSource.com and clicking on the OneSource logo.

**The PNH Community:** The PNH Community is a patient support site in partnership with National Organization for Rare Disorders (NORD) and the Aplastic Anemia & MDS International Foundation (AA&MDSIF). This site is dedicated to providing patients with PNH access to other patients as well as many free events offered throughout the country. [www.pnhcommunity.org](http://www.pnhcommunity.org)

**National Organization for Rare Disorders (NORD):** A not-for-profit organization dedicated to helping people with rare disorders, such as PNH. [www.rarediseases.org](http://www.rarediseases.org)

**Aplastic Anemia & MDS International Foundation (AA&MDSIF):** A nonprofit resource for assistance, advocacy, and support for patients living with aplastic anemia (AA), myelodysplastic syndromes (MDS), and PNH. [www.aamds.org](http://www.aamds.org)

**The PNH Research & Support Foundation:** A volunteer-based organization that helps raise funds for PNH research and offers limited financial support for PNH-related expenses to qualified applicants. [www.pnh.aamds.org](http://www.pnh.aamds.org)

**PNH Support Group:** An online support group for people with PNH. [www.pnhdisease.org](http://www.pnhdisease.org)
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 Printable Brochures. There, you can download trackers to:

- Monitor your symptoms and lab results—including your LDH—over time
- Record any changes in your everyday activities to help you understand how PNH has affected your life

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.

PNH Patient Resources app

Use the PNH Patient Resources app to stay in control of your PNH, even when you’re on the go. You can:

- Learn about PNH from actual patient experiences
- Discover more about the disease from doctors managing patients with PNH
- Access tools to actively help you manage your PNH
- Find out where to connect with others at PNH community events
- Tap into support from OneSource™—anytime, anywhere

To download tracking tools, go to PNHSource.com and click on Printable Brochures, or order them by calling OneSource at 1.888.765.4747. To access the app, go to PNHSource.com. Click on Live With PNH, then Patient Support. Choose the type of device you have. That will take you to a page where you can read about and download the app.
Frequently asked questions

Here are some 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 who are in close contact with you.

**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 (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 (AA)? What is myelodysplastic syndrome (MDS)?**
AA 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 AA and MDS, the bone marrow does not make enough new blood cells.
Notes
Know what you’re dealing with

PNH is a serious, progressive disease that can get worse over time, putting you at risk for serious health problems.

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.