This *is* PNH

Understanding PNH

A GUIDE FOR YOUR JOURNEY

PNH stands for **P**aroxysmal (meaning "sudden and irregular") **N**octurnal ("at night") **H**emoglobinuria ("hemoglobin in urine"). What's important to know is that PNH symptoms can happen at any time of day, and not everyone will have dark urine. The name has stuck around, but PNH can look different for each person.

Take a look inside to learn more about PNH for you or someone you care about.

Inside this guide, we invite you to explore:

If you have any questions regarding PNH or symptoms you may be experiencing, please speak with your doctor.

What causes PNH?

No one is born with PNH. PNH is "acquired," which means the genetic mutations responsible for the disease happen during your life. PNH is not something that is contagious, so you can't give it to anyone else. PNH is closely related to aplastic anemia, an autoimmune disease in which the body cannot produce all types of blood cells in sufficient numbers, causing fatigue, infections, bruising or bleeding. Some patients diagnosed with PNH may also have a history of aplastic anemia as well.

PNH by the numbers

First reported in medical journals in the late

1800s

Affects ~1 out of every

million

people each year

~400-500

new cases are diagnosed in the U.S. **each year**

Impacts both

men + women

of every ethnicity

Diagnosis can take up to

5 years

Many individuals may see more than

5

physicians before getting diagnosed

Most often **diagnosed** at

30-40

years of age

Approximately

44%

of patients diagnosed with PNH have a history of **aplastic anemia or hypoplastic anemia**

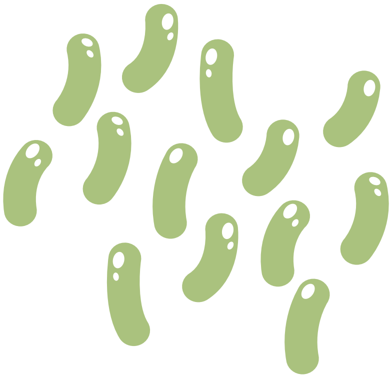
Did you know

- PNH is not cancer
- With treatment, most people with PNH can expect a normal life expectancy
- PNH is not inherited and can't be passed onto others
- Everyone' s experience with fatigue is different

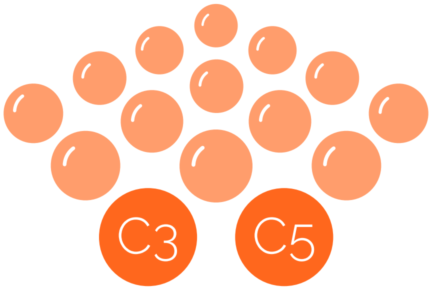
Understanding the immune system

To understand why red blood cells are destroyed, we must understand the science of PNH and the immune system.

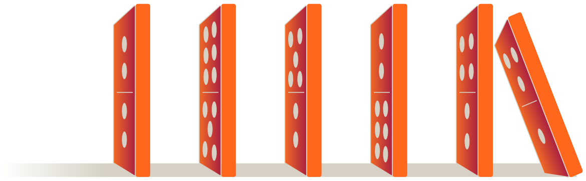
The immune system is a sophisticated defense network that keeps the body safe from dangers like disease and infection. One very complex weapon in this arsenal is called the "complement system".



← The complement system helps destroy dangerous cells, like viruses or bacteria, and gets rid of damaged or dying cells



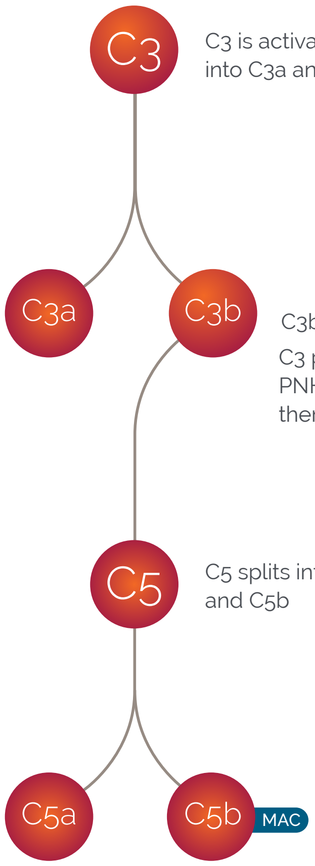
← There is an army of more than 50 different **proteins** that play a part in the complement system. Two key proteins are known as **C3** and **C5**



← Like dominoes, C3 and C5 proteins are activated in a specific order as your immune system detects viruses or bacteria

Understanding the science

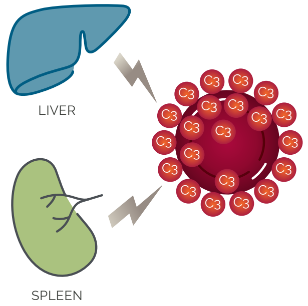
PNH occurs due to a mutation in the PIG-A gene in which red blood cells are missing normally occurring, protective proteins, subjecting them to accidental attacks from the complement system. The lack of protective proteins on the red blood cells makes them more susceptible to being destroyed and broken apart, which is a process called hemolysis. Hemolysis can occur when the immune system attacks these cells as though they were dangerous viruses or bacteria. Hemolysis causes many of the symptoms of PNH.



C3 is activated and splits into C3a and C3b

C3b activates C5 →

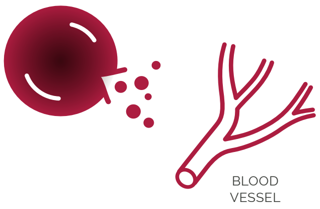
C3 proteins bind to PNH RBC's, which "tags" them for destruction



Extravascular hemolysis (EVH) occurs when red blood cells are destroyed in the liver and spleen

C5 splits into C5a and C5b

The membrane attack complex (MAC) is formed to help destroy dangerous cells, like viruses and bacteria, in the body →



Intravascular hemolysis (IVH) occurs when red blood cells are destroyed inside the blood vessels

It may be **important to control both IVH and EVH** as they can occur in your body at the same time, causing your PNH symptoms.

While your treatment works to protect your red blood cells, it's important to be aware of situations where symptoms could possibly reoccur. One such situation is called breakthrough hemolysis (BTH). BTH happens when your immune system is activated and surpasses the protection provided by your medication. It can be triggered by infections, vaccines, or other factors that stress the immune system. Symptoms can vary, **if you have any concerns or suspect BTH, be sure to contact your doctor.**

Signs and symptoms

PNH impacts every patient differently—while one individual may have only mild symptoms, another might experience severe effects.

PNH can cause symptoms like:

- Fatigue
- Headaches
- Trouble breathing
- Difficulty exercising
- A rapid heartbeat
- Abdominal and chest pain
- Trouble concentrating (often called "brain fog")
- Loss of appetite
- Small dots on the skin
- Blood in urine
- Bruising

Some people with PNH may have clear, noticeable symptoms, while others might not feel much at all. Even with management, some individuals may continue to experience challenges like anemia or fatigue.

Even if you're feeling okay, there could still be problems happening in your body that you can't see or feel. That's why it is crucial to have ongoing discussions with your provider about how you're feeling.

Here are some associated conditions that might not be obvious[1]:

- Blood clots
- Kidney disease
- Stroke
- Heart attack

Imagine your body is like a house

- The clinical symptoms a patient feels or sees, like pain, shortness of breath, fatigue, or dark urine, are like leaks in the ceiling or flickering lights. They're the things you *notice* and that tell you something might be wrong
- The hidden symptoms, or underlying internal changes, are like a growing crack in the foundation. You can't see them directly, but they could be causing, or about to cause, major problems. These issues might only show up with special tools (like blood tests or imaging), just like you'd need an inspector to find hidden problems in a house

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1. Schrezenmeier, H., Röth, A., Araten, D. J., Kanakura, Y., Larratt, L., Shammo, J. M., Wilson, A., Shayan, G., & Maciejewski, J. P. (2020). Baseline clinical characteristics and disease burden in patients with paroxysmal nocturnal hemoglobinuria (PNH): updated analysis from the International PNH Registry. *Annals of hematology*, 99(7), 1505–1514.

Lab values

Lab tests look at different markers in your blood to help determine what's happening in your body. Some of these markers include:

CBC

analyzes the amount of red and white blood cells, hemoglobin, and platelets in your blood

- Higher hemoglobin levels are associated with less fatigue and pain, and better physical, emotional, and social functioning
- Low levels are associated with losing red blood cells and may lead to a blood transfusion

Lactate Dehydrogenase (LDH)

is an enzyme found in your body's red blood cells

- Red blood cell destruction results in the release of LDH into the bloodstream
- High levels of LDH may be an indication that IVH is ongoing

Reticulocytes

are young red blood cells

- High reticulocytes could mean your body is working hard to replace the red blood cells being destroyed by PNH

Bilirubin

is a pigment produced from the destruction of red blood cells

- People with PNH may have high levels of bilirubin
- Higher than normal levels could be a sign of EVH or IVH

Haptoglobin

measures amount of free haptoglobin in blood

- Haptoglobin is a protein that attaches to hemoglobin once it has been released from red blood cells
- People with PNH typically have low free haptoglobin levels

Making sense of the numbers

Every person's experience with this disease can be unique. The way each lab process tests is different, so what they consider a "normal" range can vary. Your doctor will consider a variety of test results and all your signs and symptoms when monitoring your PNH. It's always best to speak to your doctor about your test results and what they may mean for your health.

Scan the QR code to learn more about lab tests for PNH.

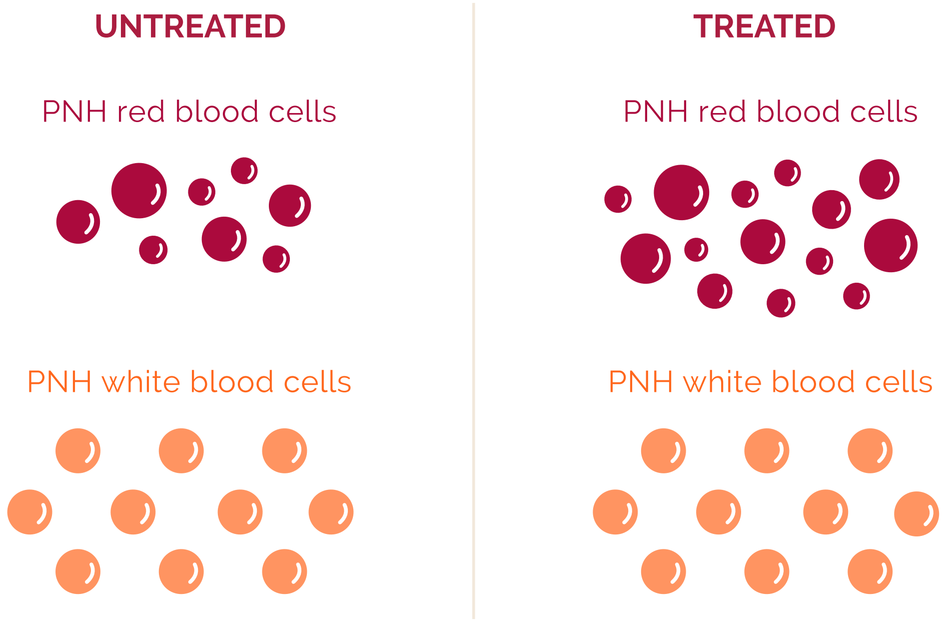
Methods of diagnosis

Flow cytometry is one of the best tests to help diagnose PNH. This blood test assesses white blood cells and red blood cells to determine if they are missing their protective shield, a key sign of PNH. In confirming a PNH diagnosis, flow cytometry focuses on detecting white blood cells, since they are able to be assayed even when red blood cells are destroyed.[1,2] Flow cytometry measures the number of WBC and RBC affected by PNH, which is called your "clone size".

Clone size

- If your PNH is untreated, you could anticipate having a higher PNH WBC and lower PNH RBC clone size, which could lead to more PNH symptoms.
- If your PNH is treated, you could anticipate an increase in your PNH RBC's clone size because therapy protects those RBCs from destruction. The WBCs will remain unaffected.

Your clone size can change over time, and your symptoms may get worse if the condition isn't carefully managed. That's why regular monitoring and ongoing care are so important when living with PNH.



A **bone marrow biopsy** can also be used for diagnosing PNH:

- It shows how well your bone marrow is making new blood cells
- It also looks at the kinds of cells being made and how many there are
- It can also look at many other things within your marrow that your provider may find useful or helpful

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1. Brando B, Gatti A, Preijers F. Flow Cytometric Diagnosis of Paroxysmal Nocturnal Hemoglobinuria: Pearls and Pitfalls - A Critical Review Article. *EJIFCC*. 2019;30(4):355-370.
2. Babushok DV. When does a PNH clone have clinical significance?. *Hematology Am Soc Hematol Educ Program*. 2021;2021(1):143-152.

What is your experience with PNH symptoms?

This worksheet is provided for your convenience only and does not contain medical advice. Please talk to your doctor about any questions you have regarding PNH, symptoms, or treatment.

Which PNH symptoms do you experience most often?

	How often?				How bad?			
Fatigue	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Shortness of breath	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Headaches	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Brain fog	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Abdominal/chest pain	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Erectile dysfunction	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Difficulty swallowing	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating
Back pain	○ Rarely	○ Sometimes	○ Often	○ All of the time	○ Not too bad	○ Manageable	○ Pretty bad	○ Debilitating

Questions for your doctor:

- Why am I **continuing to experience these symptoms**?
- What can we do to **improve these symptoms so I can try to do more of what I love**?
- **What are my lab tests telling us?**
- Do we need to make **any changes to my treatment or lifestyle**?

Partnering with your doctor

Every appointment with your doctor is an opportunity to take steps toward better health. Planning can help you get the most out of these conversations.

Planning ahead

Share your expectations when you schedule your appointment, and let the office know about any topics you'd like to discuss or questions you might have.

Consider the impact of your symptoms on your life so you can work with your friends/family/doctor to prioritize what's most important to you.

Prepare a list of medications and topics you'd like to discuss.

During your appointment

Bring someone with you who can help support you, or serve as a second set of ears or a notetaker (even if via phone).

Be open when talking about your list of concerns and asking questions. The more information you can share, the better your doctor can help. Be specific by explaining what your ideal day-to-day experience looks like.

Set clear next steps before leaving your doctor's office and create a plan for what should happen next.

After your appointment

Keep track with a journal or list of how changes to your routine or treatment plan are working for you.

Re-evaluate and be mindful of how changes in your life may need to be reflected in your treatment plan. Record any new topics or observations to discuss with your doctor at your next appointment, including how symptoms are impacting your activities.

Stay organized by keeping a record of all your appointments, lab tests, and agreements in one place.

Supporting your emotional well-being

Many people prioritize their physical health over their emotional well-being, but the latter is equally important for overall wellness. Here are some tips and strategies to help you focus on and enhance your emotional health.

Living with a chronic disease can create a range of emotions. Exploring mind-body connections, which center on reducing stress and enhancing emotional well-being, may be helpful. As always, talk to your doctor or a mental health professional for any concerns relating to your mental or emotional wellbeing.

Managing your stress

- Activities such as meditation, yoga, deep breathing, or doing other things that make you smile could also be meaningful such as taking up new hobbies, exploring nature, or anything that offers distraction
- Set short-term achievable goals

Addressing mental fatigue

- Evaluate tasks and identify top priorities
- Avoid overloading your schedule
- Plan regular rest breaks and set boundaries

Connecting with others

- Coping with your disease and navigating your treatment journey can be challenging. Using support systems can be beneficial in your journey

A tip on managing your energy

Think of your energy like a battery—some days you feel fully charged and ready to take on the day, and other days you might feel completely drained or depleted. That's perfectly normal, especially when managing a chronic illness.

What's important is to:

- Check in with yourself regularly.
- Pay attention to how you're feeling and take time to recharge when you need it. Even small actions can help restore your energy.
- Finding a healthy balance in your day and discovering what helps you feel refreshed is key to managing fatigue.
- Listen to your body, it's always communicating with you, and no one knows it better than you do.

Use this interactive wellness tool to understand the impact PNH has on your overall wellness.

Helpful resources

Being a part of a community means you never have to do it alone. This is true whether you have PNH yourself or someone you love does. A rare disease affects more than just the person who lives with it, and spouses, children, employers, and friends can all be part of your support team.

While you may not have come across someone else with PNH in your neighborhood, there are ways to connect with the larger community and find supportive resources as you navigate your everyday.

Learn More

- Visit ThisIsPNH.com to learn more about PNH and access other tools and resources to help you through your journey
- Many organizations offer information and helpful resources for people with PNH

Learn more

Make A Connection

Ask an ACE:

- Our team is here to help you learn, connect, and share. We'd love to hear from you!

Connect now

Get Social

- Join a group for people with PNH and become a regular contributor to online discussion boards
- Attend or get involved with Rare Disease Day to meet others in the PNH community
- Follow ThisIsPNH on social

> "I find my resiliency through others who have forged this road before me. I am in several PNH support groups and I'm forging my own personal connections with my PNH friends."
>
> **—Jessi, living with PNH**

Notes

Apellis