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FALL 2023

GOOD TO KNOW:

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SCAN ME

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IS YOUR **PNH** UNDER CONTROL, OR ARE YOU STILL EXPERIENCING SYMPTOMS?

Whether you're on treatment for PNH or not, you may be facing these challenges:



Fatigue or weakness



Shortness of breath



Brain fog



Headaches



Anemia



Bruising/bleeding easily



Dark-colored urine



Abdominal pain

Any symptoms, mild or severe, may be a sign that your PNH isn't fully controlled. **It's important to let your doctor know how you're feeling.**

ACCESS MORE PNH INFORMATION AND

HELPFUL RESOURCES AT [EXPLOREPNH.COM](https://www.explorepnh.com)

PNH, paroxysmal nocturnal hemoglobinuria.
Patient portrayal.



Head to the next page to see what may be behind your PNH symptoms

WHAT'S BEHIND THE ROUGH RIDE OF **PNH**?

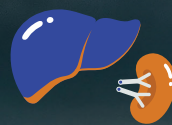
In PNH, hemolysis causes the destruction of red blood cells, which lowers hemoglobin levels and can cause symptoms.

But there are two types of hemolysis in PNH



Intravascular hemolysis (IVH)

Red blood cells are destroyed within the blood vessels (like veins and arteries).



Extravascular hemolysis (EVH)

Red blood cells are destroyed outside the blood vessels, within the liver and spleen.

Both IVH and EVH should be accounted for in the management of PNH

• C5 inhibitor PNH treatments only address IVH, not EVH



LEARN MORE ABOUT PNH, INCLUDING

IVH AND EVH, AT [EXPLOREPNH.COM](https://www.explorePNH.com)

Patient portrayal.

INSIGHT ON

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

WHAT IS PAROXYSMAL NOCTURNAL HEMOGLOBINURIA?

PNH is an extremely rare blood disorder. People with PNH develop a mutation in some of the stem cells in their bone marrow, where red blood cells, white blood cells, and platelets are made. Usually, some sort of stress on your body, like an infection or overexertion, triggers your symptoms. At this time, red blood cells break down and die earlier than they should. Protein from your red blood cells, called hemoglobin, builds up in your urine. This usually happens during the night and you may see dark-colored urine when you first go to the bathroom in the morning. The loss of red blood cells, white blood cells, and platelets can also make you extremely tired, pale-skinned, short of breath, and prone to infections and potentially life-threatening blood clots. You may have a fast heartbeat, too.

SOURCE: National Library of Medicine

6 in 1 million

Estimated number of people who are diagnosed with paroxysmal nocturnal hemoglobinuria each year.

SOURCE: Cleveland Clinic

TREATMENT TALK

When you have PNH, a part of your immune system called the complement system destroys your red blood cells. Doctors prescribe targeted therapies to treat the disease. These medicines block the complement system to prevent it from killing blood cells. While the medicines may come with some side effects, they seem to wear off soon after you start the treatment. Before these medicines were available, people with PNH had to have frequent blood transfusions.

SOURCE: Cleveland Clinic

2 in 5

Approximate number of people who see more than five specialists before they get a PNH diagnosis.

SOURCE: *Journal of Managed Care + Specialty Pharmacy*

WOMEN: WATCH OUT

People who have a defect in a gene called PIGA get PNH. You don't inherit this genetic flaw from your parents. It just happens at random. People usually develop the condition between the ages of 30 and 40. Both men and women get it, but it's a little more common in women. People of any race or ethnicity can get PNH, but certain complications, like blood clots, might be more common among people of some races than others.

SOURCES: Cleveland Clinic, *Thrombosis and Haemostasis*



JGI/TOM GRILL/VIA GETTY IMAGES

HOW PAROXYSMAL NOCTURNAL HEMOGLOBINURIA AFFECTS YOUR BLOOD

BRUSH UP ON THE BASICS

By Kendall K. Morgan | Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

You probably know that paroxysmal nocturnal hemoglobinuria (PNH) is a blood disorder. While PNH comes with fatigue and other, more troubling symptoms, many people notice that their urine is stained red or brown, says Robert A. Brodsky, MD, a hematologist at Johns Hopkins Medicine in Baltimore, MD. This is where the condition gets its name.

The reason this happens is that your immune system is attacking and damaging the red blood cells that carry oxygen through your bloodstream. Your discolored urine is a sign of the destruction taking place in your blood. You'll also have fewer healthy red blood cells than you should, a condition called anemia, as those cells break down prematurely. PNH can leave you prone to getting blood clots, too.

"Before there was effective therapy, blood clots in the abdomen and brain were the leading cause of death," Brodsky says. Fortunately, doctors now treat PNH with medicines that prevent those potentially life-threatening complications.

WHERE IT STARTS

Each year, about 6 in every 1 million people—most often men and women between the ages of 30 and 40—learn they have PNH. It's a little more common in women than men and tends to happen in people with other conditions that affect bone marrow, where blood cells are made. The trouble arises when a genetic change pops up in the stem cells that make your blood cells. This change happens in a gene called PIGA, which you need to make anchors that attach other proteins to your blood cells.


"This mutation leads to the absence of several proteins on the [blood] cell surface," Brodsky explains. "Two of these proteins are important for controlling part of our immune system known as complement. The absence of these proteins means that the body's own immune system will destroy red blood cells."

WHAT ABOUT OTHER BLOOD CELLS?

Your body has other types of blood cells, too, including white blood cells, part of your immune system, and platelets. So what happens to them? Brodsky explains that your white blood cells will miss the same surface proteins as red blood cells. They also get attacked by the complement system. The difference is that white blood cells can repair the damage in ways that red blood cells can't.

Platelets, which allow your blood to clot after you get a cut, don't fare as well. While you'll still have platelets, they'll be defective in ways that may encourage too much clotting. Thankfully, treatments that block the complement system can now stop the damage to red blood cells and platelets before it happens. As a result, you can now expect to live just as long with PNH as you would without it.



SCAN ME 

Read this article on **The Challenges of PNH**. Use your mobile phone camera to activate the QR code.

RECURRING SYMPTOMS

PHYSICAL EFFECTS TO EXPECT WITH PNH

By Rachel Reiff Ellis

Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

The symptoms you get when you have PNH happen because your body is making abnormal blood cells. Your bone marrow also isn't making enough blood cells. The type of symptoms that happen as a result vary from person to person.

You may have only mild symptoms that stay the same for many years, or your symptoms may be severe and progress to life-threatening complications.

COMMON SYMPTOMS

Your doctor may see signs of PNH in your body first by looking at blood test results and seeing low blood counts as well as evidence of red blood cells being destroyed in your blood vessels, a process called hemolysis.

"If you break down enough red blood cells, you release bilirubin into the bloodstream," says Joseph Shatzel, MD, associate professor of medicine and hematology oncology at Oregon Health and Science University in Portland. "High bilirubin sometimes causes red and dark urine, and that's usually the initial signs that I see."

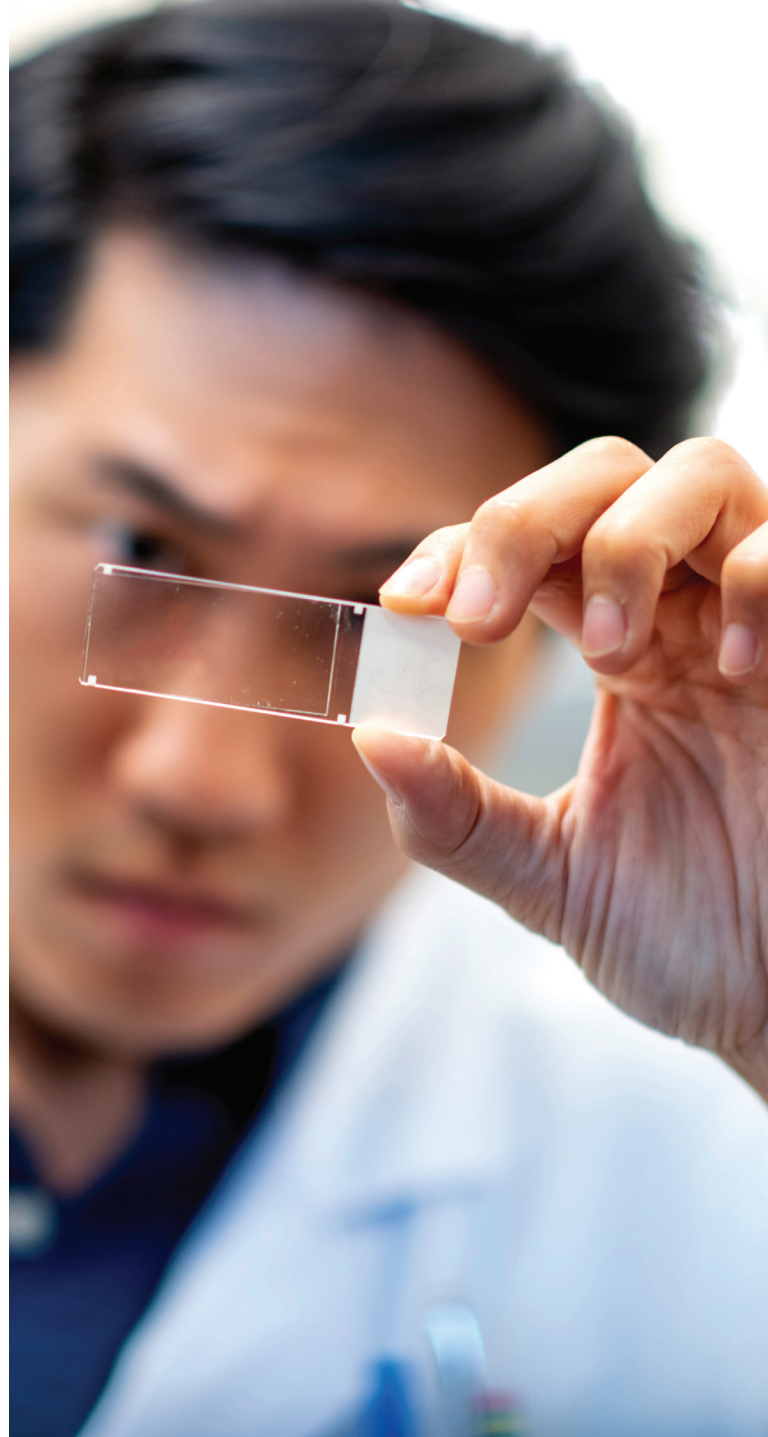
Extra bilirubin in your body can also cause jaundice, which makes your skin look yellow.

People with PNH often feel severely and constantly tired, a sign of anemia (low numbers of red blood cells). Anemia can cause other problems, too.

"Sometimes if people get really anemic, they'll report that they just get short of breath with simple activities," Shatzel says. "They'll walk up a flight of stairs and get short of breath. When it becomes severe, they can injure other organs like the kidneys."

PNH also affects your platelets—cells that help your blood clot. Your risk of blood clots goes up with PNH. Blood clots in your limbs cause throbbing or cramping pain, swelling, redness, and warmth. You may develop them in other spots, too.

"You can get them in the abdomen, which would cause



abdominal pain, and usually a CT scan will identify it," Shatzel says. "Rarely, they'll clot off the liver, a painful situation called Budd-Chiari syndrome."

SYMPTOM TRIGGERS

PNH symptoms may come on when you have certain stresses on your body, such as infections or physical exertion. These stresses prompt red blood cells to break down earlier than they should.

"Hemolysis is a weird thing," Shatzel says. "It can kind of tip in and out of it. Sometimes, a person may be doing OK and then they get an infection and go to the hospital, and they tend to get sicker. We tend to see hemolysis increase."

FATCAMERA/VIA GETTY IMAGES

OPTIONS TO CONSIDER

MEDICATIONS THAT MANAGE PNH

By Rachel Reiff Ellis

Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

PNH is a chronic disease you'll have your whole life. But there are current and emerging treatments that help ease symptoms and help prevent complications. Before the current drug options came along, people with PNH needed regular blood transfusions to treat constant anemia and lived shorter lives. Now there are multiple effective options, with more on the way.

"It's a very exciting time for PNH," says Bart L. Scott, MD, clinical director of MDS/MPN and myeloid malignancies at Fred Hutchinson Cancer Center in Seattle. "Long-term survival for PNH patients is actually quite good now in the modern era."

You might need several different treatments depending on the severity of your symptoms and the number of PNH-affected cells in your body. In some cases, doctors may decide to "watch and wait" before starting treatment if you have mild symptoms and normal blood counts. But in many cases, you'll need to take medication.

TARGETED THERAPIES

There are three FDA-approved targeted therapies for PNH. These drugs are called complement inhibitors. They help prevent your complement system—a group of proteins that fights infection—from destroying red blood cells.

"These medications work by 'blocking' or 'clamping' the complement system to try to eliminate blood cell breakdown," says Monika Oliver, MD, clinical lecturer in the Division of Hematology at University of Alberta Hospital in Alberta, Canada.

TIME TO TREAT

Your doctor may recommend you start treatment if you start having:

- + Bruising
- + Shortness of breath
- + Bleeding
- + Low blood counts
- + Tiredness



Read this article on **The Future of Treatment for PNH**. Use your mobile phone camera to activate the QR code.



The first two complement inhibitors approved are both antibody infusions you get by IV. But they have different dosing schedules. Depending on which one your doctor gives you, you might need an infusion every 2 weeks or every 8 weeks.

The most recently approved complement inhibitor works in a similar way but binds in a slightly different place "higher up the complement cascade chain," Scott says.

"The disadvantage is that it is given as a subcutaneous infusion twice a week," he says. "So that's much less convenient."

Recently, a new complement inhibitor in pill form was so effective at improving hemoglobin levels in clinical trials that the FDA is working to speed up the drug's approval so doctors can prescribe it. This option has so far been successful in keeping trial participants from needing blood transfusions.

"There are great treatment options that can improve the condition," Scott says. "We're also looking forward to new FDA approvals of therapies that would be easier for patients to take."

SUPPORTIVE TREATMENT

Alongside targeted therapies, you may also need other treatments to help manage certain symptoms.

"Occasionally you might give steroids to people who have a lot of inflammatory symptoms from their PNH," Scott says.

Blood thinners can reduce your risk of blood clots or treat ones you have.

And several options can improve your blood counts.

"Some people require supplementary folic acid and/or iron, which your bone marrow needs to produce new blood cells," Oliver says.

A common option for increasing blood counts is a blood transfusion. In this procedure, parts of blood from a donor are put into your bloodstream. Growth hormones may also help.

BONE MARROW TRANSPLANT

In a bone marrow transplant, a surgeon replaces your bone marrow with bone marrow donated from a healthy person. This gives you new stem cells that grow into different types of blood cells. It's possible for a bone marrow transplant to cure PNH, but the risks are high.

"It has such a high mortality rate that we generally don't consider that as the best treatment option," Scott says. It may become an option if you aren't responding to any other PNH treatments.

SIDE EFFECTS

You may experience the following when taking complement inhibitor infusions:

- + Headache
- + Colds
- + Back pain
- + Nausea
- + Cough
- + Fatigue

STATS & FACTS

By Sonya Collins

Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor

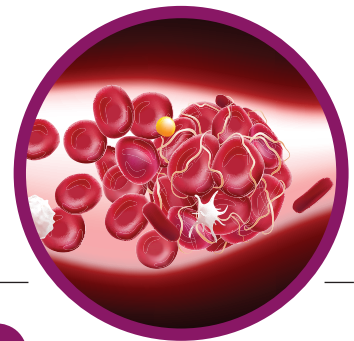
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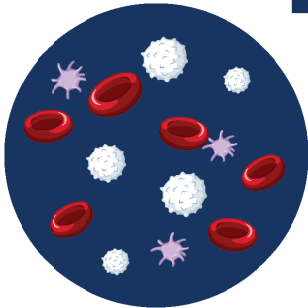
Average age when someone is diagnosed with paroxysmal nocturnal hemoglobinuria (PNH).

2 in 5

Number of people with PNH who get a blood clot.



Up to **1 in 5**



Number of people with PNH who develop aplastic anemia—when the bone marrow can't make as many new blood cells as the body needs.

1 in 20

Number of people with aplastic anemia who eventually develop PNH.

1 in 4



Number of people with PNH who took more than 5 years to get a diagnosis.

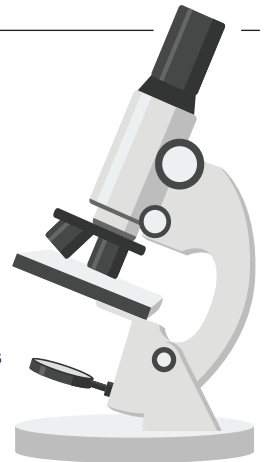
< 2 in 5

Number of people with PNH who get a diagnosis within the first year of symptoms.



2

Average number of years it takes to get a PNH diagnosis after the start of symptoms.



SOURCES: Medscape, Journal of Managed Care + Specialty Pharmacy

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