PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

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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

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

Patient portrayal.



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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 darkcolored 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 I see more than they get a PNH

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*

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STATS & FACTS

By Sonya Collins Reviewed by Neha Pathak, MD, WebMD Lead Medical Editor



SOURCES: Medscape, Journal of Managed Care + Specialty Pharmacy

HOW PAROXYSMAL NOCTURNAL HEMOGLOBINURIA AFFECTS YOUR BLOOD

BRUSH UP ON THE BASICS

By Kendall K. Morgan Reviewed by Brunilda Nazario, MD, WebMD Chief Physician Editor, Medical Affairs

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're most likely to see this in the morning when you wake up. But the process of red cells breaking down is happening all the time.

You'll also have fewer healthy red blood cells than you should, a condition called anemia, as those cells break down prematurely. Even when the breakdown of your red blood cells doesn't happen too much, loss of those cells may cause fatigue, rapid heartbeat, headaches, chest pain, and trouble breathing when you exercise. As it gets worse, you may have trouble swallowing, spasms in your belly and esophagus, and other signs. 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 affects men and women equally and tends to happen in people with other conditions that affect

DEFINING PNH

- Paroxysmal: sudden or happening in irregular episodes
- Nocturnal: at night
- Hemoglobinuria: hemoglobin
 (the red part of your blood)
 in urine



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."

The complement system normally cleans up damaged cells. Its job is to help you heal after you get hurt or have an infection. But when you have PNH, your complement system sees the defects in your blood cells and destroys them.

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.

BLOOD CELLS 101

Your blood is mostly fluid, known as plasma, with three main types of blood cells floating in it.

- Red blood cells have hemoglobin to carry oxygen through your body.
- White blood cells fight infections.
- Platelets clot your blood to stop you from bleeding.

COMPLICATIONS AND RISK FACTORS FOR OTHER CONDITIONS

LEARN THE SIGNS AND HOW TO PROTECT YOUR HEALTH

By Kendall K. Morgan **Reviewed by** Brunilda Nazario, MD, WebMD Chief Physician Editor, Medical Affairs

Paroxysmal nocturnal hemoglobinuria (PNH) is a blood disorder, and you may feel its effects in many parts of your body. Some of the most common complications include life-threatening blood clots, hemolytic anemia, and bone marrow failure, says Taha Bat, MD, a hematologist at the University of Texas Southwestern Medical Center in Dallas.

"Up to 40% of PNH patients can experience a thromboembolic event, and this can be the first sign of PNH disease," Bat says. "Seventy to 80% will have hemolytic anemia and fatigue."

A thromboembolism happens when a blood clot in your veins gets stuck and blocks your blood flow. In hemolytic anemia, red blood cells are destroyed faster than they can be replaced, leaving you weak and tired. When you have bone marrow failure, blood-forming cells in the spongy center of your bones can't make all the blood cells your body needs. Bat notes that some people with PNH also have a form of bone marrow failure called aplastic anemia and lower numbers of all the major blood cell types including red blood cells, white blood cells, and platelets.

WILL TREATMENT LOWER MY RISKS?

With treatment and careful monitoring from your doctor, your risk for blood clots and other potentially serious complications will go down. But you may still have symptoms of your PNH and complications to watch out for.

"Thankfully, treatments do lower the risk of these issues a lot, so that is a good thing," says Caroline Cromwell, MD, a hematologist and oncologist at Mount Sinai in New York City. "But certain things can still occur, especially fatigue and anemia."

TAKE EXTRA PRECAUTIONS

Cromwell recommends working closely with your doctor to be sure you're well protected from developing blood clots. Be sure to talk to your PNH doctor if you want to get pregnant or



need surgery, both of which can increase your risk for clots even more.

"In the setting of surgery, [PNH] patients are at higher risk of blood clots or hemolysis and worsening anemia," Cromwell says. "During those times, hematologists and surgeons work together to time surgery closer to treatment. We'll often put patients on blood-thinning medication if they are not on it already."

SET YOURSELF UP FOR SUCCESS

Cromwell and Bat say that

COMMON PNH SYMPTOMS

- + Being short of breath
- + Kidney trouble
- + Trouble swallowing
- + Spasms in your esophagus
- + Belly or back pain
- + Erectile dysfunction

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women with PNH who get pregnant will need to continue treatment throughout pregnancy. Talk with your doctor in advance to make sure you're taking the right one. You may need to take a blood thinning medicine, too. "Pregnancy can be very successful in this setting," Cromwell says.

When you're taking your medicines as prescribed, fatigue is typically the biggest challenge people with PNH face. "You should expect a full life expectancy overall, but you do need to work with your doctor in terms of addressing how you're feeling day to day and if there's anything to be done to improve your quality of life if you feel very fatigued," Cromwell says. "But we're in a good place [now] in terms of many treatments out there compared to in the past."

Working closely with your care team is the best way to live a healthy life and reduce your risk for complications of PNH. Along with PNH medicines, Cromwell recommends taking daily folic acid. Folic acid is a form of the B vitamin folate, which your bone marrow needs to make blood cells. Knowing the symptoms of potentially more serious complications will also go a long way in protecting your health, she says.

CATCH A BLOOD CLOT

Signs of a clot vary depending on where in your body it is and may include:

- + Swelling
- + Pain
- + Headaches + Confusion
- + Red or warm skin
- + Yellow skin (jaundice)
- + Fast or irregular heartbeat

+ Trouble breathing



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 PNHaffected 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

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

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.

The first two complement inhibitors approved are both

TIME TO TREAT

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

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

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

PUT YOUR PNH IQ TO THE TEST

By Kendall K. Morgan Reviewed by Brunilda Nazario, MD, WebMD Chief Physician Editor, Medical Affairs

1. The trouble in paroxysmal nocturnal hemoglobinuria (PNH) starts with a single change in one of your bone marrow cells.

O True **O** False

- 2. If you don't have dark pee in the morning, you can't have PNH.
- - O True ○ False
- 3. When you have PNH, you should be careful about flying in an airplane.

O True

O False

4. You can't get pregnant when you have PNH.

O False

O True

O True





around age 30, but people of any age can have it.

in people all over the world. It usually starts in adults

PNH today than in the past can have healthy babies.

4. FALSE. PNH doesn't change your fertility. If you

you should take it you're planning to fly.

and women about equally. Doctors have seen the disorder

5. TRUE. PNH is a rare condition, but it happens in men

monitoring. With the right treatment, more women with

cations and should see your doctor for advice and careful

decide to get pregnant, you'll have more risk for compli-

shortage of oxygen. Ask your doctor about any precautions

to cause PNH. makes many more copies of itself, the trouble can grow mutation, in a single gene. When that defective cell stem cells in your bone marrow picks up a mistake, or 1. TRUE. PNH starts when one of the blood-forming

a lot of people with PNH don't have this symptom. 2. FALSE. Dark pee is where PNH gets its name. But

should (anemia) from PNH, high altitudes can cause a 3. TRUE. When you have fewer red blood cells than you

