CONDITION

Paroxysmal nocturnal hemoglobinuria

Paroxysmal nocturnal hemoglobinuria is an acquired blood condition that destroys red blood cells and raises the risk of blood clots.

WHAT IT IS
Acquired blood stem-cell condition causing red-cell destruction

BODY SYSTEM
Blood and bone marrow

MAIN SYMPTOMS
Fatigue, dark urine, breathlessness, abdominal pain

WHAT CAUSES IT
Acquired stem-cell gene mutation, not inherited

HOW IT IS DIAGNOSED
Flow cytometry showing cells without protective proteins

MAIN TREATMENT
Complement-inhibiting medicines and supportive care

CAN IT BE CURED?
Sometimes - stem cell transplant can cure

IS IT AN EMERGENCY?
Sometimes - possible blood clot or serious infection

LONG-TERM OUTLOOK
Often manageable, but clot and bone-marrow risks remain

Overview

Paroxysmal nocturnal hemoglobinuria, usually called PNH, is a rare, acquired blood condition. It begins in a blood-forming stem cell in the bone marrow. The affected stem cell produces blood cells that are missing proteins that normally protect them from part of the immune system.

Without these protective proteins, a group of immune proteins called complement can damage or destroy red blood cells. This is called hemolysis . If the cells break apart inside blood vessels, they release hemoglobin, the protein that carries oxygen.

PNH matters because ongoing hemolysis can cause anemia, severe fatigue, pain, and kidney problems. It also raises the risk of dangerous blood clots. Some people have bone marrow failure, meaning the marrow does not make enough healthy blood cells.

The name can be misleading. "Paroxysmal" means occurring in episodes, "nocturnal" refers to nighttime, and "hemoglobinuria" means hemoglobin in the urine. However, red-cell destruction can happen at any time, and not everyone has dark urine.

PNH ranges from a small group of affected cells found during testing to a condition causing major symptoms. It may occur by itself or alongside bone marrow conditions such as aplastic anemia.

Symptoms

Symptoms differ according to how many blood cells are affected, how quickly red cells are being destroyed, and whether bone marrow failure or a blood clot is present.

Common symptoms include:

Dark urine may be most noticeable in the morning, but it can appear at other times or not at all. Its color comes from hemoglobin released by destroyed red blood cells, rather than bleeding from the urinary tract.

Some symptoms result from low blood counts. Anemia means too few healthy red blood cells. Low platelets can cause easy bruising, nosebleeds, or prolonged bleeding. Low white blood cells may increase the chance of infection.

PNH can also affect sexual function. Some men develop problems getting or keeping an erection, particularly during episodes of hemolysis.

A blood clot may be the first sign of PNH. Symptoms depend on where the clot forms and require prompt assessment.

- Severe tiredness or weakness
- Shortness of breath, especially with activity
- Dark red, brown, or tea-colored urine
- Headaches, dizziness, or difficulty concentrating
- Abdominal, back, or chest pain
- Trouble swallowing
- Yellowing of the eyes or skin
- A fast heartbeat or awareness of the heartbeat

Causes and risk factors

PNH is caused by a change in a gene called PIGA within a blood-forming stem cell. This change happens during a person's life. It is not usually present at birth and is not passed from parent to child.

The gene change prevents blood cells from attaching certain protective proteins to their surface. Two important proteins are CD55 and CD59. Without them, complement can attack red blood cells.

The altered stem cell can produce a group of affected cells called a PNH clone . Clone size means the percentage of tested blood cells that have the PNH features. A larger clone may be linked with more hemolysis and clot risk, but clone size alone does not show exactly how someone will feel or what treatment they need.

PNH is closely linked with acquired aplastic anemia, a condition in which immune activity damages bone marrow stem cells. Small PNH clones may also be found in some people with other bone marrow failure conditions.

Lifestyle, food, stress, or anything a person did does not cause the genetic change. PNH is also not contagious.

Diagnosis

The test that confirms PNH is flow cytometry . This laboratory method examines individual blood cells and checks whether protective surface proteins are missing.

Testing usually looks at white blood cells called granulocytes and monocytes. It may use a marker called FLAER and tests for proteins such as CD55 and CD59. Red blood cells can also be tested, although recent transfusions or red-cell destruction may make their results harder to interpret.

Other blood tests help show how PNH is affecting the body. These may include:

A bone marrow sample is not required to prove that a PNH clone exists. It may be used to investigate low blood counts, aplastic anemia, or another bone marrow condition.

Imaging may be needed if symptoms suggest a blood clot. Clots related to PNH can occur in usual sites, such as the legs or lungs, or in less common abdominal or brain veins.

- A complete blood count to check red cells, white cells, and platelets
- Lactate dehydrogenase, or LDH, which often rises during hemolysis
- Bilirubin, haptoglobin, and reticulocyte tests for red-cell destruction

- Kidney and liver function tests
- Iron, vitamin B12, and folate levels when deficiency is possible

Treatment and management

Treatment is based on symptoms, hemolysis, blood counts, clot history, clone size, and any related bone marrow failure. A small clone without symptoms may only need regular monitoring.

The main treatments for active PNH are complement inhibitors . These medicines block parts of the complement system, reducing red-cell destruction. Available treatments act at different points, including complement proteins C3 and C5 or a pathway protein called factor B. Some are given by infusion or injection, while others are taken by mouth.

Complement inhibition can reduce hemolysis, transfusion needs, symptoms, and clot risk. It does not remove the PNH clone. Some people continue to have anemia because of bone marrow failure, iron deficiency, or red cells being removed outside the bloodstream.

Complement inhibitors increase vulnerability to certain serious bacterial infections, especially meningococcal infection. Vaccination and an individual infection-safety plan are therefore important. Vaccination lowers risk but does not remove it completely. Fever or symptoms of meningitis or bloodstream infection need urgent assessment during complement treatment.

Supportive care may include blood transfusions for significant anemia and replacement of iron, folate, or other nutrients when tests confirm a need. Treatment of aplastic anemia may involve medicines that reduce immune attack on the bone marrow.

A blood clot generally requires hospital assessment and anticoagulant medicine, which reduces the blood's ability to clot. Whether long-term anticoagulation is appropriate is an individual decision because both clotting and bleeding risks must be considered.

A donor stem cell transplant can replace the affected bone marrow and is the only established treatment that may cure PNH. It carries substantial short-term and long-term risks, so it is usually considered for selected people, particularly those with severe bone marrow failure or disease not controlled by other treatment.

Medicines commonly used for this include eculizumab and ravulizumab . Which one suits you, if any, is a decision for you and your doctor.

Complications

Blood clots are among the most serious complications of PNH. They may form in the legs or lungs, but PNH can also cause clots in veins draining the liver, abdomen, skin, or brain.

Other possible complications include:

Pregnancy can increase clotting and blood-count risks in someone with PNH. Pregnancy is possible, but it usually requires coordinated care from blood-disorder and high-risk pregnancy teams.

- Persistent anemia and reduced ability to exercise
- Bone marrow failure with low red cells, white cells, and platelets
- Acute or long-term kidney injury from released hemoglobin
- High pressure in the blood vessels of the lungs
- Iron deficiency from ongoing urinary hemoglobin loss
- Iron overload after repeated blood transfusions
- Serious infection during complement-inhibitor treatment

Prevention

There is no known way to prevent PNH. The gene change is acquired by a stem cell and is not caused by everyday habits.

Complications may sometimes be reduced through effective treatment and follow-up. This can include taking prescribed treatment consistently, keeping recommended vaccinations current, having regular blood tests, and knowing the warning signs of infection and blood clots.

Stopping a complement inhibitor without a planned transition may allow severe hemolysis to return. Any interruption should be managed with the prescribing specialist.

General measures such as staying active, not smoking, and managing other cardiovascular risks support overall health, but they do not prevent the PNH clone or replace condition-specific treatment.

Living with it and what to expect

PNH is usually a long-term condition. Its course is not the same for everyone. A small clone may remain stable for years, grow, or become smaller. Symptoms and blood counts can also change over time.

Complement-inhibiting treatment has greatly changed the outlook for many people with active

hemolysis. Fatigue, pain, dark urine, and transfusion needs may improve when red-cell destruction is controlled. Regular treatment and monitoring often continue for years because the underlying clone remains.

Some people still experience breakthrough hemolysis. This means red-cell destruction returns despite treatment, sometimes during an infection or near the end of a treatment interval. New or worsening symptoms should be reported rather than assumed to be an expected episode.

Bone marrow failure may remain even when hemolysis is controlled. This can mean continued anemia or low white-cell and platelet counts. Follow-up therefore considers the whole blood count, not only the PNH clone.

Routine appointments may include blood counts, markers of hemolysis, kidney function, symptom review, and checks for treatment side effects. Flow cytometry may be repeated to monitor clone size.

Many people continue work, education, exercise, travel, and family life, although fatigue and appointment schedules can require adjustments. Carrying treatment information can be useful, especially when travelling or seeking emergency care.

When to get medical help

Seek emergency care for symptoms that could indicate a blood clot, stroke, severe anemia, or serious infection. These include:

If you take a complement inhibitor, fever, a new rash, severe headache, stiff neck, confusion, or rapidly worsening illness needs urgent medical assessment. Meningococcal infection can progress quickly even after vaccination.

Contact your usual healthcare team promptly for increasing fatigue, breathlessness, dark urine, yellowing of the eyes, reduced urination, unusual bruising, or signs of infection.

Routine follow-up is appropriate for stable symptoms, planned blood tests, vaccination reviews, medication monitoring, and discussion of work, travel, pregnancy, or treatment side effects.

- Sudden shortness of breath, chest pain, coughing blood, or collapse
- New one-sided weakness, facial drooping, confusion, or trouble speaking
- A severe, unusual headache, seizure, or loss of consciousness
- Severe abdominal pain, especially with swelling or vomiting
- A painful, swollen, warm, or discolored leg or arm

- Heavy bleeding that does not stop

Common questions

Is PNH a type of cancer?

PNH is a clonal blood stem-cell condition, meaning affected blood cells come from one altered stem cell. It is not usually described as leukemia or another typical cancer. However, it is managed by specialists in blood conditions because it affects the bone marrow and blood.

Is PNH inherited?

No. The PIGA gene change develops in a blood-forming stem cell during life. It is not normally found throughout the body and is not passed to children.

Why is my urine dark in the morning?

Destroyed red blood cells release hemoglobin, which can pass into urine and turn it red, brown, or tea-colored. Overnight concentration may make the color more noticeable in the morning. Dark urine has other possible causes, so testing is needed to identify the reason.

Can PNH go away on its own?

A PNH clone can sometimes become smaller, particularly when it is associated with aplastic anemia, but this cannot be predicted. Active PNH usually needs long-term monitoring, and treatment may be needed for continuing hemolysis or complications.

Can PNH be cured?

A donor stem cell transplant can cure PNH by replacing the affected bone marrow. Because transplantation can cause serious complications, it is not the best option for everyone. Complement inhibitors can control PNH effectively but do not remove the clone.

Can I exercise with PNH?

Many people can exercise, with the level adjusted for anemia, fatigue, and other health issues. Sudden chest pain, severe breathlessness, dizziness, or unusual limb swelling during activity needs prompt medical attention.

Sources

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