

# Understanding Paroxysmal Nocturnal Haemoglobinuria (PNH).

What you should know about the effects  
of chronic red blood cell destruction.



A resource for patients and caregivers.

## An introduction to PNH.

If you've recently been diagnosed with paroxysmal nocturnal haemoglobinuria (PNH), you may feel overwhelmed—or even confused, angry, or scared. What is PNH? How and why did I get it? How can I manage it? This brochure has been designed to help you understand more about PNH and answer some of your questions.

As you may know, PNH is a serious disease. Fortunately, much has been learned about it in recent years and advances have been made in treatment options. These new discoveries can help you and your healthcare team actively manage your PNH.

As you read through this booklet write down any questions you have for your doctor or nurse. The more you know about PNH, the more you'll be able to help your healthcare team develop the treatment plan that's best for you.

If you have any questions, talk to your doctor. You can also read more about PNH at [www.pnh.net.au](http://www.pnh.net.au).

## What is PNH?

PNH is an acquired mutation that causes some or all of your body's red blood cells (RBCs) to be destroyed by a process called haemolysis.<sup>1-3</sup> PNH is a complicated disease because the signs and symptoms are nonspecific, unpredictable, and often similar to those of other diseases. In addition, PNH presents uniquely in each person. If you have PNH, some or all of your RBCs may be missing an important protective protein. Without this protein, RBCs are prone to destruction by a part of your body's defence system called complement.<sup>1-3</sup>

Even though you can't feel it, haemolysis is constant, silent, and can be life threatening.<sup>4</sup> Like other chronic diseases, such as diabetes or hypertension, PNH can result in serious health problems if not treated. Common symptoms associated with PNH include stomach pain, difficulty swallowing, anaemia, shortness of breath, and tiredness (fatigue). More serious complications can include blood clots, kidney failure, and damage to vital organs. People with PNH may have different symptoms that can unpredictably get worse (such as during times of stress) or better from time to time. However, all people with PNH experience chronic haemolysis.

People with PNH may have other medical conditions that affect the function of their bone marrow such as aplastic anaemia (AA) or myelodysplastic syndromes (MDS). Unlike PNH, which destroys RBCs, these diseases may reduce the production of blood cells and further complicate PNH.<sup>5</sup>



### PNH RBC

PNH RBCs lack an important protein.



### Complement Attack

Without this protein, some RBCs can be destroyed by complement, one of the body's defence systems.



### PNH RBC Lysis (haemolysis)

PNH RBCs are destroyed, and the toxic contents are released into surrounding plasma (yellow-coloured liquid component of blood).

## How did paroxysmal nocturnal haemoglobinuria get its name?

When PNH was first named, not much was known about it. The name literally means episodic haemoglobin (a component of blood) in the urine, which occurs at night. But actually, less than one-third of people with PNH experience haemoglobin in their urine at diagnosis.<sup>6</sup> In fact, PNH is a complex disease that affects many parts of the body and haemolysis (the destruction of red blood cells) does not only happen at night – it happens all the time.

## How many people have PNH?

PNH is a rare disease that affects approximately 8,000 to 10,000 people in North America and Western Europe.<sup>7</sup> It can affect men and women of all races and ages but most commonly affects people between the ages of 20 to 40 years old.

Although PNH is rare, the medical community understands a lot about the way the disease works – and there are doctors who are experienced in treating it.

## What is haemolysis?

Haemolysis is a medical way of saying “destruction of red blood cells.” Haemolysis is measured by LDH (lactate dehydrogenase, an enzyme found in red blood cells) and elevated levels of LDH are an indicator of excessive haemolysis.<sup>4</sup> In healthy people, low levels of haemolysis are constant and naturally occurring. However, in people with PNH, there is excessive haemolysis resulting from a missing protective surface protein on some or all RBCs. This excessive haemolysis releases the toxic contents of RBCs into the bloodstream, which, over time, can cause many of the symptoms associated with PNH and harm important organs in your body.

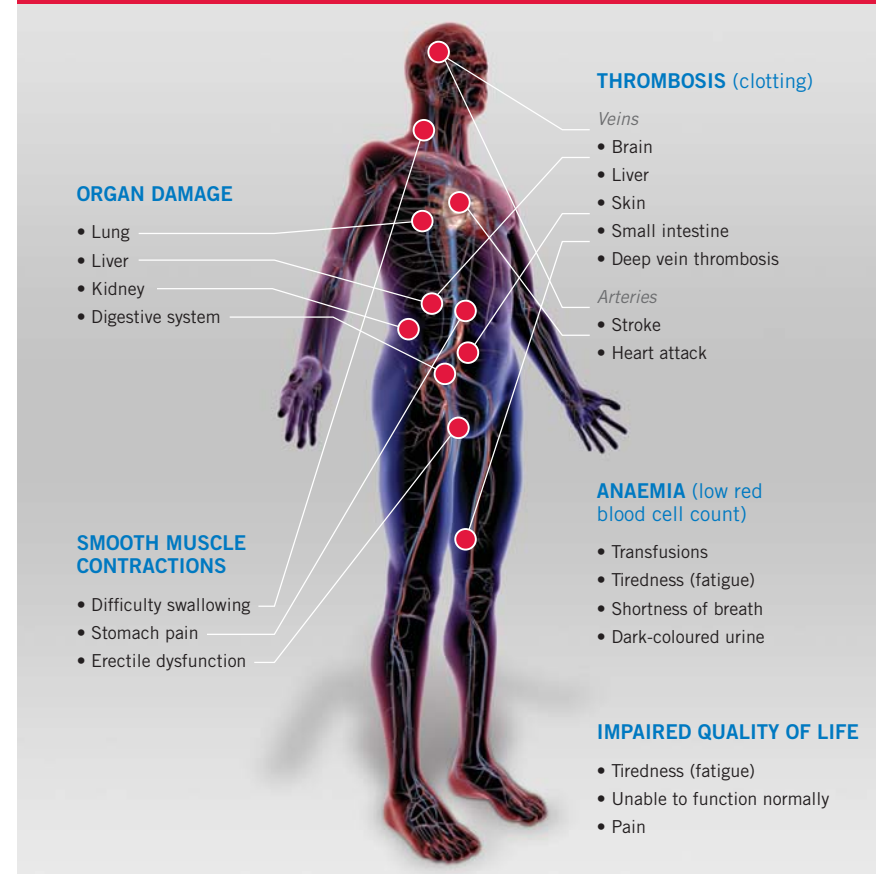
If you have PNH, haemolysis is always taking place—whether you feel OK or whether you’re having a flare-up (paroxysm), such as during times of stress or infection.<sup>1,4,8,9</sup> Excessive and continual haemolysis is the main cause of major health problems in PNH.

## Why is haemolysis important?

When blood cells are destroyed, their toxic contents are released into the bloodstream and can build up, causing health problems that can occur suddenly at any time.<sup>8,9</sup> These problems can include kidney failure and serious blood clots, which may cause damage to important organs like your liver, brain, and lungs.<sup>4</sup>

Haemolysis also affects the way you feel. Many people with PNH report that the unpredictability of the frequency and severity of their symptoms impairs their quality of life. Physicians believe reducing chronic haemolysis is an important goal in PNH treatment.

**Chronic haemolysis is the main cause of major health problems associated with PNH.<sup>7</sup>**



➔ **Talk to your doctor about what you can do to reduce the risk of chronic haemolysis.**

## If I have PNH, can I still have children?

If you have PNH and are considering pregnancy, there are risks involved to both mother and child that should be discussed with your physician – and your partner. If you do choose to become pregnant, you will likely be referred to a high-risk pregnancy specialist and monitored closely for the duration of the pregnancy.

## Can I give PNH to my children?

PNH cannot be inherited from parents, nor can it be passed on to children.

## What if I have other conditions besides PNH?

People with PNH may have other medical conditions that affect the function of their bone marrow such as aplastic anaemia (AA) or myelodysplastic syndromes (MDS). These diseases may reduce the production of blood cells and further complicate PNH.<sup>5</sup>

If you have PNH in combination with AA or MDS, talk to your doctor – it's important to effectively treat all the conditions you may have.

## What treatment options are available for PNH?

There are many treatment options available for people with PNH. As you move forward, you and your healthcare team will develop a plan that's best for you. The following approaches are most commonly used in PNH:

- A monoclonal antibody therapy: The first and only approved medication to address haemolysis and its harmful effects in people with PNH
- Palliative therapies: Include therapies that may ease the symptoms of PNH, such as transfusions, steroid hormones, androgen hormones, anticoagulants, and vitamin supplements
- Curative therapy: Bone marrow transplantation (BMT) is currently the only curative therapy available for PNH. However there are many risks associated with BMT, which your doctor can tell you more about

**→ Talk to your doctor about your PNH treatment options.**

## Know how you're feeling...

PNH symptoms can change over time, and are different from person to person. This list will help you identify some symptoms you might have. Don't be shy! Let your healthcare team know how you're feeling – it's an important part of managing your PNH.

### Signs and Symptoms of PNH

- Feeling exhausted
- Feeling weak all over
- Need help doing usual activities
- Limiting social activities because I'm tired
- Trouble taking long walks
- Not feeling hungry
- Feeling nauseated
- Pain (associated with blood clots)
- Having abdominal pain
- Having erectile dysfunction
- Trouble starting or finishing things because I'm tired
- Needing to sleep during the day
- Short of breath
- Fainting
- Yellowish skin, eyes (jaundice)
- Trouble sleeping
- Having dark urine
- Trouble swallowing
- Back pain

You may experience one or more of the symptoms listed above quite frequently or just occasionally. However, you may not immediately feel other potential complications, such as blood clots and vital organ damage.

## ...and know your lab values.

Being aware of your symptoms, as well as your lab values, can provide a more complete picture of your PNH. There are many lab values that can be helpful in measuring your PNH.

One of the most important lab values is called LDH. By measuring your LDH, your physician can determine the degree of haemolysis in your body.<sup>4,10</sup> Knowing your beginning LDH and monitoring it over time will help you and your doctor keep better track of the progression of your PNH. It can also be used to help assess the risk for developing serious complications associated with PNH.

Some other tests that your healthcare team may use to evaluate your condition include: haemoglobin (Hgb), platelets, white blood cells (WBCs), and haematocrit (HCT) – which are all part of a complete blood count (CBC) – as well as creatinine (CRT) and others. Talk to your doctor to learn more. He or she can tell you about specific tests and why they are being ordered.

➔ **Reducing chronic haemolysis is the main goal in PNH management.**

## If you have PNH, you're not alone. Learn more and connect with others at these websites.

There's an entire community dedicated to helping people with PNH. Researchers are learning more about the disease every day. Doctors are using new therapies that were unheard of only a few years ago. There's also a large community of people with PNH that you can meet online. Remember that your healthcare team, friends, and family are there for you too. On the following page, you'll find just a few of the websites where you can learn more by exploring these resources—or by talking to your doctor.

→ **If you have questions, talk to your doctor to learn more about PNH and other conditions you might have.**

### Organisations in Australia

PNHSAA (PNH Support Association of Australia): [www.pnhsaa.org.au](http://www.pnhsaa.org.au)

Leukaemia Foundation Australia (LFA): [www.leukaemia.org.au](http://www.leukaemia.org.au)

- For information about Aplastic Anaemia, Myelodysplastic Syndromes and practical support and assistance available to patients and families.
- LFA also hosts the following forum website for people with blood cancer and related blood disorders: Talk Blood Cancer – all ages: [www.talkbloodcancer.com](http://www.talkbloodcancer.com)

Red Cross: Information on blood and blood donation: [www.donateblood.com.au](http://www.donateblood.com.au)

Life Goes On: telephone and online counselling for people with a serious illness and their families: [www.lifegoeson.org.au](http://www.lifegoeson.org.au)

### Overseas Organisations

Aplastic Anemia & MDS International Foundation (AAMDS): an international not-for-profit organisation supporting people living with aplastic anaemia (AA), myelodysplastic syndromes (MDS), PNH and related bone marrow failure diseases: [www.aamds.org/aplastic/](http://www.aamds.org/aplastic/)

National Organization for Rare Disorders (NORD): a US-based non-profit, voluntary health agency for people with rare "orphan" diseases: [www.rarediseases.org](http://www.rarediseases.org)

PNH Research and Support Foundation: a US-based volunteer-run organisation for support of people with PNH: [www.pnhfoundation.org](http://www.pnhfoundation.org)

New Zealand Organisation for Rare Disorders (NZORD): a registered Charitable Trust to help people affected by rare disorders find information and support: [www.nzord.org.nz](http://www.nzord.org.nz)

PNH Support Group: US-based online support group run by people with PNH: [www.pnhdisease.org](http://www.pnhdisease.org)

*NOTE: These are suggestions only for organisations, patient support groups and disease information websites you may like to visit to learn more about PNH, PNH treatments and other blood conditions. It is strongly recommended that a medical doctor and/or other healthcare professionals are consulted for confirmation on any information that is obtained from a non-medical source.*

## Glossary

### Anaemia

A condition in which your body does not have enough haemoglobin (the oxygen-carrying component of your blood) inside the red blood cells (RBCs). Alternatively, the number of RBCs may be reduced. This may cause tiredness and other symptoms and contribute to fatigue.

### Aplastic anaemia

A condition where the bone marrow does not produce enough new red blood cells and possibly all other blood cells. The term “aplastic” means that the bone marrow is unable to produce new blood cells properly. People with aplastic anaemia have lower counts of all three blood cell types: red blood cells, white blood cells, and platelets. PNH is often found in combination with aplastic anaemia.

### Blood clot

When platelets and fibrinogen, a protein that is the essential component of the coagulation system within the blood, bind together, they form a blood clot (also called “thrombus”). These clots can block blood flow in the veins and arteries, depending on their size and location (see **Thrombosis**), and can cause serious problems in patients with PNH.

### Bone marrow

Soft tissue inside your large bones. Bone marrow contains stem cells, which form red blood cells, white blood cells, and platelets through a process called haematopoiesis.

### Complement

Part of your body's defence system that destroys foreign organisms (eg, bacteria) as well as whole cells (self or foreign). In PNH, complement is responsible for the destruction of red blood cells that lack specific protective proteins.

### Complete blood count (CBC)

Tests performed on a small amount of your blood that can provide information about the amount of each type of blood cell.

### Glycosyl-phosphatidylinositol (GPI)

An important type of anchor that attaches proteins to the cell surface. PNH red blood cells lack GPI-anchored proteins. Without these GPI anchors, certain proteins are missing from the surface of cells, leaving the cells vulnerable to destruction by the body's complement system (see **Complement**).

### Haematocrit

The amount of your blood volume that is occupied with red blood cells.

### Haemoglobin

The brownish-red substance in red blood cells that carries oxygen throughout your body.

### Haemoglobinuria

Haemoglobin in the urine. Haemoglobinuria is the technical term for the “cola-coloured” or dark urine seen in approximately 25% of patients with PNH at diagnosis. When the red blood cells that are missing the protective protein are destroyed, as they are in PNH, haemoglobin is released from the red blood cells. If haemoglobin is not all processed by the body's systems, it is sent out as waste and gives the urine a characteristic cola-brown colour.

### Haemolysis

The destruction of red blood cells. Destruction of red blood cells is the main cause of major health problems associated with PNH.

### Lactate dehydrogenase (LDH)

An enzyme that is found in many organs in the body, and is especially abundant in red blood cells. LDH is a key marker of haemolysis, the underlying cause of the signs and symptoms associated with PNH.

### Myelodysplastic syndromes (MDS)

A large and heterogenous group of blood disorders in which there are problems with the proper production of blood cells within the bone marrow. MDS typically occur in elderly people and have a certain risk of converting into so-called “acute leukemia.” For this reason, MDS sometimes are also called “preleukemic states.” PNH is sometimes, but not often, found in combination with MDS (ie, about 2% of all PNH patients also suffer from MDS).

### Paroxysmal nocturnal haemoglobinuria (PNH)

A disease characterised by chronic red blood cell destruction, often resulting in serious health problems. Signs and symptoms can include stomach pain, difficulty swallowing, anaemia, shortness of breath, tiredness (fatigue), and life-threatening complications such as blood clots, kidney failure, and damage to vital organs.

### Platelets (thrombocytes)

Cells in your blood that are essential components in the clotting process. In concert with certain proteins, platelets help stop bleeding when you've cut yourself and block blood flow inside blood vessels. In certain disease states, such as PNH, they may stick together and form a potentially harmful clot inside blood vessels.

### PNH clone

A group of cells in your body that are affected by the genetic defect that causes PNH. The extent to which your blood cells are affected by PNH is often described in terms of one's clone size.

### Red blood cells (RBCs)

Red blood cells are constantly travelling through your body delivering oxygen and removing waste (carbon dioxide). PNH red blood cells are continually attacked and destroyed by part of the body's defence system known as complement because they are missing important protective proteins.

### Thromboembolism

The blocking of a blood vessel by a particle that has broken away from a blood clot at its site of formation.

### Thrombosis

The formation or development of a blood clot that often blocks blood from flowing through a vessel (vein or artery). Blood clots can cause life-threatening complications for anyone, including patients with PNH. Haemolysis significantly increases the risk of blood clots in patients suffering from PNH (see **Blood clot**).



# Learn all you can about your PNH— and stay involved in your treatment.

- If left untreated, PNH is a serious and life-threatening disease
- PNH causes some or all of your red blood cells to be destroyed by a process called haemolysis. The toxic contents of these destroyed red blood cells can build up over time and can cause serious health problems, as well as keep you from participating in normal daily activities
- Many people with PNH also have other bone marrow disorders that may reduce the production of red blood cells and further complicate PNH; talk to your doctor about getting treatment for all the conditions you may have
- LDH and other lab tests can help keep track of your health when you have PNH—but telling your doctor how you're feeling is just as important
- There are treatments for PNH. Talk to your doctor to learn more

Together with your healthcare team, you can take control of your PNH.

If you have questions, talk to your doctor or go online at [www.pnh.net.au](http://www.pnh.net.au).

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ACN 132 343 036. Suites 226-227, 117 Old Pittwater Road, Brookvale NSW 2100.