PNH (Paroxysmal Nocturnal Hemoglobinuria)

**Introduction**

PNH stands for paroxysmal nocturnal hemoglobinuria. PNH is a rare and serious blood disease that causes red blood cells to break apart. PNH is difficult to diagnose. If not treated, it can cause pain, fatigue and possibly death.

This reference summary explains what PNH is. It discusses its causes, symptoms, diagnosis and treatment options.

**About Blood**

In order to understand PNH, it’s important to know certain facts about blood. Blood is made of blood cells floating in plasma. Plasma is mostly made of water with chemicals in it. These chemicals include proteins, hormones, minerals and vitamins.

There are 3 basic types of blood cells:

- Red blood cells normally make up almost half of blood. They are filled with hemoglobin. Hemoglobin is the red part of red blood cells. Its job is to carry oxygen around your body.
- Platelets are small pieces of cells that help blood clot and stop bleeding.
- White blood cells fight disease and infection by attacking and killing germs that get into your body. There are several kinds of white blood cells, each of which fights a different kind of germ.

All three types of blood cells are made by blood forming stem cells in the bone marrow. Bone marrow is a spongy tissue located inside some bones. Bone marrow stem cells make copies of themselves all the time. These stem cells eventually become mature blood cells. When blood cells are fully formed and functional, they leave the bone marrow and enter the blood.

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The complement system is a group of proteins in the blood that are part of the body's natural defense system. They help support the work of white blood cells by fighting infections. These proteins are always active at a very low level. But, when bacteria, viruses and other foreign or abnormal cells get into your body, these proteins become more active. They work together to attack and destroy the abnormal cells in your body.

**About PNH**

PNH is a rare and serious blood disease that causes red blood cells to break apart. Health care providers call this breaking apart “hemolysis”. It can happen when some or all your red blood cells are missing proteins that protect them from your body's complement system.

Here are few facts about PNH:
- PNH can happen at any age, but is more common in young adults.
- PNH cannot be passed down through the genes from parent to child.
- PNH cannot be passed through germs from person to person.
- PNH is closely linked to aplastic anemia, another disease of the bone marrow.

Aplastic anemia happens when the immune system attacks and kills the blood forming stem cells. This causes the bone marrow to stop making enough red blood cells, white blood cells and platelets for the body.

PNH stands for “paroxysmal nocturnal hemoglobinuria”. Paroxysmal means sudden and irregular. Nocturnal means at night. Hemoglobinuria means hemoglobin in the urine. Hemoglobin is the red part of red blood cells. Urine appears red when it contains hemoglobin. So, “paroxysmal nocturnal hemoglobinuria” literally means sudden, irregular episodes of passing dark colored urine, especially at night or in the early morning. It is important to know that many people with PNH do not have episodes of passing red or dark urine.
A lot more is known about PNH since it was first named in the late 1800s. Health care providers now know that:

- The breaking apart of blood cells, called hemolysis, is always happening at some level in people with PNH.
- Signs and symptoms of PNH can happen at any time of day or night.
- While most people will experience dark-colored urine at some point, only 1 in 4 will experience it at diagnosis.

When red blood cells break apart, the hemoglobin inside them is released. The release of hemoglobin causes most PNH symptoms. The signs and symptoms of PNH vary a lot from person to person. You may have only mild symptoms. Or, you may have severe symptoms and need medicines or blood transfusions.

Many people with PNH can live for decades. People who develop blood clots in key parts of the body or other serious medical conditions may have a shorter lifespan. Fortunately, treatments are available. They are helping people with PNH live longer.

**What Causes PNH?**

Normal red blood cells have a shield of proteins. This shield protects the cells from being attacked by the complement system. People with PNH have defective red blood cells that are missing this protective shield.

PNH happens because of a change in the gene of a single stem cell in the bone marrow. This abnormal stem cell makes copies or clones of itself. This leads to a population of stem cells that have this defective gene. Stem cells in the bone marrow make the blood cells. The stem cells with this defective gene make red blood cells with a defective shield of proteins. These are called PNH blood cells.

Hemolysis happens when the complement system becomes more active and attacks PNH blood cells. The complement system usually attacks only foreign objects, such as viruses and bacteria. But, because PNH cells lack their protective shields, it sees them as foreign and attacks them too, causing them to burst.
In general, the more PNH blood cells you have, the worse your symptoms will be. If between 10 and 20 out of every 100 red blood cells in your body are PNH blood cells, you may start to have some symptoms of PNH.

**Symptoms & Complications**

PNH can cause a number of symptoms and complications. These can vary greatly from person to person.

All PNH symptoms are caused by one of the following:
- Hemolysis (the breaking apart or destruction of red blood cells).
- Low red blood cell count (anemia).
- Thrombosis (blood clots).

When hemolysis happens, the hemoglobin inside red blood cells is released into the blood plasma. The release of hemoglobin can cause a number of symptoms. For instance, your urine may get darker.

If you have severe hemolysis, you may have spasms in your esophagus. This can cause trouble swallowing. The esophagus is the organ that connects the mouth to the stomach. It is also called the feeding tube. Others may feel pain in the stomach or belly area. Men may have trouble getting or keeping an erection. Over time, chronic hemolysis can cause permanent kidney damage.

Thrombosis is a blood clot in a vein. It is often simply called a blood clot. At least one out of three people with PNH gets a blood clot. The symptoms of a blood clot depend on where the clot happens. People who are otherwise healthy and don’t have PNH sometimes get a blood clot in the veins of a leg. But people with PNH tend to get blood clots in other parts of the body, such as in the brain or abdomen.

If you have a blood clot in your abdomen:
- You may have fluid and swelling in the belly area; this is called ascites.
- You may have belly pain, back pain or bloating.
- You may have swollen ankles.

If the blood clot in your abdomen is not treated:
- Part of your intestine may die.
• Your liver may stop working well, causing you to feel ill and confused.

You may get a blood clot in the veins covering your brain. If this happens:
• You may get a very bad headache.
• Your brain may not work as well as usual; you may have trouble speaking, seeing or moving parts of your body.

You may get a blood clot in the veins of your arm or leg. If this happens:
• That limb may get warm, blue, puffy or painful.

Sometimes a blood clot can break off and travel to your lungs where it gets stuck. This is called a pulmonary embolism and can be life threatening. If you have a pulmonary embolism, you may:
• Have a sharp pain in your chest; it may get worse when you breathe deeply.
• Have trouble breathing (shortness of breath); or you may start breathing fast.
• Suddenly feel anxious.

If you have a pulmonary embolism you may also:
• Cough up some blood.
• Feel dizzy, or even pass out.
• Sweat a lot.

Blood clots can be very dangerous. If you think you have any symptoms of a blood clot, tell your health care provider right away. You may need treatment to save your life.

Many people with PNH have a low blood cell count. That means you don’t have enough of one or more types of blood cells. The most common shortage involves red blood cells. This is called anemia. If you have a very low red blood cell count, you may:
• Feel just a little tired, or very tired.
• Have trouble breathing.
• Feel less alert or have trouble concentrating.

If you have a very low red blood cell count, you may also:
• Have paler than normal skin.
• Have rapid heartbeat and chest pain; this most often happens only in severe cases.
• Have a loss of appetite or lose weight.

PNH can cause a variety of symptoms and complications. You may have many of these symptoms, or just one or two. You may get a new symptom at any point in the course of your illness. Some people have more severe symptoms than others do. If you have PNH, it is important to track your signs and symptoms and to discuss them with your health care provider.

Diagnosis
PNH is a rare disease. Many health care providers have never seen a case of it. Also, many PNH symptoms are similar to other diseases. So, people with PNH may have symptoms for several years before they get a correct diagnosis.

Choose a health care provider who is treating people with PNH or similar bone marrow problems. He or she is more likely to be aware of new medicines and treatments.

If you have some of the symptoms of PNH or have certain bone marrow failure diseases, your health care provider may ask to screen you for PNH. He or she will take a small sample of your blood and send the sample to a lab for tests.

Your health care provider may order a CBC, also known as a Complete Blood Count test. This gives information about the quantity and quality of each type of cell in your blood. Your health care provider may order a flow cytometry test of blood cells taken from a vein in order to test for PNH. This gives information about the percentage of PNH cells in your blood.

Your health care provider may order a test that looks at your LDH level. LDH stands for lactate dehydrogenase. An elevated level of LDH enzyme in your blood can be a sign of PNH. A test called a reticulocyte count gives information about the amount of very young red cells in your blood. An elevated level can be
a symptom of PNH.

Your health care provider may ask you to get other lab tests as well. These include:
  • Ferritin test to check your iron levels.
  • Tests of your bone marrow through a bone marrow biopsy.
  • A test for the pigment bilirubin.

If you have been diagnosed with PNH it is important to include a specialist in treating people with PNH or similar bone marrow problems on your medical team. He or she is more likely to be aware of new medicines and treatments. You can often find experts in treating rare diseases, like PNH, at teaching hospitals associated with universities.

**Treatments**

PNH is considered a chronic disease. That means it may last for a long time. Eculizumab is the only FDA-approved drug currently available to treat PNH and reduce hemolysis. The only known cure is a bone marrow transplant. Other treatments are designed to ease symptoms and prevent problems.

There are a number of treatments for PNH. Here are some of them:
  • Anticoagulants, also called blood thinners.
  • Blood transfusion.
  • Bone marrow transplantation.
  • Eculizumab (Soliris®).
  • Growth factors.

Talk with your health care provider about the risks and benefits of different treatment options. That way you can make an informed choice about which treatment is best for you. For most people with PNH, the most common problem is anemia caused by hemolysis. There are several treatment options for hemolysis and anemia.

**Blood Transfusion**

In a blood transfusion, whole blood or parts of blood from a donor are put right into your bloodstream. This can temporarily improve your anemia. Your health care provider will look at your symptoms to decide if you need a transfusion.
The two types of transfusion available for PNH patients are:

- Red blood cell transfusion.
- Platelet transfusion.

Patients with PNH should only get blood that exactly matches their ABO blood type. For example, non-PNH patients who are type AB can get blood from a donor that is type A, B, AB or O. A PNH patient with type AB should only get blood from a type AB donor.

Hemolysis can lead to a shortage of iron in your body. This can make it hard for your bone marrow to make red blood cells. So, unless you are getting regular red blood cell transfusions, you probably need to take iron pills. Ask your health care provider how much iron you need. Also, ask about taking folic acid.

**Growth Factors**

Growth factors are chemicals in your body. They cause your bone marrow to make more blood cells. Man made forms of some growth factors are available. Taking a red cell growth factor can reduce the need for red blood cell transfusion in some patients. Your kidneys make a red blood cell growth factor called EPO, or erythropoietin. If you have anemia and your kidneys are not making enough natural EPO, your health care provider may recommend you take a form of EPO made in a lab. Most health care providers recommend that you get your blood EPO level checked before taking a man-made form of EPO.

**Eculizumab (Soliris®)**

Eculizumab is the only drug approved by the FDA (U.S. Food and Drug Administration) and the EMEA (European Medicines Evaluation Agency) to treat PNH. It works by making your complement system less active and reducing hemolysis, the underlying cause of PNH symptoms and complications.

Eculizumab has many benefits. It has been found to:

- Reduce hemolysis, the breaking apart of red blood cells, over both the short and the long term.
- Reduce the risk of blood clots.
- Reduce or get rid of the need for transfusions.
- Improve anemia.
Eculizumab is not right for all PNH patients. Only a qualified health care provider can determine whether eculizumab is the right course of treatment for a specific patient. It is important to know that eculizumab may increase your risk of getting certain infections. As a safety precaution, patients must be vaccinated against meningococcal infection before starting eculizumab.

Patients who take eculizumab may no longer get rid of large amounts of iron in their urine. This means that they may need to stop taking iron supplements when they go on this drug. People with PNH may also get blood clots. This is also a result of hemolysis. Blood clots are very dangerous. If you have a blood clot, you need to get help right away. There are several ways that blood clots can be treated.

**Anticoagulants**

Anticoagulants, also called blood thinners, are the most common way to treat blood clots. They decrease the ability of blood to clot. Some health care providers think some people with PNH should take blood thinners on a regular basis to prevent blood clots. Others disagree. Health care providers use several factors to help them decide whether a patient should go on anticoagulants and which anticoagulant is the best choice for a specific patient.

**tPAs (Tissue Plasminogen Activators)**

tPAs may be used to break up an existing blood clot, especially if the clot is large. These drugs usually work best if given as soon as possible after a clot. This is why it is important to go see a physician immediately if you think you have a clot. These drugs can cause bleeding.

**Bone Marrow Transplantation**

In some cases a bone marrow transplant is considered for a PNH patient. There are many factors health care providers consider when deciding whether a bone marrow transplant is a good option. Whether or when to consider this option should be discussed with a PNH specialist and a bone marrow transplant team.

In this procedure, the patient’s bone marrow is destroyed using chemotherapy and sometimes radiation. Healthy bone marrow stem cells are then taken from a matched donor. These cells are then given to the patient by IV. The donor’s stem cells make their way through your blood and into your bones. The donor marrow is called a graft.

Bone marrow transplantation is the only way to cure PNH. But it carries many risks,
including chronic illness and death.

**Summary**

PNH stands for paroxysmal nocturnal hemoglobinuria. PNH is a rare and serious chronic blood disease that causes red blood cells to break apart. Health care providers call this breaking apart hemolysis. It happens because your blood cells are missing proteins that protect them from your body’s immune system.

PNH is difficult to diagnose. If left untreated, it can cause pain, fatigue, serious complications and possibly death. PNH is not contagious, cannot be passed from parent to child and can happen at any age.

PNH can cause different symptoms in different people. Common symptoms include feeling very tired, pain, trouble swallowing and dark urine. Your health care provider may run several blood tests before diagnosing PNH.

There are several treatment options for PNH. Talk with your health care provider about the risks and benefits of different treatment options. Talk with your health care provider and make sure you ask them any questions you have about PNH.