CONTENTS

About Us ............................................................................................................................................................................... 3
Introduction from Barry Katsof ......................................................................................................................................... 4
About PNH .......................................................................................................................................................................... 5
The Future of PNH by Dr. Christopher Patriquin, MD MSc FRCPC ........................................................................... 13
What’s New in Research ......................................................................................................................................... 14
Clinical trials ............................................................................................................................................................. 15
How clinical trials work ........................................................................................................................................ 16
The PNH Journey ......................................................................................................................................................... 17
Where you have been ................................................................................................................................... 17
Where you are now ......................................................................................................................................... 18
Access to treatment ........................................................................................................................................... 19
Travelling with PNH ........................................................................................................................................ 24
Where you are going ...................................................................................................................................... 25
The Physical Journey ............................................................................................................................................... 26
The Mental Journey ....................................................................................................................................................28
The Emotional Journey ............................................................................................................................................31
How to be a mentor to a newly-diagnosed PNH patient ....................................................................................35
Tracking your progress ..................................................................................................................................36
Asking questions .................................................................................................................................................41
Resources ............................................................................................................................................................................42
Glossary ................................................................................................................................................................................44
Sources .................................................................................................................................................................................48

The Canadian Association of PNH Patients

The Canadian Association of PNH Patients is a not-for-profit Canadian organization formed in 2009. The mission of the organization is to connect Canadians affected by paroxysmal nocturnal hemoglobinuria and advocate for the best possible care for patients, and ensure they are equipped with the most current tools and information to help them live well with the condition. The organization also provides support to caregivers, and works to increase awareness and understanding of PNH.

www.pnhca.org/

Terms that are **bold and underlined** can be found in the Glossary on pages 44-47.
Introduction from **BARRY KATSOF**

If you live with PNH (or *paroxysmal nocturnal hemoglobinuria*), you have likely experienced many lows since you first noticed symptoms, through to diagnosis and living day-to-day with the condition. Perhaps you were unable to work or go to school, too fatigued and weak as a result of the disease. You may have also lived with a constant fear of developing a blood clot, having a stroke – or even dying.

So much has changed over the past decade, from the approval in Canada of the first medication to treat PNH, to the important research into new treatment options that’s going on all over the world. I hope that many of you have turned a corner and have entered a new, healthier chapter in your life. For most patients today, PNH is no longer a fatal disease, but a chronic condition that can be well-managed with treatment.

With access to treatment comes a new reality – learning to live well with PNH and entering a new stage in your life. The Guide to Living Well with PNH is designed to give you, as well as your friends and family, a road map to navigate this next chapter.

This guide, now in its second edition, contains advice from PNH experts, as well as insights from Canadians living with PNH which can assist you in adjusting your activities and mindset.

The Canadian Association of PNH Patients is pleased to bring you this information to help you take charge of your condition and live well with PNH!

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**What is PNH?**

PNH is a very rare, **progressive** and devastating disease that destroys an important part of your blood: the **red blood cells**. Red blood cells develop in your **bone marrow**. They are important because they help deliver oxygen and remove waste from your body. The constant, ongoing destruction of red blood cells is called **hemolysis** – which is the main cause of major health problems in PNH.

The name *paroxysmal nocturnal hemoglobinuria* comes from the following:

- **PAROXYSMAL** – means “sudden and irregular”
- **NOCTURNAL** – means “at night”
- **HEMOGLOBINURIA** – means “hemoglobin in urine”

So, “paroxysmal nocturnal hemoglobinuria” means sudden, irregular episodes of passing dark coloured urine, especially at night or in the early morning. The breakdown of red blood cells cause hemoglobin (the red part of red blood cells) to leak into the blood and pass into the urine. An overabundance of **hemoglobin** in the urine can make it look dark. However, some people with PNH do not have dark urine as symptoms vary from patient to patient.
What causes PNH?

People with PNH have blood cells that are missing a gene called PIG-A. This gene allows a substance called glycosyl-phosphatidylinositol (GPI) to help certain proteins stick to cells. Without PIG-A, important proteins cannot connect to the cell surface and protect the cell from substances in the blood called complement. The complement system is part of the immune system, and helps destroy invading microorganisms. Without the proteins that protect them from complement, red blood cells are destroyed through the process of hemolysis.

What are the symptoms?

- dark/unusually coloured urine
- jaundice
- nausea
- stomach/abdominal pain
- digestive problems
- bloating
- back pain
- muscular pain
- joint pain
- headaches
- insomnia
- dizziness
- tingling or numbness, particularly in the extremities

Because these symptoms are common to many diseases, and appear gradually, a diagnosis of PNH is often overlooked. Meanwhile, a patient’s chance of experiencing serious consequences of PNH is ever-present.

What are some of the consequences?

PNH starts with your blood, but it can affect your entire body. If it isn’t managed through treatment, PNH can lead to serious and life-threatening health problems. Some of these problems include:

- hemolysis – the destruction of the red blood cells
- anemia
- blood clots (thrombosis)
- kidney damage/failure
- lung problems
- heart attack
- stroke
- pulmonary hypertension

A challenge of PNH is that you cannot always see or feel its effects. This means serious health risks can take you by surprise. Also, not everyone with PNH has the same experience or feels the same way.

Who gets PNH?

PNH is an extremely rare disease, affecting about 8,000 to 10,000 people globally and about 90 people in Canada.

- Both males and females can get PNH
- PNH occurs across all races
- PNH can occur at any age; the average age at diagnosis is in the early 30s
Diagnosis

A PNH diagnosis is most commonly confirmed by a specialized blood test called flow cytometry, but several other tests are performed during the diagnostic process to rule out complications of PNH and assess its severity. These may include a bone marrow biopsy, blood tests, x-rays, CT scans, an ultrasound and other specimen tests (i.e. urine).

Flow cytometry involves suspending cells in a stream of fluid and passing them by an electronic detection apparatus. This test can track your white and red blood cell count to help determine your *clone size*, which refers to the percentage of red blood cells in your body that are affected by PNH. A larger clone size means you have more PNH cells, but even patients who have a clone size as small as 10% can have symptoms that may greatly limit their lives, such as fatigue, stomach pain, chest pain, shortness of breath and dark-coloured urine.

Ongoing exams and tests

There are three major laboratory tests which are conducted routinely among PNH patients to help your doctor monitor your disease – flow cytometry, *lactate dehydrogenase (LDH)* and *complete blood count (CBC)*. These tests, along with your signs and symptoms, will give you and your doctor the full story of your PNH and help with management.

**Lactate dehydrogenase (LDH)**

LDH is an *enzyme* found in red blood cells. This test will give you and your doctor an idea of how much hemolysis is going on in your body. LDH levels are typically elevated in patients experiencing exacerbations in their PNH. Frequent testing of your LDH is an important part of PNH management, and establishing a baseline LDH level is important to track over time, so you and your doctor can check your progress.

**Complete blood count (CBC)**

This test measures the different parts of your blood, including your red blood cells, white blood cells and hemoglobin. It can help to identify if there is anything wrong with your bone marrow.

**How is PNH treated?**

There are several treatment options available to people living with PNH, depending on the progress and severity of the disease. The only cure for PNH is a bone marrow transplant. Other treatments are supportive only, but some offer significant benefits including a reduction in the severity of symptoms.

While some people can manage their PNH symptoms with the above supportive treatments for a period of time, they are still at risk of developing deadly blood clots. Without treatment, approximately one third of PNH patients did not survive more than five years. However, there is a Health Canada-approved treatment option available to patients in Canada that has been shown to allow a patient’s life expectancy to return to that of a healthy person.
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Side effects</th>
<th>Benefits</th>
<th>Risks</th>
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<tbody>
<tr>
<td><strong>CURATIVE</strong></td>
<td></td>
<td></td>
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<tr>
<td>bone marrow/</td>
<td>side effects caused by high-dose chemotherapy that accompanies these</td>
<td>replaces unhealthy blood-forming stem cells with healthy ones,</td>
<td>infection, death (42% of PNH patients die post-transplant),</td>
</tr>
<tr>
<td>stem cell transplant</td>
<td>procedures</td>
<td>eliminating PNH from the body</td>
<td>or rejection complications including <strong>graft-versus-host disease</strong></td>
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<tr>
<td>only curative treatment for PNH</td>
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<tr>
<td>but risky and difficult to find a</td>
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<tr>
<td>well-matched donor</td>
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<td></td>
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<tr>
<td><strong>SUPPORTIVE</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>blood transfusions</td>
<td>fever, itching, wheezing and other allergic symptoms</td>
<td>raises hemoglobin levels by replacing blood cells lost through hemolysis</td>
<td>increased hemolysis, increased ferritin levels, transmission of viral infections (Hepatitis C)</td>
</tr>
<tr>
<td>iron therapy</td>
<td>diarrhea or constipation and discomfort in the upper central region of the abdomen</td>
<td>helps the bone marrow make normal blood cells, counteracts effects of hemolysis (such as fatigue, abdominal pain)</td>
<td>increased production of “bad” blood, possible increased hemolysis</td>
</tr>
<tr>
<td>folate/folic acid</td>
<td></td>
<td>helps the bone marrow make normal blood cells, counteracts effects of hemolysis</td>
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<tr>
<td><strong>SUPPORTIVE</strong></td>
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<td>corticosteroids (prednisone)</td>
<td>high blood pressure, bone loss, increased risk of infection, fluid retention, a change in the distribution of body fat, pressure or clouding in the eyes, thinning of the skin, easy bruising</td>
<td>reduces rate of hemolysis, may make the complement system less active, may also increase counts of white blood cells and platelets in some people</td>
<td></td>
</tr>
<tr>
<td>anticoagulants (warfarin, heparin)</td>
<td>premature bone loss (osteoporosis), easy bruising</td>
<td>reduces chance of blood clots forming</td>
<td>serious bleeding (may be life-threatening)</td>
</tr>
<tr>
<td>androgenic hormones [testosterone, fluoxymesterone (Halotestin), oxymetholone, stanozolol (Winstrol), and danazol (Danacrine)]</td>
<td>liver damage, acne in women: masculinization (hair growth on the face, lowering of the voice, enlargement of the clitoris, and increased masculinity)</td>
<td>increased red blood cell production</td>
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It is an exciting time for PNH. There is a great deal of research being done to understand the disease and to find new therapies. We are very likely on the verge of a significant change, as many new drugs are being evaluated in clinical trial and may soon come to market.

The availability of new medications will create a practice environment we have never had before, in which options will exist should one treatment fail or not be tolerated. It will also allow patients with PNH to have more flexibility with respect to their treatment. Currently, the only available treatment option requires infusions every two weeks. Some of the newer therapies in clinical trial will allow for longer times between treatments, while others allow for daily self-administration at home. In the future, this will hopefully increase the ability of PNH experts to consider a patient’s lifestyle and choose a therapy that fits best with it.

Beyond the ongoing clinical trials, the Global PNH Registry is helping PNH experts discover a number of insights with respect to PNH natural history (e.g. risk of blood clots, infection rates, impact of a history of aplastic anemia), disease presentation and outcomes. As a result, PNH experts are learning more about the disease on a truly international scale and with a level of confidence that hasn’t been possible in the past. This increased understanding and recognition of PNH amongst experts is extremely important, and will surely allow for further advancements in treating our patients.

Dr. Christopher Patriquin is a hematologist and PNH expert at the Toronto General Hospital, University Health Network, in Toronto, Canada.

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**The FUTURE OF PNH**

by Dr. Christopher Patriquin, MD MSc FRCPC

<table>
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<th>Treatment</th>
<th>Side effects</th>
<th>Benefits</th>
<th>Risks</th>
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<tr>
<td>Soliris* (eculizumab)</td>
<td>headaches (temporary), runny nose and colds, sore throat, back pain, and nausea (temporary headaches may also be experienced as gas dissipates as a result of hemolysis reduction)</td>
<td>improved anemia, reduced or eliminated need for transfusions, reduced hemolysis, reduced the risk of blood clots, improved energy and has been shown to return patient life expectancy to normal</td>
<td>meningococcal infections at least two weeks prior to beginning Soliris therapy, your doctor should immunize you with a meningococcal vaccine</td>
</tr>
</tbody>
</table>

Soliris is the first and only drug approved by Health Canada to treat PNH. This treatment effectively prevents the premature destruction of red blood cells, and thereby significantly reduces the development of life-threatening complications such as blood clots, stroke, heart attack and kidney failure.

Essentially, Soliris stops your body’s natural defense system from attacking red blood cells that are missing an important protective protein, thereby reducing ongoing hemolysis. The active substance in Soliris is a monoclonal antibody. This is a type of protein that recognizes and attaches to a specific structure, or antigen, found within the body. Soliris attaches to the CS complement protein, which is part of the body’s complement system. By blocking the CS complement protein, Soliris prevents complement from attacking red blood cells, reducing their destruction and relieving the symptoms and minimizing the consequences of the disease.
Clinical trials

Every year, hundreds of new clinical trials are initiated to test new “experimental” drugs, or to test new uses of already approved drugs on humans, in a wide range of disease areas. These trials are conducted by researchers in countries all around the world, including Canada, in locations like hospitals, universities, doctors’ offices, and community clinics. Through voluntary participation in clinical trials, patients get a chance to take part in research that could improve their health and help them access a drug, prior to its approval. Like all drugs, the ones used in clinical trials have potential benefits as well as risks, and since they are still being studied, there is usually limited information about safety and efficacy.

Before deciding to take part in a clinical trial, discuss the potential risks and benefits with your health care provider, so that you can make an informed decision about your health.

What’s **NEW IN RESEARCH**

For the last 20 years, there has only been one Health Canada-approved treatment for PNH patients, but that may change in the coming years. There is a significant amount of research activity underway to discover and develop new treatments for PNH, including ongoing clinical trials around the world led by companies such as Achillion Pharmaceuticals, AKARI Therapeutics, Alexion Pharmaceuticals, Alnylam Pharmaceuticals, Apellis Pharmaceuticals, Hoffmann-La Roche, Novartis Pharmaceuticals and Ra Pharmaceuticals.

The ongoing clinical trials are evaluating new medications that target different parts of the complement system. Like Soliris, there are a number of medications in clinical trial right now that target C5. Some of these are antibodies like Soliris but do not need to be given as often, some can be injected under the skin once daily at home, and others work by reducing the amount of C5 made by the body, mostly in the liver.

There are also other targets for medications in clinical trial right now, including proteins in the complement system that appear earlier in the activation process before C5, such as C3 or Factor D. Medications that target C3 or Factor D are different than those that target C5, but have the potential to be just as effective, and some are even being studied as oral therapies.

There may also come a time when targeting the complement system is not necessary. With advances in gene therapy, there is the theoretical possibility that the PIG-A mutation in PNH patients could be corrected, allowing the cells to start expressing GPI again.

Where you have been:

Every PNH patient has a very different journey through their disease – from where they started to where they are today. But most – if not all – experience extended stays in hospital, being unable to work or go to school, and living with the daily fear of blood clots.

Here are some accounts of the hopelessness and despair experienced by some PNH patients soon after being diagnosed and prior to receiving treatment:

Carrie, Niagara Falls, ON
“I was living like I was dying. I didn’t care. I was going out drinking. I was punishing my body. I just thought it’s my body shutting down.”

Barry, Montreal, QC
“It took two years to finally get a diagnosis. Once I knew I had PNH, I began to understand why I was tired all the time and how it just wasn’t my professional lifestyle. My hemoglobin levels had dropped significantly to below 70 and I had no colour. In fact, some people started telling me I looked yellow.”

Mark, Saint John, NB
“I knew that without treatment, a third of PNH patients do not survive more than five years and about half die within 10 years from the time of diagnosis. The only treatment available to me was steroids, which took their toll on my body without improving my symptoms.”

While every person living with PNH has the same disease and many will have many similar symptoms or challenging experiences leading up to a diagnosis, many will be at different stages in their PNH journey once they start treatment and can begin living well with the disease.
Where you are now:

Fortunately, most people in Canada with PNH now have access to Soliris, which has finally allowed them to live well with PNH by completely altering the course of their disease. While this is great news, it also requires a change in perspective. Simply put, people in despair, many of whom were preparing for death, can now look to the future with hope and promise. While this may be an easy feat for some, it is a huge mental shift for others, which requires understanding and support.

You may also need time to heal from symptoms and the supportive treatments which were previously a part of your life.

Some people describe the shift to living well with PNH as follows:

Access to treatment

The Canadian Association of PNH Patients has a mission to advocate for the best possible care for patients, and ensure they are equipped with the best tools and most up-to-date information to help them live well with the condition.

As part of our mandate, we are here as a resource to help you begin your journey to living better with PNH. You can contact us at any time at info@pnhca.org or by visiting www.pnhca.org.

To further assist you in your efforts to learn more about PNH, if you are considering Soliris, or are already on treatment, we recommend connecting with OneSource™ at 1-888-765-4747. A OneSource nurse case manager will answer any questions about Soliris infusions you may have, help you navigate insurance or funding issues, as well as provide ongoing support. Your OneSource case manager will also help you determine with your doctor whether or not you are eligible for Soliris through your private insurance plan or government insurance program.
Eligibility criteria for public funding for Soliris may vary from province to province.

As an example, to be eligible for public funding for Soliris in Ontario, you must meet the following criteria as set out by the Ontario Ministry of Health and Long-Term Care:

- Flow cytometry/FLAER exam with granulocytes clone ≥10% AND
- LDH > 1.5 upper limit of normal

AND at least one of the following:

- A thrombotic or embolic event which required the institution of therapeutic anticoagulant therapy
- Minimum transfusion requirement of 4 units of red blood cells in the previous 12 months
- Chronic or recurrent anemia where causes other than hemolysis have been excluded and demonstrated by more than one measure of less than or equal to 70 g/L or by more than one measure of less than or equal to 100 g/L with concurrent symptoms of anemia
- Pulmonary insufficiency: Debilitating shortness of breath and/or chest pain resulting in limitation of normal activity (New York Heart Association Class III) and/or established diagnosis of pulmonary arterial hypertension, where causes other than PNH have been excluded
- Renal insufficiency: History of renal insufficiency, demonstrated by an eGFR less than or equal to 60 mL/min/1.73 m², where causes other than PNH have been excluded
- Smooth muscle spasm: Recurrent episodes of severe pain requiring hospitalization and/or narcotic analgesia, where causes other than PNH have been excluded


Before your Soliris infusion

While your world has shifted for the better, now that you have access to a life-saving treatment, you will also need to become familiar with the delivery process associated with Soliris – the world of infusions.

You will receive Soliris through an intravenous (IV) needle placed in a vein in your hand or arm.

There are various things that you should keep in mind before and after your first Soliris infusion:

1. **Get your meningococcal vaccine.** You must receive this vaccine at least two weeks before your first dose of Soliris. If you have already received the vaccine previously, your doctor should administer a booster.

2. **Know all your medications.** Give your healthcare provider with a list of medications you are already taking.

3. **Eat and drink (non-alcoholic beverages) to your heart’s content.** There are no food or beverage restrictions before or after receiving Soliris. That said, everyone can benefit from a healthy diet.

4. **Determine your transportation needs.** While some patients prefer to have the infusions administered by a nurse in the comfort of their own home, others prefer the camaraderie of an infusion centre. For a list of in-home nurse providers and infusion centres in your area, please contact the OneSource program.

5. **Know the duration of your infusion, so you can plan your day accordingly.** The Soliris infusion time is approximately 35 minutes. Your infusions will typically start with weekly dosing for the first five weeks and then you will receive an infusion every two weeks.

6. **Be aware of side effects.** The most common side effects of Soliris in people with PNH include headaches, runny nose and colds, sore throat and nausea.
Headache is the most common side effect, but it typically occurs less frequently after the second dose. While serious side effects can occur, they are rare. Tell your health care provider immediately if you experience any of the following:

- chest pain
- trouble breathing
- swelling of the face or related areas
- feeling faint

7. Anticipate a lowered immune system. Soliris can affect the ability of your immune system to fight infections, especially meningitis, which requires immediate attention. If you experience any of the following symptoms (headache with nausea, fever or stiff neck, fever of 39°C / 103°F or higher, fever and a rash and/or muscle aches), report to the nearest emergency room.

While on treatment

Blood transfusions
Some PNH patients receiving Soliris may continue to experience anemia and require blood transfusions. This is because PNH is very often associated with malfunction of the bone marrow, with many PNH patients also having some degree of aplastic anemia (AA) or . These disorders impair the ability of the bone marrow to make new red blood cells, and so even when hemolysis, the rupturing of red blood cells in PNH patients, is prevented by Soliris, there may still be significant anemia necessitating blood transfusions.

Breakthrough hemolysis
Sometimes hemolysis continues even after Soliris treatment is started. Most of the time, the amount of complement that is made by the body is steady; however, things like infections, surgeries, and pregnancy, as examples, can increase it. Breakthrough hemolysis describes a situation when the protection provided by Soliris is overwhelmed by higher levels of complement, or its complement blocking effect runs out before the next dose is given. Symptoms of breakthrough hemolysis may be new or worse fatigue and dark urine, or may just be noted on blood tests.

There are two main explanations for breakthrough hemolysis. First, although the standard dose of Soliris is sufficient to block complement activation and hemolysis in the majority of patients, for some this dose is insufficient and a higher dose is needed. Your PNH physician will check for this by measuring your LDH level on the day of your Soliris infusion, just before you receive your dose. An elevated LDH level at this time may suggest a need to increase the dosage, or to shorten the interval between doses. Another method of verification is a test measuring your CH50 level on the day of your Soliris infusion, just before you receive your dose. If your CH50 level is greater than 10, you may experience breakthrough hemolysis, and if your CH50 level is less than 10 or undetectable, you are not experiencing breakthrough hemolysis.

A second explanation for continuing hemolysis despite Soliris treatment is the development of extravascular hemolysis. It occurs as a result of the build-up of the complement protein, C3, on the red blood cells, which marks them for destruction and signals the liver and spleen to remove them from circulation. In PNH, this is something seen only after Soliris treatment is started because the cells are no longer experiencing intravascular hemolysis, and are living long enough to be marked by C3. Although this may cause some anemia, it is usually not severe, and does not have the same risks and complications (like blood clots and kidney damage) as the usual intravascular hemolysis of PNH.

During treatment with Soliris, it will be important to keep track of your LDH and/or CH50 levels, since they are a measure of hemolysis in your body. By knowing your LDH and/or CH50 levels before beginning Soliris treatments, and monitoring them over time, you and your doctor can better manage your PNH. It is possible that your levels will fluctuate from time to time, especially if you have an infection or are under stress.

To find out more about Soliris treatment, visit www.pnhca.org/disease-and-treatment/treatment/treatment/.
Travelling with PNH

PNH Travel Protocol
If you have PNH, it is important to plan ahead for any upcoming travel – be it for work, holidays or personal reasons. Apart from the usual things to think about when travelling, having PNH means you also need to consider:

- Your current health;
- Any health needs you may have while travelling; and
- Steps you can take to avoid becoming ill while you’re away.

Even if you’ve successfully travelled in the past, things can change over time, and you must talk to your doctor as soon as you start thinking about taking a trip.

To help you plan for any upcoming travel, the Canadian Association of PNH Patients has developed a travel protocol for PNH patients. The protocol can help you answer questions like

- Do I need approval from my physician to travel?
- What information do I need when travelling with PNH?
- How do I ensure I can access treatment when travelling?

To view and download the travel protocol, please visit our website at www.pnhca.org/news/pnh-travel-protocol/.

Where you are going:
Now that you have begun treatment and are responding well, you may be facing many challenges – physical, mental and emotional. The infographic below may summarize some of the issues you are currently dealing with.

Symptoms
Stomach pain, dark urine, shortness of breath, trouble

DIAGNOSIS
I have PNH.

TREATMENT
I have been prescribed a treatment that addresses the underlying cause of my disease.

GOOD NEWS
I am living well with the disease. While I am happy to have my life back, I still have some challenges/concerns.

MENTAL CHALLENGES
1. Health setbacks may set off anxiety/stress
2. Annual review of treatment coverage which may set off anxiety/stress
3. Career and educational setbacks
4. Postponing having children
5. Financial dependence on others
6. Employment/school/schedule disruptions
7. Unable to travel

PHYSICAL CHALLENGES
1. Temporary headaches
2. Meningitis risk
3. Organ damage

EMOTIONAL CHALLENGES
1. Fear of recurrence
2. Fear of death
3. Survivorship
4. Self-consciousness
5. Why me?
6. Loneliness/isolation

Where you are going:
Now that you have begun treatment and are responding well, you may be facing many challenges – physical, mental and emotional. The infographic below may summarize some of the issues you are currently dealing with.
the PHYSICAL JOURNEY

If your specialist determines that treatment is right for you, you will likely begin to feel the results immediately. However, in some patients, improvements are experienced more gradually.

Physical changes:

Treating the underlying cause of your disease will help prevent the serious consequences associated with PNH. That means that people with PNH who are on treatment should experience less hemolysis and fewer blood clots. Patients’ need for blood transfusions will also be significantly reduced.

Your energy and overall quality of life will be improved after three weeks of treatments, and your kidney function and lung health will also improve. As you continue with treatment, commonly reported side effects will become milder.

It is important to remember that the longer you’ve been living with PNH, the more severe the damage your body may have endured. Also, you may still have blood clots in your system that developed prior to beginning treatment. Be mindful of this, and remember that your organs may need more time to restore themselves fully. Be patient and realistic about your recovery time, based on discussions with your doctor.

Work closely with your doctor by letting them know about your physical changes and improvements in symptoms.

Nutrition and exercise:

In addition to treatment, it is important to take care of your body by eating properly, and your doctor can help find the best nutrition plan for you.

While there is no special diet that can alleviate your PNH symptoms, Dr. Richard Wells, medical advisor to the Canadian Association of PNH Patients, and a PNH specialist at Sunnybrook Health Sciences Centre in Toronto, recommends eating a healthy, well-balanced diet containing lots of fruits and vegetables. To ensure your body gets enough folic acid and iron, your specialist will likely recommend an over-the-counter supplement. Folic acid and iron help your body make red blood cells. Always talk to your doctor to see which supplements are right for you, and before taking any supplements, medicines, vitamins or herbs.

It is also important to find a form of physical activity that will assist you in living as well as possible with PNH. While you may have been limited in the past to undertaking simple activities such as walking or light housekeeping duties, being on treatment may allow you to resume these activities and more. However, some of your PNH symptoms prior to treatment may have persisted, so enter into any new exercise regimen only once you are feeling better and have your doctor’s consent.
the MENTAL JOURNEY

In addition to the physical changes taking place in your body, those with PNH will also need to adapt mentally now that treatment has entered their lives. While the physical transformation is significant, the changed mindset is also important to consider.

You may not have been able to think about the future before, but it is likely all you think about now, and you may be hesitant to feel hopeful and look to tomorrow’s possibilities given all you have been through.

While setbacks or temporary side effects are still possible, the reality is that treatment is keeping many PNH patients alive. However, in addition to focusing on the future, and feeling elated over a “miracle” treatment, some patients may find it difficult transitioning into this happy or hopeful mindset.

There are also very real challenges that come with managing a chronic illness day-to-day. The mental journey of the PNH patient, after starting treatment, can be described as a series of ups and downs, as the reality of daily life sets in. Some patients have missed educational opportunities, lost jobs, or find themselves financially dependent on others as a result of a PNH diagnosis. Even for those patients who have a job, they now have to navigate a new work path, sometimes filled with anxiety, to accommodate infusions every two weeks that may impact productivity. Like heart attack patients and cancer survivors, PNH patients may be affected physically, mentally and emotionally.

You can and will prevail over these challenges. Here are some suggested solutions to help you cope with the mental journey.

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Suggested Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden health setbacks such as HEMOLYSIS, blood clots detected or worsening lab numbers</td>
<td>Talk to your doctor or nurse. Most of the time, these are normal and temporary setbacks.</td>
</tr>
<tr>
<td>Depending on the province you live in, your treatment COVERAGE MAY BE REVIEWED by the government on a yearly basis, which may create anxiety for you</td>
<td>Focus on the fact that this is required paperwork and that most provinces require annual reviews when covering a costly drug for an individual. As long as you are responding positively to the medication, there is no reason that coverage should stop.</td>
</tr>
<tr>
<td>Your PNH diagnosis has led to CAREER and EDUCATIONAL SETBACKS</td>
<td>Reach out and connect with other PNH or rare disease patients who have also encountered career or educational setbacks. Various groups can help you obtain advice, direction and support. Speak to a guidance counsellor, headhunter or life coach for advice on how to re-integrate into a professional or scholarly life.</td>
</tr>
<tr>
<td>Your PNH diagnosis has side-lined your DECISION TO HAVE CHILDREN</td>
<td>While it is possible for women with PNH to become pregnant, it can be dangerous for both the mother and infant. That said, studies have shown that the risk of complications and adverse outcomes in PNH patients during pregnancy may be minimized with ongoing treatment rather than just symptomatic therapy. If you have PNH and wish to become pregnant, you should discuss this with your partner, your PNH specialist and an obstetrician who specializes in high-risk pregnancies. It is important to understand the risks before you become pregnant. If you do become pregnant, you should be very closely monitored by your doctors.</td>
</tr>
<tr>
<td>PNH is not known to be an inherited condition; therefore, it is not passed on to children.</td>
<td></td>
</tr>
</tbody>
</table>

GUIDE TO LIVING WELL WITH PNH
The new lease on life while on treatment can take an emotional toll. Setbacks are inevitable – an abnormal lab test, perhaps indicating that the disease or a serious side-effect has surfaced, can cause despair. In some ways, the emotional challenges faced by PNH patients can be far more worrisome than the infusions.

While it makes sense to focus heavily on one’s physical health when it comes to PNH, leaving fears unaddressed can leave emotional scars. That is why it is important for PNH patients to protect themselves from the “dark side” of survival – because complete happiness is not always available, and other emotions and issues can surface that need to be addressed.

It’s important to know that you’re not alone in experiencing any of the emotions below. However, if you find that your feelings are overwhelming or interfering with your everyday life, it’s a good idea to consider getting some help.

You might consider:

**Consulting a therapist.** Your doctor may be able to refer you to a professional who can help you sort through your emotions and come up with ways to address your feelings.
Connecting with other PNH patients. Support groups, whether in your community or online, provide a great place to share your feelings and hear from others who are going through what you’re experiencing. You can learn new ways of coping with fears. The Canadian Association of PNH Patients offers a mentorship program for patients recently diagnosed with the condition. To be connected with a mentor, send an email to mentor@pnhca.org.

Devising your own plan for coping with your emotions. Have an open mind and try different strategies to find out what works best for you.

Here are some suggested solutions to possible emotional scenarios that PNH patients may encounter:

<table>
<thead>
<tr>
<th>Emotional Challenges</th>
<th>Suggested Solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of RECURRENCE</td>
<td>As long as you’re on treatment, your PNH should not worsen. Though you may feel invincible after beginning treatment, you must maintain your regular treatment schedule to continue to see the benefits. To avoid the threat of blood clots while on treatment, take care of your body, and focus on keeping yourself healthy. Eat a healthy diet with plenty of fruits and vegetables. Fit exercise into your day, with your doctor’s guidance. Go easy at first, but try to increase the intensity and amount of exercise you get. Get enough sleep so that you wake up feeling refreshed. Go to all of your follow-up appointments. You may fear the worst when it’s time for your next follow-up appointment. Don’t let that stop you from going. Use the time with your doctor to ask questions about any signs or symptoms that worry you. Write down your concerns and discuss them at your next appointment.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suggested Solutions</th>
<th>Emotional Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Being open about FEARS/CONCERNS</td>
<td>Being open is a healthy way to confront your concerns around PNH. Express your concerns to your friends, family, other PNH patients, and your doctor or a counsellor. If you’re uncomfortable with the idea of discussing your fears, try recording your thoughts in a journal or blog.</td>
</tr>
<tr>
<td>STRESS</td>
<td>When you were first diagnosed with PNH, you had to process some difficult news. Now that you have access to treatment, all those projects around the house and the things on your to-do list are competing for your attention. This can make you feel stressed and overwhelmed. Don’t feel you need to do everything at once. Take time for yourself as you establish a new daily routine. Try exercising, talking with other patients and taking time for activities you can once again enjoy.</td>
</tr>
<tr>
<td>SELF-CONSCIOUSNESS</td>
<td>If side-effects relating to PNH or other treatments (like prednisone) have changed your appearance, you might feel self-conscious about your body. Changes in skin, weight gain or loss, might make you feel like you’d rather stay home, away from other people. You might withdraw from friends and family. And self-consciousness can strain your relationship with your partner if you don’t feel worthy of love or affection. Take time to grieve, but also learn to focus on the ways PNH has made you a stronger person.</td>
</tr>
</tbody>
</table>
How to become a mentor to a newly-diagnosed PNH patient

Learning that you have a rare and unfamiliar condition can be stressful, confusing and frightening. The Canadian Association of PNH Patients can help connect Canadians recently diagnosed with PNH with peers also living with the condition. Mentors can support new members of the PNH community with practical information and advice for not only coping with a rare disease, but thriving.

The Canadian Association of PNH Patients mentors:

- are Canadian PNH patients, or caregivers to a PNH patient
- have been living with PNH for more than one year
- are currently living well with the condition
- are available to share their knowledge and give moral support and encouragement to new members of the PNH community

Volunteer as a Mentor.

If you would like to volunteer to offer peer support to Canadians recently diagnosed with PNH, please send an email to mentor@pnhca.org.

- Please note: mentors must agree to be evaluated by the Canadian Association of PNH Patients prior to being paired with a mentee.

Request a Mentor.

If you, a friend or a family member would like to be connected with a PNH mentor, please send an email to mentor@pnhca.org.

- The Canadian Association of PNH Patients will make every effort to ensure that mentors are assigned to newly-diagnosed individuals based on their age and where they live.

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DEPRESSION, ANXIETY and ANGER

Why me?

Lingering feelings of sadness and anger can interfere with your daily life. Questions like, “Why does my life have to revolve around an infusion schedule?” and “Why do I have to have this disease?” may weigh heavily on you. For many, these feelings will dissipate. But for others, these feelings can develop into depression.

Tell your doctor about your feelings. If needed, you can be referred to someone who can help you through talk therapy, medication or a combination of both. Early diagnosis and prompt treatment are keys to successfully overcoming depression.

You might feel as if others can’t understand what you’ve been through, which makes it hard to relate to other people and can lead to loneliness. Friends and family might be unsure of how to help you after you have been diagnosed with PNH.

Don’t deal with loneliness on your own. Consider joining a PNH support group, or request a mentor through the Canadian Association of PNH Patients. Mentors experienced, or perhaps continue to experience, the same emotions that you are dealing with now. To be connected with a PNH mentor, send an email to mentor@pnhca.org.

LONELINESS in survival

(TSOURCE: Cancer survivors: Managing your emotions after surviving cancer
http://www.mayoclinic.com/health/cancer-survivor/CA00071)
Tracking your progress

Before and after you begin treatment, it will be important to keep a journal of signs and symptoms to share with your doctor. With PNH, your physical symptoms only tell part of the story, and don’t reflect everything going on inside your body.

Your signs and symptoms — combined with lab results — give you and your doctor a fulsome view of your PNH.

The symptoms of PNH can be silent and unpredictable. They affect everyone differently, and they can change from day to day. Even when you can’t see or feel symptoms, you can still be at risk of serious health problems.

Keep track of your symptoms

When you track your signs and symptoms over time, you and your doctor can be more aware of changes in your health. So, take note of how you’re feeling every day and share it with your doctor.

PNH symptom checkup chart

Record your signs and symptoms of PNH before each appointment and discuss them with your healthcare team.

Please check off the severity of your signs and symptoms

**My PNH Record**

**Signs and symptoms**

- Dark-colored urine
- Shortness of breath
- Difficulty swallowing
- Yellowing of the skin and/or eyes
- Erectile dysfunction
- Have you had a cold or infection since your last visit?

**Date:** __________________________

**Severity:**

- None
- Moderate
- Severe

**Pain**

- Stomach pain
- Leg pain or swelling
- Chest pain
- Back pain

**Fatigue**

- Tiredness
- Inability to perform daily activities
- Trouble concentrating
- Dizziness
- Weakness

**Lab test results**

- Lactate dehydrogenase (LDH) Value: __________________________
- Transfusions Frequency: __________________________
- # of units: __________________________

(SOURCE: PNHSource.com)
Lab result tracking

There are a number of important lab tests that can help tell you and your doctor how your PNH is progressing. As someone living with PNH, you will always be consistently tested for the following:

- Lactate dehydrogenase (LDH)
- PNH clone size
- Complete blood count (CBC)
  - Red blood cells (RBC)
  - White blood cells (WBC)
  - Hemoglobin (Hgb)

These simple blood tests can tell a great deal of information about your PNH.

Remember, there is no one sign, symptom, or lab result that defines PNH. You may feel fine, even when your lab results show something unusual. The reverse of this can also happen. Always contact your doctor if you have any sudden changes to your health. PNH can be life-threatening, but it is manageable.

The following lab result tracker will help you and your doctor to better understand your lab test results, so you can get more out of each visit.

Understanding your lab results

To manage your PNH, your healthcare team may use many different tests. This tool can be used to track your lab values over time for the following tests:

**Complete blood count (CBC):** Provides information about the kinds and numbers of cells in the blood. Includes hematocrit, hemoglobin, platelets, and white blood cells (among other measurements):

- **Hematocrit (HCT):** Measures the volume of red blood cells in your blood. The test is given as a percentage of how much of your blood is made up of red blood cells
- **Hemoglobin (Hgb):** Hemoglobin is the substance in red blood cells that carries oxygen in the blood. This test measures the amount of hemoglobin in the blood and its ability to carry oxygen throughout the body
- **Platelets (thrombocyte) count:** Measures the amount of platelets in your blood. Platelets are used for clotting and play an important role in helping you heal from injury
- **White blood cells (WBCs):** This test measures the amount of white blood cells in your blood. WBCs protect the body against infection

**Creatinine (CRT):** Measures creatinine, a waste product in the blood. This test indicates how well your kidneys are working.
Asking questions

Members of your healthcare team are your frontline contacts, and are there to help you navigate the PNH journey. Don’t be afraid to ask questions! Please see some sample questions below to help you in speaking with your doctor, after starting treatment.

1. How can I find out if my insurance covers the treatment I have been prescribed?
2. If I do not have private health insurance does that mean I cannot have the treatment?
3. Can you put me in touch with other PNH patients?
4. Should I begin taking supplements like iron and folic acid? How much of each? What is the danger of taking too many supplements?
5. Can I get pregnant if I have PNH?
6. I am not pregnant now, but would like to have children. What do I need to know to have a healthy pregnancy with PNH and treatment?
7. I think I may be pregnant. How will PNH and treatment affect my pregnancy, and how will my pregnancy affect my PNH?
8. Have others undergoing treatment had successful pregnancies?
9. What percentage of my total blood cells are normal cells versus PNH cells? Or what is my “PNH clone size?”
10. Should I take an anticoagulant to avoid blood clots?
11. When I feel sick, how will I know if I should call you or 911?
12. Will any of my symptoms come back after being on treatment for a while?
13. Are there any clinical trials currently recruiting for patients in Canada?

It is also important to speak to your doctor about your lab results whenever you have a consultation.

Here are a few questions to consider asking:

1. What does this lab test mean?
2. Are my results normal?
3. What does it mean if my results are above or below normal?
4. Is there anything I can do to get them within a normal range?

Important lab results

<table>
<thead>
<tr>
<th>Date of Test</th>
<th>Creatinine (CRT) mg/mL</th>
<th>Hematocrit (HCT) g/dL</th>
<th>Hemoglobin (Hgb) g/dL</th>
<th>Platelets (PLT) mm³</th>
<th>White Blood Cells (WBCs) μL</th>
</tr>
</thead>
</table>

Keeping track of your other lab values, combined with monitoring your LDH level, is the best way to help you and your doctor manage your PNH.

(SOURCE: PNHSource.com)
RESOURCES

The following is a list of organizations and websites which may be useful to PNH patients, their caregivers and families.

**The Canadian Association of PNH Patients**
The Canadian Association of PNH Patients is a not-for-profit Canadian organization formed in 2009. This website represents a growing community of patients, caregivers and members of the medical community who wish to support and improve the quality of life of those with PNH.
www.pnhca.org

**Canadian Association of PNH Patients Facebook Page**
The mission of the Canadian Association of PNH Patients Facebook Page is to connect a growing community of Canadians affected by PNH, including patients, caregivers and members of the medical community who wish to support and improve the quality of life of those with PNH.
www.facebook.com/PNHCanada/

**Canadian PNH Support Group**
The Canadian PNH Support Group is a closed group on Facebook that is managed by the Canadian Association of PNH Patients, which contains information for PNH patients and caregivers only, and exists to facilitate dialogue between members of the Canadian PNH community.
www.facebook.com/groups/canadianpnhsupportgroup/

**Canadian PNH Network**
The Canadian PNH Network is a nationwide network of experts dedicated to the diagnosis, treatment, management, education and investigation of Paroxysmal Nocturnal Hemoglobinuria (PNH), for the benefit of Canadian patients and the Canadian healthcare system.
www.pnhnetwork.ca/

**Canadian Organization for Rare Disoders**
CORD is Canada’s national network for organizations representing all those with rare disorders. CORD provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders.
www.raredisorders.ca

**Aplastic Anemia and Myelodysplasia Association of Canada**
A non-profit resource for assistance, advocacy, and support for patients living with aplastic anemia, myelodysplasia, and PNH.
www.aamac.ca

**Aplastic Anemia and MDS International Foundation**
The Aplastic Anemia and MDS International Foundation supports, connects and educates patients, caregivers and health professionals on bone marrow failure diseases worldwide. It promotes and invests in collaborative clinical research to accelerate the discovery of better treatments and cures for aplastic anemia, MDS, PNH and related bone marrow failure diseases.
www.aamds.org

**OneSource**
A patient support program provided by Alexion Pharma Canada, the manufacturers of Soliris. Nurse case managers can help answer questions about PNH and provide personal support for people living with PNH and their caregivers.
1-888-765-4747

**PNH Source**
Complete information about PNH and helpful tools to manage your disease, all in one resource.
www.PNHSource.com

**PNH Support Group**
An online support group for people with PNH.
www.pnhdisease.org
Complement system
The complement system is a collection of immune molecules that provide surveillance and protection for the body against foreign organisms (e.g., viruses, bacteria) or abnormal cells (e.g., old cells, cancer). Infections and abnormal cells can be eliminated by the complement system by being tagged for elimination in the spleen and liver, or they can be destroyed on site by the body’s natural defense system. Complement activation can also recruit other immune cells to the site of injury, infection, or other damage to help control the situation. Healthy cells in the body are spared from this damage by molecules that regulate complement activity, with some circulating and others that are expressed directly on our cells. If regulators of complement activity become defective or deficient, our healthy cells can also become damaged.

Complete blood count (CBC)
A lab test that gives the amounts of different cells in your blood.

Enzyme
A type of protein that helps reactions/processes happen in the body.

Erectile dysfunction (ED)
A condition found in men that affects their ability to achieve an erection.

Graft-versus-host disease (GVHD)
When the new (donor) bone marrow creates a new immune system which then attacks the skin or digestive system.

Hemoglobin (Hgb)
The reddish-brown material found inside red blood cells that carries oxygen throughout your body. When it gets outside of your cells, it is harmful and can lead to serious health problems.

Hemoglobinuria
Hemoglobin in the urine. About 25% of patients with PNH have it at diagnosis, but most will experience it at some time. Because of the reddish-brown colour of hemoglobin, it results in dark, sometimes “cola-coloured” urine.
**Hemolysis**
When red blood cells burst. Hemolysis is the main cause of the major health problems in PNH.

**Intravascular hemolysis**
The breakdown of red blood cells while they are still circulating inside ("intra") the blood vessels ("vascular"). This is the main type of hemolysis that happens in all patients with PNH. Because the cells are missing their protection from complement activity, the body’s natural defense system can act at any point and cause destruction of the cells. When it happens in this uncontrolled way, hemolysis releases the red blood cell contents into the circulation, which can cause some of the symptoms seen in PNH patients, like shortness of breath, abdominal pain, difficulty swallowing, and blood clots.

**Extravascular hemolysis**
A more controlled breakdown of red blood cells outside ("extra") of the blood vessels ("vascular"). In PNH, it occurs as a result of the build-up of the complement protein, C3, on the red blood cells, which marks them for destruction and signals the liver to remove them from the circulation. This is something seen only after Soliris treatment is started because the cells no longer experience intravascular hemolysis, and are living long enough to be marked by C3. Although this may cause some anemia, it is usually not severe, and does not have the same risks and complications (like blood clots and kidney damage) as the usual intravascular hemolysis of PNH.

**Lactate dehydrogenase (LDH)**
An enzyme found in red blood cells, released during hemolysis. Testing for LDH can help show how much hemolysis is happening in your body.

**Meningococcal infection**
A severe bacterial infection in the blood. Soliris can lower the ability of your immune system to fight infections, especially meningococcal infection, which requires immediate medical attention.

**Myelodysplastic syndromes (MDS)**
A condition in which there’s a problem with the way bone marrow makes blood cells. About 2% of PNH patients also have MDS.

**Paroxysmal nocturnal hemoglobinuria (PNH)**
A disease where red blood cells are created without a protective protein. This causes them to burst (a process called hemolysis) and can result in serious health problems. Signs and symptoms include stomach pain, difficulty swallowing, anemia, shortness of breath, and tiredness. Life threatening complications from PNH include blood clots, kidney failure, and damage to organs. Scientific studies have shown that without treatment, approximately one third of PNH patients do not survive more than five years, and about half die within 10 years from the time of diagnosis.

**Progressive**
A progressive disease is one that gets worse over time.

**Pulmonary hypertension**
High blood pressure in the arteries that deliver blood to the lungs. This means that blood has a hard time getting to the lungs, causing your heart to pump harder.

**Red blood cells (RBCs)**
A type of cell found in your blood that delivers oxygen and removes waste (carbon dioxide) in your body. Red blood cells affected by PNH are attacked and destroyed because they are missing a protective protein.

**White blood cells (WBCs)**
A type of cell found in your blood that helps your immune system fight disease and infection.
SOURCES


What is PNH? 2012, Alexion Pharmaceuticals.


HCP Counselling Tool. 2012. Alexion Pharmaceuticals.


SOLIRIS® Product Monograph. Alexion Pharmaceuticals, Inc. June 29, 2009


OneSource Treatment Support: http://soliris.net/onesource/


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