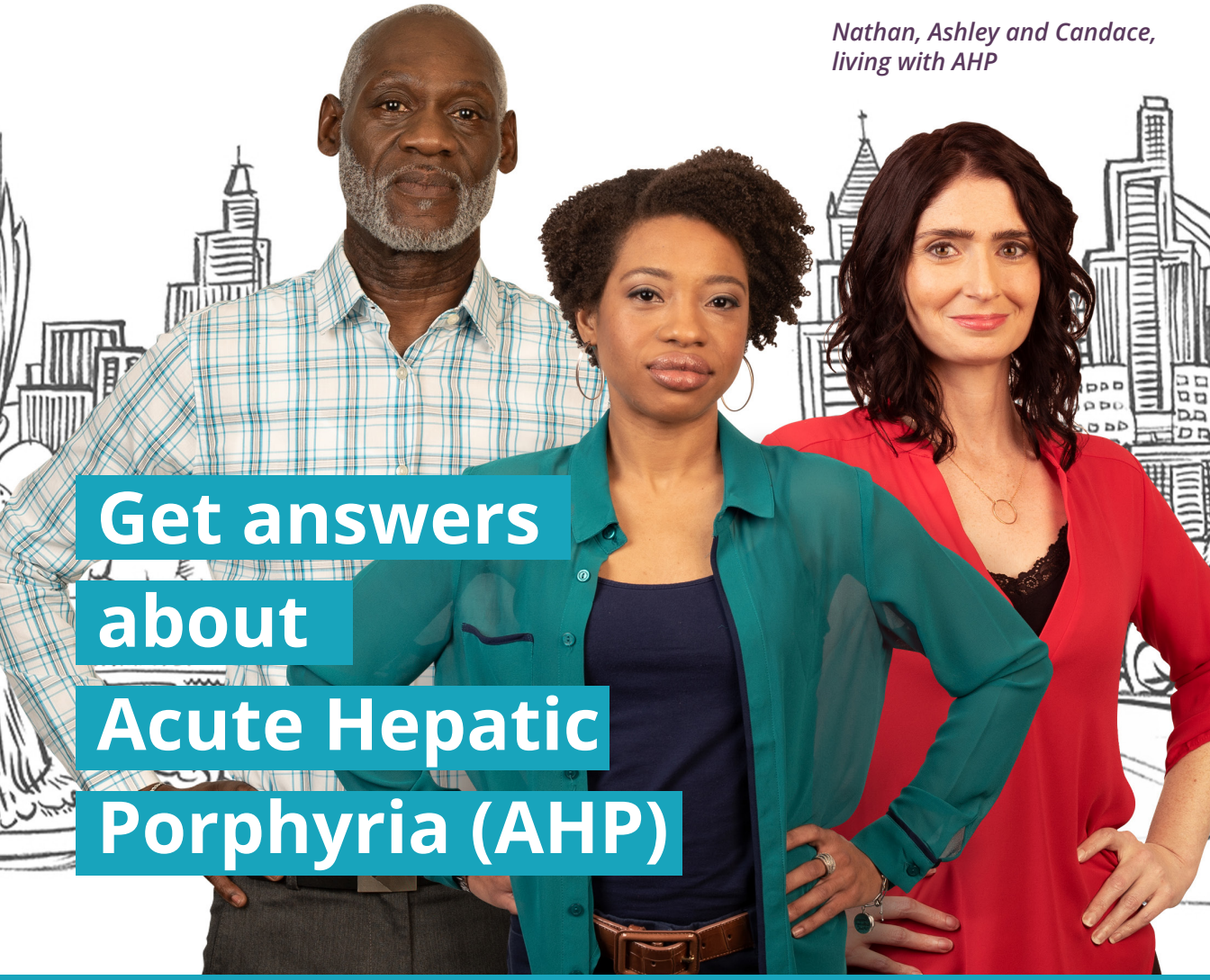


Get answers about Acute Hepatic Porphyria (AHP)

Find helpful information about symptoms, diagnosis, and living with AHP.

PORPHYRIA.ca
Acute Hepatic Porphyria

Porphyria.ca

Alnylam® PHARMACEUTICALS

Could it be Acute Hepatic Porphyria (AHP)?

Have you ever had **severe, unexplained abdominal pain**, along with at least 1 other symptom, such as:

- **Limb, back, or chest pain**
- **Nausea**
- **Vomiting**
- **Confusion**
- **Anxiety**
- **Insomnia**
- **Seizures**
- **Weak limbs**
- **Dark or reddish urine**
- **Constipation**
- **Diarrhea**
- **Hallucinations**

You may have had multiple doctor appointments, received a series of different diagnoses, and had treatments—even surgeries—that didn't help.

If this sounds at all familiar, the cause may be Acute Hepatic Porphyria, or AHP.

AHP is a rare genetic disease with a wide array of symptoms that mimic those of other conditions, often making proper diagnosis difficult. People with AHP can wait years for a confirmed diagnosis. The good news is, your doctor can check for AHP using a few simple tests.

This brochure provides education, resources, and information on how to get tested, so you can get answers.

"I can still remember sitting in the doctor's office when my test came back. He said that the results were positive—positive, not inconclusive!"

— Megan, living with AHP

What is Acute Hepatic Porphyria?

Acute hepatic porphyria (AHP) refers to a family of rare genetic diseases characterized by potentially life-threatening attacks and, for some people with AHP, chronic debilitating symptoms that negatively impact daily functioning and quality of life. AHP is comprised of four subtypes, outlined below:

AIP	VP	HCP	ADP
Acute intermittent porphyria	**Variegate porphyria**	**Hereditary coproporphyria**	**ALAD-deficiency porphyria**

MOST COMMON → EXTREMELY RARE

What AHP does to the body

- In people with the genetic defect for AHP, one of the enzymes in the heme pathway doesn't work properly
- Heme is essential to our body and is necessary for our liver to function properly
- In the liver, the heme pathway is controlled by an enzyme called ALAS1
- When ALAS1 activity is increased, the enzyme that doesn't work properly is unable to keep up. This results in the buildup of neurotoxic intermediates called aminolevulinic acid (ALA) and porphobilinogen (PBG) in the liver which are released throughout the body
- ALA and PBG are harmful to nerve cells and have been associated with the symptoms and attacks of AHP
- Sudden attacks are associated with widespread dysfunction within your nervous system and a wide array of symptoms which can mimic those of other diseases, often making proper diagnosis difficult

Everyone experiences AHP in a different way

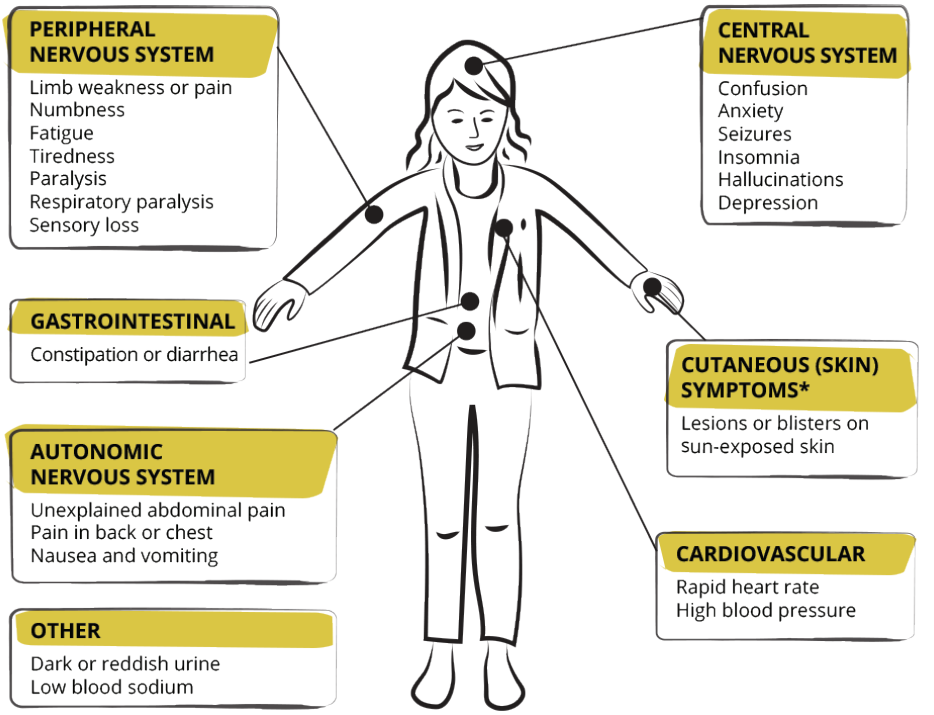
Acute attacks can be life-threatening and can last for days. Not everyone who has AHP experiences acute, sudden attacks. In some people they happen rarely – in others more often. Some people experience daily symptoms from their AHP, even when they are not having an attack. This is part of what makes diagnosis difficult.

"By the time I was 14, I had more unexplained attacks. My symptoms included tremors, seizures, sun burns and light sensitivity, frequent vomiting, abdominal pain, severe all-body pain, muscle weakness, memory loss, and diarrhea."

— Nathan, living with AHP

What are the signs and symptoms of AHP?

Severe, unexplained abdominal pain of varying intensity without fever or a high white blood cell count is the most common symptom, occurring in **more than 90% of people diagnosed with AHP**. People with AHP are also likely to experience at least one of many other, seemingly unrelated symptoms:



The symptoms of AHP can vary from person to person and change over time. Not every person with AHP will experience all the symptoms listed here and throughout this brochure, and some people will have symptoms more frequently or more severe than others.

*Hereditary coproporphyria and variegate porphyria only.

AHP can have a significant impact on a person's daily life

AHP is unpredictable and attacks are debilitating. It can take over your life with symptoms that can disrupt everything from sleep to the ability to work, attend school, and socialize. Even those who rarely experience attacks may live in constant fear of them. Long-term complications of AHP may include chronic high blood pressure, chronic kidney disease, liver cancer, and psychological problems.

How is AHP diagnosed?

If you have symptoms you think may be due to AHP, talk with your doctor about getting tested. Simple urine tests are the first step.

Download an informative guide that will help you prepare to discuss AHP, as well as testing options, with your doctor.

Diagnosing AHP early is important

Accurate diagnosis of AHP as soon as possible may make a real difference in a person's quality of life by enabling them to:

- **Take steps to manage factors that may trigger symptoms**
- **Understand what is happening in their bodies and why**
- **Avoid the complications that result from misdiagnoses and unnecessary surgeries**

The path to diagnosing AHP

1. **Rule out other conditions**
2. **Suspect AHP signs and symptoms**
3. **Test urine PBG, ALA, and porphyrins**
   (Biochemical test for ALA, PBG, porphyrins)
   - PBG (porphobilinogen)*
   - ALA (delta-aminolevulinic acid)*
   - Porphyrins†

   It is recommended to have a urine test within 48 hours of symptom onset since PBG and ALA levels drop over time, increasing the chance of a false negative result. Urine porphyrins is a nonspecific test and should not be used alone to diagnose AHP.
4. **Review the test results**

   Positive–Your doctor may perform genetic testing or porphyrin analyses to confirm the type of AHP

   Negative–If you and your doctor still suspect AHP, repeat the urine test during an attack, and/or consider genetic testing

No-charge genetic testing

Alnylam sponsors no-charge, third-party genetic testing through Alnylam Act® for individuals who may carry a gene mutation known to be associated with AHP. Your doctor must sign up for the program and confirm that you meet certain criteria in order for you to receive genetic screening at no charge. Please see the back of this brochure for more details.

*PBG and ALA are substances that are produced when the liver makes heme. Increased levels of PBG and ALA can become toxic and have been associated with the symptoms and attacks of AHP.
†Porphyrin analyses may help identify the specific AHP.

AlnylamAct®

Living with AHP: be aware of the triggers for acute attacks

It is important to lessen exposure to attack triggers when possible. The triggers listed here are common, but triggers can be different for every person.

Be aware of:

- The way some drugs in certain medication classes may affect AHP, including:
  - Some seizure medications
  - Antihistamines
  - Hormones
  - Migraine drugs
  - Sedatives

  Speak with your doctor if you have any questions about your medications and AHP.
- Hormone levels, including levels of estrogen and progesterone
  - These hormones fluctuate the most during the 2 weeks before a woman's menstrual cycle begins
- Stress caused by:
  - Infections
  - Surgery
  - Physical exhaustion
  - Emotional exhaustion

Try to avoid:

- Drinking alcohol
- Smoking
- Fasting or low-carb diets

> *"I knew from my nutritionist consult that I needed to eat a healthy, well-balanced diet."*
>
> *— Candace, living with AHP*

Living with AHP: how to get the help you need

Talk to your healthcare team

It's important to keep the communication lines open with your healthcare team. Sharing your symptoms and concerns can help them tailor a plan for managing the disease that is right for you. You'll find this discussion guide to be helpful.

Seek information and support

There are many educational resources available to you, as well as support groups for people living with AHP. Although you may not know anyone else with the disease, there are ways to find others with AHP and connect. You can also find helpful information through patient organizations such as:

- Canadian Association of Porphyria
- Canadian Organziation for Rare Diseases

Talk with trusted family and friends

The choice to talk with your family is an important first step in creating awareness. Educating your family about your diagnosis of AHP can help each of you make educated, health-conscious decisions about your future.

Consider talking to your co-workers and supervisors

Because of the unpredictability of AHP attacks and the chronic symptoms that may come and go, you might want to inform your immediate supervisor and human resources manager about your condition, so they can be supportive if an attack occurs.

"I'm a big advocate for knowledge and education—it is power. And finally having a diagnosis gave me the power to be a better advocate for myself."

— Ashley, living with AHP

Visit **Porphyria.ca** to find additional resources for understanding and living with AHP.

No-charge AHP genetic testing programs are available

NO-CHARGE
Genetic testing

Alnylam is sponsoring no-charge, third-party genetic testing a for individuals who may carry a gene mutation known to be associated with acute hepatic porphyria (AHP). The Alnylam Act® program was created to reduce barriers to genetic testing to help people make more informed decisions about their health.

AlnylamAct®

While Alnylam provides financial support for this program, tests and services are performed by independent third parties. Healthcare professionals must confirm that patients meet certain criteria to use the program. Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient identifiable information. Alnylam receives contact information for healthcare professionals who use this program. Genetic testing is available in the United States and Canada. Healthcare professionals who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use or support any Alnylam product.

Your doctor must sign up for the program and confirm that you meet certain criteria in order for you to receive genetic screening at no charge.

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