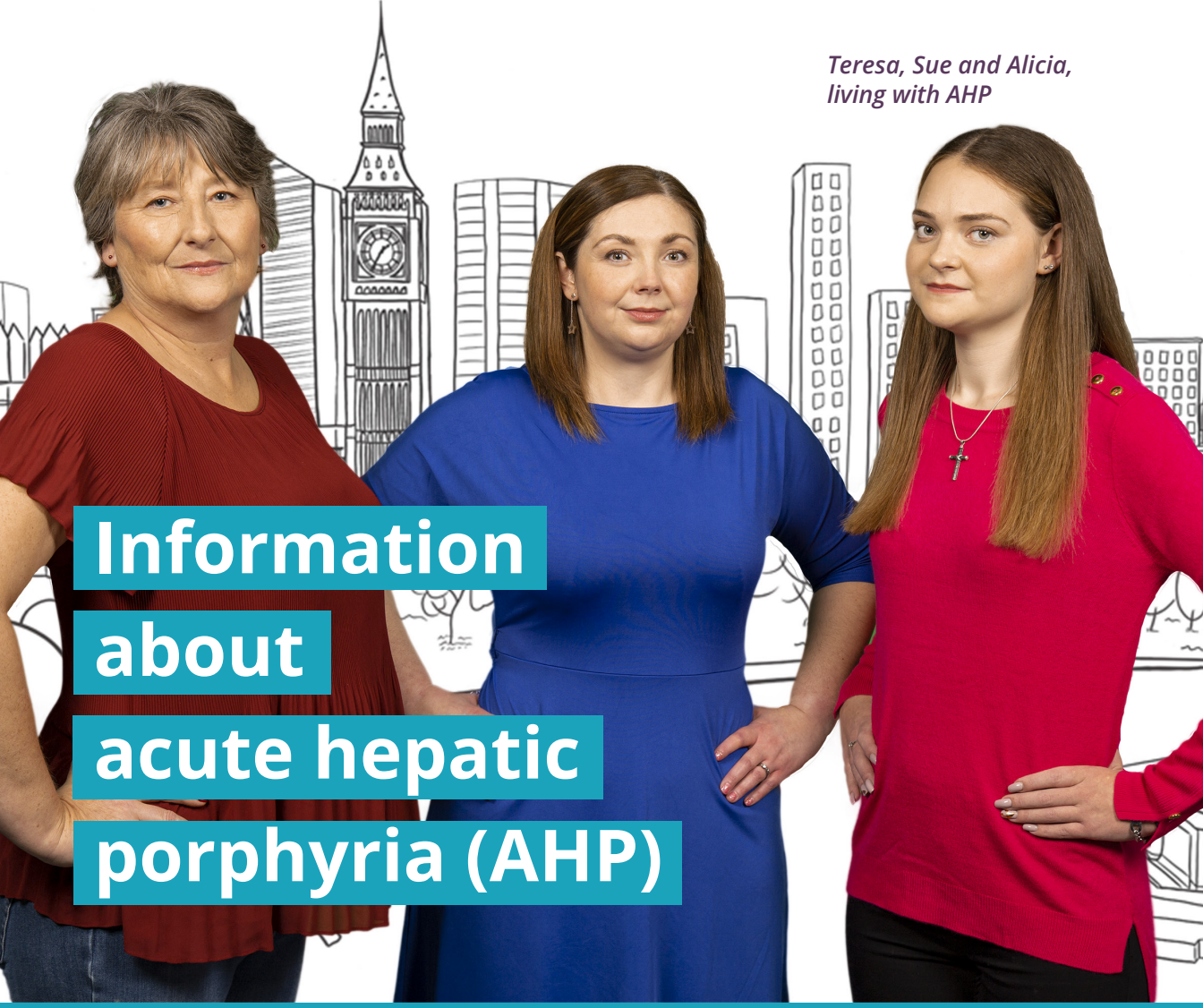


Information about acute hepatic porphyria (AHP)

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

Living with PORPHYRIA
Acute Hepatic Porphyria

Livingwithporphyria.eu

Alnylam® PHARMACEUTICALS

Could it be acute hepatic porphyria (AHP)?

Acute Hepatic Porphyria typically causes episodes of **severe, unexplained abdominal pain**, together with one or more of the following:

- **Limb, back, or chest pain**[1]
- **Nausea**[1]
- **Vomiting**[1]
- **Confusion**[1]
- **Anxiety**[2]
- **Insomnia**[3]
- **Seizures**[3]
- **Weak limbs**[1]
- **Dark or reddish urine**[1]
- **Constipation**[1]
- **Diarrhoea**[1]
- **Hallucinations**[1]

You may have had multiple doctor appointments, received a series of different diagnoses, and had treatments—even surgeries—that didn't help.[1]

If this sounds at all familiar, the cause may be acute hepatic porphyria, or AHP.[1]

AHP is a rare genetic disease with a wide array of symptoms that mimic those of other diseases, often making proper diagnosis difficult.[5] People with AHP can wait years for an accurate and confirmed diagnosis.[6] The good news is your doctor can check for AHP using appropriate tests.[2]

This brochure provides education, resources, and information on the signs and symptoms of AHP, living with AHP, and ways AHP is diagnosed so you can start a conversation with your doctor and get answers.

"As soon as I realised that I might have been having a porphyria attack, I was petrified. I thought, "This cannot be happening to me. I've avoided all of the unsafe medications. I haven't drunk. I haven't done all of these things." And it still happened."

— Sue, living with AHP

What is AHP?

AHP refers to a family of rare genetic diseases characterised by potentially life-threatening attacks and, for some people, chronic debilitating symptoms that negatively impact daily functioning and quality of life.[1,2] There are 4 types of AHP:

AIP
Acute intermittent porphyria

VP
Variegate porphyria

HCP
Hereditary coproporphyria

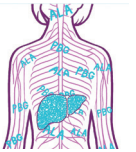
ADP
ALAD-deficiency porphyria

MOST COMMON → EXTREMELY RARE

What AHP does to the body

In AHP, **when ALAS1 activity is increased**, the haem production process is unable to keep up

This results in the **buildup of toxins** called ALA and PBG in the liver



These toxins are **released throughout your body**

ALA and PBG are **harmful to nerve cells** and have been associated with **attacks and other AHP symptoms**

In people with a genetic defect for AHP, one of the enzymes in the haem synthesis doesn't work properly.[1] Haem is essential to our body and is necessary for our liver to function properly.[7] In the liver, the haem synthesis is controlled by an enzyme called ALAS1.[8]

When ALAS1 activity is increased, the enzyme that doesn't work properly is unable to keep up. This results in the buildup of toxins called aminolevulinic acid (ALA) and porphobilinogen (PBG) in the liver which are released throughout the body.[1]

ALA and PBG are harmful to nerve cells and have been associated with attacks and other AHP symptoms.[1,8,9] Sudden attacks are associated with widespread dysfunction within the nervous system and a wide array of symptoms which can mimic those of other diseases, making a diagnosis difficult.[5]

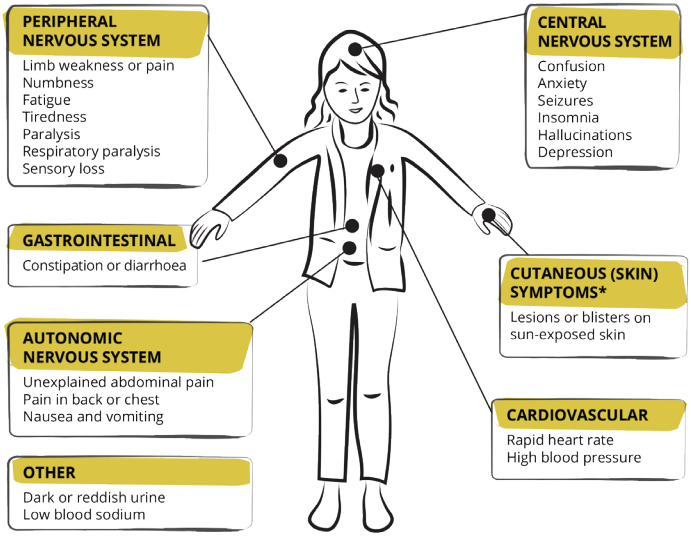
Everyone experiences AHP in a different way

Acute attacks can be life-threatening and can last for days. Acute attacks are not the only sign of AHP – some people with AHP also experience debilitating symptoms daily, so called chronic symptoms, even when they are not having attacks. This is part of what makes diagnosis difficult.[1,10]

AHP = Acute hepatic porphyria; **ALA =** Aminolevulinic acid; **PBG =** Porphobilinogen

What are the signs and symptoms of AHP?

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.[1] Severe, unexplained abdominal pain is the most common symptom, occurring in **85% to 95% of people who experience AHP attacks**.[1]
People with AHP are also likely to experience at least one of many other seemingly unrelated symptoms:



*Variegate porphyria (VP) and hereditary coproporphyria (HCP) 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, and socialise. People with AHP may live in constant fear of attacks.[10]

It was really frightening to not know what it was, or how to deal with it, or how to live with it. I'd never really experienced pain like it. Myself and my doctors didn't really know what to do.

— Alicia, living with AHP

Diagnosing AHP

If you have symptoms you think may be due to AHP, talk with your doctor.
Visit **Livingwithporphyria.eu** to download a Doctor Discussion Guide that will help you prepare to discuss AHP, as well as testing options, with your doctor.

The earlier the diagnosis, the better

Early, accurate diagnosis of AHP may make a real difference in a person's ability to maintain their quality of life by:

- **Taking steps to manage factors that may trigger attacks**
- **Understanding what is happening in their bodies and why**
- **Avoiding the complications that can result from misdiagnoses and unnecessary surgeries**[1,11]

How AHP is diagnosed

The two most common techniques a doctor uses to determine if a person has AHP are a **spot urine test** and a **genetic test.**[2,5]

SPOT URINE TEST

- AHP can be diagnosed with a urine test of PBG (porphobilinogen), ALA (aminolevulinic acid), and porphyrin levels[1,2,5]
- A 24-hour urine collection is not recommended and may result in considerable delay in confirming the diagnosis[12]
- It is recommended to have a urine test during or shortly after an attack[1,2]
- Porphyrin analyses may help identify the specific type of AHP, but are not used alone to diagnose AHP[2]

GENETIC TEST

- A genetic test using a blood or saliva sample may help to confirm a diagnosis or determine the specific type of AHP[2]
- It can rule out AHP if there is not a genetic mutation[2]
- AHP is a genetic inherited disease, so family members of someone who has AHP may also have inherited the altered gene responsible for the disorder. While most people with an altered gene may never have symptoms, they are however at risk of having an attack, or at risk of complications associated with elevated levels of ALA and PBG.[13] Knowledge of genetic risk of AHP may enable people to make informed decisions regarding lifestyle and medications with the intent to prevent attacks and complications of the disease.[1] Therefore, family members of someone who has AHP may want to talk with their doctor about genetic testing for AHP.[14]

AHP: be aware of the triggers for acute attacks

Common triggers for attacks are shown below. Since triggers can be different for every person, there may be others that are not listed here.[1,11]

Be aware of:

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

  Speak with your doctor if you have any questions about your medications and AHP and to identify which drugs could be unsafe, possibly unsafe or safe for you.
- Hormone level fluctuations during a woman's menstrual cycle
- Stress caused by:
  - Infections
  - Surgery
  - Physical stress
  - Psychological stress[1,15]

Try to avoid:

- Drinking alcohol
- Smoking
- Fasting or extreme dieting[1,2]

"It is important that we eat 3 meals a day. But that's easier said than done when you're feeling sick and you don't really want to eat. So, you have to...you do have to."

— Alicia, living with AHP

How to get the help you need

Talk to your healthcare team

If you think you have AHP, please speak to your healthcare professional.
Sharing your symptoms and concerns can help them tailor a management plan that is right for you.
Visit **Livingwithporphyria.eu** to download a helpful Doctor Discussion Guide.

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 the following independent patient organizations:

Visit **British Porphyria Association** to learn more.

- **http://www.porphyria.org.uk/**

Reach out to family

With a disease like AHP, it can be helpful if family and/or close friends understand the disease so they know how to best support you. Be sure to explain to the people close to you the importance of steps you're taking to avoid triggers.

Talking with others about AHP

Consider talking with family, friends, and possibly coworkers about AHP. Explaining AHP to them can help them understand the unique burden of this debilitating disease. It can be challenging but here are some tips that can make those conversations easier:

1. Start by saying that AHP is real
2. Tell them that some people with AHP may experience debilitating attacks
3. Explain that some people with AHP experience ongoing symptoms

It's important to do awareness because it shows that you're not alone. It's so important that the disease might be really rare, but people are suffering a lot.

— Sue, living with AHP

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Alnylam® PHARMACEUTICALS

Living with PORPHYRIA
Acute Hepatic Porphyria

Developed and produced by Alnylam Pharmaceuticals.

This brochure is intended for the general public in Europe, Middle East and Africa with the purpose of health promotion, disease prevention and providing advice to help understand the disease development and to help improve quality of life.
Nothing in this brochure constitutes individual medical advice.
Individuals are advised to consult their physician or other appropriate HCP for a correct diagnosis and management of the disease.

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