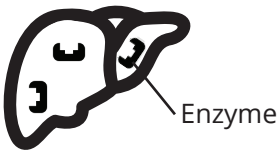
The importance of FAMILY GENETIC TESTING FOR AHP

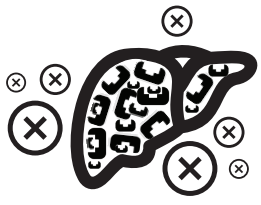
Isabelle, AHP Patient & Patient Advocate, AFMAP
(Association Française des Malades Atteints de Porphyries)

What is AHP?

Acute Hepatic Porphyria (AHP) is a family of rare genetic diseases, caused by gene mutations that affect the liver's ability to make haem.[1] Acute intermittent porphyria (AIP) is the most common type of AHP.[2]



Haem helps the liver function properly and is essential for the human body.[1]



In AHP, an enzyme involved in haem synthesis does not work correctly.[3]

The result is **the buildup of toxins** called aminolevulinic acid (ALA), porphobilinogen (PBG), and porphyrins in the liver, which are then released throughout the body.[4]

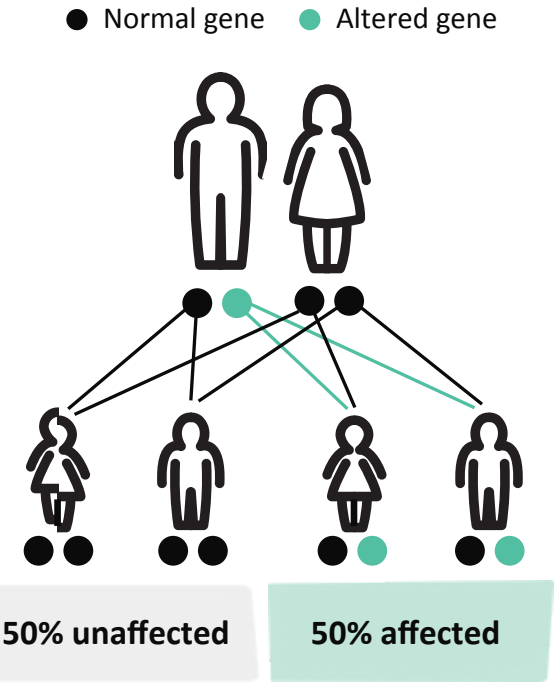
AHP attacks, chronic symptoms, and long-term complications occur when the nervous system reacts to the excess ALA, PBG, and porphyrins.[4]

Symptoms vary widely but abdominal pain, nausea and vomiting, constipation, dark urine, and confusion are common, usually appearing in women between 14 and 45 years old.[1, 3]

AHP: Acute Hepatic Porphyria AIP: Acute Intermittent Porphyria ALA: Aminolevulinic Acid PBG: Porphobilinogen

What is the genetic basis of AHP?

AHP is **hereditary,** meaning it can be passed down from one generation to the next.



It is generally passed down in an autosomal dominant pattern, which means a person only needs to inherit one copy of the altered gene from one parent in order to develop the disease risk.[1]

If you inherit the gene, you are at risk of inheriting the disease, but most people will never develop symptoms.[1]

If one parent carries the altered gene, a child has a 50% chance of inheriting the mutation.

AHP is not linked to gender, so men and women have an equal chance of inheriting the altered gene though women are often more likely to experience symptoms.[1]

Why is family genetic testing important?

Knowing if you've inherited the genetic mutation may enable you to make **informed decisions** regarding **lifestyle and medications** with the intent of **preventing attacks** and complications of the disease.[3]

Alicia, AHP Patient and British Porphyria Association Volunteer

AHP: Acute Hepatic Porphyria

Understanding genetic testing

Tests blood or saliva for an AHP gene mutation.[2]

Can help confirm diagnosis or determine the specific type of AHP.[5]

Can help inform you and your family who may be at risk for AHP symptoms.[5]

Who should have a genetic test?

Those at risk of inheriting the AHP mutation from a family member. **Identify who might be at risk in** your family by filling out the **Family Mapping Tool.**

Where can I go to have a genetic test?

If you decide genetic testing is right for you, speak with your healthcare provider about where to have a genetic test.

Support from a genetic counsellor[6]

Genetic counselors can help you understand and make informed decisions on various topics by:

Explaining the genetic basis of AHP.

Helping you understand your family history.

Helping with family planning.

Dispelling rumours and myths.

Finding solutions to individual problems.

Supporting discussions with family members.

AHP: Acute Hepatic Porphyria

Speaking to my family

- Start by saying AHP is real.
- Explain that most people with AHP don't have symptoms, but some experience acute attacks, chronic attacks, and long-term complications.
- Encourage them to be genetically tested so they can make informed decisions.

Veronica, AHP Patient and Advocate, AEP (Asociación Española de Porfiria)

Resources and information

Canadian Association for Porphyria
Association Canadienne de Porphyrie
http://canadianassociationforporphyria.ca/

CORD Canadian Organization for Rare Disorders
https://www.raredisorders.ca/

GPAC GLOBAL PORPHYRIA ADVOCACY COALITION
www.gpac-porphyria.org

You are not alone. There are many sources of information and support, plus ways to connect with other patients and families. These organisations can help.

Visit www.porphyria.ca, Alnylam's sponsored website, to find additional resources for understanding and living with AHP

Developed together with a steering committee consisting of European porphyria patient association leaders, AHP patients, caregivers and health care professionals. Funded by Alnylam.

1. Wang B, Rudnick S, Cengia B, Bonkovsky HL. Acute Hepatic Porphyrias: Review and Recent Progress. Hepatol Commun. 2018;3(2):193-206. Published 2018 Dec 20. doi:10.1002/hep4.1297.

2. Bissell DM & Wang B. J C/,n Transl Hepatol. 2015 Mar,3(1):17-26.

3. Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias [published correction appears in Ann Intern Med. 2005 Aug 16;143(4):316]. Ann Intern Med. 2005;142(6):439-450. doi:10.7326/0003-4819-142-6-200503150-00010.

4. Gouya L, Ventura P, Balwani M, et al. EXPLORE: A Prospective, Multinational, Natural History Study of Patients with Acute Hepatic Porphyria with Recurrent Attacks. Hepatology. 2020;71(5):1546-1558. doi:10.1002/hep.30936.

5. Balwani M, Wang B, Anderson KE, et al. Acute hepatic porphyrias: Recommendations for evaluation and long-term management. Hepatology. 2017;66(4):1314-1322. doi:10.1002/hep.29313.

6. Patch, C., & Middleton, A. (2018). Genetic counselling in the era of genomic medicine. British medical bulletin, 126(1), 27–36. doi:10.1093/bmb/ldy008.

AHP: Acute Hepatic Porphyria