AlnylamAct™

FOR PATIENTS

What Are the Acute Hepatic Porphyrias (Also Known as Acute Porphyrias)?[1-4]

There are four types of acute hepatic porphyria: acute intermittent porphyria (AIP), variegate porphyria (VP), hereditary coproporphyria (HCP), and ALAD-deficient porphyria (ADP). The acute hepatic porphyrias (AHPs) are characterized by acute, potentially life-threatening attacks and chronic debilitating symptoms that negatively impact patients' quality of life. Attacks are commonly characterized by severe abdominal pain, vomiting, nausea, rapid heart rate (tachycardia), and constipation. During an attack, a person may also experience muscle weakness or paralysis, seizures, low sodium levels (hyponatremia), and mental changes such as anxiety, confusion, or hallucinations in severe cases. HCP and VP are classified as acute but can also have symptoms that affect the skin—specifically blistering skin lesions on sun-exposed areas. Skin symptoms can be present with or without attacks.

For more information about the acute hepatic porphyrias, visit the American Porphyria Foundation at **www.porphyriafoundation.org**

What a Positive Genetic Test Result Means for You[3,5]

Gene mutation testing can give several possible results: a positive result, a negative result, or an ambiguous (or uncertain) result called a variant of unknown significance.

A positive test result indicates that a person has inherited a mutation that increases the risk of developing symptoms of one of the AHPs over his/her lifetime. A positive result, however, cannot predict whether someone will have any attacks, a few attacks, or many attacks.

In addition, biochemical testing—specifically testing a person's urine for elevated levels of porphobilinogens (PBG) or aminolevulinic acid (ALA)—may be used to diagnose AIP, HCP, and VP.*

These tests can be performed in a random urine sample and are more accurate when normalized per gram of urine creatinine—a 24-hour collection is not required. Biochemical testing is typically performed when a person is experiencing a suspected attack, since PBG and/or ALA are most elevated at this time.

Genetic and biochemical testing results should always be interpreted in the context of a person's symptoms, medical history, and family history. If genetic testing is positive, you are encouraged to follow up with your health care provider to interpret the results as well as to determine whether other tests, such as biochemical testing, may be indicated.

What a Positive Genetic Test Result Means for Your Family

A positive genetic test result may also have important health and social implications for your family members, as the AHPs are passed down through families.

We have two copies of most genes, one from each parent. AIP, HCP, and VP are all autosomal dominant conditions, meaning a person only needs to inherit one copy of a disease-causing gene mutation, from either parent, to be at risk for developing the condition.** When a person has a disease-causing gene mutation, his/her first-degree relatives, such as children, full siblings, and parents, have a 50% chance to also have the same mutation. Extended family members may also be at increased risk.

A conversation about the AHPs may help your family members identify symptoms sooner, reach an earlier diagnosis, and work with their health care providers to manage their health.

Genetic Counseling

Genetic counseling is a service that provides information and support to people and families who have, or may be at risk for, genetic diseases. Genetic counselors are trained health care professionals who can explain genetic diseases, genes and inheritance, and genetic test results.

Individuals in the U.S. can schedule telephone-based genetic counseling for the AHPs with InformedDNA, the independent genetic counseling provider.

To schedule telephone-based genetic counseling, call **1.888.475.3128** and reference the Alnylam Act™ program.

Note: Callers will also be asked to provide their doctor's name, address, phone, and fax number, as a detailed summary report will be sent directly to him/her following the genetic counseling session.

*Urinary aminolevulinic acid (ALA) is the first-line test for ADP. **ADP is inherited in a different manner than the other acute hepatic porphyrias.

AlnylamAct™ The Alnylam Act™ program was developed to reduce barriers to genetic testing and counseling in order to help people make more informed decisions about their health. While Alnylam provides financial support for this program, all tests and services are performed by independent third parties. At no time does Alnylam receive patient-identifiable information. Alnylam receives contact information for health care providers who use this program. Genetic testing is available in the U.S. and Canada. Genetic counseling is only available in the U.S.

References: 1. Bissell DM, et al. *J Clin Transl Hepatol*. 2015;3(1):17-26. **2.** Bonkovsky, HL et al. *Am J Med*. 2014;127:1233-1241. **3.** Anderson KE, et al. *Ann Intern Med.* 2005;142(6):439-50. **4.** Anderson, et al. In: Proceedings from AASLD 2016;64(1):285A. **5.** Bissell, et al. *N Engl J Med*. 2017;377:862-872.