Understanding Acute Hepatic Porphyria

581A

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International Foundation for Gastrointestinal Disorders (www.iffgd.org)

What is Acute Hepatic Porphyria?

Acute hepatic porphyria (**AHP) is a group** of rare genetic conditions that can cause severe gastrointestinal (GI), neurologic, psychiatric, cardiovascular, and skin symptoms. There are four types of AHP which include:

- acute intermittent porphyria,
- variegate porphyria,
- hereditary coproporphyria, and
- ALAD-deficient porphyria.

It is estimated that 5 in every 100,000 persons have AHP. Most people with AHP start to develop symptoms when they are adults. While AHP can affect anyone, it is more common in women and Caucasians.

People with AHP have a defective gene that leads to problems making heme, which is an important part of hemoglobin. Hemoglobin is a protein in red blood cells that carries oxygen throughout the body. This defect leads to the buildup of toxic chemicals in the body that can damage nerve cells and cause severe symptoms. Sometimes the AHP attacks can be life-threatening. Below are the most common symptoms of AHP, many other symptoms may occur.

Symptoms of AHP

- Severe abdominal pain - Pain that occurs inside the belly area (stomach and intestines)
- Seizures – uncontrolled electrical surges in the brain that can cause sudden and temporary changes in muscles, behaviors, and ability to sense the environment around you
- Hallucinations – experiencing something that is not there, typically through seeing or hearing
- Confusion – being unable to think as quickly or clearly as your normal
- Skin blisters – raised, fluid filled bumps on the skin
- Constipation – having bowel movements (BMs) less often, typically 3 or fewer times per week; the passing of hard pellet-like BMs, difficulty or straining when passing a BM, feeling unable to completely empty, or feeling the need to go but are not able to
- Diarrhea - loose, watery, or frequent bowel movements
- A change in urine color

Patients with AHP can go years without being correctly diagnosed. This delay in diagnosis can lead to unnecessary treatments, surgeries, and stays in the hospital. This is due to AHP being such a rare condition and that symptoms are similar with other more common conditions, such as:

- Irritable Bowel Syndrome (IBS) is a chronic and recurrent disorder of the GI tract usually accompanied by diarrhea, constipation or both.
- Fibromyalgia (FM) is a condition marked by muscle pain all over the body, sleep problems, and fatigue.
- Endometriosis is a painful condition in women where tissue like the lining of the uterus or womb grows on the outside of the organ.

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Signs and Symptoms of Acute Hepatic Porphyria

Acute hepatic porphyria (AHP) can cause a wide range of symptoms and it is different for each patient. Those with AHP can experience gastrointestinal, neurologic, psychiatric, cardiovascular, or skin symptoms. The most common symptom is abdominal pain, which can be very severe and felt throughout the belly. The pain can also last for many hours.

Patients with AHP can have sudden (acute) symptoms that can be life threatening. These symptoms can happen in many different parts of the body and often require a hospital visit. Those with AHP can also experience chronic symptoms. Chronic symptoms are ones that last a long time and may include:

- anxiety
- depression
- fatigue - feeling low energy, overly tired
- nausea - a feeling of sickness felt in the abdomen, stomach, chest, or head with feeling an urge to vomit
- pain - physical discomfort and/or suffering in the body

Gastrointestinal Symptoms of AHP

AHP often affects the GI tract and can cause the symptoms listed below.

- Pain and/or discomfort – physical discomfort and/or suffering in the belly area (stomach and intestines). 85-95% of people with AHP that experience this symptom.
- Nausea – a feeling of sickness felt in the abdomen, stomach, chest, or head with an urge to vomit. 43-88% of people with AHP that experience this symptom.
- Vomiting – bringing food back up from the stomach into the mouth. 43-88% of people with AHP that experience this symptom.
- Constipation – This can mean any or all of these: having bowel movements (BMs) less often, typically 3 or fewer times per week; the passing of hard pellet-like BMs, difficulty or straining when passing a BM, feeling unable to completely empty, or feeling the need to have a bowel movement, but are not able to. 48-84% of people with AHP that experience this symptom.
- Diarrhea – loose, watery, or frequent bowel movements. 5-12% of people with AHP that experience this symptom.

Neurological Symptoms of AHP

AHP also commonly leads to neurologic and psychiatric symptoms. The symptoms are related to the nervous system, including the brain, spinal cord, and nerves of the body. Symptoms that impact the nervous system include:

- Pain in arms, legs, chest, back, neck, or head. 50-70% of people with AHP that experience this symptom.
- Muscle weakness. 42-68% of people with AHP that experience this symptom.
- Mental symptoms like agitation, confusion, depression, hallucinations. 40-58% of people with AHP that experience this symptom.
- Seizures. 10-20% of people with AHP that experience this symptom.

Other symptoms that patients with AHP can experience are fast heart rate, high blood pressure, dark or reddish urine, and skin blisters on areas exposed to sun, among others.

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Diagnosing and Treating Acute Hepatic Porphyria

Acute hepatic porphyria (AHP) is a rare condition with symptoms that are similar with other more common conditions (e.g., irritable bowel syndrome, fibromyalgia, endometriosis). This causes some patients to go many years before the correct diagnosis is made. Irritable bowel syndrome (IBS) is a chronic and recurrent disorder of the GI tract usually accompanied by diarrhea, constipation or both. Fibromyalgia (FM) is a condition marked by muscle pain all over the body, sleep problems, and fatigue. Endometriosis is a painful condition in women where tissue like the lining of the uterus or womb grows on the outside of the organ.

Diagnosing Acute Hepatic Porphyria

Lab tests are needed to properly diagnose AHP. The type of test that should be done depends on whether the person is having symptoms at the time. When a person having symptoms from AHP, a spot urine test for porphobilinogen (PBG), a porphyrin, may be used. This test simply involves urinating in a specimen container, often a small cup. The sample is then tested in the lab for PBG levels. If PBG levels are high, a healthcare provider can tell that a person has AHP. Other tests that may be done include a urine test for aminolevulinic acid (ALA) as well as testing for total porphyrins in the urine, blood, or stool. If someone has severe kidney disease, a blood test for PBG may also be done. This is due to the kidney being unable to properly filter urine.

As AHP is caused by a gene defect, genetic testing can also be used to diagnose the condition. Unlike the urine tests mentioned above, the genetic test can be done when a patient is not experiencing symptoms. Genetic testing is also helpful for diagnosing the condition in family members of those with known AHP. The genetic test looks for problems in 4 different genes and can diagnose the specific type of AHP that one may have (acute intermittent porphyria, variegate porphyria, hereditary coproporphyria, and ALAD-deficient porphyria).

Treating Acute Hepatic Porphyria

When someone with AHP is experiencing an acute attack, treatment with intravenous (IV) hemin in the hospital can help with symptoms. At that time, it is also important to try to identify what may have caused the attack (e.g., infection, medicine, diet changes) so that they can be avoided in the future.

The Food and Drug Administration (FDA) is one of the U.S. government's regulatory agencies. This agency oversees a broad range of topics that pertain to food, drugs and other products used daily.

The FDA works to protect public health by assuring that foods and drugs for humans and animals are safe and properly labeled. The FDA also ensures that vaccines, other biological products, and medical devices intended for human use are safe and effective.

Products approved by the FDA have been deemed safe, with benefits that are worth the possible risks. This is done after reviewing studies and tests that have been done on a product.

A drug called Givosiran (Givalaari®) was approved by the U.S. Food and Drug Administration in 2019 for the treatment of adults with AHP. It is a medicine that is injected under the skin once a month. In clinical trials, patients on givosiran had fewer acute attacks from AHP when compared to those given a placebo. A placebo is a pill or treatment with no active ingredients. While taking givosiran, patients should have their liver and kidney tests monitored by their healthcare team. For patients with AHP who suffer from repeated severe attacks, do not respond to IV hemin or givosiran, or have a very poor quality of life, liver transplantation can be considered as a last resort.

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Triggers for Acute Attacks in Acute Hepatic Porphyria

Patients with acute hepatic porphyria (AHP) can have sudden (acute) symptoms that are severe and require them to go to the hospital. At times, these acute attacks can be triggered by stress, medications (drugs), diet, and environmental factors, among others. Avoiding or reducing exposure to known triggers is an important way to prevent acute AHP attacks. However, some people experiencing an attack may not know what caused the attack to happen.

Drugs can be triggers for some patients with AHP. Some examples of drugs that should be avoided when possible include carbamazepine, danazol, diclofenac, estrogens, metoclopramide, phenytoin, progesterone, rifampin, sulfonamide antibiotics, and valproic acid, among many others. A full list of safe and unsafe medicines for AHP can be found at the American Porphyria Foundation Drug Database (https://porphyriafoundation.org/drugdatabase/).

Crash dieting can also trigger acute attacks and should be avoided in those with AHP. Patients with AHP can also consider working with a dietician for help identifying foods that may be causing attacks. Alcohol, tobacco, marijuana, and recreational drugs also may lead to sudden symptoms in AHP and should be avoided.

IFFGD's **Dietitian Listing** is a resource that allows you to search for a dietitian that is in your area or treats a specific condition.

Any infection in the body, including common ones like urinary tract infections and pneumonias, can trigger acute attacks. When a person with AHP is experiencing an acute attack and is found to have an infection, both the AHP and infection should be treated at the same time. Also, those with AHP should receive all appropriate vaccinations that prevent infections, such as the flu, pneumonia, and recombinant shingles vaccines.

Any stress to the body such as surgery or physical/emotional exhaustion can also trigger acute AHP attacks. For women with AHP, some may experience frequent attacks during their menstrual cycle. As the menstrual cycle can be a trigger, some types of contraceptives (birth control) can help in preventing attacks. Common types include low-dose estradiols or low-dose estrogen-progestins which are available under many brand and generic names.

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What are Acute Hepatic Porphyria and Cutaneous Porphyria?

Porphyrias are a group of conditions where the body has problems making heme, which is an important part of hemoglobin. Hemoglobin is a protein in red blood cells that carries oxygen throughout the body. The two main classes of porphyrias are Acute Hepatic Porphyria (AHP) and cutaneous porphyria.

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Cutaneous porphyrias cause skin symptoms including sensitivity to sunlight, blisters on exposed skin (e.g., hands, arms, face), sudden painful redness and swelling, and itching, among others. The most common cutaneous porphyria is porphyria cutanea tarda (PCT). It is estimated that up to 20 in every 100,000 persons have PCT.

What Causes Acute Hepatic Porphyria and Cutaneous Porphyria?

Acute Hepatic Porphyria (AHP) runs in families and can be inherited. In this case, those with AHP have a defective gene for a protein involved in making heme. Those with porphyria cutanea tarda (PCT) often came in contact with an outside factor during their lives that made a protein in the heme pathway to not work as efficiently. Examples of these factors include alcohol use, smoking, infection with hepatitis C virus or HIV. For both AHP and PCT, these defective proteins lead to buildup of toxic chemicals in the body that cause symptoms. In order for hemoglobin to bind to toxic chemicals, such as carbon dioxide, and take them to the lungs to be filtered out of the body.

What Symptoms Do Those with Acute Hepatic Porphyria and Cutaneous Porphyria Experience?

People with AHP can experience severe attacks of gastrointestinal, neurologic, psychiatric, cardiovascular, and skin symptoms. These attacks can be life threatening and need urgent treatment in the hospital. In between episodes, those with AHP can also experience chronic pain and may later develop liver damage and kidney failure. On the other hand, those with PCT get skin blisters that can lead to permanent skin damage or become infected. Even after the skin heals, it can scar, become fragile, or become discolored.

How are Acute Hepatic Porphyria and Cutaneous Porphyria Diagnosed?

AHP is generally diagnosed through a spot urine porphobilinogen (PBG) test during an acute attack. AHP can also be diagnosed with a genetic test, even when they are not having symptoms. PCT is typically diagnosed by measuring total porphyrins in the blood or urine.

How are Acute Hepatic Porphyria and Cutaneous Porphyria Treated?

For those with AHP, symptoms during an acute attack are usually treated with IV hemin in the hospital. To help prevent attacks, a once-monthly, self-injectable medicine called givosiran (Givalaari®) can be used. For patients with PCT and active skin lesions, either phlebotomy to reduce the body's iron levels or a drug, hydroxychloroquine, can be used. Phlebotomy involves safely removing blood from the body with an IV needle, typically placed inside the elbow or on the back of the hand. To help prevent future skin lesions, patients should avoid sun, alcohol, smoking, excess iron intake, and estrogens as well as treat hepatitis C virus or HIV when present.

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About IFFGD

The International Foundation for Gastrointestinal Disorders (IFFGD) is a 501(c)(3) nonprofit education and research organization. We work to promote awareness, scientific advancement, and improved care for people affected by chronic digestive conditions. Our mission is to inform, assist, and support people affected by gastrointestinal disorders. Founded in 1991, we rely on donors to carry out our mission. Visit our website at: www.iffgd.org.

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About the Publication

This Fact Sheet is being provided in part, by Alnylam and donors of IFFGD.