Living with

Acute Intermittent Porphyria (AIP)

This brochure will help you understand what **AIP** is, how it affects your body, and how you can help manage your condition.

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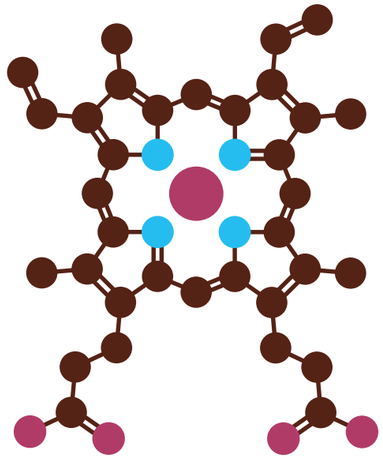
What is **AIP**?

AIP is caused by the partial lack of an **enzyme** in the body called **porphobilinogen deaminase (PBGD)**. Enzymes are proteins that carry out chemical reactions in the body. PBGD helps to make heme, which is a molecule that carries oxygen through the bloodstream and throughout the body. The production of heme involves a number of steps. If your body does not have enough PBGD activity, this process is interrupted and heme production gets backed up. This can cause other molecules to build up that are harmful to the body. And when that happens, symptoms of AIP may occur. These are called **AIP attacks**. Symptoms are **intermittent**, meaning they may occur for a set period of time, then go away – only to return later.

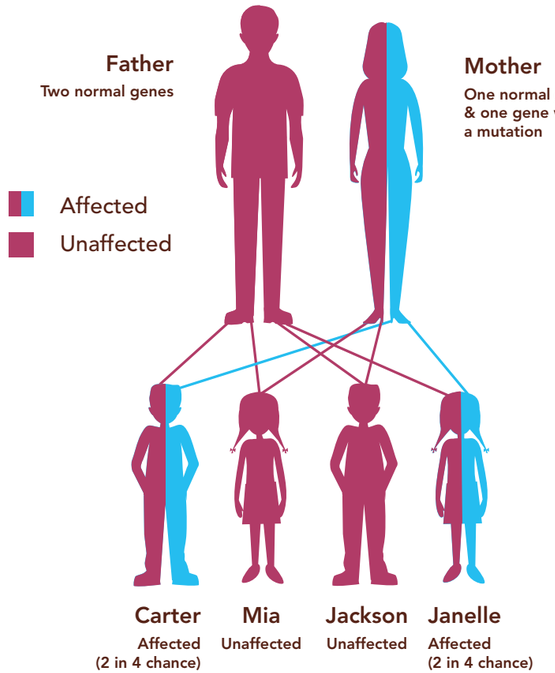


Heme molecule

How does someone get **AIP**?

AIP is a genetic disorder, which is another way of saying that the condition is inherited from one or both parents. If you have AIP, you inherited a hydroxymethylbilane synthase *(HMBS)* gene with a porphyria-causing mutation from one parent and an *HMBS* gene with no mutations from the other parent. The medical term for this kind of inheritance is **autosomal dominant**. Very rarely, someone has an *HMBS* gene mutation and neither parent does.

The job of the *HMBS* gene is to make an enzyme known as hydroxymethylbilane synthase (HMBS). Another name for this enzyme is porphobilinogen deaminase (PBGD).



- In the family shown in the diagram, the father has two normal *HMBS* genes, and the mother has one normal *HMBS* gene and one gene with a mutation. She may or may not have symptoms.
- Each child in the family has a 50% chance of inheriting the gene with a mutation from their mother.
- In this family, Carter and Janelle inherited a gene with a mutation from their mother.
- Individuals with an *HMBS* gene mutation can pass it on to the next generation.

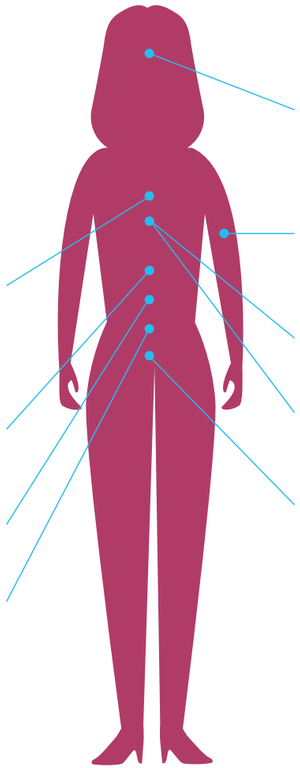
However, even if you inherit a gene mutation, you may not have symptoms of AIP. In fact, **most people with a gene mutation never have symptoms.** And if you do have a gene mutation, it is not possible to predict whether or not you will ever have symptoms, or how severe those symptoms may be.

Doctors may use these terms:

- **Overt AIP:** Someone who currently has symptoms or has had symptoms in the past
- **Latent AIP:** Someone who has never had symptoms but who is at risk for developing symptoms because they have a porphyria-causing mutation in the *HMBS* gene.

What symptoms may be caused by **AIP**?

It's important that you become familiar with symptoms of an AIP attack and that you call your doctor right away if you begin to have symptoms. If not treated right away, AIP attacks can cause serious, long-term health problems or in rare cases be life-threatening. Common symptoms of AIP attacks may include:



Mental health symptoms, such as feeling anxious, restless, or confused

Muscle weakness that usually begins in the arms and often in the shoulders

Fast heart rate

High blood pressure

Dark or reddish urine after the urine has been exposed to air and light

Pain in the arms, legs, chest, neck, or head; the pain may start in the chest or back and move to the abdomen

Nausea or vomiting, commonly along with abdominal pain

Severe pain in the abdomen

Constipation, possibly along with loss of bladder control

Warning symptoms

Some people also have symptoms that occur hours or even a few days before an AIP attack. These warning symptoms may include:

- Pain that is not abdominal pain
- "Brain fog" or feeling mentally cloudy, confused, or unfocused
- Irritability
- Extreme tiredness
- Anxiety and/or agitation
- Headache
- Insomnia or trouble sleeping

Keep a log of your warning symptoms and consider contacting your doctor if you are anticipating an AIP attack.

Chronic symptoms

Some people may have chronic symptoms between AIP attacks, or symptoms that happen occasionally or as often as every day. These symptoms are generally less severe than those that occur during AIP attacks, with pain described as soreness, dullness, aching, throbbing, or burning. Chronic symptoms may include:

- Pain in the abdomen or other parts of the body
- Symptoms involving mental health or mood, such as tiredness, trouble sleeping, and anxiety
- Gastrointestinal (GI) symptoms such as nausea
- Tingling, numbness, or loss of feeling
- Muscle pain

What is unique about the symptoms of **AIP** attacks?

The symptoms that occur during AIP attacks are common in many other diseases. This is one reason why AIP may be misdiagnosed. But there are certain things that may increase suspicion of AIP:

- Pain may be spread throughout the body rather than in focused areas.
- The pain tends to begin gradually and become worse, and it may last for hours or days.
- Pain medicines such as ibuprofen or acetaminophen usually don't help much to relieve the pain caused by AIP attacks. This is because the pain is **neuropathic**, meaning it is caused by nerves.
- You may have one or more symptoms during an AIP attack, but you may not have all of the symptoms that are common during attacks.
- Symptoms of AIP can come and go, and each new attack may be similar to or different from previous attacks.
- Symptoms are often caused by triggers, such as taking certain medicines or dieting to lose weight.

The pain caused by AIP attacks has been described by some people living with AIP as the worst imaginable level of pain:

- **"It's like digesting huge, hot rocks with bone-crushing pain." – L.C.V.**
- **"My insides feel like they're on fire!" – N.T.M.**

What situations may trigger **AIP** attacks?

People with an AIP-causing gene mutation have about half the normal amount of PBGD enzyme activity in their bodies. This is usually enough to produce the amount of heme that the body needs. But certain situations may add stress to this process, causing heme production to get backed up and an attack to become more likely. These situations, or triggers, may include:

- Monthly hormone fluctuations; symptoms are more common during the two weeks before a menstrual period starts
- Weight loss, fasting, or being on a low-carbohydrate diet or ketogenic (keto) diet
- Taking certain medicines, including some types of oral contraceptives, steroids, sedatives, antibiotics, and anti-seizure drugs
- Starting new medicines
- Smoking cigarettes
- Drinking alcohol
- Using illegal drugs
- Stress on the body caused by infections, illness, or surgery

AIP attacks are usually due to several triggers occurring at the same time.

If you have an AIP attack

If you have an AIP attack, you should call your doctor right away. This is very important because if AIP attacks are not treated promptly, they may progress to the point where they cause irreversible nerve damage or even death.

How is **AIP** diagnosed?

It's very important to get properly tested for AIP. Your doctor can order a series of tests to determine whether or not you have AIP:

- **Porphobilinogen (PBG) urine test** – If your doctor suspects AIP, your first test will be a PBG urine test. PBG is one type of molecule that builds up when heme production is disrupted during an AIP attack. During an AIP attack, the level of PBG in urine is much higher than normal. A PBG urine test must be done at or near the time of symptoms to capture a higher PBG level.
- **Follow-up tests** – If the PBG level in your urine is high, more lab tests will show whether you have AIP or another type of acute porphyria.
- **Genetic test** – A DNA test done by a laboratory with specific expertise can identify whether you have a gene that may cause AIP.

Getting an accurate diagnosis is the first step toward managing your attacks of AIP, which is vital for your health.

If a DNA test indicates that you have an *HMBS* gene mutation, your relatives may also want to learn if they have a gene mutation and are at risk of developing symptoms.

What heathcare providers may be involved in your care?

Many people with AIP see a local hematologist who manages their care. A hematologist is a doctor who specializes in diseases of the blood.

It's very important to establish **good relationships with the doctor who is treating your AIP and with nurses and other staff who may be involved in your care.** Mutual trust and respect are important in these relationships. Ideally, you should be in an environment where you are encouraged to ask questions and discuss your treatment.

The American Porphyria Foundation (APF) keeps a list of **porphyria experts** who are experienced in diagnosing and treating porphyrias, including AIP. You can contact the APF to find an expert in your area. Ideally, a doctor who is knowledgeable about AIP will be involved in diagnosing your condition and overseeing your care.

What treatments may be helpful for **AIP** attacks?

Your doctor will determine the best course of treatment. The goal is to reduce the build-up of harmful chemicals and restore balance to the process of heme production.

PANHEMATIN® (hemin for injection)

For a **mild attack**, your doctor will first consider trying carbohydrates in the form of glucose. If your doctor suspects or confirms this therapy is not working, he or she may start PANHEMATIN therapy. For a **moderate to severe attack**, your doctor may begin PANHEMATIN treatment right away. The faster the treatment is started, the better the outcome. Both glucose and PANHEMATIN are given through IV infusions. Infusions can be done on an inpatient basis at a hospital or on an outpatient basis at an infusion center or doctor's office. Your doctor can contact the pharmacist at his or her facility to order PANHEMATIN.

Other Therapies

Your doctor may also prescribe other therapies to:

- Correct any electrolyte imbalances (electrolytes are certain salts and minerals that control the balance of fluids in your body)
- Reduce pain
- Prevent other symptoms

If you have recurrent attacks before menstrual periods, your doctor may recommend a medicine to reduce the production of certain hormones.

Panhematin® (hemin for injection) Indications and Usage

PANHEMATIN is a hemin for injection prescription medication used to relieve repeated attacks of acute intermittent porphyria related to the menstrual cycle in affected women, after initial carbohydrate therapy is known or suspected to be inadequate.

Limitations of Use

- Before giving PANHEMATIN, consider an appropriate trial of carbohydrates [i.e., 400 grams of glucose (a carbohydrate or sugar) per day for 1 to 2 days].
- Attacks of porphyria may progress to a point where irreversible nerve damage has occurred. PANHEMATIN therapy is intended to prevent an attack from reaching the critical stage of nerve breakdown. PANHEMATIN is not effective in repairing nerve damage that has already occurred.

Important Safety Information

- PANHEMATIN is not for patients known to be allergic to this drug.
- Vein inflammation is possible. Use a large arm vein or a central line to administer PANHEMATIN to minimize the possibility of vein inflammation.
- Elevated iron levels may occur. Your doctor must monitor your iron levels if you receive multiple courses of PANHEMATIN.
- PANHEMATIN has a passing and mild blood thinning effect. Avoid blood thinners during PANHEMATIN therapy.
- Reversible kidney shutdown has occurred when too high a dose of PANHEMATIN was given in a single dose.
- PANHEMATIN may carry a risk of transmitting agents that can cause infections, such as viruses, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.
- Most common side effects are headache, fever, infusion site reactions, and vein inflammation.
- **To report SUSPECTED SIDE EFFECTS, contact Recordati Rare Diseases Inc. at 1-888-575-8344, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**
- When taking PANHEMATIN, do not take drugs such as estrogens (e.g., oral contraceptives), barbiturates (drugs that help with sleep and used to treat epilepsy) or steroids (body hormone-like drugs), because such drugs can trigger an attack or make an attack worse.

Please click here to see full Prescribing Information or go to www.PANHEMATIN.com

How can you meet the challenges caused by **AIP**?

If you have overt AIP, there are many things you can do on your own and with others to stay healthy and prepare for the challenges caused by AIP.

Your doctor can help you develop two different plans: an everyday plan and an emergency plan.

Develop an everyday plan

The goal of your everyday plan will be to stay healthy and prevent AIP attacks from developing. Your plan may include:

- **Identifying and avoiding AIP triggers** – substances and situations that may trigger an attack, and **keeping a log** of your attacks and what may have triggered them.
- **Exercising moderately and eating a healthy, well-balanced diet,** avoiding low-carbohydrate diets.
- **Talking to your family and friends** about your AIP. The more they know about AIP, the more they can understand what you are going through and support you.
- **Developing a list of friends and neighbors** to call when you need extra help. And when you need help, being specific about what you need, such as taking you to the doctor, caring for your pet, or bringing in your mail.
- Finding **additional information and support** through the American Porphyria Foundation.
- **Encouraging family members** to talk to their doctors about **getting tested for AIP** and finding out if they are at risk for having AIP attacks.

Develop an emergency plan

The goal of your emergency plan will be to get prompt treatment when you have an AIP attack. Having a plan in place will help ensure that you get the care you need when you need it.

Here are some questions to ask your doctor when developing your emergency plan:

- Whom should I call if I have an AIP attack? Do I have a phone number to contact my doctor?
- What should I do if my doctor is not available?
- Where should I go – hospital, infusion center, or doctor's office – if I have an attack?
- Do I have a friend or family member who will take me to the facility?
- How should I prepare myself for an attack when I'm out of town? Are there hospitals in the area with doctors who treat AIP?
- What should I do if I have warning symptoms that may lead to an attack?

Also ask your doctor to write a **"Dear doctor" letter** that explains your diagnosis and provides instructions on what to do if you have an AIP attack. Include contact information for your doctor or other support resources in the letter. You should carry the letter with you at all times so that you can give it to healthcare providers who may not be familiar with AIP attacks or their treatment.

Where can you find more information and support?

American Porphyria Foundation

www.porphyriafoundation.org
1-866-APF-3635 (273-3635)
info@porphyriafoundation.org

The mission of the American Porphyria Foundation (APF) is to improve the health and well-being of individuals and families affected by all types of porphyria, including AIP. The APF focuses on education, advocacy, support services, and research for the prevention, treatment, and cure of the porphyrias.

United Porphyrias Association

www.porphyria.org
1-800-868-1292
info@porphyria.org

The United Porphyrias Association is committed to improving the quality of life of the porphyria patient community and is relentlessly focused on advancing disease awareness, research, and therapies in all the porphyrias.

The Porphyrias Consortium

www1.rarediseasesnetwork.org/cms/porphyrias

The Porphyrias Consortium, part of the Rare Diseases Clinical Research Network founded by the NIH, benefits patients and physicians by enabling a large-scale collaborative effort to develop new strategies and methods for diagnosis, treatment, and prevention of illness and disability resulting from these rare disorders.

www.recordatirarediseases.com/us PP-PHT-US-0210v3