

# Acute Hepatic Porphyria

**Learn to recognize & test for a  
family of undiagnosed and  
potentially life-threatening, rare,  
genetic diseases**

*Intended for US Healthcare Professionals only.  
Developed and funded by Alnylam Pharmaceuticals.*



**~15 years can elapse from  
symptom onset to proper  
diagnosis<sup>1</sup>**

# What is Acute Hepatic Porphyria?

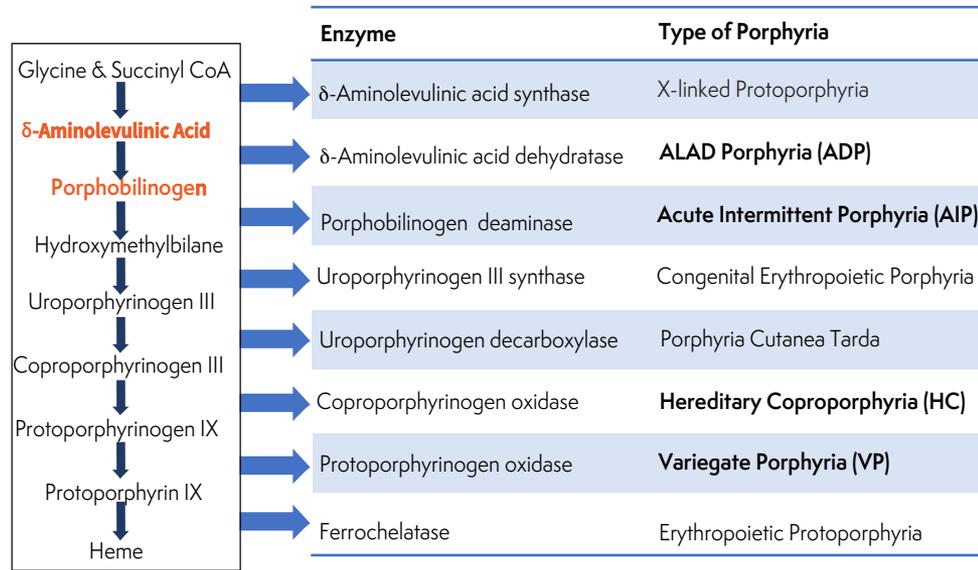
Porphyria is a group of disorders arising from a defect in one of the eight steps involved in the biosynthesis of heme in the liver or bone marrow. Acute Hepatic Porphyria (AHP) is comprised of four genetic subtypes (**bolded below**) manifesting in the liver.<sup>2</sup>

These defects may lead to the accumulation of neurotoxic intermediates, aminolevulinic acid (ALA) and porphobilinogen (PBG), causing disease manifestations of AHP.<sup>2,4</sup>

AHP is characterized by acute, potentially life-threatening neurovisceral attacks and chronic debilitating symptoms that can negatively impact patients quality of life.<sup>7,8</sup>



## Heme Biosynthesis Pathway<sup>3</sup>



Adapted from Ramanujam et al. *Porphyria Diagnostics-Part 1: A Brief Overview of the Porphyrias*. 2015.

# Abdominal Pain is the Most Common Attack Symptom of AHP

In the EXPLORE natural history study on patients (n=112) with recurrent attacks\*, pain associated with AHP attacks was most commonly found in the abdomen (92% of patients) but also occurred in the extremities (77%), back (72%), muscles (66%), and head (51%).<sup>9</sup>

## Patients in EXPLORE also reported chronic symptoms<sup>9</sup>



CHRONIC SYMPTOMS

such as:

- pain
- tiredness
- anxiety
- nausea



DAILY SYMPTOMS

## Diverse Clinical Characteristics and Associated Conditions Potentially Experienced

### CNS Manifestations<sup>9-12</sup>

- Confusion
- Anxiety
- Memory loss
- Depression
- Tiredness
- Hallucinations\*
- Seizures\*

### PNS Manifestations<sup>10,11</sup>

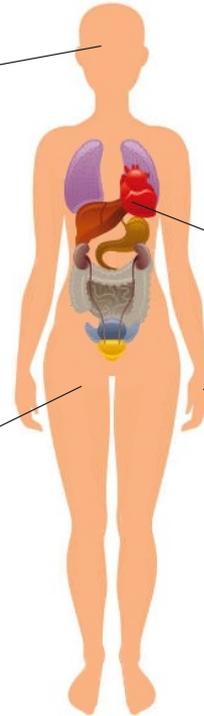
- Neuropathic pain
- Sensory loss
- Muscle weakness
- Paralysis\*
- Respiratory failure\*

### ANS Manifestations<sup>9-12</sup>

- Severe pain in the abdomen, chest, or back
- Hypertension
- Tachycardia
- Nausea and vomiting
- Constipation
- Hyponatremia

### Cutaneous Manifestations<sup>11,12</sup>

- Lesions on sun-exposed skin



\*≥3 porphyria attacks within the past 12 months or were receiving prophylactic treatments

# Potential Long-term Complications

AHP has been identified as a risk factor for **primary liver cancer**, especially hepatocellular carcinoma.<sup>13</sup>



In a population based study, the annual incidence of primary liver cancer was 0.35% (or 108-fold higher risk) in individuals with AHP compared with 0.003% in the reference population.<sup>14</sup>



Patients with AHP may have an increased risk of chronic sustained hypertension.<sup>2,15,16</sup> As the risk of hypertension is high in the general population, further research is required to detect the true excess risk in patients with AHP.<sup>16</sup>



Studies have found high levels of **chronic kidney disease** in patients with AHP<sup>14</sup>. 59% of patients with symptomatic AHP have been observed to have chronic kidney disease (eGFR <60 mL/min/ 1.73 m<sup>2</sup>).<sup>17</sup>



Patients with AHP can develop chronic pain associated with axonal motor polyneuropathy.<sup>2</sup> Chronic pain symptoms can lead to severe depression and anxiety, which may necessitate psychiatric care.<sup>8</sup> Suicidality has also been observed in patients with AHP.<sup>18,19</sup> Permanent quadriplegia may rarely occur as a result of severe attacks.<sup>20</sup>

# Recognizing and Testing for AHP

**Clinical presentation of AHP can be broad and multisystemic, but is frequently characterized by:**

**Severe, diffuse abdominal pain<sup>9,21</sup>**

+  
1 or more of the following

<b>AUTONOMIC</b> Nervous System <sup>8,11</sup>	<b>CENTRAL</b> Nervous System <sup>8,9</sup>	<b>PERIPHERAL</b> Nervous System <sup>8,21</sup>
Nausea/vomiting Constipation Tachycardia Systemic arterial hypertension	Seizures Anxiety Mental status changes	Limb weakness or pain Peripheral neuropathy
<b>CUTANEOUS<sup>8,11</sup></b>	<b>OTHER</b> Common AHP System <sup>8,11</sup>	
Skin lesions on sun-exposed areas (Cutaneous symptoms primarily in HCP and VP)*	Hyponatremia Dark, reddish urine	

**Biochemical and genetic testing are used to help diagnose AHP**

- Substantial elevations of urinary PBG is a hallmark indicator of the 3 most common types of AHP.<sup>4,22</sup>
- ALA may also be substantially elevated in all subtypes of AHP attacks.<sup>4,22</sup>
- Urine porphyrins may assist with identifying subtypes of AHP but are non specific and should not be used alone to diagnose.<sup>4,22</sup>

Genetic testing can help identify the genetic mutation involved. Due to low disease penetrance in AHP, most people with a mutation for AHP will not develop clinical symptoms of the disease.<sup>22</sup>

<b>Randon Urine Test</b>	<b>Porphobilinogen (PGB)</b>	<b>Delta Aminolevulinic Acid (ALA)</b>	<b>Porphyrins</b>
<b>CPT Code</b>	<b>84110</b>	<b>82135</b>	<b>84120</b>

Tests are more accurate when normalized per gram of urine creatinine and when sample is collected during acute episodes. A 24 hour collection is not required.<sup>23</sup> Please refer to your local lab's specific requirements.

This testing information is provided for educational and reference purposes only. It is not intended to replace the independent medical judgement of any healthcare professional.

# Management and Treatment of AHP Attacks and Symptoms

## Medications to Treat Symptoms<sup>7</sup>

Used to treat and reduce AHP symptoms like nausea, constipation, tachycardia (fast heartbeat) and seizures

## Trigger Avoidance<sup>21</sup>

Caution used with certain foods, drugs, and behaviors that may increase the risk of AHP attacks

## Hemin<sup>7</sup>

Used for the treatment of AHP attacks

## Hormone Therapy (GnRH analogs)<sup>2,21</sup>

Used for patients experiencing AHP attacks related to their menstrual cycles

## Medications to Treat Pain<sup>2</sup>

Used to manage painful AHP symptoms

## Glucose and Carbohydrate Loading<sup>2,12</sup>

Used for the treatment of AHP attacks

## RNA Interference Therapy<sup>21</sup>

Used for the treatment of AHP attacks

## Liver Transplantation<sup>6,21</sup>

Used rarely in severe cases where other approaches have been unsuccessful

# Abbreviations and References

## Abbreviations

AHP, acute hepatic porphyria; GnRH, gonadotropin-releasing hormone

## References

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