Acute Hepatic Porphyria

Acute hepatic porphyria (AHP) refers to a family of ultra-rare, genetic diseases characterized by potentially life-threatening attacks and, for some patients, chronic manifestations that negatively impact daily functioning and quality of life.\(^1,4,7\)

**AHP is comprised of four types,** each associated with distinct enzyme defects in the heme biosynthesis pathway in the liver:\(^1,3,7\)

- Acute intermittent porphyria (AIP)
- Hereditary coproporphyria (HCP)
- Variegate porphyria (VP)
- ALA dehydratase-deficiency porphyria (ADP)

In the United States and Europe,

- **\(\sim 5,000\)** people experience one or more attacks annually\(^2,18\)
- **\(\sim 1,000\)** people suffer frequent and severe attacks, requiring multiple hospitalizations each year\(^1,2,18\)

Due to the debilitating attacks and chronic symptoms of AHP, attack prevention is an important part of disease management.

**AHP Symptoms Significantly Impact Quality of Life**

- Severe, diffuse abdominal pain, vomiting/nausea, dark/reddish urine\(^8,13,14\)
- Confusion, anxiety, seizures, hallucinations, fatigue\(^1,4,5\)
- Muscle weakness, numbness, respiratory failure\(^4,5\)
- Blistering lesions, erosions or ulcers of sun-exposed skin (with VP and HCP)\(^1,13,14,15\)

AHP is an ultra-rare disease disproportionately impacting female patients of working and childbearing age. Symptoms of AHP vary widely and usually first occur between the ages of **18-45**.\(^3\)

**Misdiagnosis of AHP is Common**

The nonspecific nature of AHP signs and symptoms can often lead to **misdiagnoses of other more common conditions**, such as viral gastroenteritis, Irritable Bowel Syndrome (IBS), and addiction withdrawal.

Patients afflicted with AHP are often misdiagnosed or remain undiagnosed for up to **15 years**.\(^8,13,12,19,22\)

During attacks, delays in diagnosis can result in a higher burden of disease, which may include **unnecessary surgeries, medical complications, and paralysis**.

AHP has been associated with long-term complications and comorbidities such as **hypertension, chronic kidney disease or liver disease, including hepatocellular carcinoma (liver cancer)**.\(^5,6,8,10\)
In people with the genetic defect for AHP, one of the enzymes in the pathway that creates heme is deficient. Certain triggers can impact the pathway and can cause an increase of ALAS1 (aminolevulinic acid synthase 1).1,3,7

In patients with AHP, this increase in ALAS1 results in the buildup of neurotoxic intermediates – aminolevulinic acid (ALA) and porphobilinogen (PBG) – throughout the body.8,16,17

ALA and PBG are harmful to nerve cells and are factors associated with the attacks and disease manifestations characteristic of AHP.8,16,17,20,21

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