Acute Hepatic Porphyrias

Rare Genetic Diseases with Limited Treatment Options

Acute hepatic porphyrias (AHPs) are a family of rare, genetic diseases characterized by potentially life-threatening attacks and, for many patients, chronic debilitating symptoms that negatively impact daily functioning and quality of life.

AHPs are comprised of four subtypes, each resulting from a genetic defect leading to deficiency in one of the enzymes of the heme biosynthesis pathway in the liver:

Acute intermittent porphyria **(AIP)**

Hereditary coproporphyria **(HCP)**

Variegate porphyria **(VP)**

ALA dehydratase-deficiency porphyrias **(ADP)**[1,2]

In the United States and Europe,

~5,000 people experience one or more attacks annually

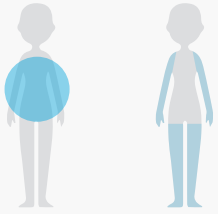
~1,000 people suffer frequent and severe attacks, requiring multiple hospitalizations each year[3]

Currently, there are no treatments approved to prevent debilitating attacks and treat the chronic symptoms of the disease.

Common Symptoms Significantly Impact Quality of Life

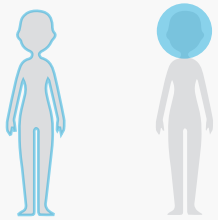
Symptoms of AHPs vary widely and usually first occur in the **prime of patients' lives** between the ages of **20 and 30**.

Severe, diffuse abdominal pain, nausea, dark/reddish urine



Weakness, numbness, respiratory failure

Lesions on sun-exposed skin; chronic/blistering (with VP and HCP)



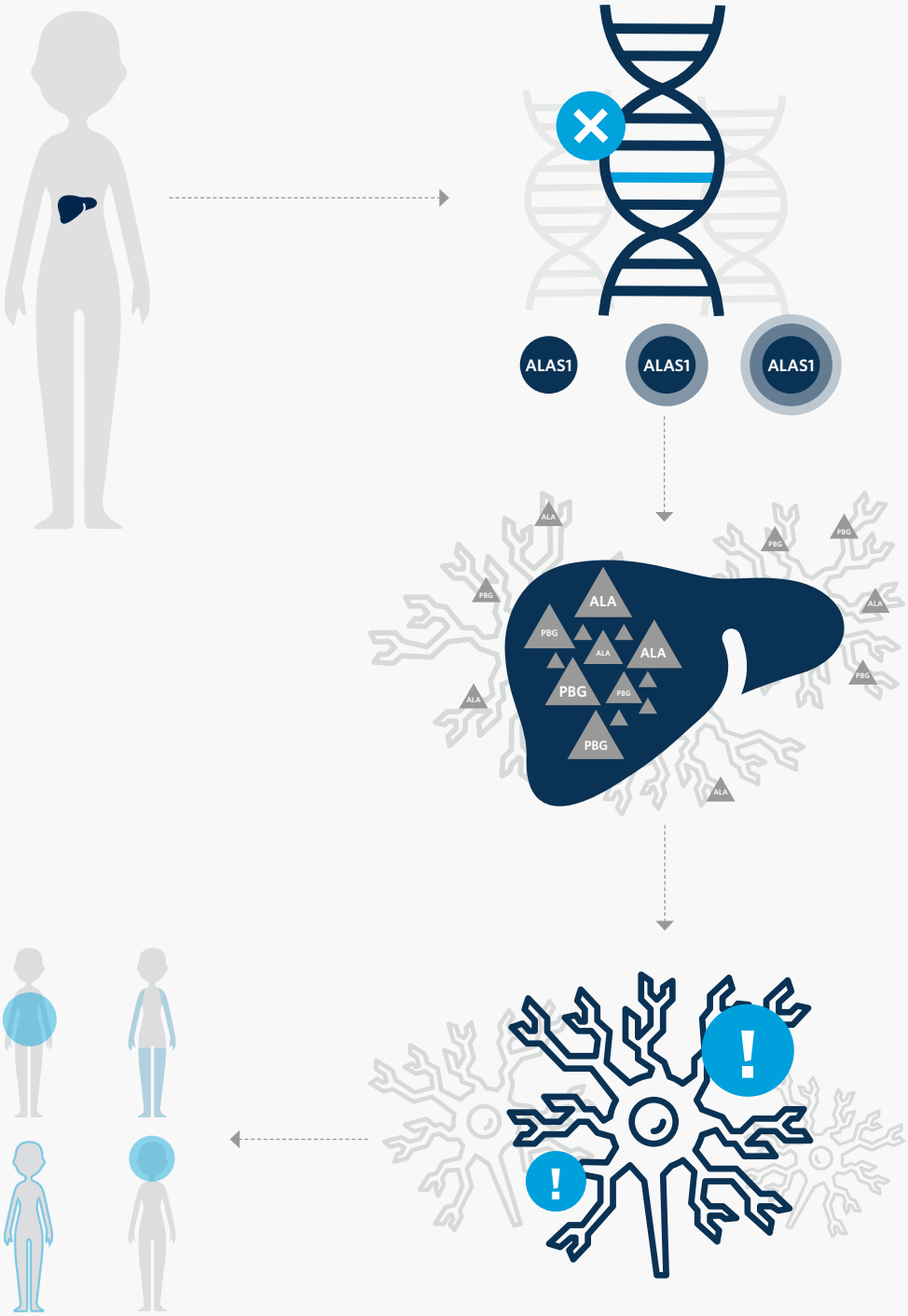
Confusion, anxiety, seizures, hallucinations, fatigue

Misdiagnosis of AHPs is Common

The symptoms of AHPs can often resemble those of other more common conditions such as irritable bowel syndrome (IBS), appendicitis, fibromyalgia, and endometriosis, and consequently, patients afflicted with AHPs are often misdiagnosed or remain undiagnosed for up to **15 years.**

These delays in diagnosis may lead to **unnecessary surgeries** and increased disease burden such as **paralysis, hypertension, chronic kidney disease, or hepatocellular carcinoma (liver cancer).**

Underlying Cause



In people with the genetic defect for AHPs, 1 of the 8 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).

This increase in ALAS1 results in the buildup of neurotoxic intermediates – aminolevulinic acid (ALA) and porphobilinogen (PBG) – throughout the body.

ALA and PBG are harmful to nerve cells and thought to cause the attacks and chronic symptoms characteristic of AHPs.

1. Bissell, Wang. *J Clin Trans Hepat*. 2015;3(1):17-26.
2. Puy, Hervé et al. *Lancet*. 2010;375:924-937.
3. Anderson, Bloomer et al. *Ann Intern Med*. 2005;142(6):439-450.