IS IT ACUTE HEPATIC PORPHYRIA (AHP)?

DETECT

Signs and symptoms of AHP* include[1-3]:

SEVERE, DIFFUSE ABDOMINAL PAIN

+

1 OR MORE OF THE FOLLOWING

PERIPHERAL Nervous System	CENTRAL Nervous System	AUTONOMIC Nervous System	CUTANEOUS†
• Limb weakness or pain	• Anxiety • Confusion • Depression • Insomnia	• Nausea • Vomiting	• Skin lesions on sun-exposed areas

92%

of patients with an AHP report abdominal pain

(mimics an acute abdomen but without specific localization)[3,5]

32% of patients with AHP report hyponatraemia[9]

*There are 4 AHP subtypes. About 80% of cases are acute intermittent porphyria (AIP), followed by hereditary coproporphyria (HCP), variegate porphyria (VP), and the extremely rare ALA dehydratase-deficiency porphyria (ADP).[1-4]

†Cutaneous symptoms occur only in HCP and VP. [1-3]

SUSPECT

Nonspecific symptoms can lead to misdiagnoses

- ✗ Irritable bowel syndrome
- ✗ Inflammatory bowel disease
- ✗ Endometriosis
- ✗ Fibromyalgia
- ✗ Psychiatric disorder

- ✓ AHPs

SELECT

Confirm suspicion by running simple spot urine tests[1-3]

- ✓ **PBG** (porphobilinogen)‡
- ✓ **ALA** (delta-aminolevulinic acid)‡
- ✓ **Porphyrins** Urine porphyrins is a nonspecific test and should not be used alone to diagnose AHPs§

‡PBG and ALA are porphyrin precursors that occur naturally in the haem biosynthesis pathway in the liver but reach neurotoxic levels in patients with a symptomatic AHP.[1,2]

§Porphyrin analyses may differentiate the specific AHP.[1]

Alnylam® PHARMACEUTICALS

Acute Hepatic Porphyria (AHP)

Elevated ALA and PBG may EXPLAIN the PAIN

A family of rare, genetic diseases

AHP features acute, potentially life-threatening attacks and, for some patients, chronic, debilitating symptoms. It may inflict years of suffering and impaired quality of life.[1-3,5]

AHP is driven by one of several enzyme defects in the haem biosynthesis pathway in the liver. These defects induce compensatory overexpression of ALA synthase 1 (ALAS1), resulting in neurotoxic accumulations of ALA and PBG and leading to disease manifestations.[1,3]

The neurotoxic burden of ALA and PBG

ALA and PBG are normal precursors of porphyrin synthesis, but they are also neurotoxic in high concentrations.[1]

ALA is believed to be the primary neurotoxin responsible for the triad of chronic symptoms, acute attacks, and long-term disease complications. Although less neurotoxic, PBG is highly specific as a diagnostic marker for AHP.[2,3]

ALA and PBG should be tested along with porphyrins to confirm an AHP diagnosis. Normal urine PBG in symptomatic patients excludes the 3 most common subtypes of AHP as the cause of symptoms. Because ALA and PBG are most likely to be elevated during symptomatic periods, the timing of testing is important.[1,2,6]

Incapacitating symptoms, mostly in females

Symptomatic disease most often occurs in women of childbearing age. The major signs and symptoms are due to effects on the nervous system.[2,3]

While presenting symptoms vary, the cardinal symptom is severe, diffuse abdominal pain in up to 92% of patients. Other common symptoms may include nausea and vomiting, dark or reddish urine, confusion and anxiety, and limb pain or weakness.[3,5]

In a cohort of patients with frequent exacerbations, up to 65% of patients also reported chronic symptoms and 46% reported daily symptoms.[5]

Consequences of delayed diagnosis

AHP often escapes diagnosis because the symptoms overlap with those of numerous common conditions.[3]

Without early diagnosis, patients may cycle from specialist to specialist and experience repeated hospitalizations, unnecessary surgeries, and long-term medical complications such as kidney disease and hypertension.[2,3]

Patients with recurrent attacks may have been previously diagnosed with:

Viral gastroenteritis, irritable bowel syndrome, cholecystitis, appendicitis, hepatitis, endometriosis, depression, psychosis, stress, seizure disorder, appendicitis, Guillain-Barré syndrome, lead poisoning, or addiction withdrawal.[2,6-8]

When the signs and symptoms make you suspect AHP, order these spot urine tests to be sure[1-3]

- **PBG** (porphobilinogen)
- **ALA** (delta-aminolevulinic acid)
- **Porphyrins** is a nonspecific test and should not be used alone to diagnose AHPs

References: 1. Balwani M, Wang B, Anderson KE, et al; for the Porphyrias Consortium of the Rare Diseases Clinical Research Network. Acute hepatic porphyrias: recommendations for evaluation and long-term management. *Hepatology*. 2017;66(4):1314-1322. **2.** Bissell DM, Anderson KE, Bonkovsky HL. Porphyria. *N Engl J Med*. 2017;377(9):862-872. **3.** Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. *Ann Intern Med*. 2005;142(6):439-450. **4.** Simon A, Pompilus F, Querbes W, et al. Patient perspective on acute intermittent porphyria with frequent attacks: a disease with intermittent and chronic manifestations [published online June 19, 2018]. *Pat ent*. doi: 10.1007/s40271-018-0319-3. **5.** Gouya L, et al. EXPLORE: A Prospective, Multinational, Natural History Study of Patients with Acute Hepatic Porphyria with Recurrent Attacks. *Hepatology*. 2020; May;71(5):1546-1558. **6.** Bissell DM, Wang B. Acute hepatic porphyria. *J Clin Transl Hepatol.* 2015;3(1):17-26. **7.** Alfadhel M, Saleh N, Alenazi H, Baffoe-Bonnie H. Acute intermittent porphyria caused by novel mutation in HMBS gene, misdiagnosed as cholecystitis. *Neuropsychiatr Dis Treat*. 2014;10:2135-2137. **8.** Kondo M, Yano Y, Shirataka M, Urata G, Sassa S. Porphyrias in Japan: compilation of all cases reported through 2002. *Int J Hematol*. 2004;79(5):448-456. **9.** Ventura P, Cappellini MD, Biolcati G, Guida CC, Rocchi E; Gruppo Italiano Porfiria (GrIP). Eur J Intern Med. 25(6):497-505.

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