Identifying the Signs and Symptoms of AHP and Subtypes Including Acute Intermittent Porphyria

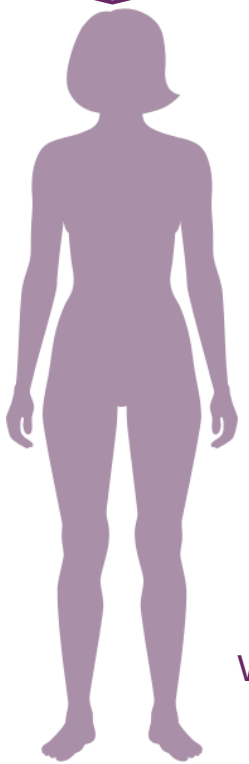
MED-US-AS1-2400026
Date of preparation: March 2025

Developed and funded by Alnylam Pharmaceuticals. This resource provides information about AHP, is intended to support scientific exchange for educational purposes, and is not intended as recommendations for clinical practice.
Not for promotional use.
For US healthcare professionals.

AHP, acute hepatic porphyria.

An Undiagnosed Patient Presents to Your Clinic…

Attacks can be “so painful that without pain medication, attacks were **not compatible with life**” – Lisa, 39-year-old with AIP[1]



Nausea and vomiting[2]

Severe, diffuse abdominal pain[2]

Weakness[2]

40-year-old female patient*,[2]

Describes their pain as like “hell on earth”[1]

Medical record describes them as opioid seeking[1]

Maybe your patient has AIP?

Has spent a large amount of time in the medical system[1] (e.g. ER five times and hospitalized numerous times, including one trip to the ICU)

Learn more about the signs of AHP in this educational module, which will:

- ✓ Illustrate the characteristics of patients with AHP
- ✓ Describe common AHP symptoms
- ✓ Summarize how patients present to the various specialties involved in managing these patients

Click to start learning

*Hypothetical patient. AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; ER, emergency room; ICU, intensive care unit.

1. American Porphyria Foundation. Voice of the patient. Available at: https://porphyriafoundation.org/apf/assets/File/public/patients/APFPFDDMeetingMarch12017-TheVoiceofthePatient_1.pdf (accessed March 2025);
2. Anderson KE et al. *Am J Med Sci.* 2022;363:1–10.

Educational Module Overview

Contents

- What Is AHP?
- Recognizing People with AHP: Symptom Profiles Per Specialty
- AHP Case-Based Scenarios
- AHP Can Be Characterized by Chronic and Acute Symptoms, Which Should Prompt Testing to Support an Early Diagnosis of AHP

Learning Objectives

After completion of this training module, you will be able to:

- Understand the chronic and acute symptoms that can be affected by the disease course of AHP
- Recognize key AHP symptoms in your patients and learn about the role other specialties have in the AHP diagnostic pathway
- Appreciate the importance of early biochemical and follow-up genetic testing to achieve an accurate diagnosis

AHP, acute hepatic porphyria; AIP, acute intermittent porphyria.

What Is AHP?

AHP Subtypes, Including AIP
Pathophysiology Symptoms
Long-Term Complications

Acute Hepatic Porphyrias Are a Group of Rare Genetic Diseases Caused by Heme Biosynthesis Dysregulation[1]

80% of patients with AHP have AIP[2]

- AHP is characterized by **chronic symptoms**, as well as **potentially life-threatening, acute attacks** that negatively impact patient functioning and QoL[3–6]

Characteristics of AHP Types

AHP Type[3,4,7,8]	Sex[9]	Age of Onset	Typical Presenting Symptoms[4]		Estimated % of AHP
			Acute Attacks	Cutaneous	
Acute intermittent porphyria (AIP)	The majority of symptomatic patients are female[4,9,10]	15–50 years[3,11]	✓		Most prevalent AHP type (~80%)[2]
Variegate porphyria (VP)			✓	✓	Less prevalent[12]
Hereditary coproporphyria (HCP)			✓	✓	Less prevalent[12]
ALA dehydratase deficiency porphyria (ADP)	All recorded symptomatic patients have been male[13]	Variable[4,13]	✓		Least prevalent; <12 cases reported worldwide[14]

Increasing prevalence

+ Other types of porphyria

AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; QoL, quality of life.

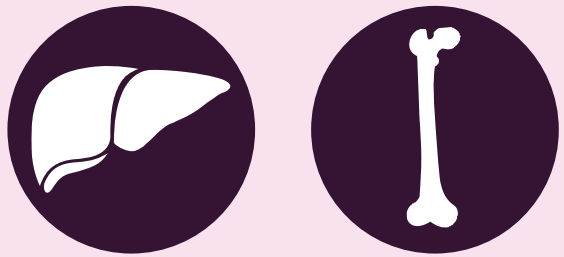
1. Anderson KE et al. *Am J Med Sci.* 2022;363:1–10; 2. Simon A et al. *Patient.* 2018;11:527–537; 3. Wang B et al. *Gastroenterology.* 2023;164:484–491; 4. Ramanujam V-MS & Anderson KE. *Curr Protoc Hum Genet.* 2015;86:17.20.1–17.20.26; 5. Cassiman D et al. *J Inherit Metab Dis.* 2022;45:1163–1174; 6. Dickey A et al. *JIMD Rep.* 202218;64:104–113; 7. Besur S et al. *Metabolites.* 2014;4:977–1006; 8. Kothadia JP et al. *Acute Hepatic Porphyria.* In: *StatPearls* [Internet]. Last update: May 2023. Available at: https://www.ncbi.nlm.nih.yv/books/NBK537178 (accessed March 2025); 9. NORD. Varigate porphyria – Affected populations. Available at: https://rarediseases.org/rare-diseases/variegate-porphyria/#affected (accessed March 2025); 10. Sam SS et al. *J Hematol.* 2016;5:67–69; 11. Bissell DM & Wang B. *J Clin Transl Hepatol.* 2015;3:17–26; 12. Elder G et al. *J Inherit Metab Dis.* 2013;36:849–857; 13. Mohan G & Madan A. *StatPearls.* [Internet]. Last update: July 2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560836/ (accessed March 2025); 14. Syed YY. *Drugs.* 2021;81:841–848.

Porphyria Is Classified According to Clinical Symptoms and Enzymatic Defects at Different Stages of Heme Biosynthesis

- Porphyrias are a group of rare metabolic disorders resulting from abnormalities in heme biosynthesis

Hepatic or Erythropoietic

- Heme precursors accumulate in either the liver or bone marrow, which are the tissues that are most active in heme biosynthesis



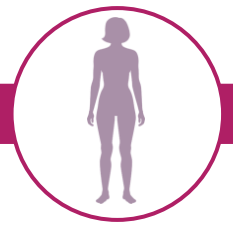
Acute or Cutaneous

- Major clinical manifestations are either neurological, usually in the form of acute attacks, or cutaneous, as a result of phototoxicity

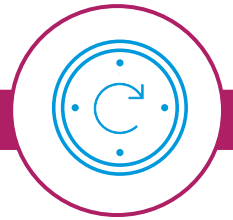
Ramanujam V-MS & Anderson KE. *Curr Protoc Hum Genet.* 2015;86:17.20.1–17.20.26.

AHP Represents a Group of Underdiagnosed and Underreported Disorders[1]

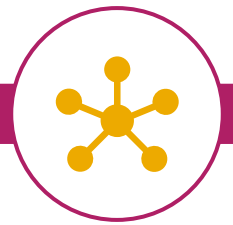
AHP Patient Profile



Women are predominantly affected[1]



Aged **15–50 years** at onset[1]



Symptom profile that includes **severe, diffuse abdominal pain** and **one or more of** CNS, PNS, ANS, or cutaneous symptoms[2,3]

AIP is the **most prevalent AHP type** (5–10 per 100,000 of the US population)[4]

+ Presenting symptoms prompting suspicion of AHP

AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; ANS, autonomic nervous system; CNS, central nervous system; PNS, peripheral nervous system.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450; 3. Ventura P et al. *Eur J Intern Med.* 2014;25:497–505; 4 Syed YY. *Drugs.* 2021;81:841–848.

Key Disease Characteristics During an Acute Attack that Should Prompt Suspicion of AHP and Subsequent Biochemical Testing[1–3]

Severe, diffuse abdominal pain

Occurred in 92% of patients at presentation[4,*]

AND

one or more of these symptoms:

PNS	CNS	ANS	Other	Cutaneous
• Limb weakness or pain	• Anxiety • Confusion	• Nausea • Vomiting	• Hyponatremia • Dark, reddish urine	• Skin lesions on sun-exposed areas

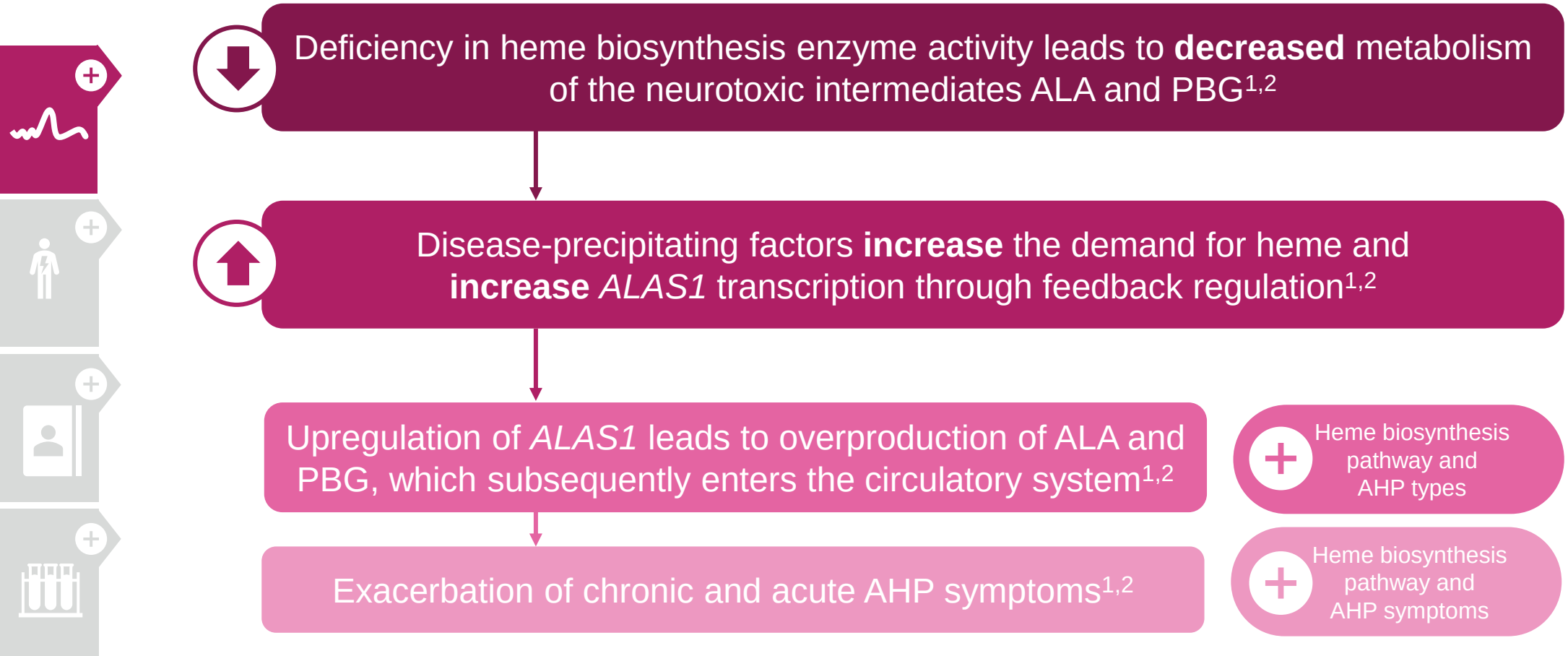
All AHPs HCP and VP only

***Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks (N=112). Eligible patients had experienced ≥3 attacks in the prior 12 months or were receiving prophylactic treatment.[4]**

AHP, acute hepatic porphyria; ANS, autonomic nervous system; CNS, central nervous system; HCP, hereditary coproporphyria; PNS, peripheral nervous system; VP, variegate porphyria.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450; 3. Ventura P et al. *Eur J Intern Med.* 2014;25:497–505;
4. Gouya L et al. *Hepatology.* 2020;71:1546–1558.

AHP Arises from Disruptions in the Heme Biosynthesis Pathway[1,2]



AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; ALAS1, ALA synthase 1; PBG, porphobilinogen.

1. Pischik E & Kauppinen R. *Appl Clin Genet.* 2015;8:201–214; 2. Balwani M et al. *Hepatology.* 2017;66:1314–1322.

Heme Biosynthesis Pathway and Association with AHP Types

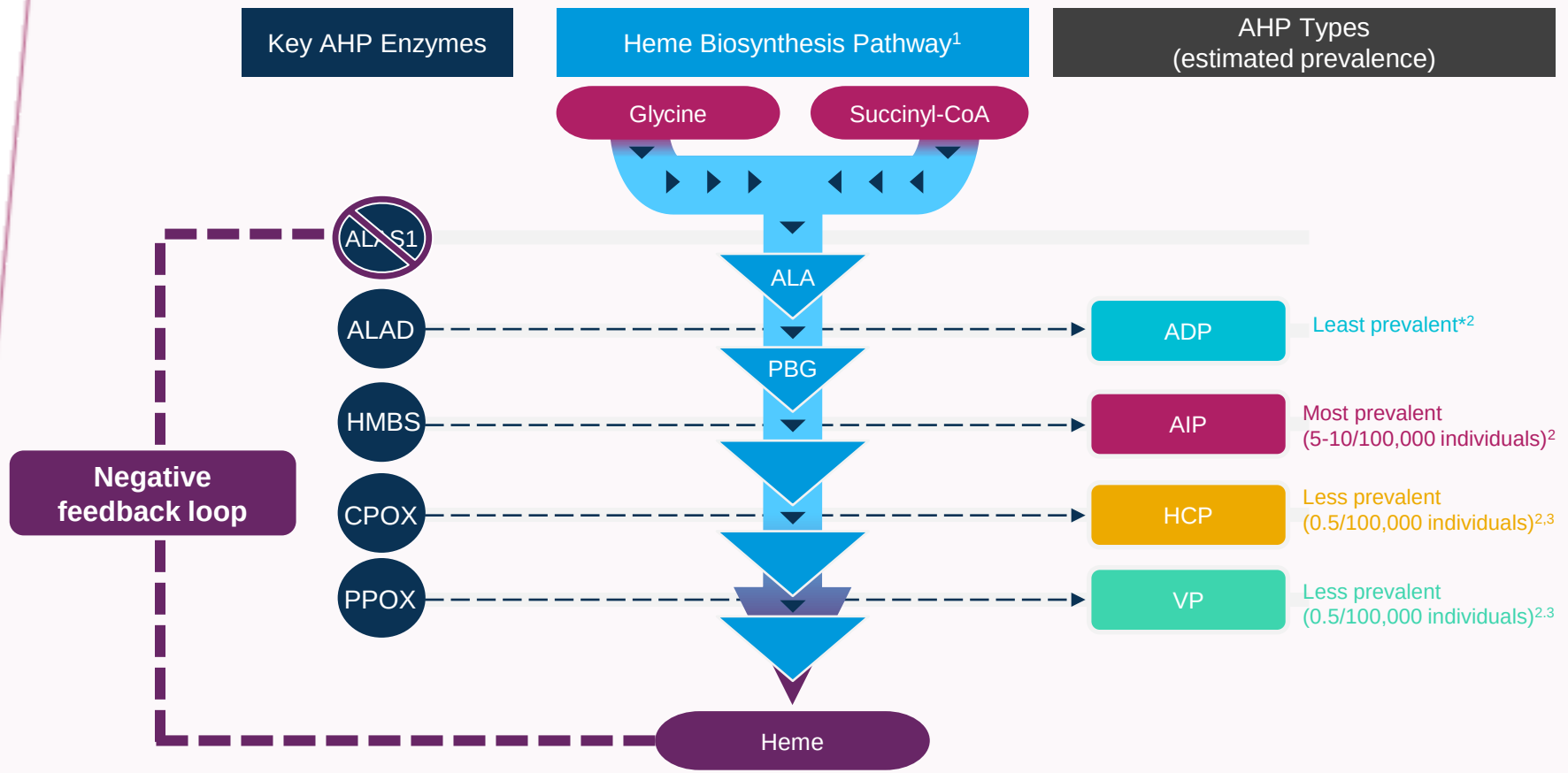


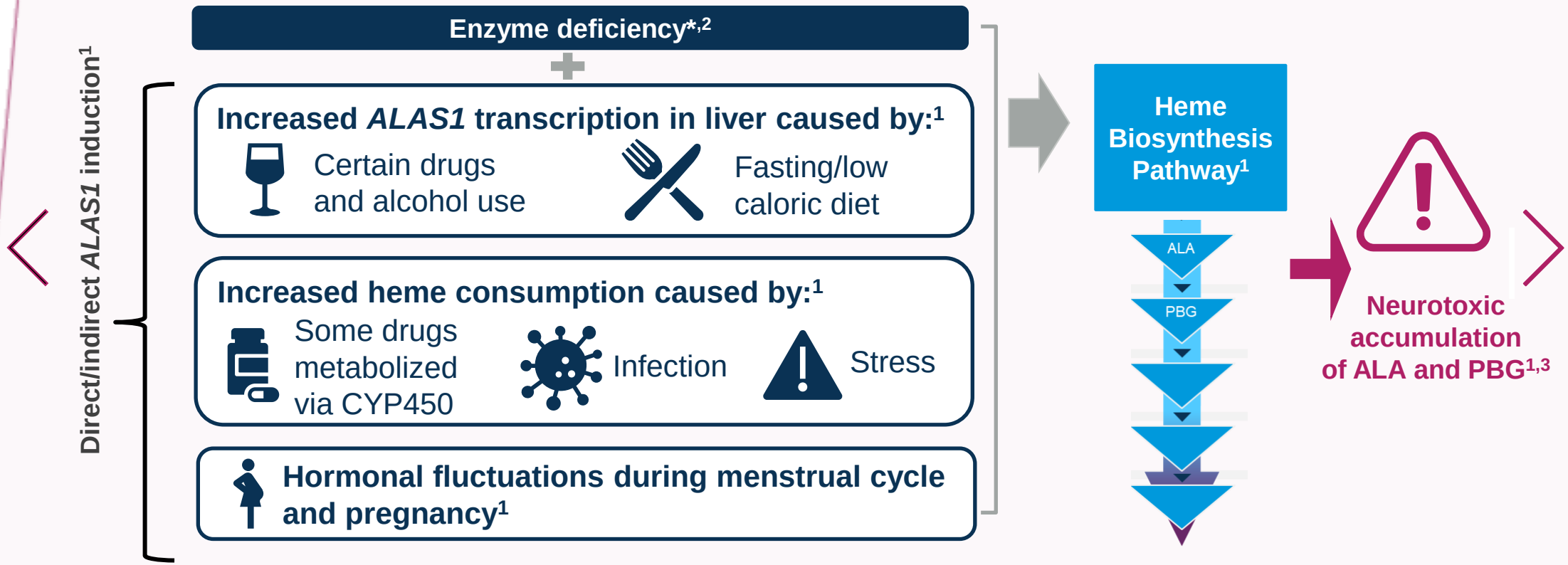
Figure adapted from Ramanujam V-MS & Anderson KE. 2015. *12 cases reported worldwide.[2]

ADP, ALA dehydratase deficiency; AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; ALAS1, ALA synthase 1; ALA, δ-aminolevulinic acid; ALAD, d-aminolevulinate dehydratase; CoA, coenzyme-A;CPOX, coproporphyrinogen oxidase; HCP, hereditary coproporphyria; HMBS, hydroxymethylbilane synthase; PBG, porphobilinogen; PPOX, protoporphyrinogen oxidase; VP, variegate porphyria.

1. Ramanujam V-MS & Anderson KE. *Curr Protoc Hum Genet.* 2015;86:17.20.1–17.20.26; 2. Syed YY. *Drugs.* 2021;81:841–848; 3. Elder G et al. *J Inherit Metab Dis.* 2013;36:849–857..

Heme Biosynthesis Pathway and Association with AHP Symptoms

- Triggers induce heme synthesis through direct/indirect *ALAS1* activation, with resulting accumulation of toxic heme metabolites, leading to symptoms in several organ systems[1]



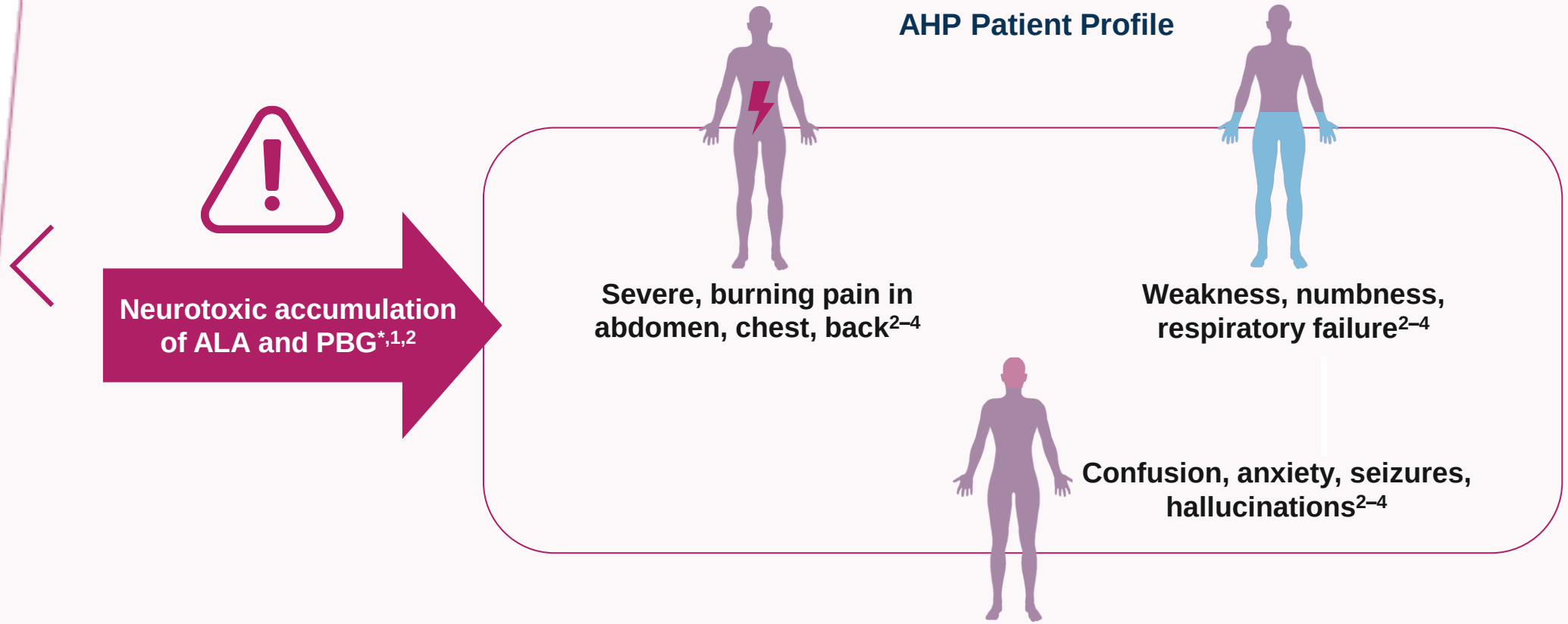
***Enzyme deficiency in the heme synthesis pathway.[2]**

AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; ALAS1, ALA synthase 1; CoA, coenzyme A; CYP450, cytochrome P450; HCP, hereditary coproporphyria; PBG, porphobilinogen.

1. Pischik E & Kauppinen R. *Appl Clin Genet.* 2015;8:201–214; 2. Besur S et al. *Metabolites.* 2014;4:977–1006; 3. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121.

Heme Biosynthesis Pathway and Association with AHP Symptoms

- Triggers induce heme synthesis through direct/indirect *ALAS1* activation, with resulting accumulation of toxic heme metabolites, leading to symptoms in several organ systems[1]



***Neurotoxic accumulation of ALA and PBG can also lead to lesions on sun-exposed skin and chronic blistering which occurs primarily in VP and HCP.[2,5]**

AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; ALAS1, ALA synthase 1; CoA, coenzyme A; CYP450, cytochrome P450; HCP, hereditary coproporphyria; PBG, porphobilinogen.

1. Pischik E & Kauppinen R. *Appl Clin Genet.* 2015;8:201–214; 2. Besur S et al. *Metabolites.* 2014;4:977–1006; 3. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121; 4. Ventura P et al. *Eur J Intern Med.* 2014;25:497–505.

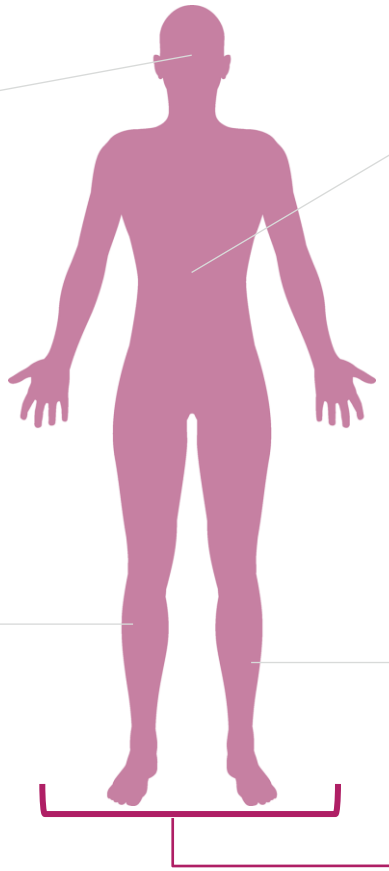
Symptoms Experienced by Patients with AHP are Numerous and Diverse[1–4]

CNS Manifestations[1–4]

- Confusion
- **Anxiety**
- Memory loss
- Depression
- **Trouble sleeping**
- Hallucinations
- Seizures

PNS Manifestations[1–4]

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



ANS Manifestations[1–5]

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

Symptoms in Pink →
Frequent symptoms (≥50% of patients) occurring during an attack, as reported at baseline in EXPLORE A[‡,2]

Cutaneous Manifestation[†,1,3]

- Lesions on sun-exposed skin

65% of patients reported experiencing chronic symptoms[‡,2]

≥50% of patients reported experiencing any pain symptoms chronically[2,‡]

AHP is a multisystem disease characterized by numerous clinical manifestations arising from acute and recurrent attacks[6]

The symptoms presented are not all of the possible symptoms of AHP.

*Only occurs in severe cases;[4] †Primarily occurs in VP and HCP;[1] ‡EXPLORE A (N=112) included patients who had three or more attacks or were receiving prophylactic treatment.[2]

AHP, acute hepatic porphyria; ANS, autonomic nervous system; CNS, central nervous system; HCP, hereditary coproporphyria; PNS, peripheral nervous system; VP, variegate porphyria.

1. Anderson KE. *Mol Genet Metab.* 2019;128:219–227; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Pischik E & Kauppinen R. *Appl Clin Genet.* 2015;8:201–214; 4. Simon A et al. *Patient.* 2018;11:527–537; 5. Anderson KE et al. *Am J Med Sci.* 2022;363:1–10; 6. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345.

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Impact Patients' Daily Functioning and Quality of Life[1–5]

Hypothetical AHP disease course[1–4]

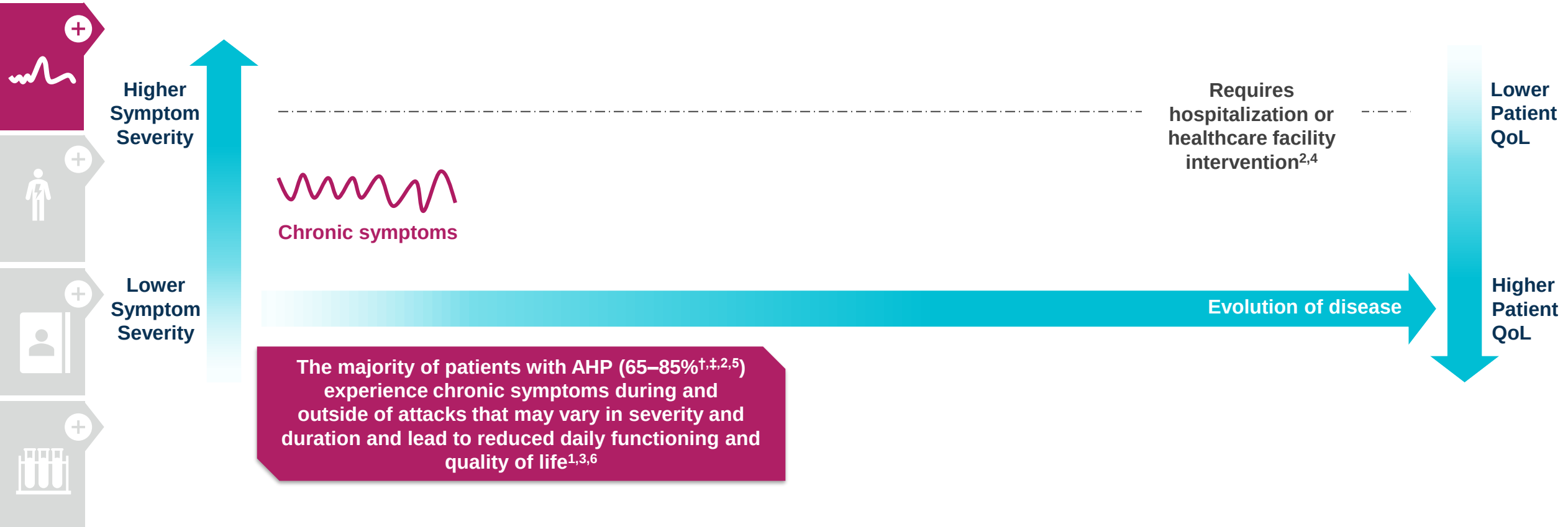


Illustration depicts a hypothetical disease course based on reported experiences of AHP from POWER, EXPLORE A, Simon et al. 2018, and Wheeden et al. 2022.[1–4]

*The mean (SD) duration of attacks requiring treatment at a health care facility and/or hemin administration was 7.3 (6.0).†Chronic symptoms were reported by 65% of patients with AHP (n=73) in the EXPLORE-A study (N=112) which included patients who had 3 or more attacks or were receiving prophylactic treatment;[2] ‡Chronic symptoms were reported by 85% of patients with AHP with<3 attacks and no prophylaxis (n=26) and by 72% of patients with AHP with ≥3 attacks or were receiving prophylactic treatment (n=110) in the EXPLORE-B Study (N=136).[5]

AHP, acute hepatic porphyria; SD, standard deviation [5]

1. Simon A et al. *Patient.* 2018;11:527–537; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Cassiman D, et al. *J Inherit Metab Dis.* 2022;45:1163–1174; 6. Pischik E, et al. *Liver Int.* 2024;44:2197–2207.

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Impact Patients' Daily Functioning and Quality of Life[1–5]

Hypothetical AHP disease course[1–4]

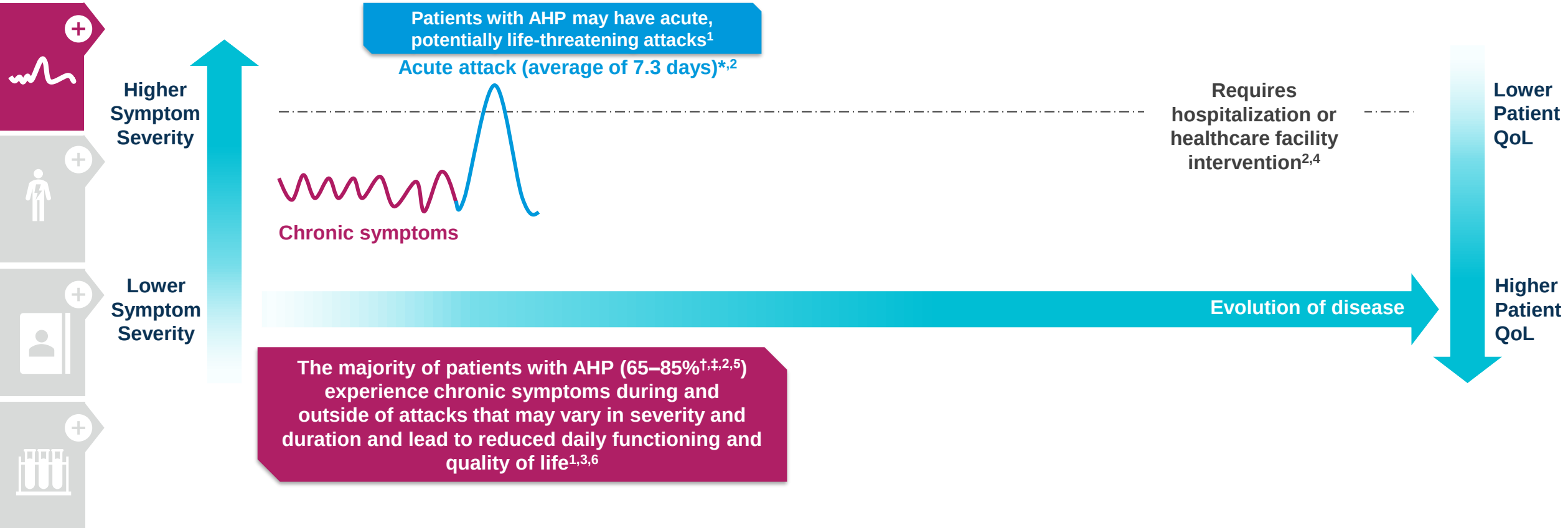


Illustration depicts a hypothetical disease course based on reported experiences of AHP from POWER, EXPLORE A, Simon et al. 2018, and Wheeden et al. 2022.[1–4]

*The mean (SD) duration of attacks requiring treatment at a health care facility and/or hemin administration was 7.3 (6.0). †Chronic symptoms were reported by 65% of patients with AHP (n=73) in the EXPLORE-A study (N=112) which included patients who had 3 or more attacks or were receiving prophylactic treatment;[2] ‡Chronic symptoms were reported by 85% of patients with AHP with<3 attacks and no prophylaxis (n=26) and by 72% of patients with AHP with ≥3 attacks or were receiving prophylactic treatment (n=110) in the EXPLORE-B Study (N=136).[5]

AHP, acute hepatic porphyria; SD, standard deviation

1. Simon A et al. *Patient.* 2018;11:527–537; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep* 2022;64:104–113; 5. Cassiman D, et al. *J Inherit Metab Dis.* 2022;45:1163–1174; 6. Pischik E, et al. *Liver Int.* 2024;44:2197–2207.

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Impact Patients' Daily Functioning and Quality of Life[1–5]

Hypothetical AHP disease course[1–4]

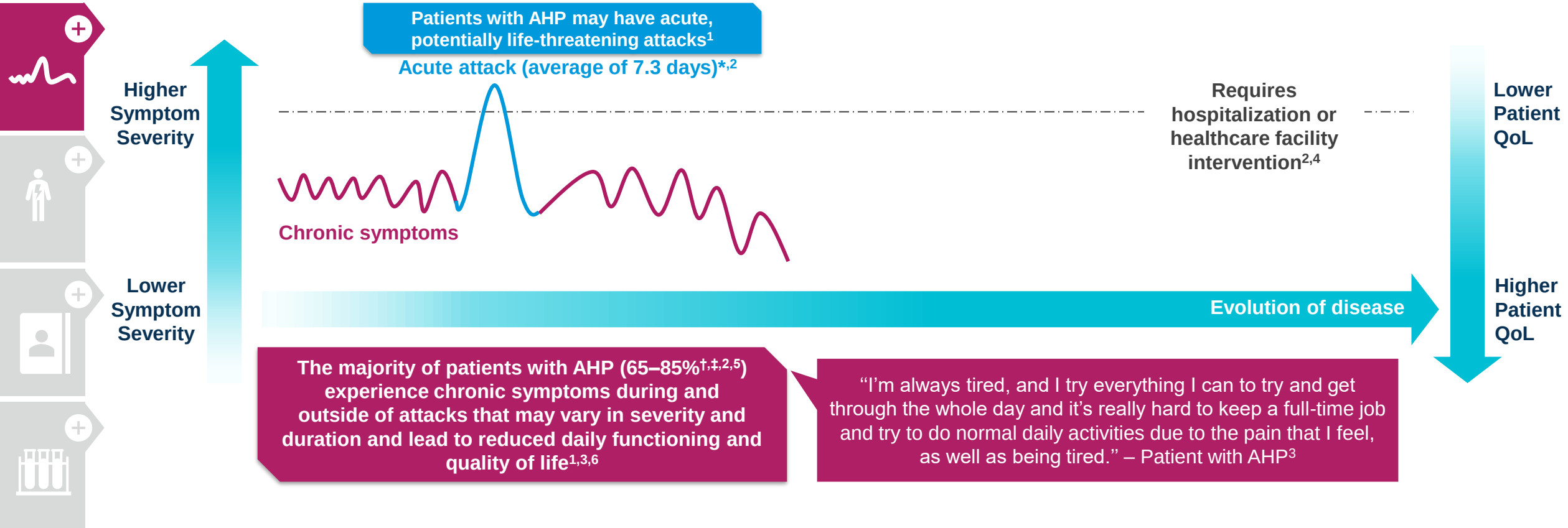


Illustration depicts a hypothetical disease course based on reported experiences of AHP from POWER, EXPLORE A, Simon et al. 2018, and Wheeden et al. 2022.[1–4]

*The mean (SD) duration of attacks requiring treatment at a health care facility and/or hemin administration was 7.3 (6.0).†Chronic symptoms were reported by 65% of patients with AHP (n=73) in the EXPLORE-A study (N=112) which included patients who had 3 or more attacks or were receiving prophylactic treatment;[2] ‡Chronic symptoms were reported by 85% of patients with AHP with<3 attacks and no prophylaxis (n=26) and by 72% of patients with AHP with ≥3 attacks or were receiving prophylactic treatment (n=110) in the EXPLORE-B Study (N=136).[5]

AHP, acute hepatic porphyria; SD, standard deviation

1. Simon A et al. *Patient.* 2018;11:527–537; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Cassiman D, et al. *J Inherit Metab Dis.* 2022;45:1163–1174; 6. Pischik E, et al. *Liver Int.* 2024;44:2197–2207.

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Impact Patients' Daily Functioning and Quality of Life[1–5]

Hypothetical AHP disease course[1–4]

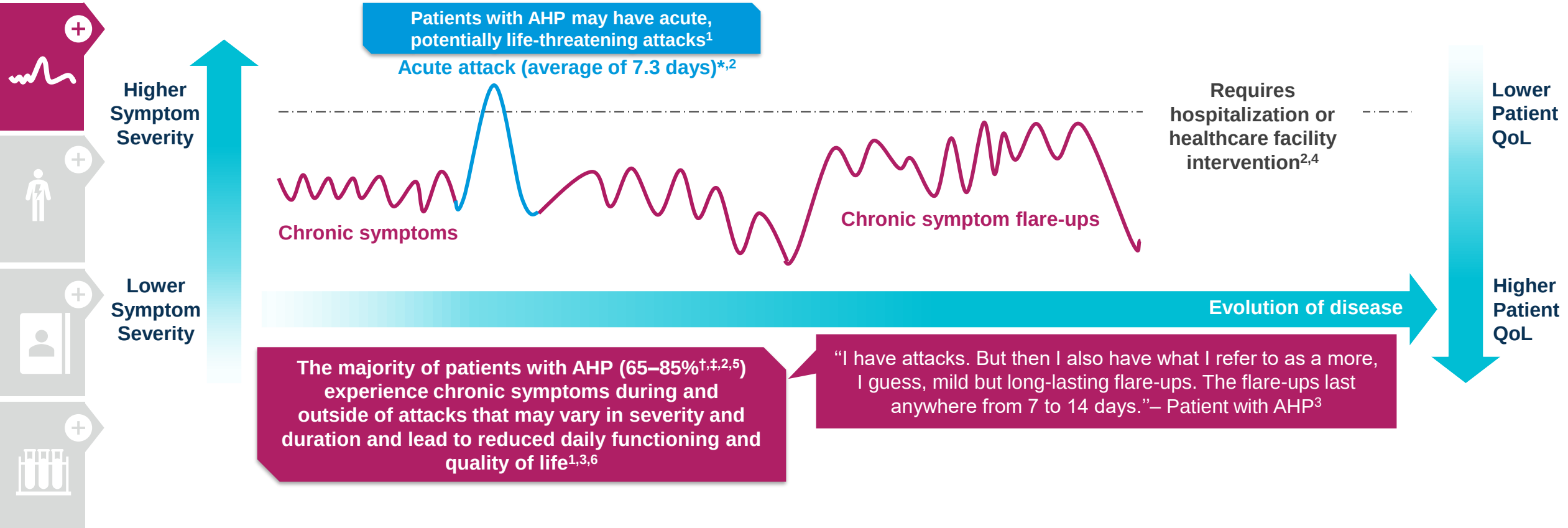


Illustration depicts a hypothetical disease course based on reported experiences of AHP from POWER, EXPLORE A, Simon et al. 2018, and Wheeden et al. 2022.[1–4]

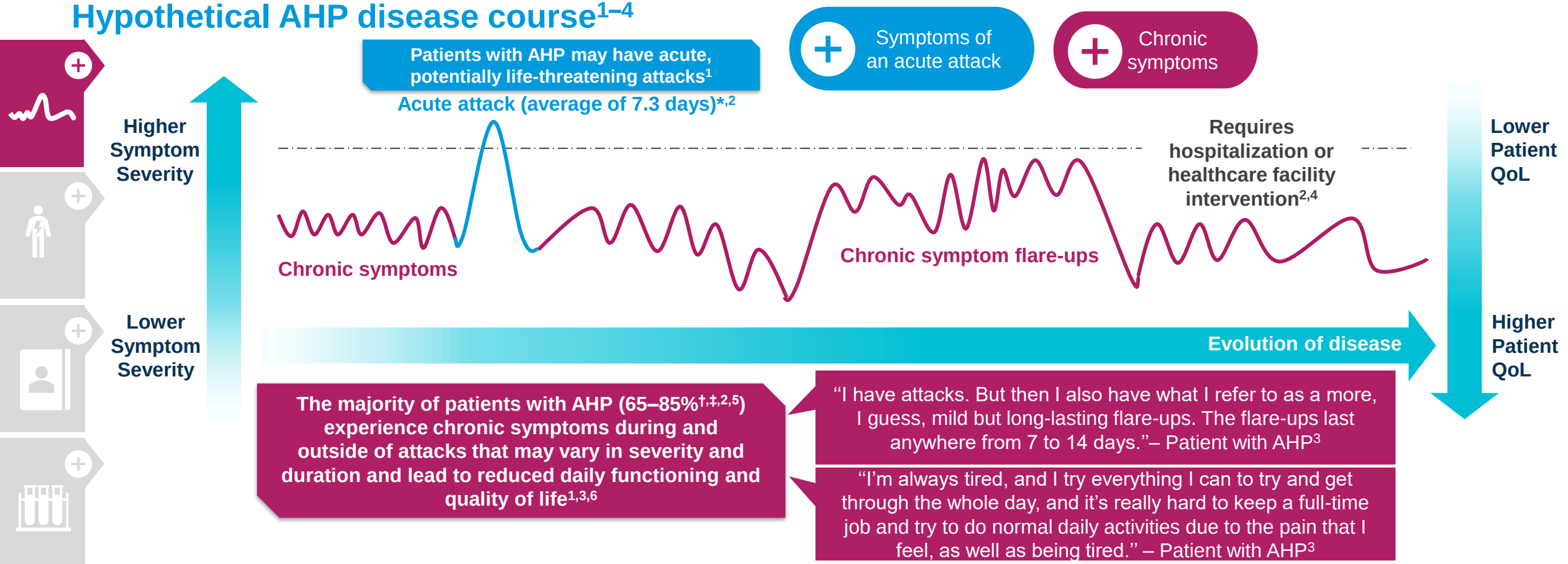
*The mean (SD) duration of attacks requiring treatment at a health care facility and/or hemin administration was 7.3 (6.0). †Chronic symptoms were reported by 65% of patients with AHP (n=73) in the EXPLORE-A study (N=112) which included patients who had 3 or more attacks or were receiving prophylactic treatment;[2] ‡Chronic symptoms were reported by 85% of patients with AHP with<3 attacks and no prophylaxis (n=26) and by 72% of patients with AHP with ≥3 attacks or were receiving prophylactic treatment (n=110) in the EXPLORE-B Study (N=136).[5]

AHP, acute hepatic porphyria; SD, standard deviation

1. Simon A et al. *Patient.* 2018;11:527–537; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Cassiman D, et al. *J Inherit Metab Dis.* 2022;45:1163–1174; 6. Pischik E, et al. *Liver Int.* 2024;44:2197–2207.

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Impact Patients' Daily Functioning and Quality of Life[1–5]

Hypothetical AHP disease course[1–4]



The majority of patients with AHP (65–85%[†,‡,2,5]) experience chronic symptoms during and outside of attacks that may vary in severity and duration and lead to reduced daily functioning and quality of life[1,3,6]

"I have attacks. But then I also have what I refer to as a more, I guess, mild but long-lasting flare-ups. The flare-ups last anywhere from 7 to 14 days."– Patient with AHP[3]

"I'm always tired, and I try everything I can to try and get through the whole day, and it's really hard to keep a full-time job and try to do normal daily activities due to the pain that I feel, as well as being tired." – Patient with AHP[3]

Illustration depicts a hypothetical disease course based on reported experiences of AHP from POWER, EXPLORE A, Simon et al. 2018, and Wheeden et al. 2022.[1–4]

*The mean (SD) duration of attacks requiring treatment at a health care facility and/or hemin administration was 7.3 (6.0).†Chronic symptoms were reported by 65% of patients with AHP (n=73) in the EXPLORE-A study (N=112) which included patients who had 3 or more attacks or were receiving prophylactic treatment;[2] ‡Chronic symptoms were reported by 85% of patients with AHP with<3 attacks and no prophylaxis (n=26) and by 72% of patients with AHP with ≥3 attacks or were receiving prophylactic treatment (n=110) in the EXPLORE-B Study (N=136).[5]

AHP, acute hepatic porphyria; SD, standard deviation.

1. Simon A et al. *Patient.* 2018;11:527–537; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Cassiman D, et al. *J Inherit Metab Dis.* 2022;45:1163–1174;6. Pischik E, et al. *Liver Int.* 2024;44:2197–2207.

AHP Symptoms According to Disease Phase: Chronic Symptoms

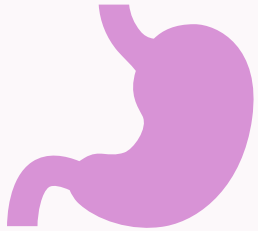
- In total, **65%** of patients with AHP (n=73) reported experiencing **chronic symptoms** in the **EXPLORE A study** (N=112), with 46% of patients reporting **daily chronic symptoms***[1]

"I never feel well rested when I wake up, ever. **I can't remember the last time I felt rested**."
– Patient with AHP[2]

"When it's chronic, it's something I'm constantly having to manage… **there will be pains where I feel like I'm getting stung by a swarm of bees** or something like that. But it doesn't get to the point where I'm having to go to the emergency room and vomiting."
– Patient with AHP[3]

Most Common (≥20%) Chronic Symptoms Reported by Patients in EXPLORE A[1]

Anxiety



Nausea

Tiredness

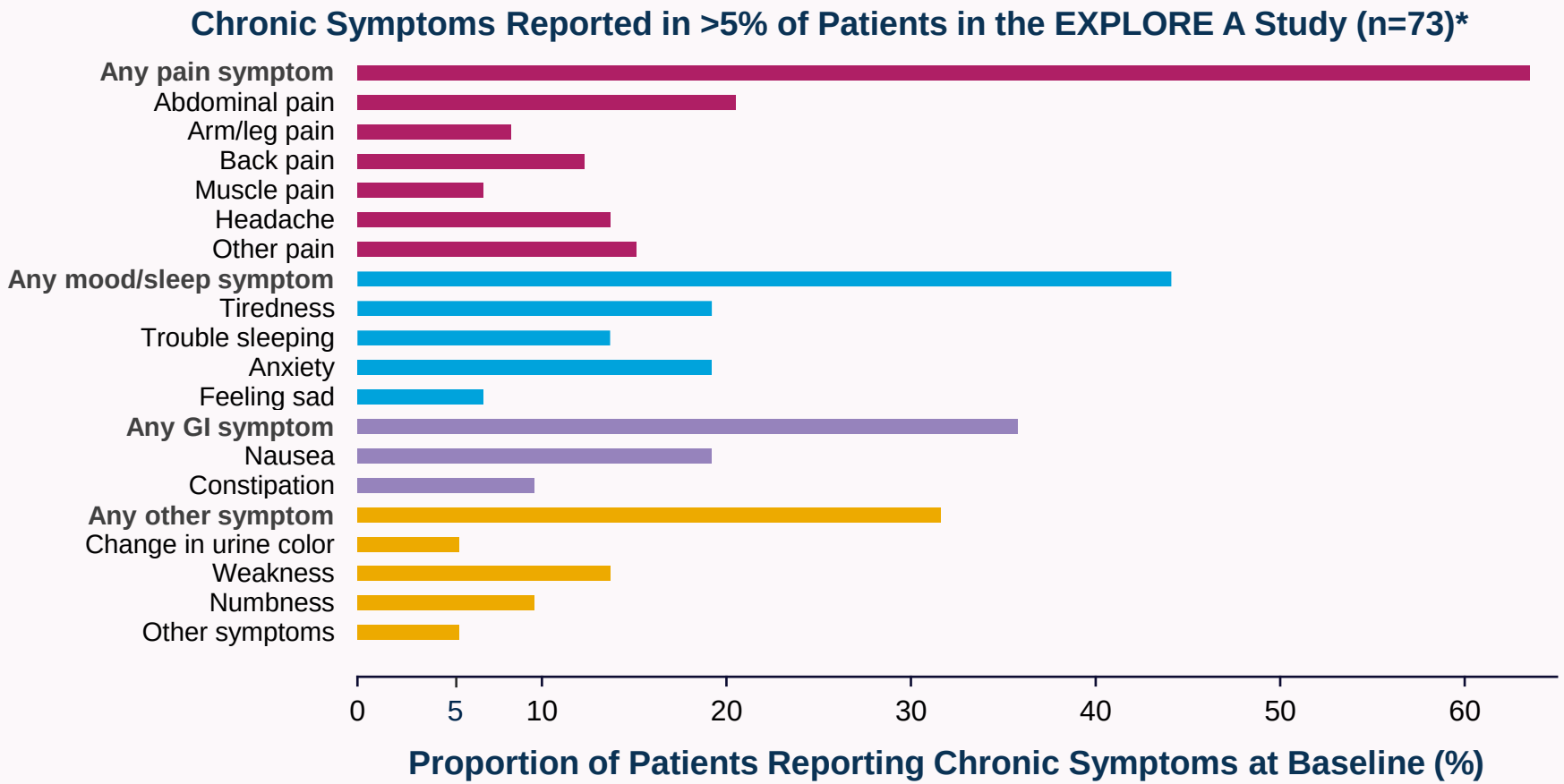
Pain

***Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks. Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.[1]**

AHP, acute hepatic porphyria.

1. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 2. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 3. Simon A et al. *Patient.* 2018;11:527–537.

AHP Symptoms According to Disease Phase: Chronic Symptoms



***Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks. Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.**

AHP, acute hepatic porphyria; GI, gastrointestinal.

Gouya L et al. *Hepatology.* 2020;71:1546–1558.

AHP Symptoms According to Disease Phase: Chronic Symptoms

Flare-Ups Vary, and Some Patients with AHP Describe the Potential for Ongoing, Chronic Symptoms to Turn into an Attack:[1]

"I'd say, one episode that's wicked bad every, I'd say, 6 to 8 weeks, where I feel [bad] for several days and barely get out of bed… That's on an irregular basis, **but it does not mean that I am getting an attack**." – *Patient with AHP*

"The pain in my legs [has] increasingly gotten worse with time, which is scary to me, like it started out a little bit, and then it became a little bit more, and now it's a little bit more often, and it just feels like I just don't want to stand for long periods." – *Patient with AHP*

"If I take it easy and—or take a day off work or do—you know, adjust what I'm eating or trying to get more sleep, it'll usually calm down. But it's when I try to do those things and the **pain continues to get worse** that it then turns more into an attack." – *Patient with AHP*

During an acute attack, multiple symptoms are experienced simultaneously, caused by multisystem dysfunction[2–4]

It is crucial that AHP is diagnosed and managed quickly because delayed management can result in severe neurological damage, which may result in prolonged recovery periods or even death[2]

AHP, acute hepatic porphyria.

1. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Bonkovsky HL et al. *Mol Genet Metab.* 2019;128:213–218; 4. Anderson KE. *Mol Genet Metab.* 2019;128:219–227.

AHP Symptoms According to Disease Phase: Acute Symptoms

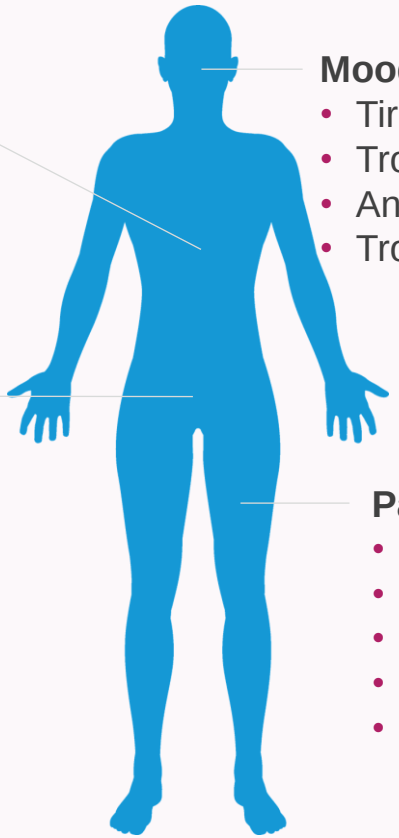
In **EXPLORE A**, an observational, multinational, prospective natural history study, **pain was the most prominent symptom** experienced during acute attacks, with abdominal pain being the most frequently reported (92%)[1]

Patients with AHP describe attacks as "completely unbearable" and pain symptoms as "agonizing" and "stabbing, knife-like"[2]

Frequent symptoms (≥50% of patients) occurring during an attack, as reported at baseline in EXPLORE-A (N=112)[1]

GI symptoms
- Nausea
- Constipation
- Loss of appetite
- Vomiting

Other symptoms
- Changes in urine color
- Weakness
- Fast heartbeat
- Sweating



Mood or sleep symptoms
- Tiredness
- Trouble sleeping
- Anxiety
- Trouble concentrating

Pain symptoms
- Abdominal pain
- Arm/leg pain
- Back pain
- Muscle pain
- Headache

AHP, acute hepatic porphyria; GI, gastrointestinal.

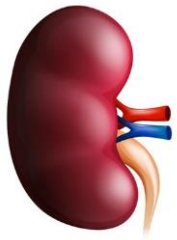
1. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 2. Simon A et al. *Patient.* 2018;11:527–537.

Potential Long-Term Complications of AHP

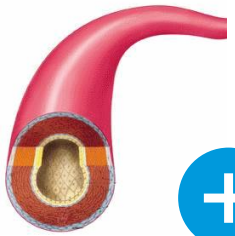
Potential for liver cancer, kidney disease, hypertension, and chronic neuropathy in patients with AHP

Primary Liver Cancer

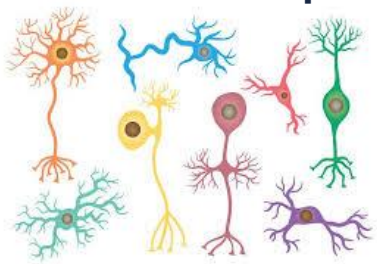
Chronic Kidney Disease



Hypertension



Chronic Neuropathy



Click on each button to learn more about each long-term complication of AHP

AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PLC, primary liver cancer.

1. Peoc'h K et al. *Mol Genet Metab.* 2019;128:236–241; 2. Baravelli CM et al. *J Intern Med.* 2017;282:229–240; 3. Pallet N et al. *Clin Kidney J.* 2018;11:191–197; 4. Pallet N et al. *Kidney Int.* 2015;88:386–395; 5. Buendia-Martinez J et al. *Orphanet J Rare Dis.* 2021;16:106; 6. Stewart MF. *J Clin Pathol.* 2012;65: 976–980; 7. Wang B et al. *Hepatol Commun.* 2018;3:193–206; 8. Wikberg A et al. *J Intern Med.* 2000;248:27–32.

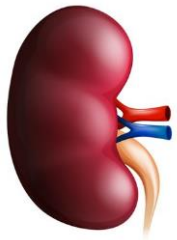
Potential Long-Term Complications of AHP

Potential for liver cancer, kidney disease, hypertension, and chronic neuropathy in patients with AHP

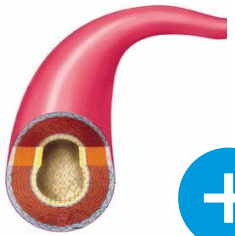
Primary Liver Cancer

- AHP has been identified as a risk factor for developing PLC, particularly **hepatocellular carcinoma**[1]
  - In a population-based study, the annual incidence of PLC was 0.35% in individuals with AHP (108-fold higher compared with 0.003% in the reference population)[2]

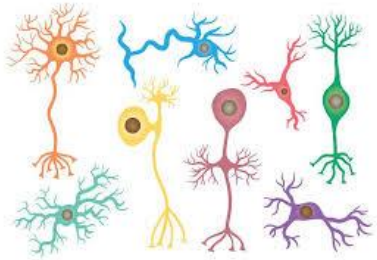
Chronic Kidney Disease



Hypertension



Chronic Neuropathy



AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PLC, primary liver cancer.

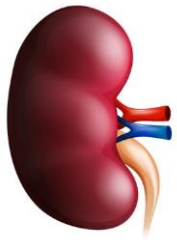
1. Peoc'h K et al. *Mol Genet Metab.* 2019;128:236–241; 2. Baravelli CM et al. *J Intern Med.* 2017;282:229–240; 3. Pallet N et al. *Clin Kidney J.* 2018;11:191–197; 4. Pallet N et al. *Kidney Int.* 2015;88:386–395; 5. Buendia-Martinez J et al. *Orphanet J Rare Dis.* 2021;16:106; 6. Stewart MF. *J Clin Pathol.* 2012;65: 976–980; 7. Wang B et al. *Hepatol Commun.* 2018;3:193–206; 8. Wikberg A et al. *J Intern Med.* 2000;248:27–32.

Potential Long-Term Complications of AHP

Potential for liver cancer, kidney disease, hypertension, and chronic neuropathy in patients with AHP

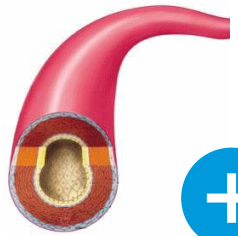
Primary Liver Cancer

Chronic Kidney Disease

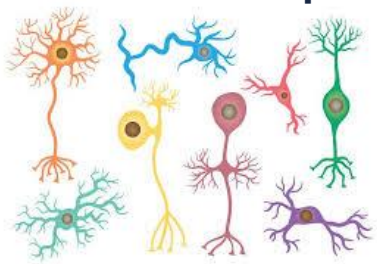


- Studies have found high levels of CKD in patients with AHP[3]
- In total, **59% of patients with symptomatic AIP have been observed to have CKD** (eGFR <60 mL/min/1.73 m^2)[4]
- Patients with sporadic AIP (<4 attacks/year) have been observed to have a significantly increased risk of CKD versus patients with latent AIP (p=0.0018)*,[5]

Hypertension



Chronic Neuropathy



*Patients with sporadic AIP were defined as having had at least one previous neurovisceral attack and an annual rate of attacks lower than four per year. A neurovisceral attack was considered to have occurred when the patient was admitted to hospital due to clinical compatible symptoms with raised urinary porphobilinogen levels and received specific treatment. Latent AIP status was defined when there was no neurovisceral attack background.
AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PLC, primary liver cancer.

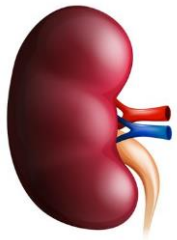
1. Peoc'h K et al. *Mol Genet Metab.* 2019;128:236–241; 2. Baravelli CM et al. *J Intern Med.* 2017;282:229–240; 3. Pallet N et al. *Clin Kidney J.* 2018;11:191–197; 4. Pallet N et al. *Kidney Int.* 2015;88:386–395;
5. Buendia-Martinez J et al. *Orphanet J Rare Dis.* 2021;16:106; 6. Stewart MF. *J Clin Pathol.* 2012;65: 976–980; 7. Wang B et al. *Hepatol Commun.* 2018;3:193–206; 8. Wikberg A et al. *J Intern Med.* 2000;248:27–32.

Potential Long-Term Complications of AHP

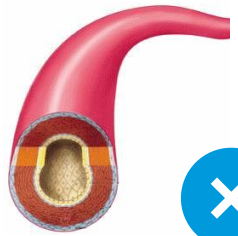
Potential for liver cancer, kidney disease, hypertension, and chronic neuropathy in patients with AHP

Primary Liver Cancer

Chronic Kidney Disease

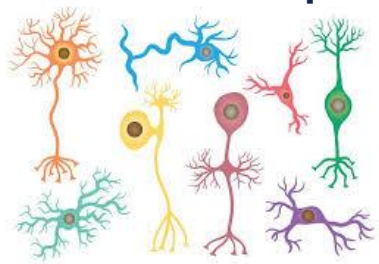


Hypertension



- Patients with AHP may have an increased risk of **chronic, sustained hypertension**[3,6,7]
  - 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[6]

Chronic Neuropathy



AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PLC, primary liver cancer.

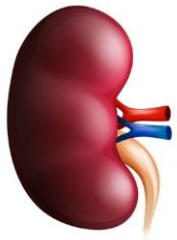
1. Peoc'h K et al. *Mol Genet Metab.* 2019;128:236–241; 2. Baravelli CM et al. *J Intern Med.* 2017;282:229–240; 3. Pallet N et al. *Clin Kidney J.* 2018;11:191–197; 4. Pallet N et al. *Kidney Int.* 2015;88:386–395; 5. Buendia-Martinez J et al. *Orphanet J Rare Dis.* 2021;16:106; 6. Stewart MF. *J Clin Pathol.* 2012;65: 976–980; 7. Wang B et al. *Hepatol Commun.* 2018;3:193–206; 8. Wikberg A et al. *J Intern Med.* 2000;248:27–32.

Potential Long-Term Complications of AHP

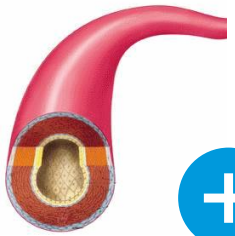
Potential for liver cancer, kidney disease, hypertension, and chronic neuropathy in patients with AHP

Primary Liver Cancer

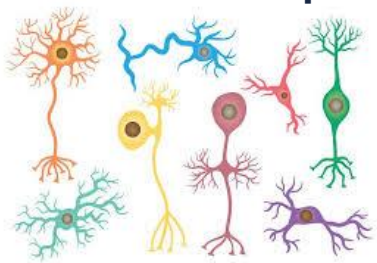
Chronic Kidney Disease



Hypertension



Chronic Neuropathy



- Patients with AHP can develop **chronic pain associated with axonal motor polyneuropathy**[7]
  - Chronic pain symptoms can lead to severe depression and anxiety, which may necessitate psychiatric care[7]
- Permanent quadriplegia may rarely occur as a result of severe attacks[8]

AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; PLC, primary liver cancer.

1. Peoc'h K et al. *Mol Genet Metab.* 2019;128:236–241; 2. Baravelli CM et al. *J Intern Med.* 2017;282:229–240; 3. Pallet N et al. *Clin Kidney J.* 2018;11:191–197; 4. Pallet N et al. *Kidney Int.* 2015;88:386–395; 5. Buendia-Martinez J et al. *Orphanet J Rare Dis.* 2021;16:106; 6. Stewart MF. *J Clin Pathol.* 2012;65: 976–980; 7. Wang B et al. *Hepatol Commun.* 2018;3:193–206; 8. Wikberg A et al. *J Intern Med.* 2000;248:27–32.

Knowledge Check 1

Question

- **What percentage of patients experienced chronic symptoms?**

A. 5%

B. 25%

C. 45%

D. 65%

Answer

Knowledge Check 1

Answer

- **What percentage of patients experienced chronic symptoms?**

A. 5%

B. 25%

C. 45%

D. 65% of patients with AHP (n=73) reported experiencing chronic symptoms between attacks, with 46% (n=52) of patients reporting daily chronic symptoms*

***Results from EXPLORE A (N=112), a prospective, multinational, natural history study of patients with AHP with recurrent attacks. Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.**

AHP, acute hepatic porphyria.

Gouya L et al. *Hepatology.* 2020;71:1546–1558.

Knowledge Check 2

Question

- **Which one of the following statements is incorrect?**

A. Women are predominantly affected by AHP

B. Men and women with AHP inherit mutations with equal frequency

C. Onset occurs at 15–50 years of age in most patients

D. Severe, diffuse abdominal pain is a key symptom of AHP

Answer

AHP, acute hepatic porphyria.

Knowledge Check 2

Answer

- **Which one of the following statements is incorrect?**

A. Women are predominantly affected by AHP

B. Men and women with AHP inherit mutations with equal frequency

C. Onset occurs at 15–50 years of age in most patients

D. Severe, diffuse abdominal pain is a key symptom of AHP

Return to Educational Module Overview

AHP, acute hepatic porphyria.

Wang B et al. *Gastroenterology.* 2023;164:484–491.

Recognizing People with AHP

Symptom Profiles Per Specialty

Recognizing People with AHP

The diagnostic journey for AHP is multidisciplinary and commonly involves many specialties

Please pick your specialty to learn more about common presenting symptoms of AHP

- Gastroenterology
- Hepatology
- Neurology
- Other
- Hematology
- Psychiatry

AHP, acute hepatic porphyria.

Key AHP Symptoms Prompting Referral for Testing Include Severe Diffuse Abdominal Pain, Nausea, and Vomiting[1–5]

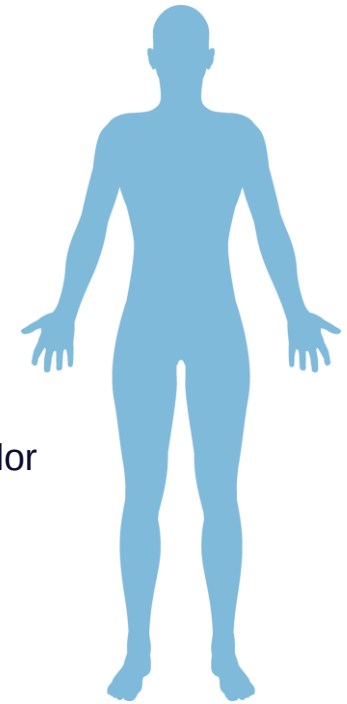
As a **gastroenterologist**, consider **GI symptoms** in your patients that may be suggestive of AHP

GI symptoms

- ✓ **Nausea**
- ✓ **Constipation**
- ✓ **Loss of appetite**
- ✓ **Vomiting***
- ✓ **Heartburn**

Other symptoms

- Changes in urine color
- Weakness
- Numbness
- Fast heartbeat
- Sweating*
- Blisters/rashes



Mood or sleep symptoms

- Tiredness
- Trouble sleeping
- Anxiety
- Trouble concentrating
- Feeling unmotivated†
- Hallucinations

Pain symptoms

- Abdominal pain
- Arm/leg pain
- Back pain
- Muscle pain
- Headache
- Other pain

All symptoms can be both acute and chronic unless otherwise stated. *Acute symptom only. †Chronic symptom only.

- Also consider **other symptoms** that fit the AHP symptom profile

Does your patient's symptom profile fit AHP?
✓ Consider testing for **AHP** as a **differential diagnosis**

Most (92%)‡ patients present with abdominal pain during an **acute attack**[2]

‡Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks (N=112). Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.[2]

AHP, acute hepatic porphyria; GI, gastrointestinal.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121.

Key AHP Symptoms Prompting Referral for Testing Include Severe Diffuse Abdominal Pain, Nausea, and Vomiting[1–5]

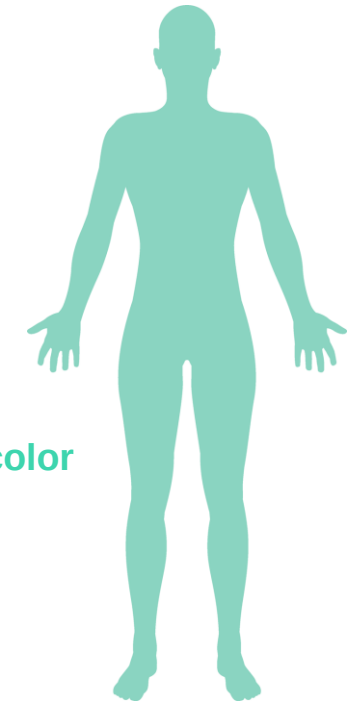
As a **hepatologist**, consider **symptoms of hepatic disorder** in your patients that may be suggestive of AHP

GI symptoms

- ✓ **Nausea**
- Constipation
- ✓ **Loss of appetite**
- ✓ **Vomiting***
- Heartburn

Other symptoms

- ✓ **Changes in urine color**
- Weakness
- Numbness
- Fast heartbeat
- Sweating*
- Blisters/rashes



Mood or sleep symptoms

- ✓ **Tiredness**
- Trouble sleeping
- Anxiety
- Trouble concentrating
- Feeling unmotivated†
- Hallucinations

Pain symptoms

- ✓ **Abdominal pain**
- Arm/leg pain
- Back pain
- Muscle pain
- Headache
- Other pain

All symptoms can be both acute and chronic unless otherwise stated. *Acute symptom only; †Chronic symptom only.

- Also consider **other symptoms** that fit the AHP symptom profile

Does your patient's symptom profile fit AHP?
✓ Consider testing for **AHP** as a **differential diagnosis**

Most (92%)‡ patients present with abdominal pain during an **acute attack**[2]

‡Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks (N=112). Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.[2]

AHP, acute hepatic porphyria; GI, gastrointestinal.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121.

Key AHP Symptoms Prompting Referral for Testing Include Severe Diffuse Abdominal Pain, Nausea, and Vomiting[1–5]

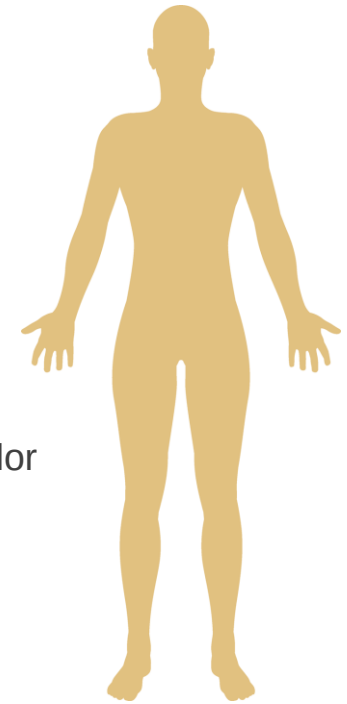
As a **neurologist**, consider **neurological symptoms** in your patients that may be suggestive of AHP

GI symptoms

- Nausea
- Constipation
- Loss of appetite
- Vomiting*
- Heartburn

Other symptoms

- Changes in urine color
- ✓ **Weakness**
- ✓ **Numbness**
- Fast heartbeat
- Sweating*
- Blisters/rashes



Mood or sleep symptoms

- ✓ **Tiredness**
- ✓ **Trouble sleeping**
- ✓ **Anxiety**
- ✓ **Trouble concentrating**
- ✓ **Feeling unmotivated†**
- ✓ **Hallucinations**

Pain symptoms

- ✓ **Abdominal pain**
- ✓ **Arm/leg pain**
- ✓ **Back pain**
- ✓ **Muscle pain**
- ✓ **Headache**
- ✓ **Other pain**

All symptoms can be both acute and chronic unless otherwise stated. *Acute symptom only; †Chronic symptom only.

- Also consider **other symptoms** that fit the AHP symptom profile

Does your patient's symptom profile fit AHP?
✓ Consider testing for **AHP** as a **differential diagnosis**

Most (92%)‡ patients present with abdominal pain during an **acute attack**[2]

‡Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks (N=112). Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.[2]

AHP, acute hepatic porphyria; GI, gastrointestinal.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121.

Key AHP Symptoms Prompting Referral for Testing Include Severe Diffuse Abdominal Pain, Nausea, and Vomiting[1–5]

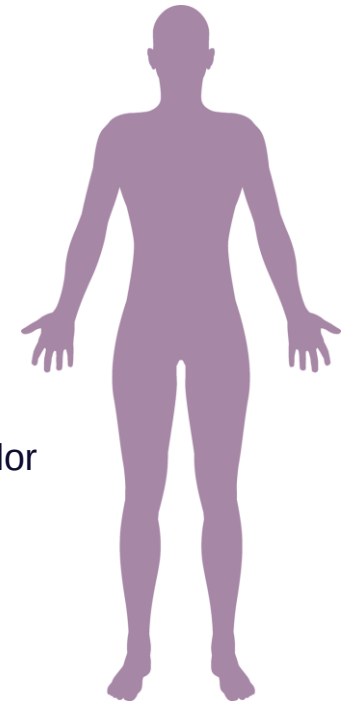
Consider symptoms in your patients that may be suggestive of AHP

GI symptoms

- Nausea
- Constipation
- Loss of appetite
- Vomiting*
- Heartburn

Other symptoms

- Changes in urine color
- Weakness
- Numbness
- Fast heartbeat
- Sweating*
- Blisters/rashes



Mood or sleep symptoms

- Tiredness
- Trouble sleeping
- Anxiety
- Trouble concentrating
- Feeling unmotivated†
- Hallucinations

Pain symptoms

- Abdominal pain
- Arm/leg pain
- Back pain
- Muscle pain
- Headache
- Other pain

All symptoms can be both acute and chronic unless otherwise stated. *Acute symptom only; †Chronic symptom only.

Does your patient's symptom profile fit AHP?
✓ Consider testing for **AHP** as a **differential diagnosis**

Most (92%)‡ patients present with abdominal pain during an **acute attack**[2]

‡Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks (N=112). Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.[2]

AHP, acute hepatic porphyria; GI, gastrointestinal.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121.

Key AHP Symptoms Prompting Referral for Testing Include Severe Diffuse Abdominal Pain, Nausea, and Vomiting[1–5]

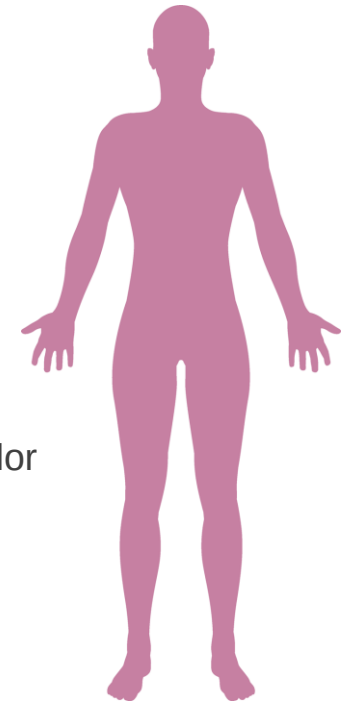
As a **psychiatrist**, consider **psychological symptoms** in your patients that may be suggestive of AHP

GI symptoms

- Nausea
- Constipation
- Loss of appetite
- Vomiting*
- Heartburn

Other symptoms

- Changes in urine color
- Weakness
- Numbness
- Fast heartbeat
- Sweating*
- Blisters/rashes



Mood or sleep symptoms

- ✓ **Tiredness**
- ✓ **Trouble sleeping**
- ✓ **Anxiety**
- ✓ **Trouble concentrating**
- ✓ **Feeling unmotivated†**
- ✓ **Hallucinations**

Pain symptoms

- Abdominal pain
- Arm/leg pain
- Back pain
- Muscle pain
- Headache
- Other pain

All symptoms can be both acute and chronic unless otherwise stated. *Acute symptom only; †Chronic symptom only.

- Also consider **other symptoms** that fit the AHP symptom profile

Does your patient's symptom profile fit AHP?
✓ Consider testing for **AHP** as a **differential diagnosis**

Most (92%)‡ patients present with abdominal pain during an **acute attack**[2]

‡Results from EXPLORE A, a prospective, multinational, natural history study of patients with AHP with recurrent attacks (N=112). Eligible patients had experienced three or more attacks in the prior 12 months or were receiving prophylactic treatment.[2]

AHP, acute hepatic porphyria; GI, gastrointestinal.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Gouya L et al. *Hepatology.* 2020;71:1546–1558; 3. Wheeden K et al. *Adv Ther.* 2022;39:4330–4345; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Anderson KE et al. *Am J Med Sci.* 2021;362:113–121.

Knowledge Check 3

Question

- **Which of the following are AHP symptoms to be aware of in patients presenting to the clinic?**

A. Abdominal pain
B. Headache
C. Trouble sleeping
D. Muscle pain
E. Nausea and vomiting
F. Tiredness
G. Heartburn
H. Topical skin issues

Answer

AHP, acute hepatic porphyria.

Knowledge Check 3

Answer

- **Which of the following are AHP symptoms to be aware of in patients presenting to the clinic?**

A. Abdominal pain

B. Headache

C. Trouble sleeping

D. Muscle pain

E. Nausea and vomiting

F. Tiredness

G. Heartburn

H. Topical skin issues

These are all potential symptoms of AHP

Return to Educational Module Overview

AHP, acute hepatic porphyria.

Wheeden K et al. *Adv Ther.* 2022;39:4330–4345.

AHP Case Scenarios

AHP Case-Based Scenarios

Click to Explore Each AHP Case Study

1 AHP with Neurological Manifestations

Steinberg T et al, 2021 — Gastroenterologist | Neurologist | Psychiatrist

2 AIP Associated with Hyponatremic Seizure in an Adolescent

Lau L et al, 2024 — ED doctor | Pediatrics

3 AIP Associated with Hyponatremia and Delirium

Fabian E et al, 2023 — Gastroenterologist | Psychiatrist | Nephrologist | Intensivist

4 VP After Etonogestrel Placement

Strome A et al, 2022 — Dermatologist

5 AIP Associated with hCG Injections

Mahesheema A and Iqbal S, 2024 — ED doctor | Intensivist

All based on published case studies.

AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; ED, emergency department; hCG, human chorionic gonadotropin; VP, variegate porphyria.

AHP Case Scenario: Acute Hepatic Porphyria with Neurological Manifestaions*

Steinberg T et al, 2021

*Based on a published case study.

Case of Neurologically Manifesting Acute Hepatic Porphyria*

Background and clinical history

Background Testing Diagnosis

- **56-year-old female**
- Presented to psychiatry with psychosomatic abdominal pain and new onset depression
- Transferred to neurology after progressive tetraparesis
- **Initial diagnosis:** Guillain–Barre syndrome complicated by axonal neuropathy
- Symptoms worsened (impaired consciousness, psychosis, dark urine) despite treatment

Click to reveal the initial signs of AHP in this patient

In this patient, neurological symptoms were attributed to uncontrolled type 1 diabetes mellitus

*Based on a published case study.
AHP, acute hepatic porphyria.
Steinberg T et al. *J Neurol Sci.* 2021;422:117334.

The 56-Year-Old Patient Demonstrated Characteristics Consistent With the AHP Symptom Profile

Background

Testing

Diagnosis

- **56-year-old female**
- Presented to psychiatry with psychosomatic **abdominal pain** and new onset depression
- Transferred to neurology after **progressive tetraparesis**
- **Initial diagnosis:** Guillain–Barre syndrome complicated by axonal neuropathy
- Symptoms worsened (**impaired consciousness**, **psychosis**, **dark urine**) despite treatment

In this patient, neurological symptoms were attributed to uncontrolled type 1 diabetes mellitus

Key AHP symptoms in this patient:

Abdominal pain | **Progressive tetraparesis** | **Dark urine**

Other potential symptoms of AHP in this patient

- New onset depression
- Impaired consciousness
- Psychosis

AHP, acute hepatic porphyria.

Steinberg T et al. *J Neurol Sci.* 2021;422:117334.

The Patient's Diagnostic Journey Highlights Symptoms Prompting Suspicion of AHP

Symptom history

1 month before psychiatric admission:

- Non-specific epigastric **pain** that resolved during diagnostic work-up

Psychiatric evaluation

At psychiatric admission:

- Evaluated due to psychosomatic **abdominal pain** and onset of a new depressive episode

Neurological evaluation

Transfer to neurology after progressive tetraparesis developed:

- On neurological examination, evidence of psychomotor retardation and flaccid **tetraparesis**
- Initially diagnosed with Guillain–Barre syndrome complicated by axonal neuropathy from poorly controlled type 1 diabetes mellitus

Clinical history and worsening of current symptoms (impaired consciousness, psychosis, dark urine) despite treatment **prompted testing for suspected AHP**

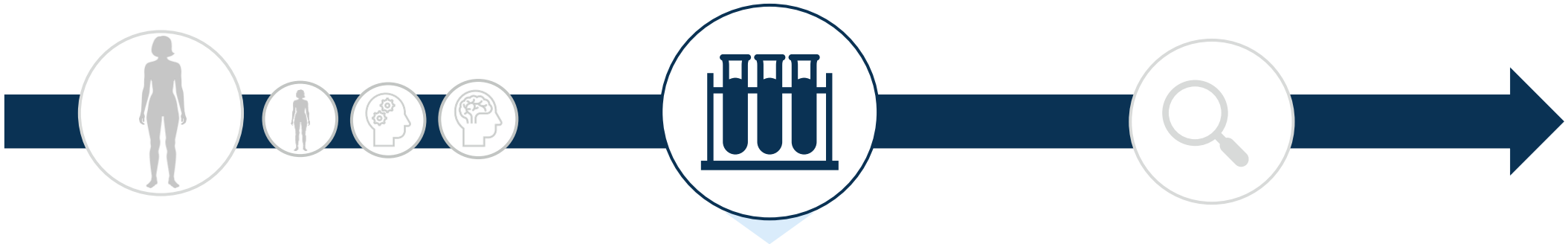
HCP Specialties Involved in Initial Work-up

Gastroenterologist* | Psychiatrist | Neurologist

*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up.
AHP, acute hepatic porphyria; HCP, healthcare professional.
Steinberg T et al. *J Neurol Sci.* 2021;422:117334.

Suspected AHP Symptoms Prompted Further Imaging and Biochemical Testing

Background | Testing | Diagnosis



Additional diagnostic tests were conducted

Biochemical tests used to diagnose AHP

- cMRI: Acute infarction of left corona radiata and posterior part of left corpus callosum
- TCCS: Showed increased blood flow velocity in cerebral arteries, however repeated TCCS was normal, consistent with vasospasm rather than multiple stenoses as cause
- **Urinalysis of ALA and PBG:**

Laboratory test	Laboratory value	Result
Urine PBG	125.4 µmol/24 hour of creatinine (normal <7.5 µmol/24 hour)	Elevated
Urine ALA	160.1 µmol/24 hour of creatinine (normal <49 µmol/24 hour)	Elevated

Laboratory values are clinic specific.
AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; cMRI, cerebral magnetic resonance imaging; PBG, porphobilinogen; TCCS, transcranial color-coded sonography.
Steinberg T et al. *J Neurol Sci.* 2021;422:117334.

Overview of Biochemical Tests Used to Achieve a Diagnosis of AHP

Random (spot) urine tests for **PBG**, ALA, creatinine, and porphyrins levels can help to diagnose AHP*,†,1–4

Urine porphyrins is a **non-specific test** and **should not be used in isolation for diagnosing AHP‡,1,4**

Ideal time to test is during or shortly after an acute attack; however, testing can be performed at any time if there is suspicion of AHP[1,3]

Additional biochemical tests, including plasma or fecal porphyrins and plasma fluorescence scanning, can be performed to help diagnose or confirm a diagnosis of AHP type, but are not specific for AHP when tested alone[3,4]

*PBG and ALA should be normalized to urinary creatinine;[1] †ALA and PBG levels can vary depending on time measured and AHP type, therefore repeat testing may be required for a diagnosis;[1]
‡The availability of biochemical tests for AHP are dependent on institution.[1]
AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; PBG, porphobilinogen.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Bonkovsky HL et al. *Am J Med.* 2014;127:1233–1241;
3. Whatley SD & Badminton MN. Acute Intermittent Porphyria. In: Adam MP et al. eds. *GeneReviews.* [Internet]. Seattle, WA: University of Washington; 2013;1993–2021;
4. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450.

Following Disease-Specific Testing, the Patient Was Diagnosed with AIP

Background | Testing | Diagnosis

After multiple tests, the patient was diagnosed with AIP[1]

- Medical history and symptoms presented by the patient were **highly suggestive of AHP**[1]
- Elevated urinary PBG and ALA levels confirmed the suspected diagnosis[1]

Practice guideline recommendations

- After an AHP diagnosis is confirmed, subsequent genetic sequencing analysis can then be used to **identify the specific sequence variant**, determining the subtype of AHP[2,3]
- Once the genetic variant is identified, **first-degree family members should be screened** to identify at-risk individuals[2]

Complications of AIP in this patient

Progressive neuropathy led to tetraplegia and **respiratory failure requiring invasive mechanical ventilation**[1]

HCP Specialties Involved in Complication Management*

- Pulmonologist
- Neurologist
- Intensivist

*Not specified in case report, assumed based on complications reported.

AHP, acute hepatic porphyria; AIP, acute intermittent porphyria; ALA, δ-aminolevulinic acid; HCP, healthcare professional; PBG, porphobilinogen.

1. Steinberg T et al. *J Neurol Sci.* 2021;422:117334; 2. Wang B et al. *Gastroenterology.* 2023;164:484–491; 3. Balwani M et al. *J Hepatol.* 2017;66:1314–1322.

AHP Case Scenario: AIP Associated with Hyponatremic Seizure in an Adolescent *

Lau L et al, 2024

*Based on a published case study.

A Hyponatremic Seizure in an Adolescent*

Background and clinical history

Background | Testing | Diagnosis

- **18-year-old female**
- Presented to ED with 4 days of acute onset of chronic abdominal pain and vomiting
- For the past 6 months, she had presented to multiple EDs for abdominal pain and back pain
- The patient had been diagnosed with gastroparesis 1 year earlier and had a history of anxiety
- **Initial diagnosis:** Pancreatitis
- Admitted to adolescent service for fluid resuscitation and pain control
- On Day 2 of admission, the patient had a seizure and was transferred to the PICU in a postictal state

Click to reveal the initial signs of AHP in this patient

In this patient, previous symptoms were attributed to gastroparesis and anxiety

*Based on a published case study.
AHP, acute hepatic porphyria; ED, emergency department; PICU, pediatric intensive care unit.
Lau L et al. *Pediatr Rev.* 2024;45:350–353.

The 18-Year-Old Patient Demonstrated Characteristics Consistent with the AHP Symptom Profile

Background | Testing | Diagnosis

- **18-year-old female**
- Presented to ED with 4 days of **acute on chronic abdominal pain** and **vomiting**
- For the past 6 months, she had presented to **multiple EDs** for **abdominal pain** and **back pain**
- The patient had been diagnosed with gastroparesis 1 year earlier and had a history of **anxiety**
- **Initial diagnosis:** Pancreatitis
- Admitted to adolescent service for fluid resuscitation and pain control
- On Day 2 of admission, the patient had a seizure and was transferred to the PICU in a postictal state

In this patient, previous symptoms were attributed to gastroparesis and anxiety

Key AIP symptoms/indicators in this patient

Abdominal pain | **Vomiting** | **Back pain**

Anxiety | **Presenting to multiple EDs**

Other potential symptoms of AIP in this patient

- Clinical seizure

AIP, acute intermittent porphyria; ED, emergency department; PICU, pediatric intensive care unit.

Lau L et al. *Pediatr Rev.* 2024;45:350–353.

The Patient's Diagnostic Journey Highlights Symptoms and Findings Prompting Suspicion of AIP

Symptom history

Prior history:

- Diagnosed with gastroparesis 1 year earlier and history of anxiety
- Weight loss of 15 kg in the past 6 months, and 4 kg in the preceding 2 weeks
- **Multiple presentations to EDs for abdominal and back pain** over the past 6 months

Initial evaluation

At admission:

- Physical examination revealed low BMI and **diffuse abdominal tenderness**
  - Worse in the periumbilical and epigastric areas
- Abnormal laboratory findings and imaging led to the patient's initial diagnosis of pancreatitis
- **Seizure** on Day 2 of admission

PICU evaluation

Transfer to PICU after seizure:

- Repeated laboratory test results showed severe **hyponatremia** post-seizure
  - Normal urine osmolality, elevated urine sodium level, low serum osmolality
- **Revised diagnosis:** SIADH
  - Treated with hypertonic saline and fluid restricted, and did not have any additional seizures after sodium level improved but continued to experience persistent symptoms of:
    - Hypokalemia, **hypophosphatemia, hypomagnesia, hypertension, constipation, pain, proximalmuscle weakness**

Clinical history plus persistence of abnormal laboratory findings and current symptoms despite treatment **prompted testing for suspected AIP**

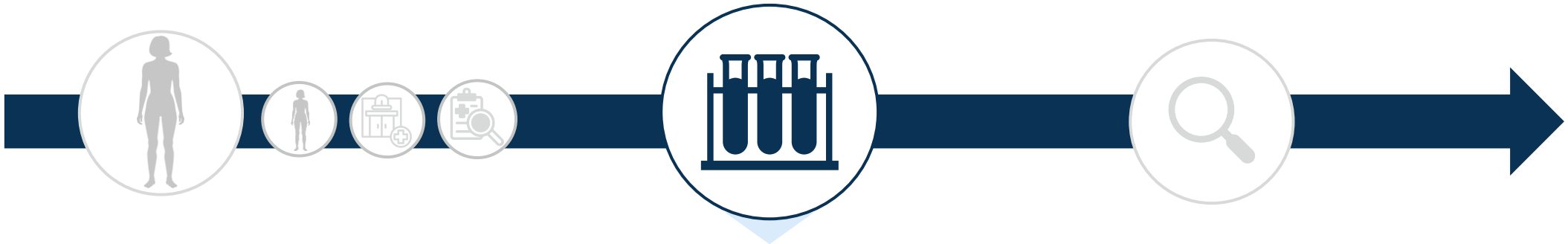
HCP Specialties Involved in Initial Work-up

Gastroenterologist* | ED doctor* | ED doctor* | Neurologist* | Intensivist*

*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up.
AIP, acute intermittent porphyria; BMI, body mass index; ED, emergency department; HCP, healthcare professional; PICU, pediatric intensive care unit; SIADH, syndrome of inappropriate antidiuretic hormone.
Lau L et al. *Pediatr Rev.* 2024;45:350–353.

Suspected AIP Symptoms Prompted Confirmatory Testing

Background | Testing | Diagnosis



Additional information that prompted AIP diagnostic testing:[1]

- Throughout admission she has persistent **hypertension** as well as hypokalemia, hypophosphatemia, and hypomagnesemia requiring supplementation
- She continued to have **persistent diffuse abdominal pain** despite treatment for constipation
- She complained of **headache** and **proximal muscle weakness** that interferes with daily living
- Her **urine** was noted to be **orange-colored** multiple times, despite multiple normal urinalyses (except for persistently elevated urobilinogen level)

Biochemical tests used to diagnose AHP

Urinalysis:[1]

- Her urine was ultimately tested for urine porphyrins, which showed **elevated porphyrin** levels confirming the diagnosis of AIP*

*ALA and PBG are porphyrin precursors and are not tested typically in porphyrin tests. Urine porphyrins should not be used alone as a screening test for AHP.[2]

AIP, acute intermittent porphyria, ALA, δ-aminolevulinic acid; PBG, porphobilinogen.

1. Lau L et al. *Pediatr Rev.* 2024;45:350–353; 2. Wang B et al. *Gastroenterology.* 2023;164:484–491.

Overview of Biochemical Tests Used to Achieve a Diagnosis of AHP

Random (spot) urine tests for **PBG**, ALA, creatinine, and porphyrins levels can help to diagnose AHP*,†,[1–4]

Urine porphyrins is a **non-specific test** and **should not be used in isolation for diagnosing AHP‡,[1,4]**

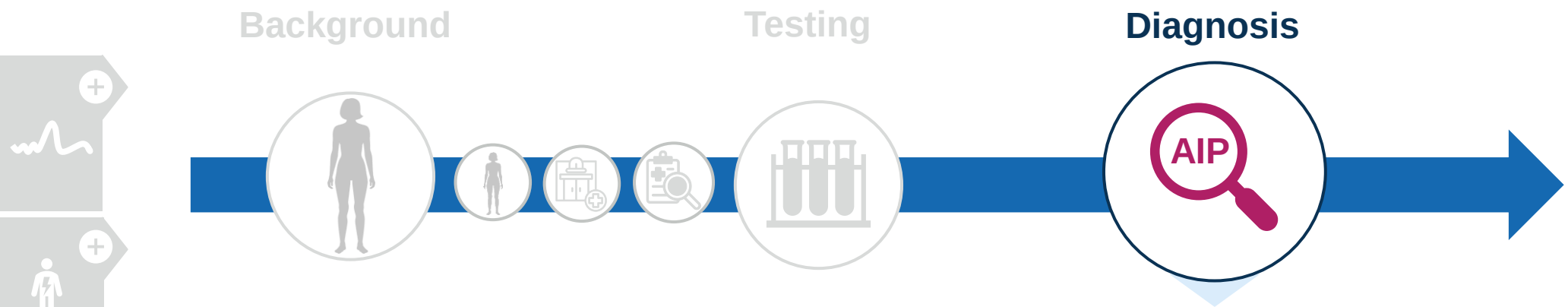
Ideal time to test is during or shortly after an acute attack; however, testing can be performed at any time if there is suspicion of AHP[1,3]

Additional biochemical tests, including plasma or fecal porphyrins and plasma fluorescence scanning, can be performed to help diagnose or confirm a diagnosis of AHP type, but are not specific for AHP when tested alone[3,4]

*PBG and ALA should be normalized to urinary creatinine;[1] †ALA and PBG levels can vary depending on time measured and AHP type, therefore repeat testing may be required for a diagnosis;[1]
‡The availability of biochemical tests for AHP are dependent on institution.[1]
AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; PBG, porphobilinogen.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Bonkovsky HL et al. *Am J Med.* 2014;127:1233–1241;
3. Whatley SD & Badminton MN. *Acute Intermittent Porphyria*. In: Adam MP et al. eds. *GeneReviews.* [Internet]. Seattle, WA: University of Washington; 2013;1993–2021;
4. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450.

Following Disease-Specific Testing, the Patient Was Diagnosed with AIP



HCP Specialties Involved in Ongoing Management:

- Hematologist
- Pediatrics
- Gastroenterologist
- Gynecologist

After confirmatory urinalysis, the patient was diagnosed with AIP

- This patient's presentation with hyponatremic seizures demonstrates a severe and unusual presentation of AIP
- The cause of the patient's SIADH was likely multifactorial:
  - Hypothalamic involvement from AIP
  - ADH release from vomiting and pancreatitis
- The patient's history of substantial weight loss with concern for disordered eating is a common trigger for recurrent AIP attacks
- Autonomic dysfunction due to AIP may have contributed to hypertension and tachycardia

ADH, antidiuretic hormone; AIP, acute intermittent porphyria; HCP, healthcare professional; SIADH, syndrome of inappropriate antidiuretic hormone.

Lau L et al. *Pediatr Rev.* 2024;45:350–353.

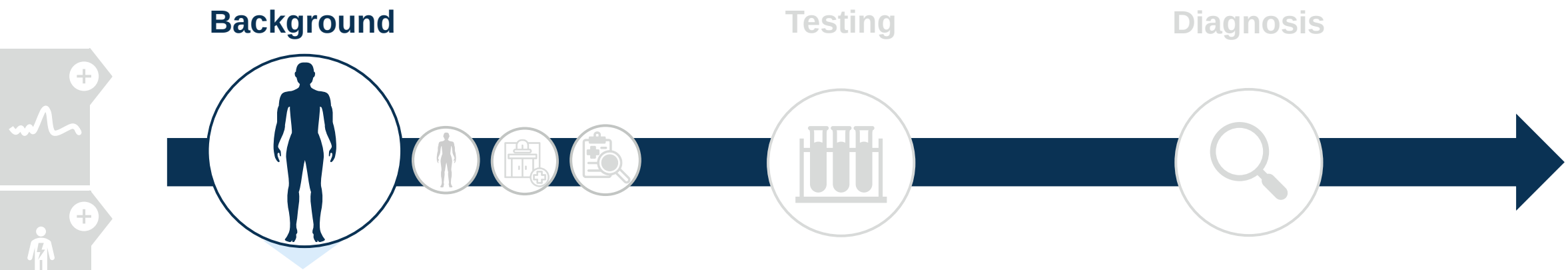
AHP Case Scenario: AIP Associated with Hyponatremia and Delirium*

Fabian E et al, 2023

*Based on a published case study.

Case of Hyponatremia and Delirium*

Background and clinical history



- **54-year-old male**
- Sciatica led to identification of massive disc prolapse managed by flavectomy and disc extraction
- Developed severe constipation after surgery
- Blood test revealed hyponatremia, which was severe and led to hospital readmission
- Prior to readmission, the patient was disorientated and confused
- After readmission, the patient was fatigued and not alert; he later developed acute delirium with visual hallucinations and was transferred to ICU for sodium replacement
- **Initial diagnosis:** Delirium with psychomotor symptoms

Click to reveal the initial signs of AHP in this patient

In this patient, symptoms were attributed to his recent surgery

*Based on a published case study. AHP, acute hepatic porphyria; ICU, intensive care unit.

Fabian E et al. *Wien Klin Wochenschr.* 2023;135:203–209.

The 54-Year-Old Patient Demonstrated Characteristics Consistent with the AIP Symptom Profile

Background

Testing

Diagnosis

- **54-year-old male**
- Sciatica led to identification of massive disc prolapse managed by flavectomy and disc extraction
- Developed **severe constipation** after surgery
- Blood test revealed **hyponatremia**, which was severe and led to hospital readmission
- Prior to readmission, the patient was disorientated and confused
- After readmission, the patient was **fatigued** and not alert; he later developed acute delirium with visual hallucinations and was transferred to ICU for sodium replacement
- **Initial diagnosis:** Delirium with psychomotor symptoms

In this patient, symptoms were attributed to his recent surgery

Key AIP symptoms in this patient

Hyponatremia **Fatigue**

Severe constipation

Other potential symptoms of AIP in this patient

- Visual hallucinations

AIP, acute intermittent porphyria; ICU, intensive care unit.

Fabian E et al. *Wien Klin Wochenschr.* 2023;135:203–209.

The Patient's Diagnostic Journey Highlights Symptoms Prompting Suspicion of AIP

Differential diagnosis excluded other causes of hyponatremia, therefore **AIP suggested**

Prior history:

- Chronic constipation
- UTI with suspected macrohematuria and lower **abdominal pain** 6 months prior to admission
- History of prolonged hangovers with abdominal pain and **headache** after alcohol consumption

At admission:

- Severe hyponatremia led to hospital admission (8 days after initial flavectomy surgery)
- Acute delirium with **visual hallucinations** led to ICU admission and initial psychiatric evaluation

Clinical evaluations:

- Acute hyponatremia confirmed
  - Given the development of hyponatremia within 48 hours after surgery
- Acute hypo-osmolar hyponatremia confirmed

Differential diagnosis of hypo-osmolar hyponatremia:

- Euvolemia confirmed
  - Volume status was normal, excluding hyper- and hypovolemia

Differential diagnosis of hypo-osmolar hyponatremia and euvolemia:

- AIP suspected
  - Cortisol deficiency, hypothyroidism, and SIADH excluded

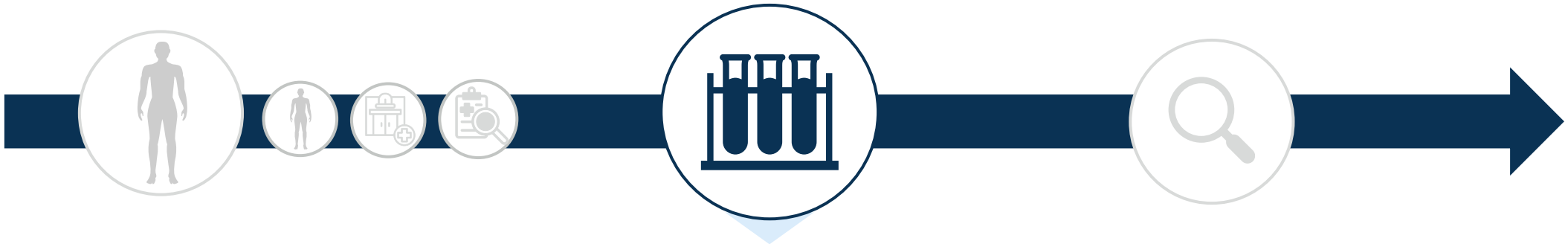
HCP Specialties Involved in Initial Work-up

Gastroenterologist* | Intensivist* | Psychiatrist | Nephrologist*

*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up.
AIP, acute intermittent porphyria; HCP, healthcare professional; ICU, intensive care unit; SIADH, syndrome of inappropriate antidiuretic hormone secretion; UTI, urinary tract infection.
Fabian E et al. *Wien Klin Wochenschr.* 2023;135:203–209.

Suspected AIP Symptoms Prompted Confirmatory Testing

Background | Testing | Diagnosis



Confirmatory tests for diagnosis of AIP were conducted:

- Porphyrins and their precursors analyzed in 24-hour urine were elevated

Laboratory test	Laboratory value	Result
Porphyrins (µg/24-hour urine)	576.30 (normal 0.00–150.00)	Elevated
ALA (µg/24-hour urine)	39.95 (normal 0.25–6.40)	Elevated
PBG (mg/24-hour urine)	121.71 (normal 0.10–1.70)	Elevated

- Genetic testing revealed a pathogenic heterozygous *HMBS* mutation

Biochemical tests used to diagnose AHP

AIP, acute intermittent porphyria; ALA, δ-aminolevulinic acid; HMBS, hydroxymethylbilane synthase; PBG, porphobilinogen.

Fabian E et al. *Wien Klin Wochenschr.* 2023;135:203–209.

Overview of Biochemical Tests Used to Achieve a Diagnosis of AHP

Random (spot) urine tests for **PBG**, ALA, creatinine, and porphyrins levels can help to diagnose AHP*,†,[1–4]

Urine porphyrins is a **non-specific test** and **should not be used in isolation for diagnosing AHP‡,[1,4]**

Ideal time to test is during or shortly after an acute attack; however, testing can be performed at any time if there is suspicion of AHP[1,3]

Additional biochemical tests, including plasma or fecal porphyrins and plasma fluorescence scanning, can be performed to help diagnose or confirm a diagnosis of AHP type, but are not specific for AHP when tested alone[3,4]

*PBG and ALA should be normalized to urinary creatinine;[1] †ALA and PBG levels can vary depending on time measured and AHP type, therefore repeat testing may be required for a diagnosis;[1]
‡The availability of biochemical tests for AHP are dependent on institution.[1]
AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; PBG, porphobilinogen.

1. Wang B et al. *Gastroenterology..* 2023;164:484–491; 2. Bonkovsky HL et al. *Am J Med.* 2014;127:1233–1241;
3. Whatley SD & Badminton MN. *Acute Intermittent Porphyria*. In: Adam MP et al. eds. *GeneReviews.* [Internet]. Seattle, WA: University of Washington; 2013;1993–2021;
4. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450.

Following Disease-Specific Testing, the Patient Diagnosis of AIP was Confirmed

Background

Testing

Diagnosis

HCP Specialties that may be Involved in AIP Management*,[1]

- Nephrologist
- Gastroenterologist
- Hematologist

After multiple tests, the patient was diagnosed with AIP[1]

- Medical history and symptoms presented by the patient were **highly suggestive of AIP**
- Elevated urinary porphyrins, PBG, and ALA levels, and genetic testing confirmed the suspected diagnosis

Practice guideline recommendations

- Genetic testing for *HMBS* homozygous mutations can confirm diagnosis in patients with suspected AIP[1–3]
- If a genetic variant is identified, **first-degree family members should be screened** to identify at-risk individuals[2]

*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up.

AIP, acute intermittent porphyria; ALA, δ-aminolevulinic acid; HCP, healthcare professional; HMBS, hydroxymethylbilane synthase; PBG, porphobilinogen.

1. Fabian E et al. *Wien Klin Wochenschr.* 2023;135:203–209; 2. Wang B et al. *Gastroenterology.* 2023;164:484–491; 3. Balwani M et al. *J Hepatol.* 2017;66:1314–1322.

AHP Case Scenario: Variegate Porphyria After Etonogestrel Placement*

Strome A et al, 2022

*Based on a published case study.

Case of VP After Etonogestrel Placement*

Background and clinical history

Background | Testing | Diagnosis

- **18-year-old female**
- Multiple painful, pruritic erythematous, crusted and eroded papules on the dorsal aspect of the hands and several lesions on the face
- The lesions had been present for 1 month
- **Initial diagnosis:** Impetigo
- Symptoms persisted despite treatment with topical mupirocin, and new lesions on the face and crusting of the eyelids developed

Click to reveal the initial signs of AHP in this patient

This patient had no significant past medical history

*Based on a published case study.
AHP, acute hepatic porphyria; VP, variegate porphyria.
Strome A et al. *JAAD Case Rep.* 2022;22:104–106.

The 18-Year-Old Patient Demonstrated Characteristics Consistent with the AHP Symptom Profile

- **18-year-old female**
- Multiple **painful, pruritic erythematous, crusted and eroded papules** on the dorsal aspect of the hands and several lesions on the face
- The lesions had been present for 1 month
- **Initial diagnosis:** Impetigo
- Symptoms persisted despite treatment with topical mupirocin, and new lesions on the face and crusting of the eyelids developed

This patient had no significant past medical history

Key AHP symptoms/indicators in this patient

Blisters

AHP, acute hepatic porphyria.

Strome A et al. *JAAD Case Rep.* 2022;22:104–106.

The Patient's Diagnostic Journey Highlights Symptoms Prompting Suspicion of VP

Persistence of symptoms following initial treatment for impetigo led to suspicion of **porphyria or pseudo-porphyria**

Prior history:

- No significant past medical history
- Had an **etonogestrel† implant** placed 4 months prior to presentation

At presentation:

- **Bilateral painful and pruritic erythematous crusted and eroded papules** on dorsal aspect of hands
- Several **lesions** on the face

Clinical evaluations:

- Impetigo
  - Mupirocin ointment prescribed to apply to the affected areas
  - **Persistence of symptoms despite treatment**

Differential diagnosis porphyria and pseudo-porphyria:

- Biopsy of 2 lesions
  - Histologic features were consistent with reparative changes associated with porphyria
  - Direct immunofluorescence revealed an immune deposition pattern consistent with porphyria‡

HCP Specialties Involved in Initial Work-up

Primary care physician* | Dermatologist*

Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up. †Progesterone-only contraceptive implant. ‡Smooth IgG, IgA (weak), IgM (weak) and C3 binding in the superficial vessel walls, and weak linear IgG deposition along the dermo-epidermal junction.

C3, Complement component 3; HCP, healthcare professional; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; VP, variegate porphyria.

Strome A et al. *JAAD Case Rep.* 2022;22:104–106.

Suspected VP Symptoms Prompted Confirmatory Testing

Background | **Testing** | Diagnosis

Confirmatory tests for diagnosis of VP were conducted:

- Laboratory tests revealed elevated porphyrins and porphyrin precursors in urine, fecal, and plasma samples
- Genetic testing showed a heterozygous variant of uncertain significance in the *PPOX* gene*

Biochemical tests used to diagnose AHP

The patient did not report any other acute porphyria symptoms such as abdominal pain, neuropathy, nausea, or confusion

*Variant c.23T>C[p.Leu8Pro].
AHP, acute hepatic porphyria; PPOX, protoporphyrinogen oxidase; VP, variegate porphyria.
Strome A et al. *JAAD Case Rep.* 2022;22:104–106.

Overview of Biochemical Tests Used to Achieve a Diagnosis of AHP

Random (spot) urine tests for **PBG**, ALA, creatinine, and porphyrins levels can help to diagnose AHP*,†,[1–4]

Urine porphyrins is a **non-specific test** and **should not be used in isolation for diagnosing AHP‡,[1,4]**

Ideal time to test is during or shortly after an acute attack; however, testing can be performed at any time if there is suspicion of AHP[1,3]

Additional biochemical tests, including plasma or fecal porphyrins and plasma fluorescence scanning, can be performed to help diagnose or confirm a diagnosis of AHP type, but are not specific for AHP when tested alone[3,4]

*PBG and ALA should be normalized to urinary creatinine;[1] †ALA and PBG levels can vary depending on time measured and AHP type, therefore repeat testing may be required for a diagnosis;[1]
‡The availability of biochemical tests for AHP are dependent on institution.[1]
AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; PBG, porphobilinogen.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Bonkovsky HL et al. *Am J Med.* 2014;127:1233–1241;
3. Whatley SD & Badminton MN. *Acute Intermittent Porphyria*. In: Adam MP et al. eds. *GeneReviews.* [Internet]. Seattle, WA: University of Washington; 2013;1993–2021;
4. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450.

Following Disease-Specific Testing, the Patient was Diagnosed with VP

Background

Testing

Diagnosis

HCP Specialties that may be Involved in VP Management*

- Primary care physician
- Dermatologist

After multiple tests, the patient was diagnosed with VP

- Results of histological and immunogenic analyses of lesions were indicative of porphyria
- **Elevated urinary, fecal, and plasma porphyrins, followed by genetic testing confirmed the suspected diagnosis**

The timing of the patients first use of hormonal birth control 4 months prior to presentation, led to the conclusion that the etonogestrel implant was the trigger for her VP

- Progesterone is an **inducer of heme synthesis** and can provoke porphyria symptoms in women
- Cyclical acute porphyria attacks have been reported during the luteal phase of the menstrual cycle, at which point progesterone is particularly elevated

*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up.
HCP, healthcare professional; VP, variegate porphyria.
Strome A et al. *JAAD Case Rep.* 2022;22:104–106.

AHP Case Scenario: AIP Associated with hCG Injections*

Mahesheema A and Iqbal S, 2024

*Based on a published case study.
hCG, human chorionic gonadotropin.

Case of AIP Associated with hCG Injections*

Background and clinical history

Background | Testing | Diagnosis

- **34-year-old female**
- Presented to ED with severe abdominal pain, diffuse body aches and fatigue
- She reported a stabbing chest pain that radiated to her back, numbness, tingling in both hands and feet, and a burning sensation
- Admitted to the ICU for monitoring and to restore electrolyte imbalances
- Following initial discharge, the patient continued to experience symptoms prompting multiple ED visits
- **Initial diagnosis:** Keto flu
- Symptoms of whole-body pain, muscle pain, and abnormal sensations continued to worsen

Click to reveal the initial signs of AIP in this patient

In this patient, symptoms were initially attributed to inadequate nutrient intake associated with a calorie-restricted ketogenic diet and injection of hCG for weight loss

*Based on a published case study.
AIP, acute intermittent porphyria; ED, emergency department; hCG, human chorionic gonadotropin; ICU, intensive care unit.
Ali M and Iqbal S. *Cureus.* 2024:16:e68651.

The 34-Year-Old Patient Demonstrated Characteristics Consistent With the AIP Symptom Profile*

Background | Testing | Diagnosis

- **34-year-old female**
- Presented to ED with **severe abdominal pain, diffuse body aches and fatigue**
- She reported a **stabbing chest pain that radiated to her back**, **numbness**, tingling in both hands and feet, and a burning sensation
- Admitted to the ICU for monitoring and to restore electrolyte imbalances
- Following initial discharge, the patient continued to experience symptoms prompting multiple ED visits
- **Initial diagnosis:** Keto flu
- Symptoms of **whole-body pain**, **muscle pain,** and abnormal sensations continued to worsen

In this patient, symptoms were initially attributed to inadequate nutrient intake associated with a calorie-restricted ketogenic diet and injection of hCG for weight loss

Key AIP symptoms in this patient

Severe abdominal pain

Diffuse body aches

Fatigue

Pain

Numbness

Other potential symptoms of AIP in this patient

- Tingling in both hands and feet
- Burning sensation

*Based on a published case study.

AIP, acute intermittent porphyria; ED, emergency department; hCG, human chorionic gonadotropin; ICU, intensive care unit.

Ali M and Iqbal S. *Cureus.* 2024:16:e68651.

The Patient's Diagnostic Journey Highlights Symptoms Prompting Suspicion of AIP

Follow-up laboratory testing of the patient's urine revealed abnormal porphyrins and consideration of a potential **porphyria diagnosis**

Prior history:

- Diffuse **abdominal and muscle pain** in the 5 months leading up to the acute episode
- **Calorie-restricted diet** (500 calories/day)
- hCG injections for weight loss

At presentation:

- **Abdominal pain, diffuse body aches, fatigue**
- Severe **chest pain**
- **Shortness of breath**
- **Numbness** in both **hands and feet**

Clinical evaluations:

- Keto flu
  - Blood pressure 155/110 and **heart rate of 130 bpm**
  - Laboratory tests, EKG, and imaging studies were unremarkable with exception of low sodium levels of 128 mmol/L (reference range: 135–148 mmol/L)†

Recommended to undergo further laboratory testing and genetic consultation

- Porphyria suspected after urinalysis **revealed elevated porphyrins and ALA**

HCP Specialties Involved in Initial Work-up

ED doctor* | Intensivist* | Dietician*

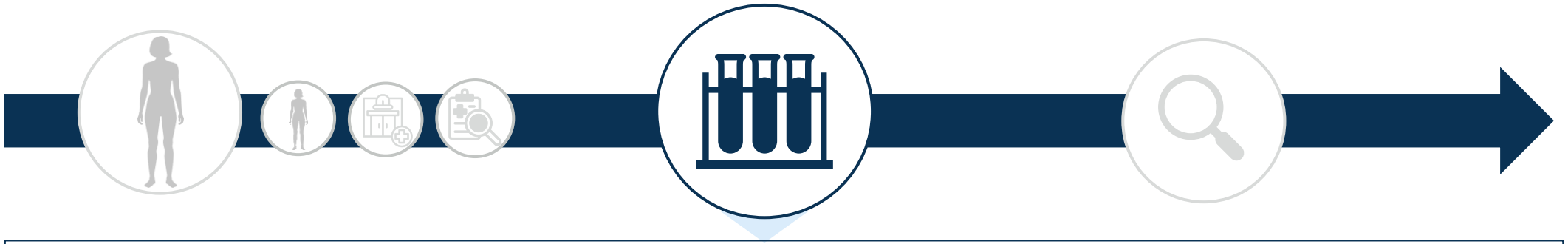
*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up. †In the case report, it was also noted that the patient had low potassium levels at 3.9mmol/L which were within normal levels (reference range 3.3-5.3mmol/L).

ALA, δ-aminolevulinic acid; AIP, acute intermittent porphyria; EKG, electrocardiogram; hCG, human chorionic gonadotropin; HCP, healthcare professional; bpm, beats per minute.

Ali M and Iqbal S. *Cureus.* 2024:16:e68651.

Suspected AIP Symptoms Prompted Confirmatory Testing

Background | Testing | Diagnosis



Additional laboratory tests were suggestive of a porphyria diagnosis:

Biochemical tests used to diagnose AHP

Laboratory test	Laboratory value	Result
Total porphyrins (µg/g creatinine)	1859.0 (normal 27.0–153.6)	Elevated
5-ALA (µg/g creatinine)	34.4 (normal <5.4)	Elevated

- Genetic testing revealed a sequence mutation in a donor splice site* of the *HMBS* gene

*c.771+2T>C.
AIP, acute intermittent porphyria; ALA, δ-aminolevulinic acid; HMBS, hydroxymethylbilane synthase.
Ali M and Iqbal S. *Cureus.* 2024:16:e68651.

Overview of Biochemical Tests Used to Achieve a Diagnosis of AHP

Random (spot) urine tests for **PBG**, ALA, creatinine, and porphyrins levels can help to diagnose AHP*,†,[1–4]

Urine porphyrins is a **non-specific test** and **should not be used in isolation for diagnosing AHP‡,[1,4]**

Ideal time to test is during or shortly after an acute attack; however, testing can be performed at any time if there is suspicion of AHP[1,3]

Additional biochemical tests, including plasma or fecal porphyrins and plasma fluorescence scanning, can be performed to help diagnose or confirm a diagnosis of AHP type, but are not specific for AHP when tested alone[3,4]

*PBG and ALA should be normalized to urinary creatinine;[1] †ALA and PBG levels can vary depending on time measured and AHP type, therefore repeat testing may be required for a diagnosis;[1]
‡The availability of biochemical tests for AHP are dependent on institution.[1]
AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; PBG, porphobilinogen.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Bonkovsky HL et al. *Am J Med.* 2014;127:1233–1241;
3. Whatley SD & Badminton MN. *Acute Intermittent Porphyria*. In: Adam MP et al. eds. *GeneReviews.* [Internet]. Seattle, WA: University of Washington; 2013;1993–2021;
4. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450.

Following Disease-Specific Testing, the Patient was Diagnosed with AIP

Background

Testing

Diagnosis

HCP Specialties that may be Involved in AIP Management*,[1]

- ED doctor
- Intensivist
- Dietician

After multiple tests, the patient was diagnosed with AIP[1]

- Medical history and symptoms were highly suggestive of AIP
- Elevated urinary porphyrins and ALA levels and genetic testing confirmed the suspected diagnosis

The patient was advised to continue her low-calorie diet, but to discontinue hCG injections

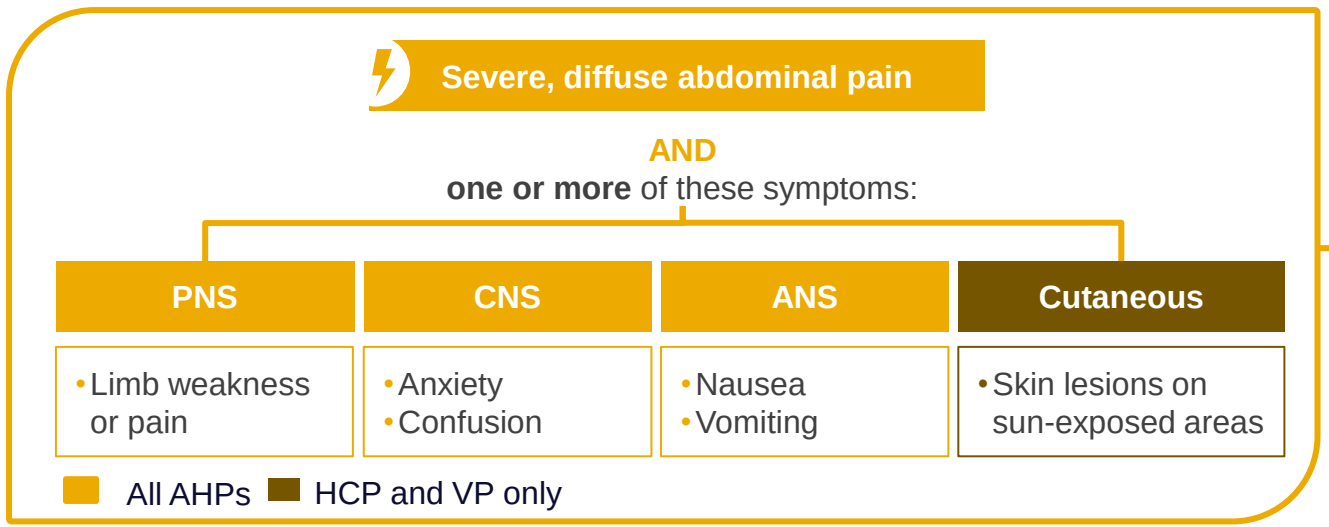
- hCG stimulates estrogen and progesterone
- Progesterone is a known trigger for AIP as an inducer of the heme biosynthesis pathway

*Not specified in case report, assumed based on symptom presentation and detail regarding extensive work-up.
AIP, acute intermittent porphyria; ALA, aminoleuvulinic acid; ALAS1, hepatic 5-ALA synthase; hCG, human chorionic gonadotropin; HCP, healthcare professional.
Ali M and Iqbal S. *Cureus.* 2024:16:e68651.

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Should Prompt Testing to Support an Early Diagnosis of AHP

AHP Can Be Characterized by Chronic and Acute Symptoms, Which Should Prompt Testing to Support an Early Diagnosis of AHP

- **AHP** represents a group of rare, genetic diseases, which can be **characterized by chronic symptoms** as well as potentially **life-threatening acute attacks** that negatively impact patient functioning and QoL[1–4]
- AHP should be considered in **any patient**, especially any **woman of childbearing age**, who presents with **unexplained recurrent, severe abdominal pain**[1]
- Key symptom clusters can support early identification of AHP[1,5,6]



Initial diagnosis of AHP should be made in suspected patients by biochemical testing measuring levels of ALA, PBG, porphyrins, and creatinine in a random urine sample followed by confirmatory genetic testing[1]

AHP, acute hepatic porphyria; ALA, δ-aminolevulinic acid; ANS, autonomic nervous system; CNS, central nervous system; HCP, hereditary coproporphyria; PBG, porphobilinogen; PNS, peripheral nervous system; QoL, quality of life; VP, variegate porphyria.

1. Wang B et al. *Gastroenterology.* 2023;164:484–491; 2. Kothadia JP et al. *Acute Hepatic Porphyria.* In: *StatPearls.* [Internet]. Last update: May 2023. Available at: https://www.ncbi.nlm.nih.gov/books/NBK537178 (accessed March 2025); 3. Cassiman D et al. *J Inherit Metab Dis.* 2022;45:1163–1174; 4. Dickey A et al. *JIMD Rep.* 2022;64:104–113; 5. Anderson KE et al. *Ann Intern Med.* 2005;142:439–450; 6. Ventura P et al. *Eur J Intern Med.* 2014;25:497–505.