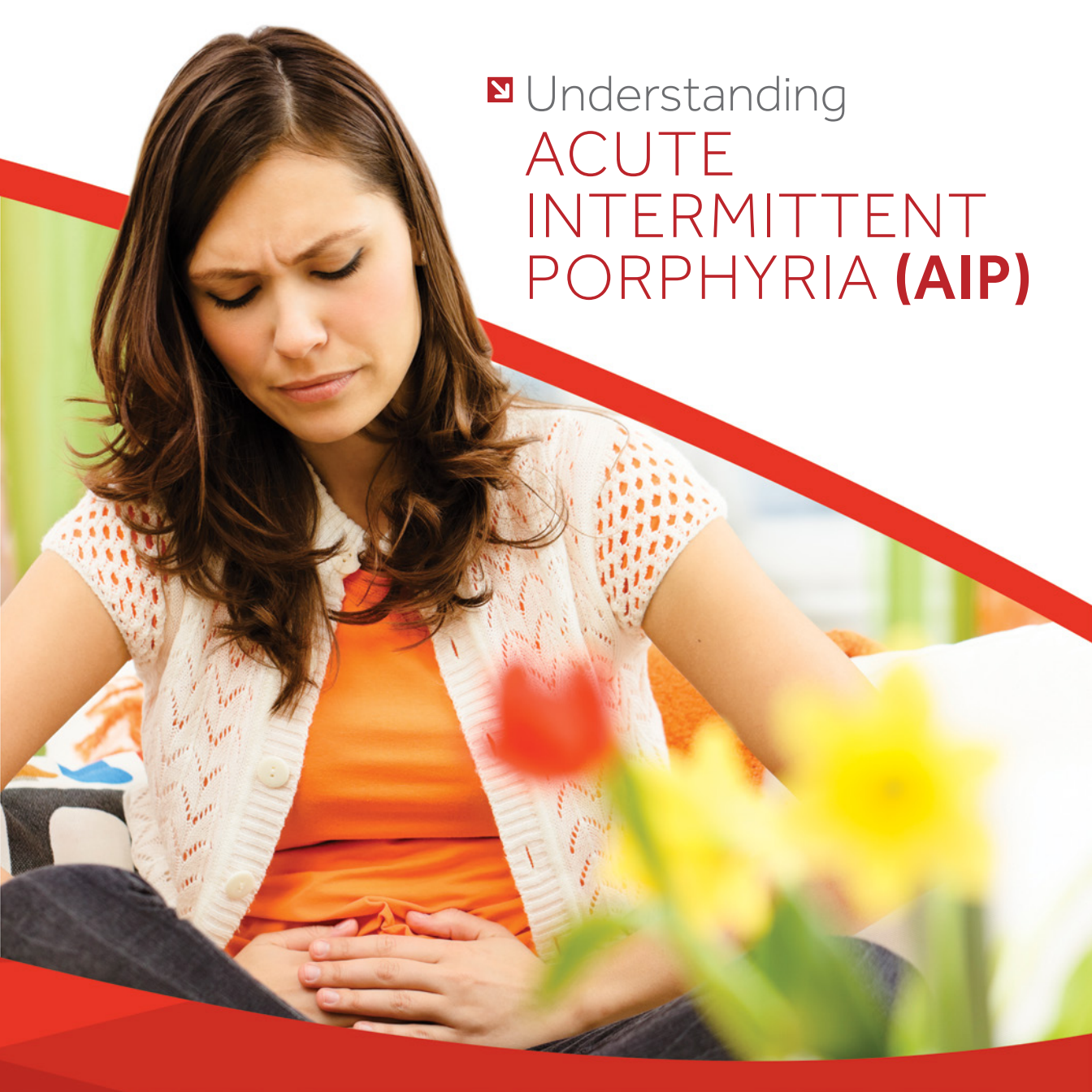


Understanding ACUTE INTERMITTENT PORPHYRIA **(AIP)**

Understanding AIP

The porphyrias are metabolic diseases that cause accumulation of intermediate compounds in the heme biosynthetic pathway. They occur chiefly due to mutations in the genes encoding the enzymes involved in heme production.[1]

The 4 hepatic acute porphyrias are:[1,2]

Autosomal dominant	Very rare autosomal recessive disorder
↘ Variegate porphyria ↘ Acute intermittent porphyria ↘ Hereditary coproporphyria	↘ δ-aminolevulinate dehydratase deficiency porphyria

The prevalence of acute porphyrias in most European countries is 1-2 per 100,000 inhabitants; most of these have AIP.[2]

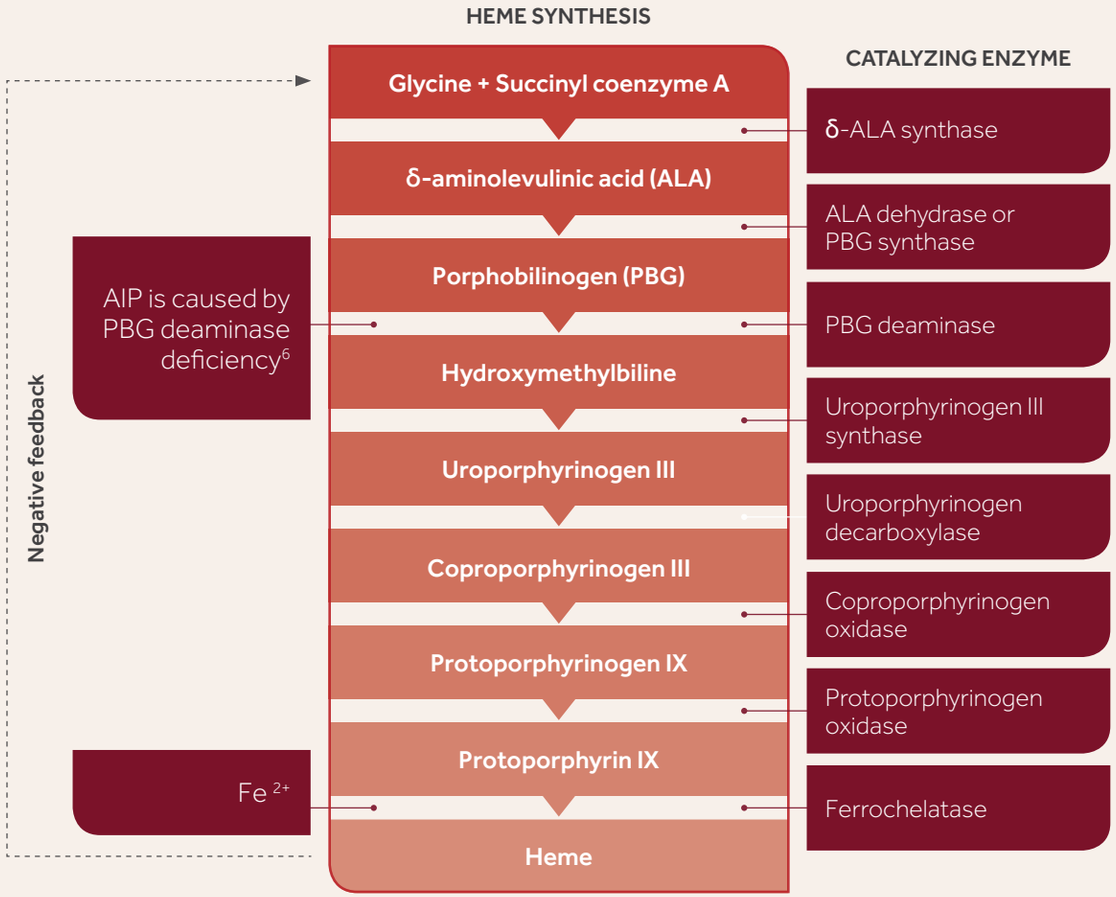
- Using the European studies as a reference (there is no prevalence information on AIP in Canada), there could be between 360-720 Canadians with AIP.[3]
- Since AIP has low penetrance, approximately 1 in 5 AIP patients present with symptoms.[4,5]

AIP defined

AIP is a rare inherited disease caused by a partial deficiency of the enzyme porphobilinogen (PBG) deaminase in the heme biosynthetic pathway.[6]

- PBG deficiency disrupts normal heme production, which leads to overproduction of porphyrin precursors that cause diverse pathologic changes.[7]
- Accumulation of heme intermediates in the liver, plus precipitating factors, can lead to AIP attacks.[6]
- Abdominal pain, the most common symptom, is neuropathic in origin and is usually severe, unremitting, and diffuse.[6]

Simplified metabolic pathway for heme synthesis[7,8]

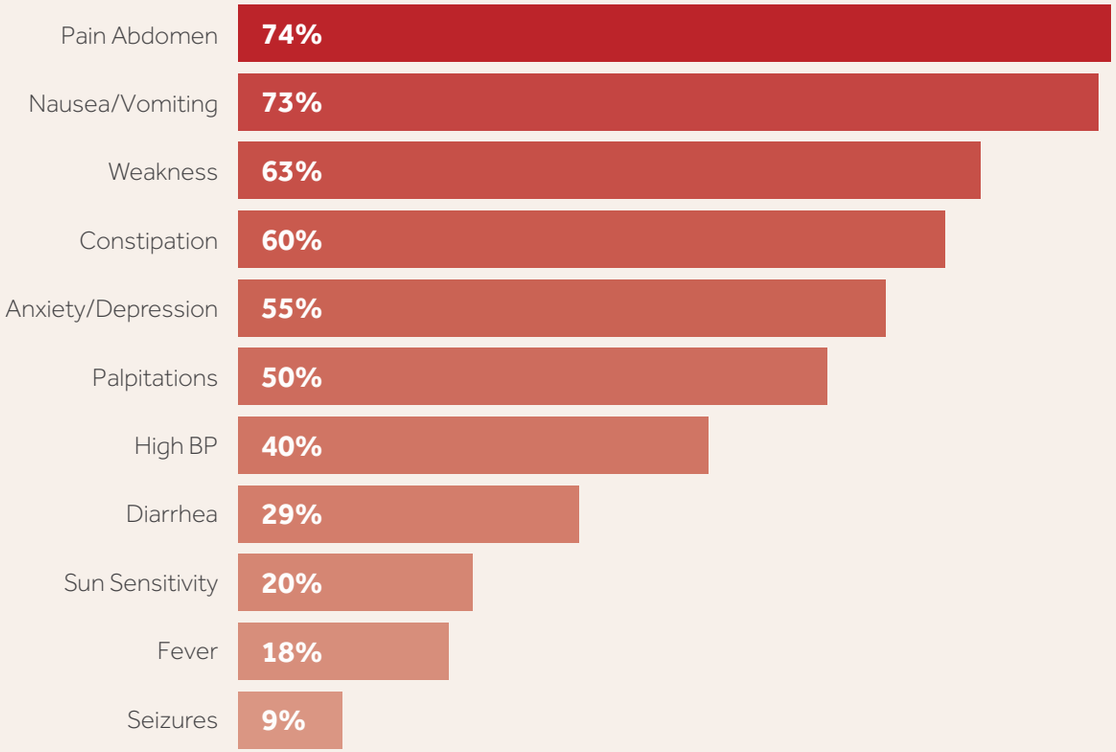


Adapted from Gonzalez-Arriaza 2003.

Clinical features of AIP[9]

- Symptoms may develop after puberty, especially in women.
- Acute attacks almost always start with severe pain in the abdomen but sometimes in the chest, back, or thighs, and are often accompanied by nausea, vomiting, and constipation.
- Heart rate and blood pressure are commonly increased.
- Confusion, convulsions, and muscular weakness, due to impairment of the nerves controlling the muscles, may lead to paralysis.
- An acute attack usually lasts for days or weeks.
- Recovery from severe paralysis is generally slow.

Prevalence of signs and symptoms during acute attacks of AIP[1,†]



Adapted from Bonkovsky 2014.

† Between September 2010 and December 2012, 108 subjects with acute porphyrias (90 acute intermittent porphyrias, 9 hereditary coproporphyrias, 9 variegate porphyrias) were enrolled into an observational study. Genetic testing was performed at a central genetic testing laboratory and clinical information entered into a central database. Selected features were compared with data for adults in the US.

Exacerbating factors for AIP attacks

Attacks are usually due to the additive effects of several exacerbating factors, including (not all-inclusive):

- Luteal phase of menstrual cycle[6]
- Use of alcohol or illicit drugs[6,10]
- Endogenous hormones[6]
- Crash dieting[6]
- Smoking[6,10]

Diagnosis of AIP is challenging because signs and symptoms mimic other, more common conditions.[6]

How is AIP diagnosed?

A urine test for porphobilinogen (PBG) should be used to confirm a diagnosis of AIP in a symptomatic patient.[6]

- The test must be ordered at or near the time of acute symptoms.
- Urinary PBG level is markedly increased during acute attacks of AIP.

If a patient's PBG level is increased, additional tests should be done. Laboratory findings that can confirm the diagnosis include:[6]

- ↑ **Urine porphyrin levels (mostly uroporphyrin) markedly increased**
- ↑ **Fecal porphyrin levels normal or slightly increased**
- ↑ **Plasma porphyrin levels normal or slightly increased**
- ↓ **Erythrocyte PBG deaminase levels decreased by ~50%**

AIP is an inherited disease. Diagnostic enzymatic and DNA tests are available to identify family members who may be at risk.[6]

AIP at a glance

- AIP is a rare inherited disease caused by a partial deficiency of the enzyme porphobilinogen (PBG) deaminase in the heme biosynthetic pathway.[6]
- Abdominal pain, the most common symptom, is neuropathic in origin and is usually severe, unremitting, and diffuse.[6]
- Diagnosis of AIP is challenging because signs and symptoms mimic other, more common conditions.[6]

For more information, visit **www.canadianassociationforporphyria.ca**

The mission of the Canadian Association for Porphyria is to deliver evidence-based information and support to patients with porphyria, their families, health care providers and the general public across Canada.

Canadian Association for **Porphyria**

Association Canadienne de **Porphyrie**

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