

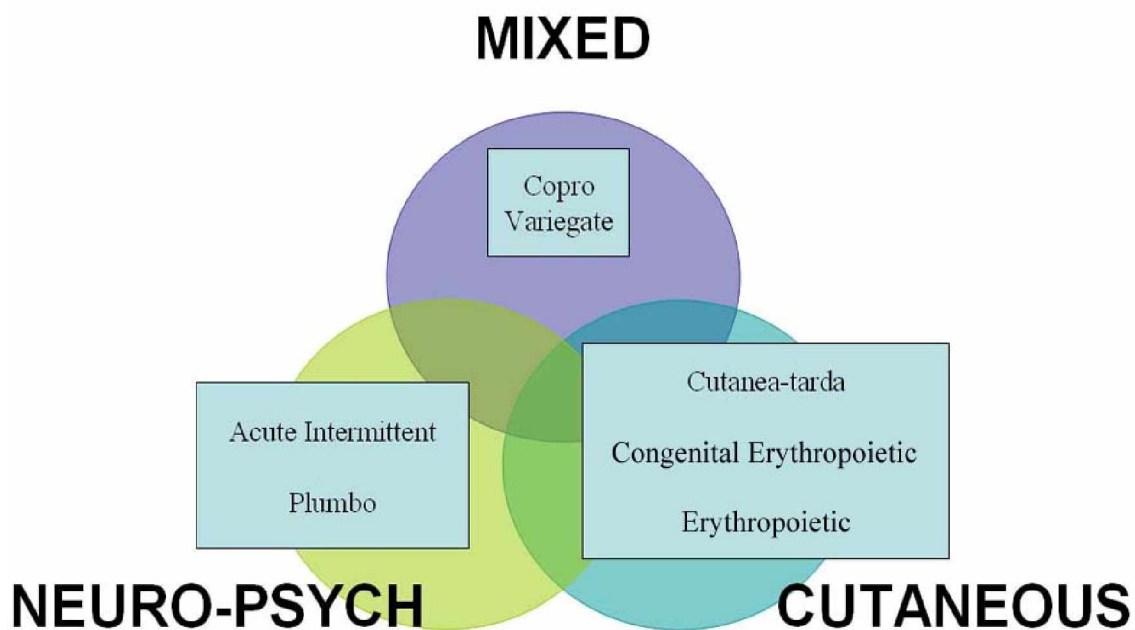
Porphyria Overview

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Background

Porphyria is named from the ancient Greek word *porphura*, meaning purple.¹ Porphyrins are precursors of heme, a part of the hemoglobin molecule. Heme is manufactured in a multistep process. Defects of enzymes needed at various steps of heme synthesis result in distinct clinical syndromes known as porphyrias. These syndromes can be clinically classified into those predominantly involving the skin, those manifesting as disorders of the liver/nervous system, and a combination involving all 3 entities (see Image 1, or below).



Clinical classification of porphyrias.

Porphyrias can be inherited or (rarely) acquired.² With the exception of congenital erythropoietic porphyria (CEP), which is autosomal recessive, all other porphyrias are inherited as autosomal dominant disorders. They invariably result in accumulation and increased excretion of porphyrins and their precursors. Some porphyrias have acute presentations (acute intermittent, variegate, hereditary coproporphyria), whereas others have a chronic, relatively stable presentation (congenital, erythropoietic).³

King George III of England had symptoms of abdominal pain, rashes, reddish urine, and psychotic episodes that are

consistent with porphyria, although the account is disputed by many.⁴

During the period 1955-1959, approximately 4000 people in southeast Anatolia (Turkey) developed porphyria due to the ingestion of hexachlorobenzene (HCB), a fungicide that was added to wheat seedlings.⁵

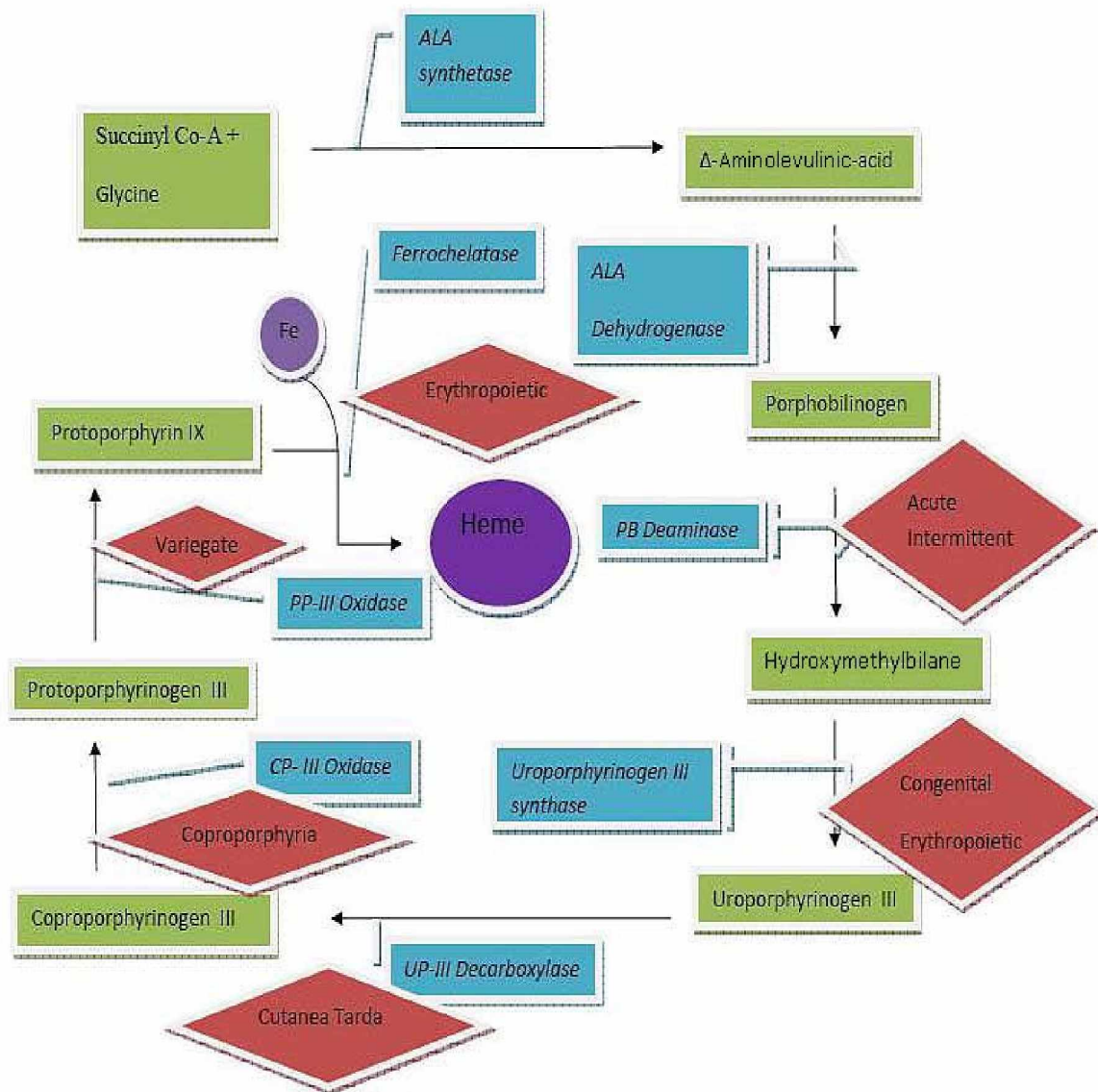
Pathophysiology

Urine and stool studies in various types of porphyria are summarized in Image 2.

Porphyria Type	Urine	Stool
Acute Intermittent	ALA/PBG ?	ALA/PBG ?
Variegata	ALA/PBG/Copro ?	Copro ?
Coproporphyrinuria	ALA/PBG/Copro ?	Copro ?
Delta-ALA dehydratase deficiency porphyria	ALA	---
Congenital Erythropoietic	Uro	Iso-Copro
Congenital Erythropoietic	Uro/Copro	Copro
Erythropoietic	---	Proto

Porphyryns in stool and urine in different porphyrias.

Heme synthesis is summarized in Image 3. In some porphyria patients and families, however, these diagnostic tools can reveal simultaneous findings that are compatible with 2 different forms of porphyria, a phenomenon referred to as dual porphyria.⁶



Heme biosynthesis and the porphyrias.

Porphyrias present in 2 distinct syndromes, acute and chronic.

Acute porphyrias

The acute porphyrias are characterized by periodic acute attacks of neurovisceral symptoms and may stay occult for a long time. Four major disorders in this group are the Doss porphyria, acute intermittent porphyria, hereditary coproporphyrria, and variegate porphyria. These porphyria syndromes are characterized by abdominal pain, neurologic deficits, psychiatric symptoms, and colored (red) urine.

Chronic porphyrias

The chronic porphyrias are dermatologic diseases that may or may not involve the liver and nervous system and do not present with acute attacks as described for the acute porphyrias above. These syndromes include congenital

erythropoietic porphyria, erythropoietic porphyria, and porphyria cutanea tarda.

Clinical manifestations

Clinical manifestations depend on the step in which the enzymatic defect occurs. If the enzymatic defects are in the initial steps of the metabolic cascade, early metabolic intermediates will accumulate (ie, aminolevulinic acid [ALA] and porphobilinogen [PBG]), which are responsible for attacks of neurologic dysfunction. If the enzymatic defects are in the final steps, sunlight-induced cutaneous lesions (photosensitivity) due to porphyrin accumulation in the skin will develop.⁷

Doss porphyria / plumboporphyria

Doss porphyria, also known as plumboporphyria (ALA dehydratase deficiency), is extremely rare.⁸ Abdominal pain and polyneuropathy are typical of this syndrome. Urinary ALA and coproporphyrin are markedly increased. Molecular genetic studies of the ALA dehydratase gene reveal the mutated nucleotides. In some patients, the development of the acute porphyria syndrome while the patient received pharmacologic doses of erythropoietin, which resolved when the drug was stopped, suggests that by stimulating heme synthesis, erythropoietin may unmask an enzyme deficiency resulting in the clinical expression of ALA dehydratase deficiency porphyria.⁹ Sometimes, exposure to lead may unmask occult plumboporphyria.¹⁰

Acute intermittent porphyria

Acute porphyria attacks are brought about by uncontrolled upregulation of the ALA synthase enzyme. This can be precipitated by certain lipophilic drugs (see the Drugs to Avoid section), hypoglycemia ("the glucose effect"),¹¹ and a deficiency of heme, the end-product of the heme pathway (see Image 3) that acts as a negative feedback mechanism in normal circumstances.¹²

Hereditary coproporphyria

Hereditary coproporphyria results in most cases from half-normal activity (50%) of coproporphyrin oxidase.¹³ The disease is an acute hepatic porphyria that is characterized by abdominal pain, neuropsychiatric symptoms, and cutaneous photosensitivity¹⁴ In rare homozygous cases, enzyme activity decreases to <10% and the term harderoporphyria is used.¹⁵

Variegate porphyria

Variegate porphyria is an autosomal dominant inherited trait that results in decreased activity of protoporphyrinogen oxidase. It is characterized clinically by photosensitive skin disease and a propensity to acute neurovisceral crises. Variegate porphyria is found worldwide but has an exceptionally high frequency in South Africa.¹⁶

Erythropoietic porphyria

In erythropoietic porphyria, the protoporphyrin molecule accumulates and can be excited by absorbing light energy. This causes the generation of free radicals and, thereby, photosensitivity of all tissues exposed to light. In the dark, several other toxic mechanisms have been described: deposition of protoporphyrin crystals in hepatocytes and bile canaliculi, interference with redox systems and, recently, formation of cytotoxic bile. Clinical manifestations of erythropoietic porphyria are photosensitivity, insignificant hematologic abnormalities, and liver disease.¹⁷ The hepatic manifestations of the disease are diverse: mildly disturbed liver enzymes in 20% to fatal hepatic failure in less than 5%.¹⁸

Porphyria cutanea tarda

Porphyria cutanea tarda (PCT) is characterized by the defective uroporphyrinogen III decarboxylase enzyme. There are 3 types of porphyria cutanea tarda with typical skin manifestations; patients present with skin fragility, erosions, vesicles, bullae, and milia in sun-exposed areas of the skin. Sometimes, there is the presence of periorbital mottled hyperpigmentation and hypertrichosis, sclerodermoid changes, and ulceration.

Hemochromatosis gene (HFE) mutations and the hepatitis C virus (HCV) are both risk factors for PCT. In a French cohort of PCT patients with both C282Y and H63D were more frequent in PCT+ patients than in controls, but there was no difference in HFE genotype according to HCV seropositivity.¹⁹ Up to two thirds of Saxon patients with PCT carry the classic HFE mutations (C282Y and/or H63D). PCT is associated with antibodies to HCV. PCT is an important extrahepatic manifestation of HCV-infection.²⁰ In a Swedish cohort, 38% of male patients with PCT had a history of alcohol abuse.²¹

Congenital erythropoietic porphyria (Gunther's disease)

Congenital erythropoietic porphyria, or Gunther's disease, is one of the least common porphyrias.²² It results from a deficient activity of uroporphyrinogen III synthase (URO-synthase). Hemolysis may be a feature in homozygous cases.²³ Prolonged exposure to sunlight may precipitate a blistering rash, red urine, and even blindness.²⁴

Prevalence

- The combined prevalence of the acute porphyrias is approximately 5 cases per 100,000 persons.²⁵
- Porphyria cutanea tarda is the most common porphyria.²⁶
- The prevalence of erythropoietic porphyria in a study was estimated at 1.75 per 100,000 population.²⁷
- Congenital erythropoietic porphyria is extremely rare. Less than 200 cases have been reported in the literature.²⁸

History

Abdominal pain

The most common presenting symptom (90%) of an acute porphyria is abdominal pain.²⁹ This is usually colicky in nature, located in the left lower abdomen, and lasts hours to days. The abdominal pain is rarely accompanied by fever, leukocytosis, or peritoneal signs. Nausea and vomiting appear common.³⁰ There is a very characteristic discrepancy between the serious complaints and the actual clinical findings.³¹

In a minority of patients, paresis may be the only presentation without abdominal pain.³² When a patient has repetitive visits to the emergency department because of severe abdominal pain without reasonable causes and needs narcotics for pain control, acute porphyria should be taken into consideration.³³

Muscle weakness and neurologic deficits

Muscle weakness and focal neurologic deficit such as tetraparesis³⁴ may be the presenting feature,³⁵ especially in women of reproductive age. Limb pain is common.

The lifetime prevalence of acute intermittent porphyria-associated seizures has been reported as 2.2% of all those with known acute intermittent porphyria and 5.1% of all those with manifest acute intermittent porphyria. Epileptic seizures

among persons with acute intermittent porphyria are less common than has been previously described.³⁶

Psychiatric symptoms

Some patients develop psychiatric symptoms such as psychosis similar to schizophrenia. Diagnostic difficulty may lead to underdiagnosis of patients who present with strictly psychiatric symptoms. This assumption is supported by a high prevalence of acute intermittent porphyria in psychiatric hospitals.³⁷

Anxiety is raised in patients with acute intermittent porphyria and with variegate porphyria, in males and females, compared with the normal population.³⁸

Other

Acute intermittent porphyria should be suspected in individuals presenting with unexplained acute abdominal pain following international air travel.³⁹

The relative risk of an acute attack in acute intermittent porphyria compared with that in variegate porphyria was 14 in a series of 112 patients from South Africa with porphyria attack.⁴⁰

A thorough family history for porphyria and the patient's occupational history must be obtained.

Physical Examination

- In acute porphyrias presenting as abdominal pain, attention should be paid to peritoneal signs. The presence of localized tenderness, rebound tenderness, vaginal discharge, cervical motion tenderness, and/or genitourinary bleeding should raise "red flags" even in patients known to carry a diagnosis of porphyria, and alternative diagnoses should be sought.
- Jaundice may or may not be present.⁴¹
- A focused neurologic exam should be performed to identify motor and sensory deficits and peripheral neuropathy.
- In some but not all acute porphyrias, a skin rash may be seen. Variegate porphyria and, much less commonly, hereditary coproporphyria can also cause chronic, blistering lesions on sun-exposed skin that are identical to those in porphyria cutanea tarda, a much more common condition.
- Gross, biochemical, and microscopic examination of the patient's urine is paramount if porphyria is on the differential diagnosis. The urine of patients with porphyria cutanea tarda is red to brown in natural light and pink to red in fluorescent light.⁴²

Laboratory

- Urine
 - Urine porphyrin studies are the mainstay in the diagnosis of acute porphyria attacks. Establish the diagnosis promptly by testing for increased porphobilinogen in a single-void urine. An expert guidelines panel recommended the Trace PBG Kit [Thermo Trace/DMA, Arlington, Tex].²⁹
 - Patients with acute exacerbations of porphyria have logarithmic increases (5-100 times) in metabolic precursors (ALA, PBG, etc). Minor elevations of these precursors are nondiagnostic and nonspecific.⁴³

- Significantly increased ALA and PBG in urine have 100% specificity (ie, rules in) for acute intermittent (hepatic) porphyria, variegate porphyria, and coproporphyria. A normal urine PBG result has a sensitivity of almost 100% (ie, rules out) in the diagnosis of porphyria in acutely symptomatic patients.⁴⁴
- Stool
 - Stool coproporphyrin and protoporphyrin are the most commonly measured porphyrins in feces. The ratio of fecal coproporphyrin to fecal protoporphyrin varies among the porphyrias. For example, fecal protoporphyrin always exceeds coproporphyrin ($P > C = V$) in variegate porphyria, whereas the reverse is true in hereditary coproporphyria.⁴⁵
- Erythrocyte uroporphyrinogen decarboxylase
 - Erythrocyte uroporphyrinogen decarboxylase activity is a specific and intrinsic defect in porphyria cutanea tarda; measurement of this enzyme is a reliable diagnostic test for this disease.⁴⁶
- Electrolytes
 - Hyponatremia is typical.⁴⁷ In 1966, lesions of the median eminence of the hypothalamus and both hypothalamic–hypophyseal tracts were described in a patient with acute intermittent porphyria and syndrome of inappropriate antidiuretic hormone (SIADH). It was suggested that SIADH occurred because of damage to these areas of the brain from excessive exposure to porphyrins.⁴⁸
- C73R mutation
 - Prenatal diagnosis is possible in some types of porphyria. For example, in congenital erythropoietic porphyria, pink fluorescence of the amniotic fluid examined fortuitously in sunlight is suggestive. DNA analysis may show the mutation C73R in the gene for URO-synthase.⁴⁹
 - A mutation screening for family members should be conducted to identify symptom-free carriers, especially in cases where there is a positive family history.³⁴

Imaging

Computed tomography (CT) scanning of the abdomen and pelvis

CT scanning helps clinicians to rule out other diagnoses of excruciating abdominal pain, such as a ruptured viscus or vessel, and may help to pick up concomitant pathology, such as intussusception or infarction.⁵⁰ Focal, fatty nodularity of the liver may be noted in some patients.⁵¹

Magnetic resonance imaging (MRI)

MRI of acute intermittent porphyria demonstrates multiple large, contrast-enhancing, subcortical white matter lesions, which regress with glucose and hematin infusions. Diffusion-weighted MRI is normal, and MR spectroscopy excludes acute demyelination or tissue necrosis. MRI findings of acute intermittent porphyria can differ from those in posterior reversible encephalopathy syndrome by virtue of intense contrast enhancement. Because diffusion-weighted MRI and MR spectroscopy are normal, the lesions are likely caused by reversible vasogenic edema and transient breakdown of the blood-brain barrier.⁵²

T2-weighted MRI sequences demonstrated multiple white-matter, high-signal lesions in 4 of 16 acute intermittent porphyria gene carriers (25%).⁵³ Kupferschmidt and colleagues⁵⁴ described 2 patients with acute intermittent porphyria who presented with cortical blindness. MRI showed bilateral occipital lesions, and the investigators speculated that these lesions were caused by vasospasm-induced ischemia due to unopposed cerebral vasoconstriction that resulted from a deficiency of nitrous oxide synthase, a major vascular dilator.

The striking feature of the MRI findings in these cases and in those of acute intermittent porphyria described in the literature is that the lesions are bioccipital and partially or totally reversible. These characteristics are typical of MRI findings seen in patients with hypertensive encephalopathy, and many patients presenting with acute intermittent porphyria attacks have high blood pressure on presentation.⁵⁵

In cases of porphyria cutanea tarda, MRI of the liver shows poorly defined areas, which, on T2-weighted sequences, exhibit a hypersignal with fat saturation. Treatment of porphyria cutanea tarda may lead to clinical remission and resolution of radiologic abnormalities.⁵⁶

Treatment

- Withdrawal of any culprit medications, alcohol, drugs, toxins, and chemicals is the key to therapy.
- Supportive care such as fluid, electrolytes, and nutrition is paramount.
- Monitor for hyponatremia or hypomagnesemia, and treat vigorously if found.
- Aggressively treat respiratory failure, which may ensue once muscle weakness involves the diaphragm, and ventilate in an intensive care unit as appropriate.
- Monitor patients on telemetry for prompt identification and treatment of arrhythmias, which are a common occurrence.
- Treat pain with parenteral meperidine or morphine. Complicated and debilitating chronic cases may require celiac plexus injection.⁵⁷
- Administer phenothiazines for nausea, vomiting, agitation, etc.
- Treat tachycardia and/or hypertension with propranolol or nadolol, which can be safely used for beta blockade.
- Promptly start glucose infusion in the form of 10% dextrose. At least 300-400 g should be given in 24 hours. The infusion is a time-buying measure to bridge the patient to more definitive treatment with hemin; by itself, glucose infusion is only effective for mild symptoms.⁵⁸
- Treat acute porphyria attacks with hemin (intravenous heme); 3-4 mg/kg/d for 3-5 days is the definitive treatment and mainstay of management. Thrombophlebitis is the major adverse effect.
 - At least two thirds of the patients have a good response, with resolution of pain and neurologic deficits.^{59,60,61} Tin protoporphyrin appears to have a synergistic effect with hemin.⁶²
 - Recombinant PBG deaminase has been tested in phase I studies of acute hepatic porphyria and found to be effective and promising.⁶³ Further data are awaited.
 - Hemodialysis has been used in dire circumstances with some benefit when hemin was not available.⁶⁴
 - Termination of pregnancy may have to be considered in acute fulminant attacks presenting during pregnancy.⁶⁵
 - Gonadotropin-releasing hormone (GdRH) analogues have been reportedly effective in some cases of acute intermittent porphyria, but these agents are not widely used.⁶⁶
- Avoidance of sunlight is the key in treating cutaneous porphyrias.⁶⁷
- Other
 - Magnesium sulfate has been used to control seizures, as many regular anti-seizure medications are contraindicated.⁶⁸
 - Neither red blood cell exchange transfusion nor plasmapheresis prevented progressive hepatic deterioration in 2 cases of advanced hepatic erythropoietic protoporphyria despite a significant decrease in protoporphyrin levels.⁶⁹
 - Hematopoietic stem cell transplantation (HSCT) has been applied with success in severe cases of congenital erythropoietic porphyria.^{70,71}
 - Liver transplantation is an option in cases in which cirrhosis complicates hepatic porphyria.

- The use of beta-carotene has shown some benefit for cutaneous porphyrias.
- Porphyria cutanea tarda can be effectively treated by phlebotomy.⁷²
 - § High-dose chloroquine therapy for porphyria cutanea tarda is rarely used now because of its hepatic side-effects.⁷³

Prognosis

Among 206 adult Finnish patients with acute intermittent porphyria or variegate porphyria, 47 patients had a total of 117 acute attacks during the period of 1967-1989.⁷⁴ Six of these patients died during an attack, and 21 attacks were associated with paresis; the frequency of severe attacks was significantly smaller than before 1967. Most pareses and deaths occurred because of a delay in diagnosis and inappropriate treatment of porphyria. Milder symptoms of porphyria were more common among those who had had previous attacks than among those who had not.

In cases of acute intermittent porphyria, the risk of attacks correlated with the excretion of PBG in the urine during remission among adults; a low rate of excretion predicted freedom from acute attacks. Two percent of the surgical operations and 4% of the pregnancies were associated with acute attacks. Nearly one third of the women had symptoms of porphyria associated with the menstrual cycle, but these seldom proceeded to an acute attack. Forty-six percent of the women had used sex-hormone preparations regularly; 2 (4.5%) of the women experienced associated acute attacks. Patients with acute intermittent porphyria or variegate porphyria showed increased incidences of hepatocellular carcinoma.⁷⁴

Erythropoietic porphyria is a persistent, severely painful, socially disabling disease with a marked impact on quality of life.⁷⁵

Prevention

- Educate patients about their porphyria disease, inheritance, precipitating drugs and events, and the importance of seeking treatment in early stages of an attack.
- Encourage patients to wear medical alert bracelets.²⁹
- Perioperative management includes the use of filters on operative lights to prevent skin burns and intestinal perforation.⁷⁶ To prevent burn injuries, astral lamps in the operating room are covered with yellow film filters.⁷⁷

Expertise, Testing, and Centers of Excellence

A listing of experts, testing, and centers of excellence in the porphyrias is available at the American Porphyria Foundation Website (www.porphyrifoundation.com).

The European Porphyria Initiative (EPI) (www.porphyrria-europe.org) network was formed in 2001 to compare the experience among countries in an attempt to develop a common approach to the management of the porphyrias, particularly concerning the recommendations of safe medications and warnings against unsafe drugs, and to facilitate international collaborative clinical and biologic research. The main achievements of the EPI during this period have been: the drafting of and agreement to consensus protocols for the diagnosis and management of acute hepatic porphyrias, as well as the creation of a multilingual Website, particularly focusing on guidelines for common prescribing problems in acute porphyrias and providing information to patients that is now available in more than a dozen languages.⁷⁸

Diet and Nutrition

Smoking, which increases hepatic cytochrome P450 enzymes and presumably heme synthesis, is associated with more frequent porphyria attacks.⁷⁹

Drugs to Avoid

The list of drugs to avoid continues to grow. Major culprits include barbiturates, anticonvulsants, progestins, and rifampin.

Individual medications can be checked against a safe and unsafe drug database that is maintained by the American Porphyria Foundation.

Acute intermittent porphyrias are rare complications of ovulation induction with clomiphene citrate, but these syndromes should be considered in patients who develop unexplained hyponatremia or neurovisceral symptoms.⁸⁰

Different drugs in the same class may have different effects in the porphyrias. For example, although lidocaine should be avoided, dental treatment using bupivacaine or levobupivacaine as local analgesic agents was successfully and safely provided for 5 children with a diagnosis of latent acute intermittent porphyria or who had a family history of acute intermittent porphyria.⁸¹

Differential Diagnosis

- Acute abdomen
- Hereditary tyrosinemia type I⁸²
- Lead poisoning
- Pseudoporphyria is a bullous photosensitivity, the commonest etiology being secondary to various ingested medications, such as voriconazole (a relatively new second-generation triazole antifungal agent)⁸³
- Psychosis

References

1. Lane N. Born to the purple: the story of porphyria. *Scientific American* [serial online]. December 16, 2002; Accessed September 30, 2009. Available at <http://www.sciam.com/article.cfm?articleID=000B1BEF-C051-1DF8-9733809EC588EEDF>.
2. Champe PC, Harvey RA, eds. Conversion of amino acids to specialized products. *Biochemistry*. 2nd ed. Philadelphia, Pa: Lippincott, Williams & Wilkins; 1994:260-1.
3. Forbes CD, Jackson WF, eds. Endocrine, metabolic and nutritional. *Color Atlas and Text of Clinical Medicine*. 2nd ed. Barcelona, Spain: Times Mirror International / Mosby; 1997:349.
4. Cooper J. King George's illness -- porphyria. Queen Charlotte, 1744-1818: A Bilingual Exhibit. Available at <http://people.virginia.edu/~jlc5f/charlotte/porphyria.html>. Accessed February 4, 2008.
5. Gocmen A, Peters HA, Cripps DJ, Bryan GT, Morris CR. Hexachlorobenzene episode in Turkey. *Biomed Environ Sci*. Mar 1989;2(1):36-43. [[Medline](#)].

6. Poblete-Gutierrez P, Badeloe S, Wiederholt T, Merk HF, Frank J. Dual porphyrias revisited. *Exp Dermatol*. Sep 2006;15(9):685-91. [\[Medline\]](#).
7. Canavese C, Gabrielli D, Guida C, Cappellini MD. [Nephrologists and porphyrias] [Italian]. *G Ital Nefrol*. Jul-Aug 2002;19(4):393-412. [\[Medline\]](#).
8. Doss MO, Stauch T, Gross U, et al. The third case of Doss porphyria (delta-amino-levulinic acid dehydratase deficiency) in Germany. *J Inherit Metab Dis*. 2004;27(4):529-36. [\[Medline\]](#).
9. Hedger RW, Wehrmacher WH, French AV. Porphyria syndrome associated with diabetic nephrosclerosis and erythropoietin. *Compr Ther*. 2006;32(3):163-71. [\[Medline\]](#).
10. Dyer J, Garrick DP, Inglis A, Pye IF. Plumboporphyria (ALAD deficiency) in a lead worker: a scenario for potential diagnostic confusion. *Br J Ind Med*. Dec 1993;50(12):1119-21. [\[Medline\]](#). [\[Full Text\]](#).
11. Taira MC, Mazzetti MB, Lelli SM, de Viale LC. Glycogen metabolism and glucose transport in experimental porphyria. *Toxicology*. Apr 15 2004;197(2):165-75. [\[Medline\]](#).
12. Furuyama K, Kaneko K, Vargas PD. Heme as a magnificent molecule with multiple missions: heme determines its own fate and governs cellular homeostasis. *Tohoku J Exp Med*. Sep 2007;213(1):1-16. [\[Medline\]](#). [\[Full Text\]](#).
13. Lee DS, Flachsova E, Bodnarova M, et al. Structural basis of hereditary coproporphyria. *Proc Natl Acad Sci U S A*. Oct 4 2005;102(40):14232-7. [\[Medline\]](#). [\[Full Text\]](#).
14. Elder GH, Hift RJ, Meissner PN. The acute porphyrias. *Lancet*. May 31 1997;349(9065):1613-7. [\[Medline\]](#).
15. Nordmann Y, Grandchamp B, de Verneuil H, et al. Harderoporphyria: a variant hereditary coproporphyria. *J Clin Invest*. Sep 1983;72(3):1139-49. [\[Medline\]](#). [\[Full Text\]](#).
16. Kirsch RE, Meissner PN, Hift RJ. Variegate porphyria. *Semin Liver Dis*. 1998;18(1):33-41. [\[Medline\]](#).
17. Todd DJ. Erythropoietic protoporphyria. *Br J Dermatol*. Dec 1994;131(6):751-66. [\[Medline\]](#).
18. Meerman L. Erythropoietic protoporphyria. An overview with emphasis on the liver. *Scand J Gastroenterol Suppl*. 2000;(232):79-85. [\[Medline\]](#).
19. Cribier B, Chiaverini C, Dali-Youcef N, et al. Porphyria cutanea tarda, hepatitis C, uroporphyrinogen decarboxylase and mutations of HFE gene. A case-control study. *Dermatology*. 2009;218(1):15-21. [\[Medline\]](#).
20. Teubner A, Richter M, Schuppan D, Kostler E, Stolzel U. [Hepatitis C, hemochromatosis and porphyria cutanea tarda] [German]. *Dtsch Med Wochenschr*. Mar 31 2006;131(13):691-5. [\[Medline\]](#).
21. Rossmann-Ringdahl I, Olsson R. Porphyria cutanea tarda in a Swedish population: risk factors and complications. *Acta Derm Venereol*. 2005;85(4):337-41. [\[Medline\]](#). [\[Full Text\]](#).
22. Madan P, Schaaf CP, Vardhan P, et al. Hans Gunther and his disease. *Photodermatol Photoimmunol Photomed*. Dec 2007;23(6):261-3. [\[Medline\]](#).

23. To-Figueras J, Badenas C, Mascaro JM, et al. Study of the genotype-phenotype relationship in four cases of congenital erythropoietic porphyria. *Blood Cells Mol Dis.* May-Jun 2007;38(3):242-6. [\[Medline\]](#).
24. Madan P, Vardhan P. Images in clinical medicine. Congenital erythropoietic porphyria. *N Engl J Med.* Sep 7 2006;355(10):1047. [\[Medline\]](#).
25. Anderson KE, Sassa S, Bishop DF, Desnick RJ. Disorders of heme biosynthesis: X-linked sideroblastic anemia and the porphyrias. In: Scriver CR, Beaudet AL, Sly WS, et al, eds. *Metabolic and Molecular Basis of Inherited Disease.* New York, NY: McGraw Hill; 2001:2991-3062.
26. Bulat V, Lugovic L, Situm M, Buljan M, Bradic L. Porphyria cutanea tarda as the most common porphyria. *Acta Dermatovenerol Croat.* 2007;15(4):254-63. [\[Medline\]](#).
27. Marko PB, Miljkovic J, Gorenjak M, Povalej P, Kansky A. Erythropoietic protoporphyria patients in Slovenia. *Acta Dermatovenerol Alp Panonica Adriat.* Sep 2007;16(3):99-102, 104. [\[Medline\]](#). [\[Full Text\]](#).
28. Maniangatt SC, Panicker JN, Thomas M, Pavithran K. A rare case of porphyria. *Ann Acad Med Singapore.* May 2004;33(3):359-61. [\[Medline\]](#). [\[Full Text\]](#).
29. Anderson KE, Bloomer JR, Bonkovsky HL, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. *Ann Intern Med.* Mar 15 2005;142(6):439-50. [\[Medline\]](#).
30. Tasnadi G, Bor M, Pusztai A. [Treatment of acute porphyrias. The importance of follow-up of patients and carriers] [Hungarian]. *Orv Hetil.* May 11 2003;144(19):933-8. [\[Medline\]](#).
31. Tasnadi G, Bor M, Pusztai A, Szekely E. [Acute porphyrias in differential diagnosis] [Hungarian]. *Orv Hetil.* Apr 27 2003;144(17):811-8. [\[Medline\]](#).
32. Andersson C, Nilsson A, Backstrom T. Atypical attack of acute intermittent porphyria--paresis but no abdominal pain. *J Intern Med.* Sep 2002;252(3):265-70. [\[Medline\]](#). [\[Full Text\]](#).
33. Liu YP, Lien WC, Fang CC, et al. ED presentation of acute porphyria. *Am J Emerg Med.* Mar 2005;23(2):164-7. [\[Medline\]](#).
34. Zimmermann M, Bonaccorso C, Valerius C, Hamann GF. [Acute intermittent porphyria. A clinical chameleon: case study of a 40-year-old female patient] [German]. *Nervenarzt.* Dec 2006;77(12):1501-5. [\[Medline\]](#).
35. Diot E, Corcia P, Zannad N, et al. [Favorable outcome of acute porphyric neuropathy after treatment with heme arginate] [French]. *Rev Neurol (Paris).* Nov 2007;163(11):1100-2. [\[Medline\]](#).
36. Bylesjo I, Forsgren L, Lithner F, Boman K. Epidemiology and clinical characteristics of seizures in patients with acute intermittent porphyria. *Epilepsia.* Mar 1996;37(3):230-5. [\[Medline\]](#).
37. Ellenweig N, Schoenfeld N, Zemishlany Z. Acute intermittent porphyria: psychosis as the only clinical manifestation. *Isr J Psychiatry Relat Sci.* 2006;43(1):52-6. [\[Medline\]](#). [\[Full Text\]](#).
38. Millward LM, Kelly P, King A, Peters TJ. Anxiety and depression in the acute porphyrias. *J Inherit Metab Dis.* 2005;28(6):1099-107. [\[Medline\]](#).

39. Peters TJ, Deacon AC. International air travel: a risk factor for attacks in acute intermittent porphyria. *Clin Chim Acta*. Sep 2003;335(1-2):59-63. [\[Medline\]](#).
40. Hift RJ, Meissner PN. An analysis of 112 acute porphyric attacks in Cape Town, South Africa: Evidence that acute intermittent porphyria and variegate porphyria differ in susceptibility and severity. *Medicine (Baltimore)*. Jan 2005;84(1):48-60. [\[Medline\]](#).
41. Park KH, Park DY, Kim JB, et al. [Porphyria cutanea tarda presenting as jaundice] [Korean]. *Korean J Hepatol*. Dec 2004;10(4):308-12. [\[Medline\]](#). [\[Full Text\]](#).
42. Rich MW. Porphyria cutanea tarda. Don't forget to look at the urine. *Postgrad Med*. Apr 1999;105(4):208-10, 213-4. [\[Medline\]](#).
43. Kahn MJ, Gregory SA, eds. Iron metabolism, iron overload and the porphyrias. *American Society of Hematology Self Assessment Program*. 3rd ed. Lancaster, Pa: Cadmus Communications; 2007:75.
44. Beganovic S, Hendler F, Herzig R, Josepgh G. Porphyria: diagnosis. In: Djulbegovic B, ed. *Reasoning and Decision Making in Hematology*. 1st. New York, NY: Churchill Livingstone; 1992:67/15.
45. Lin DL, He LF, Li YQ. Rapid and simultaneous determination of coproporphyrin and protoporphyrin in feces by derivative matrix isopotential synchronous fluorescence spectrometry. *Clin Chem*. Oct 2004;50(10):1797-803. [\[Medline\]](#). [\[Full Text\]](#).
46. Felsher BF, Norris ME, Shih JC. Red-cell uroporphyrinogen decarboxylase activity in porphyria cutanea tarda and in other forms of porphyria. *N Engl J Med*. Nov 16 1978;299(20):1095-8. [\[Medline\]](#).
47. Armestar F, Catalan B, Perez Picanol E, Mesalles E. [Severe hyponatremia due to inappropriate antidiuretic hormone in a patient with acute intermittent porphyria] [Spanish]. *Med Clin (Barc)*. May 19 2007;128(19):757-8. [\[Medline\]](#).
48. Lopez Montes A, Lorenzo I, Perez Martinez J. [Porphyria and inappropriate antidiuretic hormone syndrome] [Spanish]. *Nefrologia*. 2004;24 suppl 3:85-8. [\[Medline\]](#).
49. Daïkha-Dahmane F, Dommergues M, Narcy F, et al. Congenital erythropoietic porphyria: prenatal diagnosis and autopsy findings in two sibling fetuses. *Pediatr Dev Pathol*. Mar-Apr 2001;4(2):180-4. [\[Medline\]](#).
50. Griffith JC, Jardine DL, Bailey W, Florkowski CM. Variegate porphyria presenting with acute autonomic dysfunction, intussusception and renal infarction. *Scand J Gastroenterol*. May 2004;39(5):500-3. [\[Medline\]](#).
51. Flueckiger F, Steiner H, Leitinger G, Hoedl S, Deu E. Nodular focal fatty infiltration of the liver in acquired porphyria cutanea tarda. *Gastrointest Radiol*. 1991;16(3):237-9. [\[Medline\]](#).
52. Maramattom BV, Zaldivar RA, Glynn SM, Eggers SD, Wijdicks EF. Acute intermittent porphyria presenting as a diffuse encephalopathy. *Ann Neurol*. Apr 2005;57(4):581-4. [\[Medline\]](#).
53. Bylesjo I, Brekke OL, Prytz J, Skjeflo T, Salvesen R. Brain magnetic resonance imaging white-matter lesions and cerebrospinal fluid findings in patients with acute intermittent porphyria. *Eur Neurol*. 2004;51(1):1-5. [\[Medline\]](#).

54. Kupferschmidt H, Bont A, Schnorf H, et al. Transient cortical blindness and bioccipital brain lesions in two patients with acute intermittent porphyria. *Ann Intern Med.* Oct 15 1995;123(8):598-600. [\[Medline\]](#). [\[Full Text\]](#).
55. Sze G. Cortical brain lesions in acute intermittent porphyria. *Ann Intern Med.* Sep 1 1996;125(5):422-3. [\[Medline\]](#). [\[Full Text\]](#).
56. Chevallier P, Bahadoran P, Buckley MJ, et al. Hepatic multi-nodular focal fatty metamorphosis in acquired porphyria cutanea tarda. Sonographic, CT, and MRI features. *Clin Imaging.* Nov-Dec 1998;22(6):418-21. [\[Medline\]](#).
57. Ferrari AP, Ardengh JC. Endosonography-guided celiac plexus neurolysis in the treatment of pain secondary to acute intermittent porphyria. *Endoscopy.* Apr 2002;34(4):341-2. [\[Medline\]](#).
58. Li D. PGC-1alpha: looking behind the sweet treat for porphyria. *Cell.* Aug 26 2005;122(4):487-9. [\[Medline\]](#). [\[Full Text\]](#).
59. Anderson KE, Collins S. Open-label study of heme for acute porphyria: clinical practice implications. *Am J Med.* Sep 2006;119(9):801.e19-24. [\[Medline\]](#).
60. Mustajoki P, Nordmann Y. Early administration of heme arginate for acute porphyric attacks. *Arch Intern Med.* Sep 13 1993;153(17):2004-8. [\[Medline\]](#).
61. Herrick AL, McColl KE, Moore MR, Cook A, Goldberg A. Controlled trial of haem arginate in acute hepatic porphyria. *Lancet.* Jun 10 1989;1(8650):1295-7. [\[Medline\]](#).
62. Dover SB, Moore MR, Fitzsimmons EJ, Graham A, McColl KE. Tin protoporphyrin prolongs the biochemical remission produced by heme arginate in acute hepatic porphyria. *Gastroenterology.* Aug 1993;105(2):500-6. [\[Medline\]](#).
63. Sardh E, Rejkjaer L, Andersson DE, Harper P. Safety, pharmacokinetics and pharmacodynamics of recombinant human porphobilinogen deaminase in healthy subjects and asymptomatic carriers of the acute intermittent porphyria gene who have increased porphyrin precursor excretion. *Clin Pharmacokinet.* 2007;46(4):335-49. [\[Medline\]](#).
64. Prabahar MR, Manorajan R, Sathiyakumar D, Soundararajan P, Jayakumar M. Hemodialysis: A therapeutic option for severe attacks of acute intermittent porphyria in developing countries. *Hemodial Int.* Jan 2008;12(1):34-8. [\[Medline\]](#).
65. Weinzierl A, Brezinka C, Engelhardt K. Unusual manifestation of acute hepatic porphyria in pregnancy. *Fetal Diagn Ther.* 2007;22(2):136-8. [\[Medline\]](#).
66. Anderson KE, Spitz IM, Bardin CW, Kappas A. A gonadotropin releasing hormone analogue prevents cyclical attacks of porphyria. *Arch Intern Med.* Jul 1990;150(7):1469-74. [\[Medline\]](#).
67. Harper P, Wahlin S. Treatment options in acute porphyria, porphyria cutanea tarda, and erythropoietic protoporphyria. *Curr Treat Options Gastroenterol.* Dec 2007;10(6):444-55. [\[Medline\]](#).

68. Sadeh M, Blatt I, Martonovits G, Karni A, Goldhammer Y. Treatment of porphyric convulsions with magnesium sulfate. *Epilepsia*. Sep-Oct 1991;32(5):712-5. [\[Medline\]](#).
69. Eichbaum QG, Dzik WH, Chung RT, Szczepiorkowski ZM. Red blood cell exchange transfusion in two patients with advanced erythropoietic protoporphyria. *Transfusion*. Feb 2005;45(2):208-13. [\[Medline\]](#).
70. Faraci M, Morreale G, Boeri E, et al. Unrelated HSCT in an adolescent affected by congenital erythropoietic porphyria. *Pediatr Transplant*. Feb 2008;12(1):117-20. [\[Medline\]](#).
71. Taibjee SM, Stevenson OE, Abdullah A, et al. Allogeneic bone marrow transplantation in a 7-year-old girl with congenital erythropoietic porphyria: a treatment dilemma. *Br J Dermatol*. Mar 2007;156(3):567-71. [\[Medline\]](#).
72. Badminton MN, Elder GH. Management of acute and cutaneous porphyrias. *Int J Clin Pract*. May 2002;56(4):272-8. [\[Medline\]](#).
73. Rossmann-Ringdahl I, Olsson R. Porphyria cutanea tarda: effects and risk factors for hepatotoxicity from high-dose chloroquine treatment. *Acta Derm Venereol*. 2007;87(5):401-5. [\[Medline\]](#). [\[Full Text\]](#).
74. Kauppinen R, Mustajoki P. Prognosis of acute porphyria: occurrence of acute attacks, precipitating factors, and associated diseases. *Medicine (Baltimore)*. Jan 1992;71(1):1-13. [\[Medline\]](#).
75. Holme SA, Anstey AV, Finlay AY, Elder GH, Badminton MN. Erythropoietic protoporphyria in the U.K.: clinical features and effect on quality of life. *Br J Dermatol*. Sep 2006;155(3):574-81. [\[Medline\]](#).
76. Seth AK, Badminton MN, Mirza D, Russell S, Elias E. Liver transplantation for porphyria: who, when, and how?. *Liver Transpl*. Sep 2007;13(9):1219-27. [\[Medline\]](#). [\[Full Text\]](#).
77. Yotsumoto G, Masuda H, Iguro Y, et al. Aortic valve replacement in a patient with erythropoietic protoporphyria. *Ann Thorac Surg*. Mar 2003;75(3):1003-5. [\[Medline\]](#).
78. Deybach JC, Badminton M, Puy H, et al. European porphyria initiative (EPI): a platform to develop a common approach to the management of porphyrias and to promote research in the field. *Physiol Res*. 2006;55 suppl 2:S67-73. [\[Medline\]](#). [\[Full Text\]](#).
79. Lip GY, McColl KE, Goldberg A, Moore MR. Smoking and recurrent attacks of acute intermittent porphyria. *BMJ*. Mar 2 1991;302(6775):507. [\[Medline\]](#). [\[Full Text\]](#).
80. Wang JG, Guarnaccia M, Weiss SF, Sauer MV, Choi JM. Initial presentation of undiagnosed acute intermittent porphyria as a rare complication of ovulation induction. *Fertil Steril*. Aug 2006;86(2):462.e1-3. [\[Medline\]](#).
81. McGovern E, Fleming P, O'Marcaigh A. The dental management of five paediatric patients with a history of acute intermittent porphyria. *Eur Arch Paediatr Dent*. Dec 2007;8(4):215-8. [\[Medline\]](#).
82. Bonkovsky HL. Neurovisceral porphyrias: what a hematologist needs to know. *Hematology Am Soc Hematol Educ Program*. 2005;24-30. [\[Medline\]](#). [\[Full Text\]](#).
83. Tolland JP, McKeown PP, Corbett JR. Voriconazole-induced pseudoporphyria. *Photodermatol Photoimmunol Photomed*. Feb 2007;23(1):29-31. [\[Medline\]](#).

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porphyria overview, porphyria, hepatic porphyria, erythropoietic porphyria, acute porphyria, acute intermittent porphyria, cutaneous porphyria, porphyria cutanea tarda, hepatoerythropoietic porphyria, variegate porphyria, Doss porphyria, plumboporphyria, hereditary coproporphyrin, congenital erythropoietic porphyria, Gunther's disease, Gunther disease, EPP, PCT, AIP, CEP

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- Congenital Erythropoietic Porphyria [in the Dermatology section]
- Diseases of Tetrapyrrole Metabolism - Refsum Disease and the Hepatic Porphyrins [in the Neurology section]
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- Porphyria, Acute [in the Pediatrics: General Medicine section]
- Porphyria, Acute Intermittent [in the Hematology section]
- Porphyria, Chester
- Porphyria Cutanea Tarda [in the Dermatology section]
- Porphyria, Cutaneous [in the Pediatrics: General Medicine section]
- Porphyria, Hereditary Coproporphyrinemia
- Pseudoporphyria [in the Dermatology section]
- Variegated Porphyria [in the Dermatology section]

Clinical Trials

- Does Exercise and Heat Increase the Photosensitivity in Patients With Erythropoietic Protoporphyrinemia
- Phase III Confirmatory Study in Erythropoietic Protoporphyrinemia (EPP)
- Pilot Trial of Deferasirox in the Treatment of Porphyria Cutanea Tarda
- Studies in Porphyria I: Characterization of Enzyme Defects

Additional Resources

- American Porphyria Foundation. Available at: <http://www.porphyrifoundation.com/>. Accessed September 30, 2009.
- European Porphyria Initiative (EPI). Available at: <http://www.porphyrria-europe.com/>. Accessed September 30, 2009.
- Thadani H, Deacon A, Peters T. Diagnosis and management of porphyria. *BMJ*. Jun 17 2000;320(7250):1647-51. [Medline]. [Full Text].

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