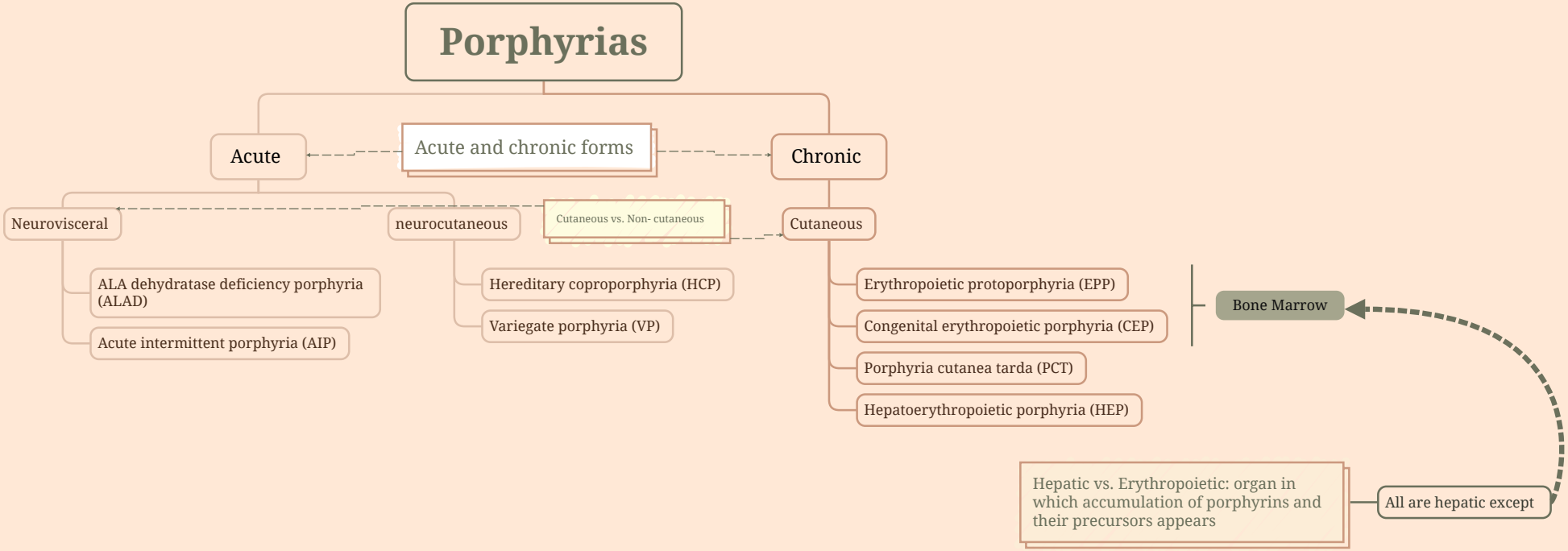

Introduction	The porphyrias are caused by deficiencies of enzymes involved in heme biosynthesis which lead to
	- blockade of the porphyrin pathway
	- subsequent accumulation of porphyrins and their precursors
	
	Either
	- genetic
	  - autosomal dominant
	  - autosomal recessive
	  - X-linked
	- acquired
	
	Classified depending on site of overproduction and accumulation of porphyrin, overlapping features common
	
	Diagnosis is difficult because of
	- variable clinic course
	- lack of understanding about diagnostic process
	- lack of a universal standard for test result interpretation

	Heterozygotes are asymptomatic in between acute attacks

Porphyrias

	Acute intermittent porphyria	Porphyria cutanea tarda	Congenital erythropoietic porphyria (Gunther's disease)
	Heterozygotes are asymptomatic between acute attack More frequent in women than men. Risk factors for exacerbation include: medications, diet, weight loss, surgery, infection, menstrual hormones, smoking Prevalence of 5-10 per 100,000 and thought to be higher in psychiatric populations Psychiatric symptoms: anxiety, depression, hallucinations, paranoia Common symptoms include: Abdominal pain.; Tachycardia, arrhythmia.; Orthostatic hypotension.; Peripheral neuropathy	Most common porphyria which causes skin manifestations Precipitants frequently include: alcohol, estrogen, iron Deficiency of hepatic urodecarboxylase Cutaneous photosensitivit: fluid filled vesicles on sun exposed areas, friable skin, wounds heal slowly, hyperpigmentation on face No neurologic manifestations Higher incidence of hepatocellular carcinoma	It is a very rare autosomal recessive disorder. Patients usually present during infancy and rarely present in adult life with milder forms. Clinical features: Very severe photosensitivity; phototoxic burning and blistering leading to burning sensation in the light exposed parts; Hypersplenism.; Hemolytic anemia; Thrombocytopenia
Diagnosis	Caused by a deficiency of PBG deaminase resulting in an accumulation of PBG and ALA		Patients usually present during infancy and rarely present in adult life with milder forms.
Treatment	Discontinue all unnecessary or potentially harmful drugs as: Sulfa drugs, barbiturates, ACEI, Antiepileptics, Antifungals 300-400 grams of carbohydrates per day. IV heme at 3-5 mg/kg/day. Treat any infection. Pain control with Morphine Treat sympathetic hyperactivity with propranolol.	Avoid sunlight, use sunscreen Chloroquine or hydroxychloroquine to form complexes with porphyrins to enhance excretion Superactivated charcoal β- carotene may increase tolerance of sunlight through Vitamin A.	Superactivated charcoal Splenectomy Hypertransfusion Bone marrow transplantation

Porphyrias

	Erythropoietic protoporphyria	Pseudoporphyria
	It is the most common childhood porphyria. It is usually evident by 2 years of age.	Most commonly due to medications especially NSAIDs and tetracycline. Some patients on hemodyalisis develop a similar PCT-like picture.
Diagnosis	Protoporphyrin levels are elevated because of deficient activity of ferrochelatase enzyme.	In certain settings patient develop blistering and skin fragility identical to PCT with the histological features but with normal urine and serum porphyrins. -This condition called →pseudoporphyria.

Hepatic	Neurologic, mental disturbances Abdominal pain Extremity pain, paresthesias Motor neuropathy
Erythropoietic	Cutaneous photosensitivity (long wave UV) light excites porphyrins in skins causing: - Cell damage - Hemolytic anemia

acute porphyrias	Symptoms of acute attacks increase the potential for misdiagnosis. clinically indistinguishable during acute attacks, except the neurocutaneous porphyrias cause dermatologic changes lead to an increase in PBG and ALA which can be detected in urine Cutaneous features are not seen in acute intermittent porphyria or the very rare ALA dehydratase deficient porphyria
Chronic	

Cutaneous	Excessive concentrations of porphyrins exposed to day-light generate free radicals, leading to cell membrane damage and cell death The type of cellular damage depends on the solubility and tissue distribution of the porphyrins. Two main patterns of skin damage are seen i the porphyrias: - accumulation of water soluble uro - and coproporphyrins leads to blistering. - accumulation of the lipophilic protoporphyrins leads to burning sensations in the exposed skin
Neurotoxicity	Most current thinking focuses on accumulations of toxic metabolites ALA and PBG are neurotoxins ALA may be a false transmitter for GABA, it also blocks one of ATPases (perhaps a sodium pump) Another hypothesis