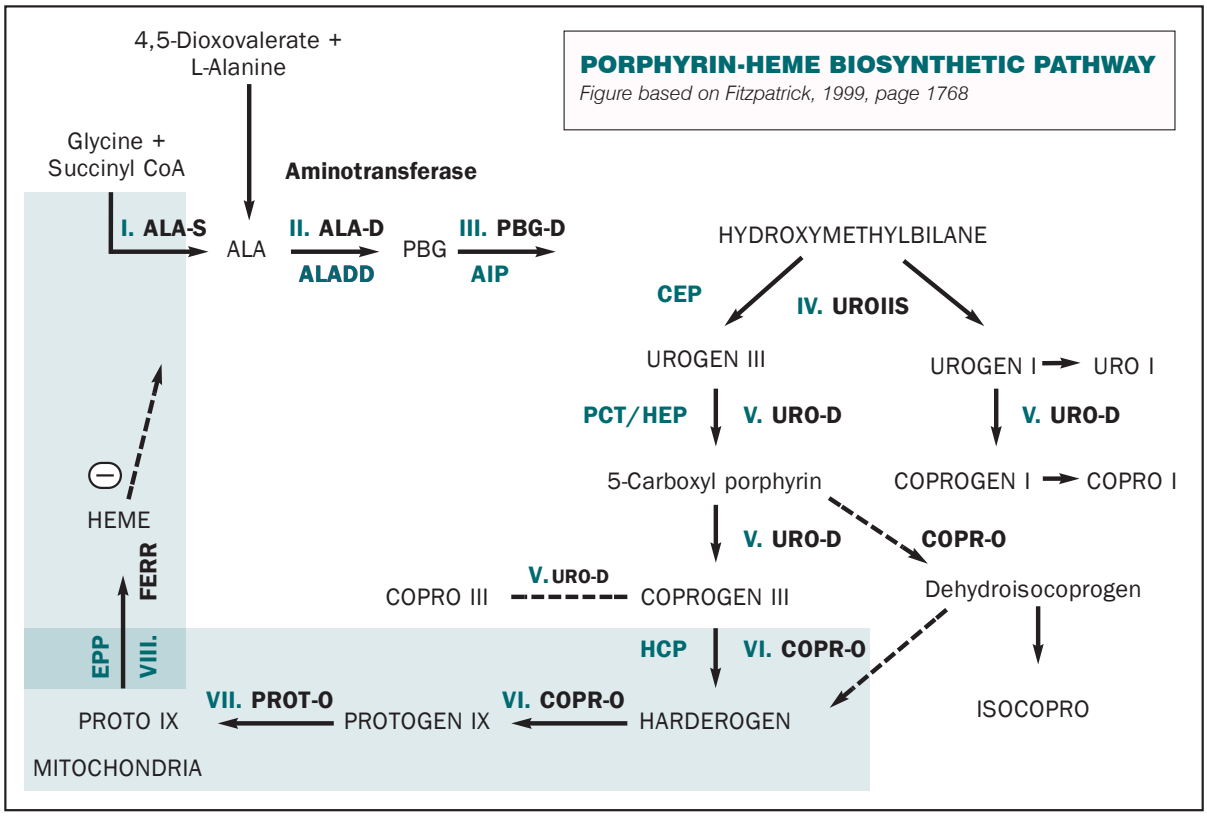
Porphyrias

Sharon E. Jacob, MD, and Hari Nadiminti, MD. (Updated July 2015)*



KEY:

Roman numerals represent chronological order, starting with ALA-s (rate limiting step enzyme)

Diseases in teal, enzymes in bold.

Light teal indicates mitochondria

MNEUMONICS and TIPS:

4 mitochodrial enzymes: "**ALAS**, **FERR**ous **OXID**izes" (**ALAS**, **Ferr**ochelatase, the **Oxid**ases)

AIP & **A**LADD: **A**bsent skin findings

HCP, **A**IP, and **V**IP: **HAV**e acute attacks of ALA, PBG

"No pee pee in EPP" (no porphyrins in the urine in EPP)

ABBREVIATIONS:

ALA-S: aminolevulinic acid synthase

ALADD: ALA dehydratase deficiency

AIP: acute intermittent porphyria

ALA-D: ALA dehydratase

CEP: congenital erythropoietic porphyria

COPR-O: corproporphrin oxidase

COPROGEN: coproporphyinogen

EPP: erythropoietic protoporphyria

FERR: ferrochelatase

HARDEROGEN: harderoporphyinogen

HCP: hepatic coproporphyria

HEP: hepatic erythropoietic porphyria

PBG-D: porphobilinogen deaminase

PCT: porphyria cutanea tarda

PROT-O: protoporphyrin

PROTOGEN: protoporphyrinogen

URO: uroporphyrin

UROGEN: uroporphyrinogen

URO-D: urogen decarboxylase

UROIIIS: urogen synthase III

VP: variegate porphyria

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	ENZYME DEF	DISEASE INHERITANCE	INHERITANCE	CLINICAL FEATURES	TREATMENT	RBC	URINE	STOOL	FLUORO
I	ALAS					Proto	ALA/ Copro	ALA	
II	ALA-D	ALADD	A^R	Rare (< 10 reported cases); sxs can mimic AIP & are highly variable; failure to thrive in infant & polyneuropathy in a 63 y/o; r/o exposure to styrene (inhibitor of ALAD)	Acute attacks: Hematin				
		Tyrosinemia		Can mimic ALADD, b/c pts with hereditary tyrosinemia accumulate succinylacetone (inhibitor of ALAD)	Diet to minimize the phenylalanine-tyrosine				
III	PBG-D	AIP	A^D	Incidence: 5 / 100,000; women > men (2:1);	Glucose load,	PBG	ALA, PBG	N/	
				onset: 18 -40 y/o; sx sequence: abd colic → psychiatric sxs, ie hysteria → peripheral neuropathy; NO SKIN FINDINGS; SIADH → hyponatremia; urine discoloration; risk Hepatic CA	Hematin/cimetidine Pain: narcotics; Liver transplant – cure (1 case report)	deami-nase	Watson-Scharwtz test	ALA/ PBG in attacks	
IV	UROIIIS	CEP (Gunther's)	A^R	Rare (<200 reported cases); onset: infancy: marked photosensitivity (vesiculo-bullous-scaring), increased fragility and ulcers lead to scarring; "werewolf-facies"; hypertrichosis, erythrodontia; hemolytic anemia; splenomegaly; port wine urine; corneal scarring → blindness; acro-osteolysis; contractures	Sun avoidance, Splenectomy, BMT, ß-carotene, transfusions, alphatocopherol	Uro> Copro	Uro> Copro	Copro> Uro	Teeth Urine, RBC
V	URO-D	PCT	A^D Types: I: Sporadic II: Familial	Most common porphyria; onset: middle age; Associated with Hepatitis C; moderate photosensitivity, fragility of sun-exposed skin after trauma → erosions & bullae → scars, hyper/hypopigmentation, milia; hypertrichosis; scarring alopecia; photo-oncholysis; sclerodermoid plaques; dystrophic calcifications; serum iron normal; DM 25%; liver iron overload; mutation: HFE C2a2	EtOH elimination, sun protection, Phlebotomy to Hb<10, antimalarials	N	Uro> copro	Isocopro	Urine
		HEP	A^R	Homozygous form of PCT; URO-D <10%; onset: infancy; extreme photosensitivity; similar sxs as PCT (earlier onset)	Strict sun avoidance, Phlebotomy ineffective	Proto	Uro	Isocopro	Teeth
VI	COPR-O	HCP	A^D	Incidence: 1-4 / 1,000,000; onset; 18-40; similar sxs to AIP, but less severe; 30% have skin findings: Hematinphotosensitivity → blistering, scarring; during attacks urine pink/red; mutation in CPOX	Glucose load, Hematin Pain: narcotics	N	Copro	Copro	
		Hardero-porphyria		Rare form of HCP; onset: infancy; sxs similar to HCP, with jaundice and anemia					
		ECP		Rare (3 reported cases); mild skin photosensitivity		Copro		Copro	
VII	PROT-O	VP	A^D	Common in South Africans; 15-30 y/o; clinically similar to AIP (abd colic, paralysis, psychosis) + PCT skin findings (photosensitivity); mutation PPOX; 624-626 nm band	Glucose load, Hematin	N	Copro> Uro*	Proto> Copro	RBC
VIII	FERR	EPP	A^D (A^R)	Photosensitivity beginning in first decade; burning and tingling (non-pruritic); edematous plaques- purpura, waxy scars; pox-like scarring on nose & cheeks; circumoral linear scars; weather-beaten skin; cholelithiasis; hepatic failure	Sun avoidance, ß-carotene, Cholestyramine	Proto	N	Proto	RR

Buzz words-Diagnostic hints: Blistering associated with PCT, VP, CEP, HCP, HEP.

If blistering with normal porphyrin labs, screen known associations with Pseudoprophyria (HD, tanning booths, drug [NSAID, abx, diuretics]).

Burning, erythema, without blisters, is seen in EPP or XLDPP.

No skin findings, AIP or ALADD. Red teeth: CEP or HEP..

***Reviewed and updated July 2015: Alina Goldenberg, MD, Elise Herro, MD, Emily deGolian, MD & Sharon Jacob, MD.**