

Porphyria



Porphyria Categories

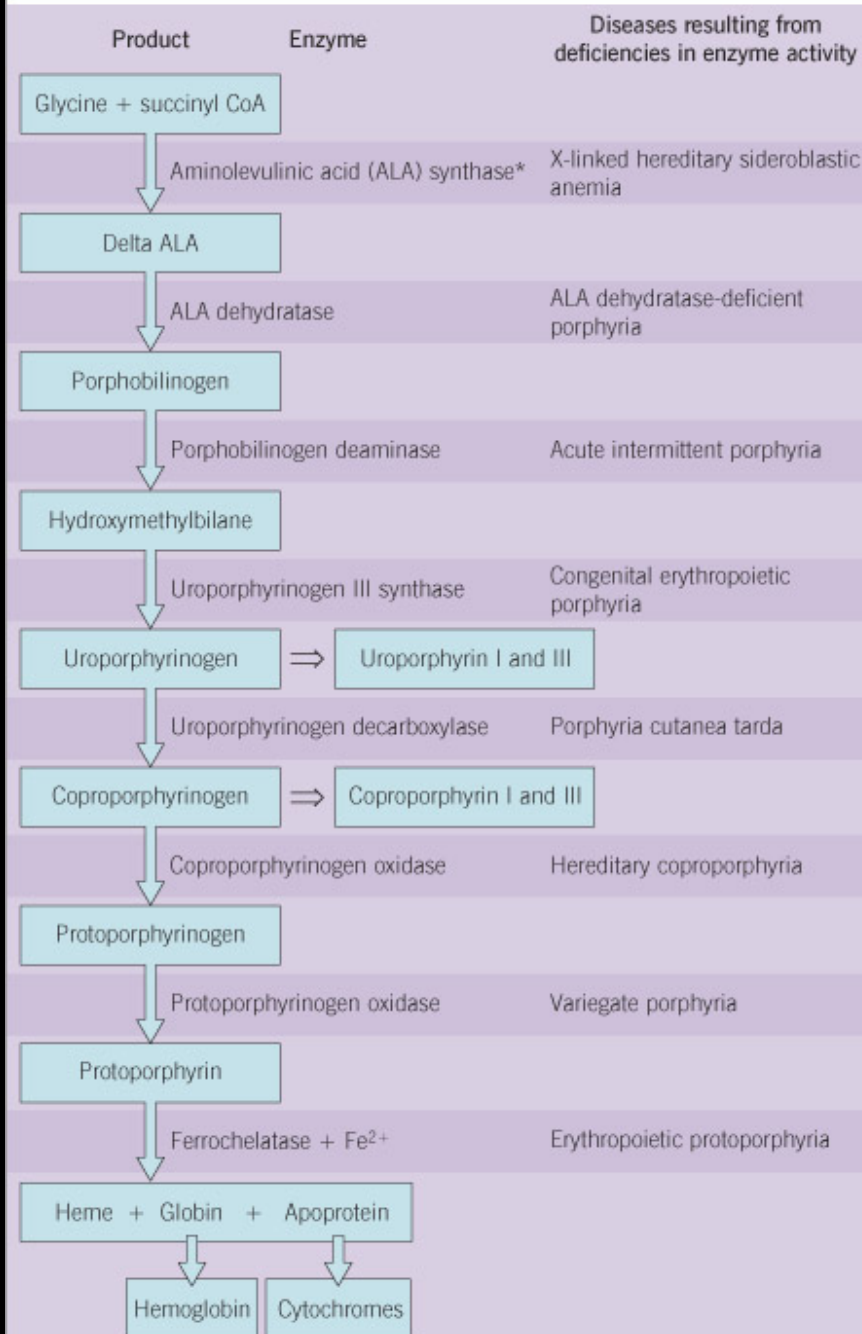
- Bone Marrow

- Erythropoietic protoporphyria (EPP)
- Congenital Erythropoietic porphyria (CEP)

- Liver

- Porphyria Cutanea Tarda (PCT)
- Acute Intermittent Porphyria (AIP), **no** skin findings.
- Variegate Porphyria (VP)
- Hereditary Coproporphyria (HCP)
- Hepatoerythropoietic Porphyria (HEP)

THE HEME BIOSYNTHETIC PATHWAY





CASE #1

- 45yo male alcoholic house painter with c/o blisters on hands and tight skin.









Labs

- Urine: elevated Uroporphyrin > Coproporphyrins
- Feces: elevated Isocopro
- RBC: nl
- CBC: wbc=8, Hg=16, Hct=50, Plt=250
- LFT: elevated



DIAGNOSIS

- PORPHYRIA CUTANEA TARDA
- Enzyme def: Uroporphyrinogen Decarboxylase
- Pneumonic: People Can Tell U Drink Constantly
- PCT basics: Sporadic and familial, forms I & II, Familial is associated with Hemochromatosis. Exacerbated by high estrogen states, sun exposure, hemodialysis, iron overload, etoh, hep c, HIV.



Clinical Presentation

- Blistering
- Milia and dystrophic Ca⁺
- Facial hypertrichosis
- Sclerodermoid changes, classically in V of neck and preauricular area.
- Port wine colored urine with pink fluorescence under woods light.



Labs to Know

- Urine porphyrins
- RBC porphyrins
- Fecal porphyrins
- Plasma porphyrins
- CBC
- LFT's
- Hep A,B,C
- HIV?
- Hemochromatosis?



Therapy

- Sun avoidance, i.e.: physical blockers
- Decrease Iron load, phlebotomy at 500ml biweekly to hg 10-11, or low nl ferritin.
- Plaquenil 200mg biw, or Chloroquine
- Vit C
- Enteric absorbents
- Life style changes (etoh etc.)



Differential Diagnosis

- Variegate Porphyria
- Hereditary Coproporphyria
- Congenital Erythropoietic Porphyria
- Pseudo PCT
- Epidermolysis Bullosa Acquisita
- Bullous LE



Case Scenario #2

- 45yo wm with 1 month history of blistering, and milia formation on hands.
- Pmhx: Severe joint pain for 3 months on naprosyn





Pseudo PCT

- PCT like skin lesions, except **hypertrichosis** and **sclerodermoid** changes.
- Will **NOT** have elevated porphyrin levels
- Same Histo
- Most often secondary to drugs, also reports of tanning beds and hemodialysis.



Drugs that cause pseudo PCT

- Naprosyn
- Oxaprosin
- Lasix
- Ketoprofen
- Tetracycline
- Dapsone
- Rifampin
- Fluoroquinolones
- HCTZ
- Vit B6
- Cyclosporine
- Nifedipine
- Erythropoietin
- Celecoxib
- 5-FU



Tx of Pseudo PCT

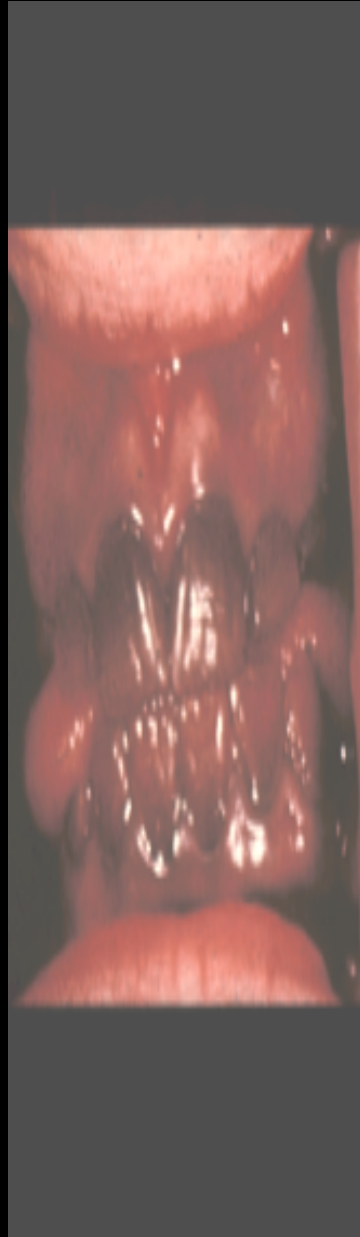
- DC offending Drugs
- Sun Protection
- Hemodialysis associated is much more difficult to tx.
Must continue to monitor these patients for true PCT because they may develop elevated porphyrins over time.

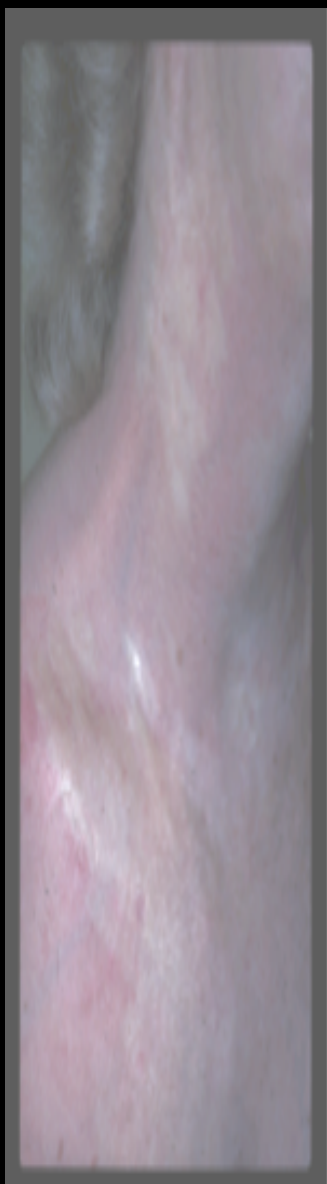


Case # 3

- Mother comes in with 3yr old child. She says used to cry after going out in the sun. He would often turn red and blister afterwards.
- In your office you notice sclerodermoid changes of the face along with excessive hair growth along the temples.
- Mother states that both she and the father have problems with blistering of their hands with extensive sun exposure.









Hepatoerythropoietic Porphyria

- Presents in infancy with marked photosensitivity, bullae, erosions, scarring and hypertrichosis.
- Late clinical findings: Scleroderma like changes, mutilating scars in acral areas, Acral osteolysis (short digits), scarring alopecia, erythrodontia, ectropion.
- Anemia, hepatosplenomegally,

HEP genetics and Labs

- Inherited AR, PCT X₂
- Uroporphyrinogen Decarboxylase Def.
- **Urine:** elevated, Uroporphyrin I-III 7-carboxyl porphyrin
- **Feces:** elevated, Uroporphyrin, Isocopro, coproporphyrin
- **RBC:** Elevated Zinc-protoporphyrin
- Anemia, with normal iron levels



HEP Tx

- Sun avoidance
- Do **NOT** phlebotomize may be anemic already!
- Consider oral charcoal



Case scenario #4

- 40yo w m from S. Africa. C/o blisters and scarring of the hands since age of 20. Recently admitted to the GI service for N/V/D with abdominal pain.







Variegate Porphyria

- **One of the four Acute Attack Porphyrias**
- Variegate Porphyria
- Acute Intermittent Porphyria
- Hereditary Coproporphyria
- ALAD deficiency Porphyria



Clinical Findings

- AD inheritance, most common in South African colonists
- Skin findings are identical to PCT, except they appear earlier 20's vs. 40's.
- Neurovisceral attacks, as adults.



Laboratory Findings

- Genetic defect in **Oxidase** **Protoporphyrinogen**
- Increased ALA and PBG in urine, during acute attacks
- Urine: Copro > Uro (**opposite of PCT**)
- Feces: Proto > Copro
- Specific fluorescence of plasma porphyrins at **627nm** peak.



Acute Attacks

- Neurological Dysfunction
 - Pain: Abd, chest, back and limb
 - GI: N/V/D/C, Abd distention, and ileus
 - Gu: retention, renal failure, frequency
 - Symp. Outflow: Fever, tachy, HTN, sweating
 - Neuropathies: Seizure, paralysis, coma
 - Death



Acute Attack Therapies

- Remove inducers ie: drugs
- Glucose infusions
- Hematin infusions
- Analgesics: Chlorpromazine, opiates
- OCP's to minimize attacks with menses
- B-blockers
- Fluids and electrolytes



Inducers of Acute Attacks

- Drugs
- Starvation (restriction of Carbs)
- Hormonal fluctuations (menses, preg.)
- Infections
- Generalized stressors



Pearls for Acute Attack Porphyrrias

- All have elevated ALA, and PBG during attacks
- **Hereditary Coproporphyria**
 - Inh. AD Def: Coproporphyrinogen oxidase
 - Harry Crazy People Can Pee Orange.
 - Copro always elevated in feces
 - Mild to no skin involvement
- **Acute Intermittent Porphyria**
 - Inherited AD, **most common**, No skin findings
 - Defect in PBG deaminase
 - An Insane Prussian Peed Blue Die
 - Ain't in Poop



Case # 5

- 3yo female who cries when she goes outside, and then runs inside to stand in front of AC vent. She now presents to you with elliptical scars on the face and pebbling of the nose and hands.









Erythropoietic Protoporphyrria

Clinical Presentation

- Immediate photosensitivity with pain and pruritis, then erythema and edema.
- Waxy, thickening of hands that causes a pebbling of the skin
- Superficial elliptical scarring over the bridge of the nose.
- 10% have anemia
- Cholelithiasis
- 5% develop hepatic failure

Erythropoietic Protoporphyrria Labs and Genetics

- Complex inherited defect in **Ferrochelatase**.
- Easily Produces Pebbly Fingers.
- Ain't in Pee Pee.
- Accumulation of Protoporphyrin IX in RBC, plasma, feces **NOT** in urine.
- Protoporphyrin is excreted by hepatic system in feces.



EPP Tx

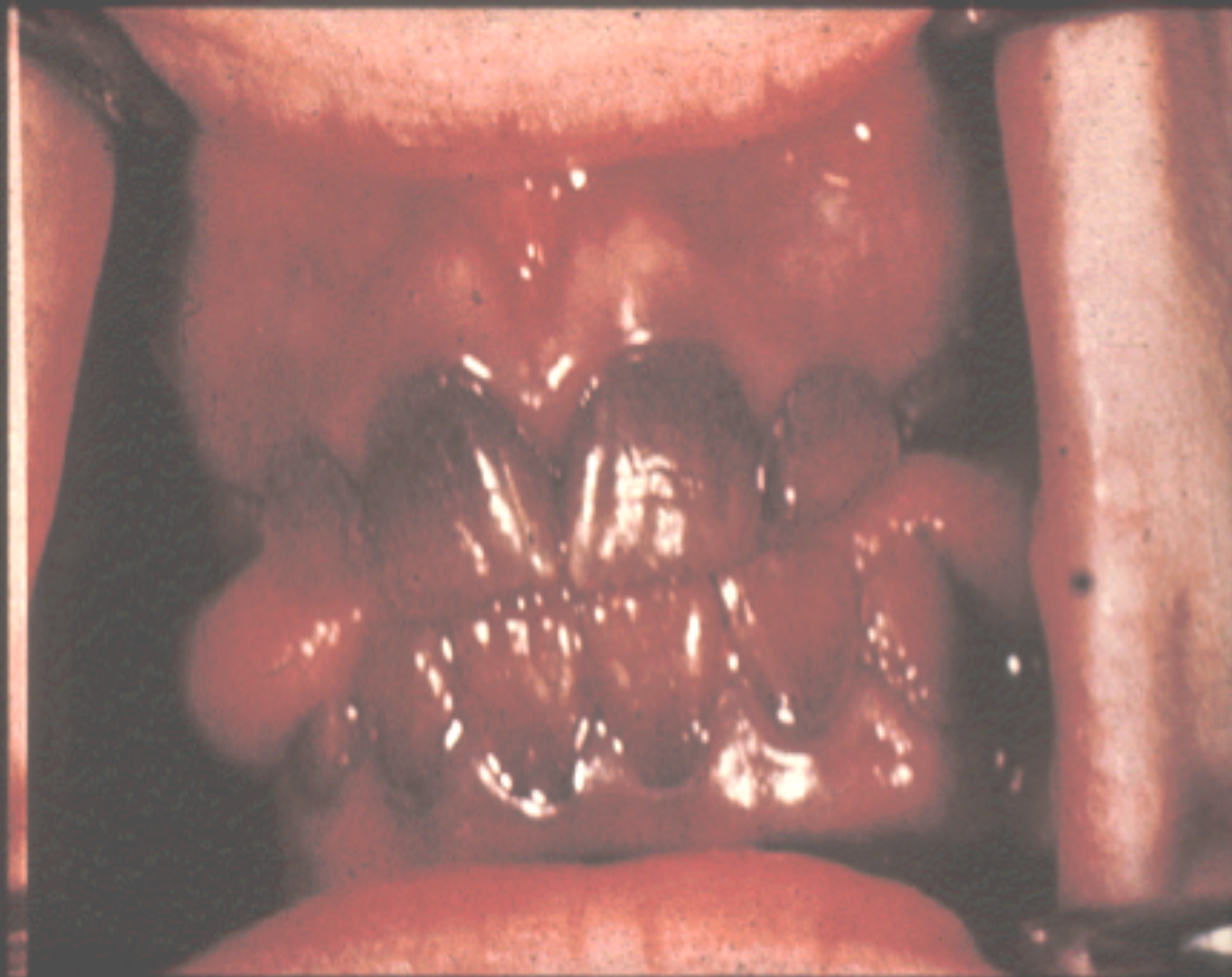
- Physical sun blocks
- Beta-carotene 80mg bid
- L-cysteine 500 bid
- Cholystyramine, charcoal
- Bile acids
- Exchange transfusion
- Hematin
- Cholecystectomy



Case #6

- You receive a 6yo male from an outside physician. Referred for “skin rash, funny teeth, and splenomegaly”. Labs sent by the MD show a CBC with hemolytic anemia. You examine the pt, get a urine sample, labs and you find...







A



Labs

- CBC, anemia with schistocytes
- Urine: Elevated Uroporphyrin I, Copro I
- Feces: Elevated Uro I > Copro I
- Plasma: Elevated Uro I, Copro I
- RBC: Elevated Uro I, Copro I, Zinc proto

Congenital Erythropoietic Porphyria

- Gunther's Disease
- Autosomal recessive dz
- Defect in **Uroporphyrinogen III Cosynthetase**
- Carrot Eating Prevents Usual Terrible Complications
- Delayed photo toxicity, with blisters, milia, deforming scars of nose and ears, hypertrichosis, eye involvement, hyper and hypopigmentation.
- Bone involvement: Erythrodontia, fragile bones, short stature, acral osteolysis
- Hemolytic anemia, and splenomegaly



CEP Treatment

- Sun Avoidance, Zinc or Titanium blocks
- Beta-carotene: Not proven
- Hypertransfusion
- Splenectomy
- Cholestyramine, Charcoal
- Chemosuppression: MTX, HU
- Bone Marrow Transplant
- Cosmetic Dental bonding
- Avoid Bili lights in the Babies

Porphyria Pneumonics

“Erythropoietic forms”

- Congenital Erythropoietic Porphyria
 - Carrot Eating Prevent Usual Terrible Complications
 - Uroporphyrinogen III Cosynthetase
- Erythropoietic Protoporphyria
 - Easily Produces Pebbly Fingers
 - Ferrochelatase

Porphyria Pneumonics

“Hepatic Forms”

- Porphyria Cutanea Tarda
 - People Can Tell U Drink Constantly
 - Uroporphyrinogen Decarboxylase
- Variegate Porphyria
 - Veld People aPpear Pretty Odd
 - Protoporphyrinogen Oxidase
- Hereditary Coproporphyria
 - Hairy Crazy People Can Pee Orange
 - Coproporphyrin oxidase
- Acute Intermittent Porphyria
 - An Insane Prussian Peed Blue Dye
 - PBG Deaminase