NOTES
PORPHYRIA

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Metabolic diseases; accumulation of heme precursors
  - Porphyrin; neurologic/cutaneous disorders
- Mostly hereditary
  - Porphyria cutanea tarda (most common)
  - Acute intermittent porphyria
  - Aminolevulinic acid dehydratase deficiency porphyria (AKA Doss porphyria)
  - Hereditary coproporphyria
  - Variegate porphyria
  - Congenital erythropoietic porphyria

CAUSES

- Sporadic/inherited enzyme mutations in heme production → porphyrin accumulates in tissues

RISK FACTORS

- Smoke, alcohol, hormonal changes, fasting, stress, certain drugs, sunlight exposure, lead poisoning

COMPLICATIONS

- Paralysis, seizures

SIGNS & SYMPTOMS

Acute

- Resolve once attack passes (e.g. acute intermittent porphyria, doss porphyria)
- Abdominal pain, vomiting, hypertension, tachycardia, neurological/psychiatric symptoms (e.g. seizures, neuropathy, anxiety, confusion, hallucinations), red urine

Chronic

- E.g. porphyria cutanea tarda, erythropoietic porphyria
- Skin manifestations
- Photosensitivity
  - Pain, discomfort, burning of sunlight-exposed areas
- Vesiculo-erosive manifestations (e.g. erosions, blistering)
- Increased skin fragility

DIAGNOSIS

LAB RESULTS

- Blood, urine tests
  - Increased levels of porphobilinogen in urine
- Genetic testing

TREATMENT

MEDICATIONS

- Acute intermittent porphyria (AIP)
  - Hospitalization during acute attack, intravenous hemin, etc.
- Porphyria cutanea tarda (PCT)
  - Phlebotomy, chloroquine/hydroxychloroquine sulfate, etc.

ACUTE INTERMITTENT PORPHYRIA (AIP)

osms.it/acute-intermittent-porphyria

PATHOLOGY & CAUSES

- Neurovisceral disease
  - Acute, recurrent attacks of abdominal pain + other clinical manifestations (neuropsychiatric, gastrointestinal, urinary)

CAUSES

- Autosomal dominant mutation of hydroxymethylbilane synthase (*HBMS*) gene → alterated codification of enzyme hydroxymethylbilane synthase (AKA porphobilinogen deaminase/ uroporphyrinogen I synthase) → impaired heme production → accumulation of metabolites: porphobilinogen (PBG), aminolevulinic acid (ALA)

RISK FACTORS

- Drugs (e.g. barbiturates, antiepileptics, rifampin)
- Alcohol
- Exposure to tobacco smoke
- Hormonal fluctuations (e.g. menstruation)
- Dietary changes (e.g. reduced caloric intake)
- Stress (e.g. illness, psychological stress)

COMPLICATIONS

- Hypertension, kidney failure, neuromuscular respiratory failure, hepatocellular carcinoma

SIGNS & SYMPTOMS

- Acute episodes lasting several hours to few days
  - Severe, diffuse abdominal pain
  - Palpitations, sweating
  - *GI:* nausea, vomiting, constipation
  - *Neurological:* seizure, peripheral neuropathy (e.g. tingling sensations in limbs), muscle weakness
  - *Psychiatric:* irritability, anxiety, hallucinations
  - *Urinary:* dysuria, urinary retention, discolored (reddish, red-brown) urine

MNEMONIC: 5Ps

Features of Acute intermittent porphyria

Pain in the abdomen

Polyneuropathy

Psychological abnormalities

Pink urine

Precipitated by drugs: including barbiturates, oral contraceptives, sulfa drugs

DIAGNOSIS

LAB RESULTS

- Elevation of heme precursor in urine (PBG)
- Genetic testing

TREATMENT

MEDICATIONS

- Intravenous hemin
- Symptomatic treatment (e.g. antiemetics, pain medications)

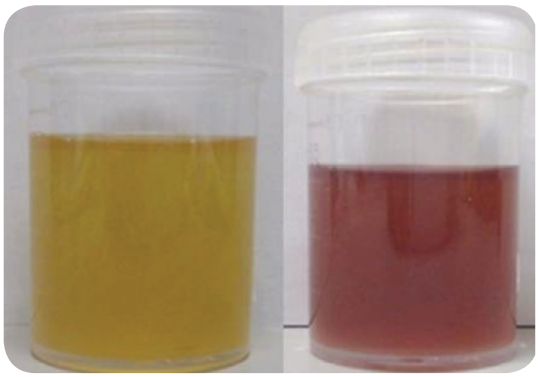

Figure 57.1 The urine of an individual with porphyria (right).

PORPHYRIA CUTANEA TARDA (PCT)

osms.it/porphyria-cutanea-tarda

PATHOLOGY & CAUSES

- Blistering cutaneous lesions of sunlight-exposed skin

TYPES

- *PCT Type I:* acquired disease
- *PCT Type II:* autosomal dominant disease

CAUSES

- Impaired function of uroporphyrinogen decarboxylase (UROD) enzyme → porphyrins overproduction, accumulation → photosensitizing porphyrins in skin damage proteins, lipids, basement membrane → cutaneous lesions

RISK FACTORS

- Alcohol
- Exposure to tobacco smoke
- Hormonal imbalances
- Infectious disease (e.g. HIV, hepatitis C)
- Hemochromatosis, iron overloading

COMPLICATIONS

- Cirrhosis, hepatocellular carcinoma

SIGNS & SYMPTOMS

- Increased mechanical fragility after sunlight exposure → painful vesicles, blisters on hands/face (minor trauma)
- Increased facial hair growth (e.g. hypertrichosis)
- Hardened yellow skin lesions (e.g. scleroderma-like plaques)
- Hypermelanosis (brownish skin pigmentation)
- Abnormal urine color

DIAGNOSIS

LAB RESULTS

- Elevated porphyrins level (orange-red fluorescence on Wood lamp)
- Elevated porphyrins level in stool
- UROD activity in blood cells

Skin biopsy of lesions

- Subepidermal bullae, inflammation
- Immunofluorescence
  - Immunoglobulins at dermal-epidermal junctions

TREATMENT

MEDICATIONS

- Low doses of chloroquine/ hydroxychloroquine sulfate

OTHER INTERVENTIONS

- Avoid sunlight exposure
- Discontinue aggravating substances (alcohol, estrogen)
- Blood removal (e.g. phlebotomy)
  - Decrease body iron load
- Limit iron-rich food

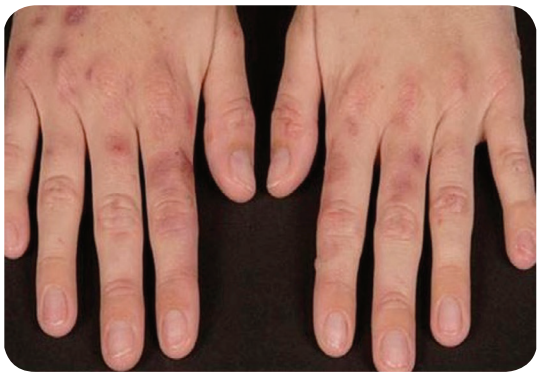

Figure 57.2 Skin lesions on the dorsum of both hands in a case of porphyria cutanea tarda.