

Porphyrias - A review

Mohammed Mohy El-Din Selim*
Hamda Al Ansari

The term porphyria is derived from the Greek word "Purphura" which means "Purple Pigment". The name refers to purple discoloration in some body fluids in patients during an attack and the biochemical characteristics of the disease was first explained by Felix⁽¹⁾ and its clinical presentation was first described by Stokvis.⁽²⁾

Porphyrias are inherited or acquired diseases that result from abnormal metabolism of Heme biosynthesis pathway.

The main causes are enzyme deficiencies that lead to defect in heme biosynthesis leading to over production and accumulation of porphyrins and their precursors. Heme is synthesized in every human cell and is a key component of several important proteins and plays a central role in cell metabolism.⁽³⁾ Heme contains iron and is incorporated in hemoglobin and gives blood its red color and its essential function is to bind oxygen and carry it from lungs to all parts of the body. Heme is a component of cytochromes in the liver as P450 cytochrome which metabolize chemicals, drugs and hormones, so that their metabolites are easily removed and excreted from the body.⁽³⁾

Porphyrias are life long recurrent diseases caused by enzyme defect in heme biosynthesis. Heme biosynthesis occurs almost entirely in liver and bone marrow through a complex process composed of 8 reactions each of which is catalyzed by a specific enzyme.

As this heme biosynthesis process progresses, several intermediate heme precursors are created and modified. Partial or complete deficiency of these enzymes will result in certain heme precursors known as porphyrins to accumulate in tissues especially bone marrow or liver, they appear in excess in blood and get excreted in urine and stool and will result in different clinical pictures of porphyrias as shown in Heme biosynthesis pathway in table one.⁽⁴⁾

* Consultant Dermatologist
Actg. / Chairman of Dermatology Department
Rumailah Hospital – Hamad Medical Corporation,
Doha – Qatar.

Most porphyrias are autosomal dominant (AD) except congenital erythropoietic porphyria (CEP) which is autosomal recessive (AR). Porphyrin abnormalities may occur in association with many conditions that include:

- lead poisoning
- sideroblastic anemia which is rarely associated with photosensitivity⁽⁵⁾
- hemolytic anemia
- iron deficiency
- renal failure
- cholestasis
- liver disease
- gastrointestinal hemorrhage
- tryosinemia associated with high aminolevulonic acid (ALA) level⁽⁴⁾

The main clinical findings in porphyrias can be summarized as follows^(6,7,8):

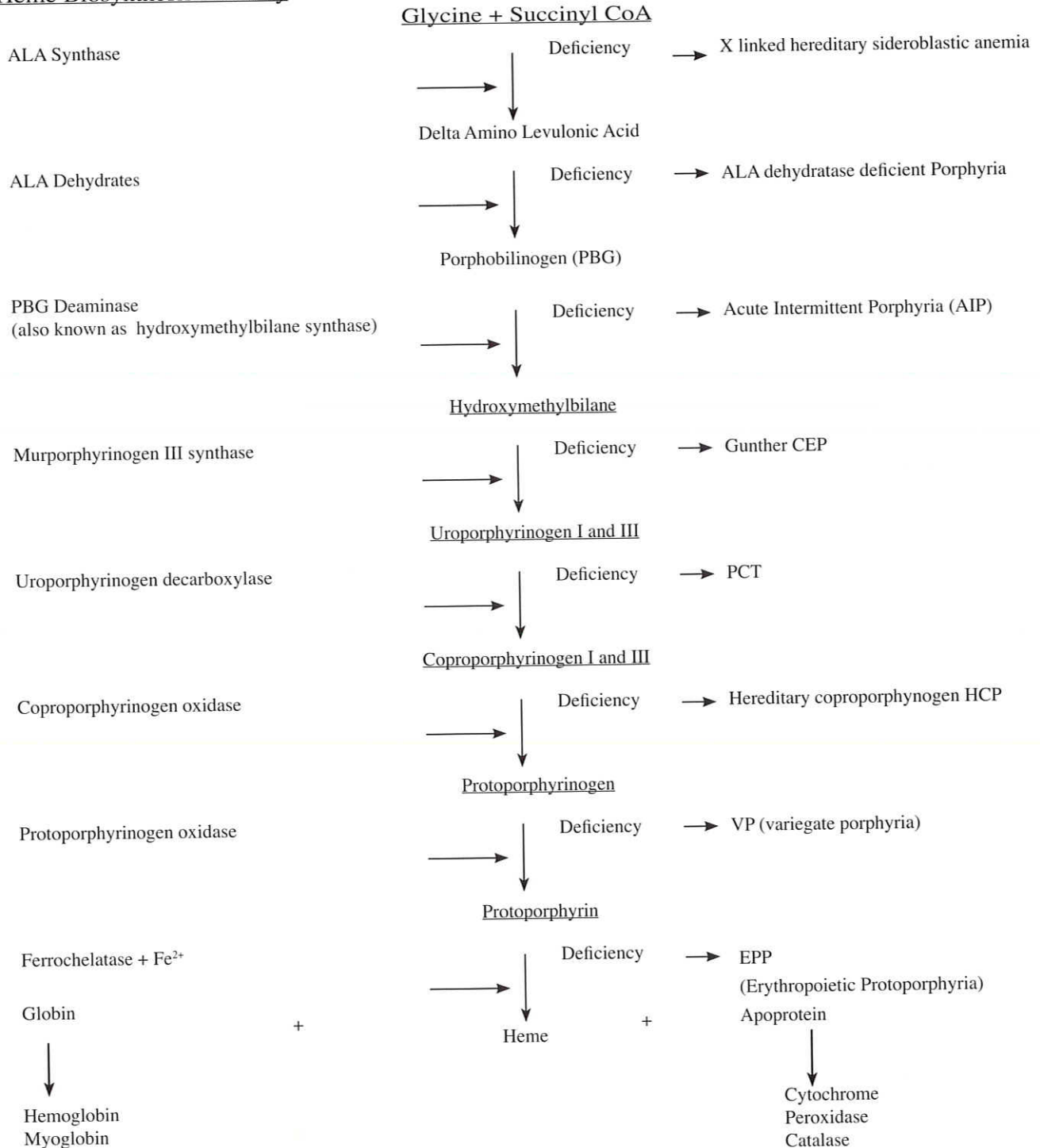
- 1- acute attacks of porphyria can be life threatening and usually last 1 – 2 weeks and include:
 - Acute Intermittent Porphyria (AIP),
 - ALA dehydratase deficient porphyria which is very rare.
 - During the attack, patients complain of abdominal pain or cramp, nausea, vomiting, diarrhea, constipation, severe electrolyte imbalance, low blood pressure (BP) and shock.
- 2- All porphyrias are photosensitive except AIP and ALA dehydratase deficient porphyria
- 3- Neuromuscular manifestation with muscle pain, muscle weakness or paralysis, numbness, tingling, pain of arms and legs, back pain, personality changes, increased pulse rate and raised B.P.
- 4- Possible complication are coma, gall bladder stones, lung failure and skin scarring.
- 5- All porphyrias predispose to liver cancer due to hemosiderosis and even asymptomatic gene carriers may get liver cancer.

Classification of Porphyrias^(9,10,11,12)

There are two main groups based on the site of over production and accumulation of porphyrins:

Table One

Heme Biosynthesis Pathway



I- Erythropoietic Type: (Bone marrow porphyrias)

They are non-acute and include:

- 1) Congenital Erythropoietic Porphyria (CEP) (Gunther's)
- 2) Erythropoietic Protoporphyrinemia (EPP)
- 3) Erythro Coproporphyrinemia (ECP)

II- Hepatic Porphyrias which may be acute and include:

- 1) Acute Intermittent Porphyria (AIP)
- 2) Hereditary Coproporphyrinemia (HCP)
- 3) Variegate Porphyria (VP)
- 4) Porphyria Cutanea Tarda (PCT)
- 5) Hepatoerythropoietic porphyria (HEP)
- 6) ALA dehydratase deficiency porphyria

The three most common types of Porphyrias are:

- 1) Porphyria Cutanea Tarda (PCT)
- 2) Acute Intermittent Porphyria (AIP)
- 3) Erythropoietic Protoporphyrinemia (EPP)

Classification of Porphyrias on clinical bases includes:

- I- Acute episodes with no skin changes and this includes:
 - 1- AIP
 - 2- ALA dehydratase deficiency porphyria
- II- Acute episodes with skin changes and this includes:
 - 1- Hereditary coproporphyrinemia
 - 2- Variegate Porphyria (VP)
- III- Skin changes only (Porphyrias with skin changes only) and this include:
 - 1- PCT
 - 2- EPP
 - 3- CEP
 - 4- Hepatoerythropoietic porphyria (HEP)

Laboratory Diagnosis of Porphyrias aims at:

- Finding characteristic porphyrias profile in plasma, erythrocytes, urine and stool.
- Avoiding missing diagnosing porphyrias and

minimize false negative laboratory tests.

- The requested investigations must be done in a laboratory that is experienced in technical methods and quality control.
- Deterioration of samples in transit lead to false negative results and it was found that ethylene diamine tetracetic plasma samples are more stable than serum sample.⁽¹³⁾
- Spectrofluorometric scanning of plasma will detect all Cutaneous Porphyrias during the symptomatic phase and is a useful screening test.^(14,15)

Pathogenesis of Porphyrias

In human beings, the porphyrins are the main precursors of heme which is an essential constituent of hemoglobin, myoglobin, catalase, peroxidase, respiratory cytochrome and P450 liver cytochrome. There are 8 enzymes in the heme synthesis. Defects in any of these enzymes will lead to accumulation of porphyrins (heme precursors) which are toxic to tissues in high concentration. The heme porphyrin synthesis and the corresponding porphyrias associated with enzyme deficiency and the laboratory diagnosis of porphyrias are summarized in Tables 2 a, b, c and d.

Porphyrin molecules absorb visible light and generate free radicals with lipid peroxidation and protein cross linking leading to cell membrane damage and death. The cell damage depends on the solubility and tissue distribution of porphyrins.^(5,15)

Two main types of damage to the skin are seen in porphyrias.

- 1- Accumulation of water soluble uroporphyrins lead to blistering
- 2- Accumulation of lipophilic protoporphyrins causes immediate burning sensation in the skin on exposure to light. Soreness may occur alone or be followed by swelling, redness, purpura and/or erosions. These features are typical of erythropoietic protoporphyrinemia. Porphyrin abnormalities may occur in iron deficiency and lead poisoning.

Table (2 – a)

Heme porphyrin synthesis corresponding porphyrias associated with enzyme deficiency
 Laboratory Diagnosis of Porphyrias

Steps of Heme synthesis			Laboratory Findings						
S.#	Metabolite	Enzyme	Enzyme Location	Porphyria & Its class	Urine	Stool	Plasma	R.B.C.	Inheritance
1	Glycine + Succinyl CoA	ALA Synthase	Cytosol	X-linked hereditary Sideroblastic anemia					
2	Delta Amino Levulonic acid	ALA dehydratase	Cytosol	Hepatic ALA dehydratase deficiency porphyria	ALA +++ Coproporphyrin III	-	-	Protozn	AR
3	Porpho Bilinogen	Porphy Bilinogen deaminase also known as hydroxyl methyl bilane synthase	Cytosol	AIP hepatic	ALA +++ PBG +++ During and between attacks	+	-	-	AD

Table (2 – b)

Heme porphyrin synthesis corresponding porphyrias associated with enzyme deficiency
 Laboratory Diagnosis of Porphyrias

Steps of Heme synthesis			Laboratory Findings						
S.#	Metabolite	Enzyme	Enzyme Location	Porphyria & Its class	Urine	Stool	Plasma	R.B.C.	Inheritance
4	Hydroxy-methylbilane	Uro-Porphyrinogen decarboxylase	Cytosol	CEP Hepatic	Uro - I Copro - I	Copro - I	+	Uro- I Uro - III Blood and bone marrow and organs Proto Zn	AR
5	Uro-Porphyrinogen I & II	Uro-Porphyrinogen decarb oxylase	Cytosol	PCT Hepato Erythro-Poietic-Porphyria (HEP)	Uro +++ Copro +	Iso-Copro ++ Copro +	Uro +	In HEP Protoporphyrin +	AD

Table (2 – c)

Heme porphyrin synthesis corresponding porphyrias associated with enzyme deficiency
Laboratory Diagnosis of Porphyrias

Steps of Heme synthesis			Laboratory Findings						
S.#	Metabolite	Enzyme	Enzyme Location	Porphyria	Urine	Stool	Plasma	R.B.C.	Inheritance
6	Copro-Porphyrinogen III	Copro-Porphyrinogen Oxidase	Mitochondria	(hepatic) HCP Hereditary Copro-Porphyria	ALA ++ PBG ++ Uro + Copro ++	Copro +	+	+	AD
7	Protoporphyrinogen IX	Protoporphyrinogen Oxidase	Mitochondrion	VP (mixed)	ALA + PBG + Uro ++ Copro ++	ALA + PBG +++ Protoporphyrin ++	625-627 nm Peek	-	AD
8	Protoporphyrin IX	Ferro-Chelatase + Fe ²⁺	Mitochondrion	EPP Erythropoietic	Normal	Proto-Porphyrin	Proto-Porphyrin	Proto-Porphyrin +	AD Sometime AR
Heme + Globin = hemoglobin									

Table (2 – d)

Heme porphyrin synthesis corresponding porphyrias associated with enzyme deficiency
Laboratory Diagnosis of Porphyrias

Steps of Heme synthesis			Laboratory Findings						
S.#	Metabolite	Enzyme	Enzyme Location	Porphyria & Its class	Urine	Stool	Plasma	R.B.C.	Inheritance
	Tyrosinemia	-	-	-	ALA	-	-	-	-
	Iron deficiency	Ferro-Chelatase	-	-	-	-	-	Protoporphyrin Zn ++	-
	Lead Poisoning	- ALA dehydratase - Coproporphyrinogen Oxidase - Ferro-chelatase	-	-	ALA ++ Copro +	-	-	Proto Zn	-

Clinical features of Porphyrias

[1] Porphyria Cutanea Tarda (PCT)

It is the most common porphyria ⁽¹¹⁾ and is characterized by photosensitivity and no acute attacks. Its incidence is estimated to be one in 70,000, ⁽¹²⁾ Male to female ratio is 3:2 and most of them are older than 40 years old. ⁽⁴⁾

In PCT, there is deficiency of Uroporphyrinogen decarboxylase enzyme (UROD) or diminished activity of UROD to 25% of normal.

Familial cases of PCT (Type II) show AD inheritance while sporadic cases (Type I) affect individuals who have genetic predisposition after being exposed to environmental factors. Both type I and II of PCT are excited by multifactorial risk factors ⁽¹⁶⁾ that adversely affect hepatocytes leading to hemosiderosis. Such risk factor includes:

- Alcoholism and drugs as estrogen
- Hemochromatosis ^(17, 18, 19)
- Iron overload ⁽²⁰⁾
- Lupus Erythematosus ^(21, 22)
- Haematological malignancy ^(23, 24)
- Some viral infections, hepatitis A, B and C, ^(25, 26) cytomegalovirus, ⁽²⁷⁾ HIV ⁽²⁸⁾
- α thalassemia
- Diabetes Mellitus
- Renal failure
- Renal dialysis
- Hepatocellular Carcinoma ⁽²⁹⁾
- Exposure to poly-halogenated hydrocarbon compounds.

In PCT, porphyrins accumulate in liver and are disseminated in plasma to other organs and uroporphyrins are excreted primarily in urine while coproporphyrin and isocoproporphyrin are chiefly excreted in stool.

Porphyrins are photoactive and absorb energy in visible spectrum and become photoexcited in the skin and mediate oxidative damage causing skin lesions.

The clinical signs of PCT vary in severity and include:

- skin fragility
- blistering with trivial trauma
- skin abrasions and sores
- depigmented and pigmented atrophic scars
- hyperpigmentation (melasma like) and hypopigmentation

- milia
- hypertrichosis ⁽³⁰⁾
- scarring alopecia
- scleroderma like changes ⁽³¹⁾ which may develop dystrophic calcifications
- plethora of central face, neck and upper chest and shoulders
- port wine color of urine
- abnormal liver function
- skin lesions usually affect hands, forearms and occasionally face and feet

In the familial type of PCT (Type II), the patient has one gene mutation at UROD locus and this is found in 20% of PCT patients and is inherited as AD with incomplete penetrance and 90% of gene carriers are asymptomatic. ⁽⁴⁾

If a child inherits 2 UROD gene mutation one from each parent, then the infant or child will present with Hepatoerythropoietic Porphyria (HEP) which usually starts in infancy and is characterized by being clinically like CEP and biochemically like PCT. HEP is inherited as AR while familial PCT is AD ⁽³¹⁾ and at least 30 different mutations of the UROD gene have been identified in patients with HEP and familial PCT. ⁽³²⁾

Severely affected child with HEP will show digital shortening, atrophy, contractures and separation of nail plate from its bed (photoonycholysis). It has to be differentiated from

- epidermolysis bullosa,
- epidermalysis bullosa acquisita,
- hydroa vaciniform
- bullous LE
- pseudoporphyria
- variegate porphyria
- erthropoietic porphyria

Laboratory diagnosis for PCT ⁽³³⁾

- 1- Uroporphyrin in urine
- 2- Coproporphyrin in stool
- 3- 7 carboxylase porphyrin in urine

A base line investigation for PCT includes:

- 1- Fresh random urine for uroporphyrin and coproporphyrin and coproporphyrin
- 2- If screening is positive, do:
 - o quantitative porphyrin analysis for 24 hours urine ⁽³⁴⁾
 - o plasma and stool for coproporphyrin and isocoproporphyrin

- 3- complete CBC, LFT, KFT
- 4- screen for hepatitis A, B, C
- 5- autoimmune screening
- 6- serum ferritin
- 7- serum iron and total iron binding capacity
- 8- blood sugar and glucose tolerance curve
- 9- HIV
- 10- Ultrasound for liver
- 11- Liver biopsy
- 12- Alfa fetoprotein
- 13- Assessment for hemochromatosis gene
- 14- Vitamin C was found deficient in some patients ⁽³⁵⁾
- 15- Mutation analysis of genes encoding UROD
- 16- UROD enzyme activity assay
- 17- Skin biopsy for pathology and immunofluorescence

Skin histologic findings:

- 1- Subepidermal inflammatory infiltrate
- 2- Dermal papillae protrude upwards into the blister
- 3- Capillary walls in upper dermis are thickened
- 4- Basement membrane area show positive for PAS stain
- 5- Hyaline deposit may be seen in the dermis
- 6- Direct Immunofluorescence show ⁽³⁶⁾ deposition of immunoglobulin (IgG and less commonly IgM and C3) around papillary dermal capillaries and at basement membrane zone
- 7- Caterpillar bodies are eosinophilic elongated segmented bodies located within the roofs of blisters and represent a specific histologic feature of porphyric blisters including PCT, EPP ⁽³⁷⁾ they are PAS positive and type IV collagen stain. Caterpillar like bodies or clusters do not stain for PAS or collagen IV and may be seen in PCT, EPP, Pseudoporphyria, B.P., EB and EBA

Liver Biopsy

- 1- Show increased iron deposit, steatosis, chronic inflammatory infiltrate and fibroses.
- 2- Hepatocytes show needle like intracytoplasmic inclusions which are believed to be uroporphyrin crystals.

Therapeutic Protocol in PCT

- avoid sun
 - sun protection
 - no alcohols and no estrogens
 - charcoal
 - plasmapheresis combined with somatostatin may be considered to treat exacerbation of porphyria
 - iron chelation with desferrioxamine to mobilize iron
 - Patients with PCT who are anemic (resulting from immunodeficiency viral infection). Erythropoietin (Epoetin alfa) (Epogen) (Procrit) is given subcutaneous or Intravenous in the dose of 50 – 100 IU/kg 3 times per week. This may help utilization of body iron store with no need for phlebotomy – so it is also done for PCT patients who cannot do phlebotomy.
 - IFN α given to treat hepatitis C may improve PCT
 - Phlebotomy reduces iron stores and this improves heme synthesis and reduces serum ferritin level. 500 c.c. blood are withdrawn once or twice weekly up to 2 – 4 liters. This leads to remission for 6-months up to 10 years.
 - If phlebotomy cannot be done, give oral chloroquin phosphate (Aralen) 125 – 250 mg PO twice weekly. Pediatric dose over two-years old is 12.5 mg PO 2/week, children 4 – 6 years, the dose is 100mg PO 2/week for five-months. Also patients may be given hydroxychloroquin sulfate (Plaquinil) in the dose of 200 – 400 mg PO 2 – 3 times per week will lead to remission up to 4 – 18 months.
- Pediatric dose is 3mg/kg PO 2/week for over 14 months.

Acute Porphyrias ^(38, 39, 40, 41) include:

- 1- Acute Intermittent porphyria (AIP)
- 2- Hereditary coproporphyria (HCP)
- 3- Variegate Porphyria (VP)

Acute porphyria may cause life threatening neurovisceral symptoms that mimic acute medical and psychiatric conditions.

Acute attacks of AIP are often precipitated by barbiturates, sulfonamides, diphenhydantoin and many other drugs as well as stress, infection, over indulgence of alcohol, low calorie, low carbohydrate

diet and administration of hormones as progesterone and related drugs.

General features of acute porphyrias are as follows:

- attacks are clinically indistinguishable in the three diseases
- clinical manifestations arise after puberty
- attacks are more frequent in women and is precipitated by menstrual cycle
- later onset may be associated with hepatomas

Clinical features of acute attack:

- onset with minor behavioral changes (anxiety, restlessness, insomnia)
- autonomic neuropathy
 - o abdominal pain treated with opiates
 - o vomiting treated with chlorpromazine
 - o constipation treated with lactulose
 - o pain of back and extremities
 - o hypertension and tachycardia treated with betablockers
 - o arrhythmias

Acute Porphyrias

Clinical manifestations and diagnosis

Acute Intermittent Porphyria

- 65% are females
35% are males
- There is porphobilinogen deaminase deficiency (also known as hydroxymethylbilane synthase deficiency).
- This deficiency leads to accumulation of delta aminolevulonic acid and porphobilinogen
- The disorder is inherited as a single dominant gene from one parent. Rarely, the disease is inherited from both parents with two genes and symptoms may then appear in childhood and include developmental anomalies. The gene is on chromosome 11q24.1q24.2 – (there may be more than 60 gene mutations)
- Majority of cases are asymptomatic
- Attacks are precipitated by drugs
- Onset from post puberty till 5th decade. It rarely starts before puberty
- The initial and commonest manifestation is abdominal pain which may be localized,

diffuse or colicky and may simulate acute inflammatory abdominal disease and the pain is caused by altered autonomic activity.

- Peripheral neuropathy is primary motor and begin in proximal muscles and more often in the arms, may be symmetric or asymmetric and may be severe and cause respiratory failure
- CNS affection includes:
 - (1) cranial nerve affection and may lead to optic atrophy
 - (2) seizures delirium and coma
 - (3) confusion
- reduced Tendon reflexes
- sensory Neuropathy lead to pain which is usually diffused, proximal or distal – sensory loss may occur distal and is symmetrical
- Hepatic dysfunction is common
- No photosensitivity
- Autonomic sympathetic and para sympathetic affection leading to:
 - o Circulatory effect and tachycardia
 - o Urinary retention
 - o Nausea, vomiting, diarrhea, abdominal pain, dysphagia and constipation
 - o Psychosis, depression and dementia

Diagnosis is made on:

- 1) Clinical picture
- 2) Rule out hyponatremia
- 3) Laboratory findings
 - increased Porphobilinogen and reduced PBG deaminase in RBC
 - ask for ALA in 24-hours urine
 - ask for ALA dehydratase in RBCS
 - increased ALA in RBCS
 - increased Porphobilinogen in urine (in 88% between attack)
 - increased ALA in Urine
 - normal Coproporphyrin in stools in between attacks

Treatment:

- Avoid precipitating factors
- Administer large doses of glucose
- Intravenous infusion of hematin 3mg/kg/day once daily for four days, hematin suppresses symptoms in acute attack.

- Chlorpromazine for abdominal pain and psychiatric attack
- Meperidine for pain
- Phenytoin – anti-convulsant

Side Effects of I.V. Hematin:

- thrombophlebitis
- coagulopathy
- Anaphylaxis

Hereditary Coproporphyrria (HCP)

- There is deficiency of Coproporphyrinogen 3 oxidase
- Autosomal Dominant Inheritance, the gene is on chromosome 3q12
- Clinically it is characterized by:
 - o Acute attack of pain as seen in AIP and VP
 - o Photosensitivity in 33.3% of cases similar to PCT
 - o Precipitated by estrogens and other drugs as in AIP, VP and PCT

Laboratory Findings:

- Reduced coproporphyrinogen oxidase in RBCS
- Elevated fecal coproporphyrin III ± protoporphyrin between attacks
- Urine shows increased
 - o Coproporphyrin III in attack
 - o Increased ALA in remission
 - o Increased Porphobilinogen in remission

Treatment:

- as in AIP

Variegate Porphyria (VP)

- It is due to protoporphyrinogen oxidase deficiency
- Autosomal Dominant and the gene is on chromosome 1q22
- Onset in childhood with growth retardation and mental abnormality.
- Characterized clinically by neurologic manifestation as in AIP (attacks of pain) and skin manifestations as in PCT. All patients have photosensitivity in sun exposed areas as in PCT.

Laboratory Findings in VP

- Protoporphyrinogen oxidase deficiency
- ALA and PBG are increased in acute attack and in remission in urine
- Urine and stool show increased protoporphyrin and coproporphyrin
- RBCS are normal
- Stools are normal
- Plasma of VP readily fluorescence at 625 – 627 nm using spectrophotometer fitted with red sensitive photomultiplier to increase its sensitivity. Spectrophotometric scanning of plasma will detect all cutaneous porphyrias during symptomatic phase ⁽¹⁴⁾ and is useful screening test ⁽¹⁴⁾
- Carriers of VP among patient relatives can be detected by
 - o Protoporphyrinogen oxidase activity in fibroblast or lymphocyte
 - o Plasma fluorescence screening is sensitive for patients over age of 15 years. Adult carriers are 86% sensitive and more than 35% have stool porphyrin sensitive test.

Treatment:

- 1- Avoid sun and adverse use of sunscreen
- 2- CHate loading
- 3- I.V. hematin infusion

Erythropoietic Protoporphyrria (EPP)

- Due to deficiency of Ferrochelataze enzyme and the defect is at level of bone marrow.
- It is the most common porphyria of childhood and is usually evident by the age of 2- 4 years and is AD.
- The disease is suspected when the child gives history of screaming on going outdoor or complains of pain of skin on exposure to sun.
- Clinical features include:
 - o Mild photosensitivity characterized by
 - Stinging sensation
 - Pruritus
 - Erythema and urticarial plaques
 - Sometimes edema
 - Purpura, vesicles, crust, erosion
 - Scarring – shallow, circular or linear, pits on nose, dorsum of hands and cheek

- Waxy thickening of the skin of the nose and knuckles
 - Hypertrichoses
 - Hyperkeratosis and thickening and mild scarring on dorsum of hands
 - Mild abnormality of liver function and biliary tract in about 10% of cases and liver biopsy is indicated
 - Liver failure may occur in 5% of cases and its early diagnosis is necessary as liver transplant may be life saving
 - Protoporphyrin Gall Stones may develop at an early age
 - EPP is linked in adults with excessive alcohol intake
 - Many patients may have an apparent mild anemia with microcytic hypochromic blood film. However, by Electron Microscopy iron is seen deposited in RBC with round sideroblast because of inability to produce heme due to partial ferrochelatase deficiency. If iron is given in such situation it may exacerbate porphyria by suppressing erythroid ALA synthase and so increase porphyrin synthesis
 - It is due to Ferrochelatase enzyme deficiency with defect in heme synthesis
 - Diagnosis is made by detecting:
 - Protoporphyrin in erythrocyte ++ while ALA and PBG are normal in urine or feces
 - Estimate Ethylenediamine acetic acid in blood
 - Quantify porphyrins in red cells and differentiate Zn and free protoporphyrin
 - Full blood count
 - Serum iron
 - Total iron binding capacity
 - Ferritin
 - LFT once / year
 - US, CT, MRI of liver
 - Liver Bx.
 - D.D :
 - Hydroa vacciniforme
 - Hutchinson summer prurigo
 - Solar urticaria
 - Polymorphic light eruption
 - Treatment:
 - Avoid sun
 - β carotene 50 – 200 mg once daily
 - N – acetyl cysteine = free radical scavenger
 - Cysteine 500mg BID = free radial scavenger
 - Anti histamine = reduce weal, flare
 - NBUVB for skin tanning
 - Cholestyramine to increase protoporphyrin excretion and decrease hepatic porphyrin and photosensitivity
 - Liver transplant
- NB:** If patient is undergoing operative interference the viscera must be protected from light (visible) because severe burn may occur and light should be reduced to 380 – 420 nm. Peripheral neuropathy and confusion may develop post operative.
- NBUVB (311 – 313 nm to increase epidermal thickening
 - Decrease hepatic accumulation of protoporphyrin by:
 - I.V. hematin
 - Increase carbohydrate intake
 - Blood
 - Oral iron
 - Oral bile acid to increase excretion of protoporphyrin
 - Gene treatment of Ferrochelatase deficiency
- Congenital Erythropoietic Porphyria (CEP)**
- Autosoma Recessive
 - Very rare – less than 200 cases reported and start in infancy
 - Very severe photosensitivity with phototoxic burning and blistering leading to mutilation of light exposed parts
 - Stunted growth and life expectancy is decreased
 - Hypertrichoses of face and larugo hair
 - Erythrodontia and severe photosensitivity with swelling, blisters on exposed areas with ulceration and scar formation
 - Hypersplenism

- Hemolytic anemia
- Thrombocytopenia
- Ocular complication as scleromalacia, photophobia and loss of vision
- There is deficiency of uroporphyrinogen III cosynthase in bone marrow
- Mutilation of ears, fingers and nose
- Pink urine and nappies (this is also seen in HEP)
- Alopecia, nail changes, hypo and hyperpigmentation
- Teeth and RBCs fluoresce red with Wood's light
- Osteoporosis and fractures, vertebral compression and acroosteolysis
- Thrombocytopenia may be the presenting feature in adults years before skin signs
- Urine contains high amounts of:
 - Uroporphyrin 1
 - Coproporphyrin – 1
- stool show coproporphyrin 1 +++
- RBC show
 - Uroporphyrin 1
 - Coproporphyrin 1
 - Protoporphyrin
- D.D.
 - 1- HEP
 - 2- EPP
 - 3- PCT
- Treatment:
 - 1- avoid solar radiation 360 – 500 nm for skin and eye
 - 2- oral super activated charcoal to reduce enterohepatic porphyrin circulation
 - 3- hypertransfusion to reduce porphyrin giving packed RBCS
 - 4- oral β carotene
 - 5- Splenectomy to reduce hemolysis and platelet consumption
 - 6- Bone marrow transplant

NB:

- 22 different CEP mutation have been described
- Prenatal diagnosis is possible by aminosynthesis
- Desferrooxamine
- Gene treatment

Δ Aminolevulinic acid dehydratase deficiency Porphyria (present since infancy)

- Autosomal recessive – on chromosome 9q34
- Clinical features (like AIP)
 - Most cases with acute infantile hepatic disorder
 - Peripheral neuropathy not well described
 - Hemolysis in some patient
 - Susceptible to lead intoxication and clinically has the features of lead poisoning but no connection to lead.
 - Laboratory finding
- elevated fecal coproporphyrin and protoporphyrin in between attacks
- normal porphobilinogen
- urine shows increased
 - ALA and
 - Coproporphyrin

Erythrocytic Coproporphyrin ECP

The rarest type of porphyria. Clinically is similar to Erythropoietic Protoporphyrin seen in childhood as photosensitivity. RBCs show increased Coproporphyrin, Protoporphyrin.

Pseudoporphyria

Clinically and histologically like PCT but is biochemically negative.

Seen in:

- 1- 4 – 18% of hemodialysis patients
- 2- Sun bed
- 3- Drugs due to photoreactive release
 - Amoidarone
 - Etretnate
 - Isotretinoin
 - Frusemide
 - Nalidixic acid
 - Naproxen
 - Tetracycline

New lesions continue to appear up to five-weeks after discontinuation of drugs and skin fragility goes on for up to six-months.

Treatment:

Avoidance of causative drug.

Comparing erythropoietic to Hepatic porphyrias is shown in the following table:

Compared Items	Erythropoietic Porphyrias			Hepatic Porphyrias		
	CEP	EPP	PCT	VP	AIP	HCP
Inheritance	AR	AD	AR – AD	AD	AD	AD
Enzyme Defect	Uroporphyrinogen Synthetase	Ferrochelatase	Uroporphyrinogen Decarboxylase	Protoporphyrinogen Oxidase	PBG Deaminase	Coproporphyrinogen oxidase
Onset	Infancy	Childhood	Middle age	Young adults	Young adults	Young adults
Photosensitivity	Yes	Yes	Yes	Yes	No	Yes
Skin lesion	Yes	Yes	Yes	Yes	No	Yes
Attacks of abdominal pain	No	No	No	Yes	Yes	Yes
Neuro Psychiatric	No	No	No	Yes	Yes	Yes

Key:
 AR = autosomal recessive - AD = autosomal dominant

Comparing erythropoietic to Hepatic porphyrias is shown in the following table:

Compared Items	Erythropoietic Porphyrias			Hepatic Porphyrias		
	CEP	EPP	PCT	VP	AIP	HCP
RBCS Uroporphyrin	+++	N	N	N	N	
Coproporphyrin	++	+	N	N	N	N
Protoporphyrin	(+)	+++	No	No	No	N
Urine Porphobilinogen	N	N	N	(+++)	(+++)	(+++)
Uroporphyrin	+++	N	++	+++	+++	
Feces Protoporphyrin	+	++	Copro-Isocorprotoporphyrin	+++	N	N

Key:
 N = Normal
 ++ = moderately increased
 (+++) = frequently increased
 + = above normal
 +++ = markedly increased
 (+) = increased in some patients

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