

# SOLAR URTICARIA AND PORPHYRIAS

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**SUMMARY:** The importance of disturbances of porphyrin metabolism in solar urticaria is discussed 15 cases of porphyrias with sun sensitivity are presented comprising 5 cases of erythropoietic protoporphyria, 8 cases of coproporphyria hereditaria and 2 cases of porphyria variegata, 9 out of these 10 patients presented neuroabdominal symptoms and in 4 cases anticonceptive pills have triggered the disease.

Due to the risk of severe forms of disease sometimes drugs induced porphyrias must be considered in all cases of solar urticaria and a correct laboratory study done in the suspected cases.

**Key-words:** Solar urticaria - Porphyrins.

Solar urticaria, solar erythema or polymorphic solar eruption are the more common forms of photosensitivity (BLACK, DICE, GRATTAN, KAPLAN, CHARLESWORTH, KONTOU-FILI, MERKLEN). Solar urticaria although not very common and in cause only in 0,5% of urticaria (DICE) is very distressing and can interfere with the quality of life of patients (KAPLAN, DICE).

Solar urticaria can be classified into six types depending on the wave length of light that induces lesions and the ability or inability to passively transfer the disorder with serum (HARBER, KAPLAN).

Types I and IV can be passively transferred and are probably mediated by IgE antibodies. These types are associated with wave length of 2 800 to 3 200, Å and 4 000 to 5 000 Å respectively (HARBER, KAPLAN). The release of histamine and chemotactic factors for neutrophils and eosinophils after challenge of patients with solar urticaria suggests degranulation of mast cells (KAPLAN, HARBER).

The mechanism producing light urticaria in types II, III and IV is unknown. These urticaria are induced by inciting wavelengths of 3 200 to 4 000 Å, 2 800 to 5 000 Å 4 000 to 5 000 Å respectively and cannot be passively transferred with serum. As a simple screen for solar urticaria fluorescent tubes that emit a broad continuous spectrum can be used with the addition of different filters to define the spectrum that causes urticaria. Type VI solar urticaria is activated at 4 000 Å and corresponds to erythropoietic protoporphyria or other forms of porphyria (KAPLAN, COSTA, GAJDOS, PALMA-CARLOS).

This classification has been largely quoted. However some patients fail to react to monochromatic light

and others demonstrate an action spectrum that changes overtime (MURPHY, HASEI, RYCAERTS). Therefore this classification system may not be useful in categorizing all patients (DICE, UETSU, RYCAERTS).

Erythropoietic protoporphyria is a metabolic disorder caused by an enzymatic deficiency on the last step of hemesynthesis, the incorporation of iron in protoporphyrin run by ferrochelatase. In contrast with other forms of porphyria the level of porphyrin excretion in urine is normal because protoporphyrin is not hydro soluble (GAJDOS, PALMA-CARLOS, DESNICK, BONKOSWKY).

However, the level of protoporphyrin in red blood cells and the levels of coproporphyrin and protoporphyrin in feces are increased (DESNICK, ANDERSON, GAJDOS, PALMA-CARLOS).

There is evidence for complement activation when the plasma of patients with protoporphyria is exposed to light 4 000 Å wavelength. There is generation of C5 a chemotactic activity proportional to the serum level of protoporphyrin (GIGLI).

Irradiation of the forearm of the patients with erythropoietic protoporphyria also resulted in complement activation as assessed by a decrease of C3 and C5 and generation of C5a. In the derm a deposition of C3 and accumulation of neutrophils are observed. Complement fragments can be detected in the serum and suction blister fluid of irradiated skin.

Photosensitivity is also observed in other forms of porphyria, Porphyria Cutanea tarda, porphyria variegata and coproporphyria hereditaria but not in acute intermittent porphyria (ANDERSON, DESNICK, GAJDOS, PALMA-CARLOS 1992).

These forms are due to different enzymatic errors in the pathway of heme synthesis leading to the accumulation of porphyrins which can be excited by light

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causing photosensitivity (ANDERSON, DESNICK, GAJDOS, PALMA-CARLOS).

In contrast with erythropoietic protoporphyria where solar urticaria with classic wheals is the clinical major presentation the other cutaneous porphyrias present vesicles, bullae and skin fragility. However, in all the forms of porphyria slight exposure to the sun or the absence of other factors, drugs or toxics for instance some episodes present only erythema, itching or a sensation of burning. In erythropoietic protoporphyria the lesions in sun exposed areas are said to be typically painful rather than itching (DICE). In forms where photosensitivity is less marked solar urticaria or erythema can be the presenting or only symptom (DESNICK, GAJDOS, PALMA-CARLOS).

Porphyrias are usually classified in hepatic and erythropoietic porphyrias depending on the site of major metabolic defect (GAJDOS and GAJDOS-TÖRÖK, PALMA-CARLOS, NORDMAN, WITH).

Hepatic porphyrias include acute intermittent porphyria, porphyria cutanea tarda, hereditary coproporphyria and porphyria variegata (ANDERSON, DESNICK, GAJDOS and GAJDOS, TÖRÖK, PALMA-CARLOS, WINTROBE, WITH).

The erythropoietic porphyrias comprise congenital porphyria (GUNTHER'S disease) and erythropoietic protoporphyria. This last form is very rare (1 case in our series of 200 porphyrias) autosomic dominant and present very severe lesions, scarring and even mutilations (ANDERSON, DESNICK, GAJDOS, GAJDOS-TÖRÖK, PALMA-CARLOS).

Erythropoietic protoporphyria usually has a typical aspect of solar urticaria, with solar erythema or polymorphic solar eruption after slight exposure to sun (KAPLAN).

In hepatic porphyrias the greater photosensitivity is present in porphyria cutanea tarda with vesicles skin fragility and hypertrichosis (ANDERSON, DESNICK, PALMA-CARLOS).

In acute intermittent porphyria there is no photosensitivity but only neuro abdominal symptoms. The 2 mixed forms, porphyria variegata and coproporphyria hereditaria present simultaneously neuro-visceral symptoms and photosensitivity (ANDERSON, DESNICK, GAJDOS, GAJDOS-TÖRÖK, NORDMAN, PALMA-CARLOS).

Enzymatic defects in the different forms of porphyria have been characterized in the last decades:

Uro I synthetase or hydroxyl methylbilane synthase in acute intermittent porphyria; UIII co-synthetase in congenital erythropoietic porphyria (Gunther's disease), uro decarboxylase in cutaneous porphyria, copro-oxydase in coproporphyria, protogene oxydase in porphyria variegata and ferrochelataze in erythropoietic protoporphyria (ANDERSON, DESNICK, NORDMAN).

## METHODS

In 40 patients presenting solar urticaria assay of red blood cells protoporphyrin and of uro and coproporphyrin in urine and copro and protoporphyrin in stool have been done by the current methods.

Laboratory diagnosis is crucial for a correct evaluation of different porphyrias. Porphyrins must be studied in red blood cells, urine and stools. Hydro-soluble porphyrins could also be assayed in plasma but until now in our experience plasma dosages are less sensible than in urine. For porphyrias associated with solar urticaria the usual findings are:

➤ *Erythropoietic protoporphyria* increase of protoporphyrin in red blood cells of proto and coproporphyrins in stools.

➤ *Coproporphyria hereditaria*: coproporphyrin increased in urine and feces.

➤ *Porphyria variegata*: Uroporphyrin and intermediate porphyrins in urine and protoporphyrin in stools. For these two porphyrias porphyrin precursors delta ALA and PBG are usually increased in urina only during neuro-visceral crises.

➤ *Porphyria cutanea tarda* Uroporphyrin in urine (ANDERSON, DESNICK, NORDMAN, PALMA-CARLOS, 1974, 1999).

## RESULTS

In 40 cases of solar urticaria a complete research of disturbances of porphyrin metabolism has been done. By the conjunction of clinical data with laboratory data we have been able to diagnose 15 cases (30%) of porphyrias presenting solar urticaria or erythema. This group comprises: 5 cases of erythropoietic protoporphyria; 8 cases of coproporphyria hereditaria and 2 cases of porphyria variegata.

■ *Erythropoietic protoporphyria* - this is the classic form of solar urticaria in porphyrias.

In these 5 cases some particular features must be emphasized.

In one case (female) the sun sensitivity was triggered by anticonceptive pills. This is as long as we know the first report of erythropoietic protoporphyria triggered by estrogens, drugs which have been linked to hepatic porphyrias (PALMA-CARLOS and PALMA-CARLOS, 1973 PERLROTH, GAJDOS AND GAJDOS-TÖRÖK, DEAN).

A second case present only pain on solar exposure. In the another case aside of solar urticaria neurologic and abdominal eruptions pain vomiting and asthenia were present without any disturbance in the excretion of porphyrins and precursors even during crises and hydroxyl methyl bilane synthase (uroporphyrinogen III Synthetase) was normal. Therefore, other form of

porphyria was not confirmed. Beta carotene could be useful in these cases (MATHEWS-ROTH MOSHELL).

■ **Coproporphyria hereditaria:** The high number of cases in this group must be emphasized, sensitivity is not so marked in mixed porphyrias coproporphyria hereditaria and porphyria variegata than in porphyria cutanea tarda. No vesicles, bullae or scarring has been observed in our patients but only solar erythema and also in 4 cases clear solar urticaria. 2 patients have taken estrogens before symptoms and one have been exposed to organic solvent in a research laboratory. Relation with estrogens has been reported before for cutaneous or mixed porphyrias (DEAN, LEVERE, PERLROTH, VALL). 7 out of these 6 patients have neuroabdominal symptoms.

This distribution with a large number of coproporphyria has been previously reported in Portugal in another series of human Porphyrias (PALMA-CARLOS ML., SANTOS MC., PALMA-CARLOS 2000

■ **Porphyria variegata** Porphyria variegata, a common form of porphyria in South African Boers is less common in Portugal than coproporphyria. Both forms are mixed presenting photosensitivity and neurovisceral symptoms during crisis. In these 2 forms sensitivity is less marked than in porphyria cutanea tarda and can only cause as in our patients solar urticaria or erythema. In our series most of the patients, 10 out of twelve presented abdominal symptoms pain, false acute leading in 2 cases to laparatomies.

## DISCUSSION

Porphyrias either erythropoietic or mixed are the cause of solar urticaria or erythema in some patients. Due to the severity of neuro-visceral crisis in mixed forms and associated hepatopathies in same cases of erythropoietic protoporphyria a correct study of porphyrins levels in blood, urine and stools must be done in all the cases of solar urticaria. The incidence of porphyrias in solar urticaria and erythema in our series is very high (30%). However this number could be biased by patients referred to us due to our experience in the field of porphyrias.

In most of the mixed forms neuro visceral crisis which could be fatal are triggered by drugs and is mandatory to know these risks and exclude potentially dangerous treatment.

Due to the risk of serious complications in neuro visceral crisis of mixed porphyrias which are often triggered by drugs a precise and early diagnosis of porphyrias is mandatory (DESNICK, NORDMAN, PALMA-CARLOS).

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## RESEARCHERS DEVELOP NEW METHOD FOR DETERMINING MOLDINESS OF HOME, FROM THE JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY

**MILWAUKEE** - Comparing the levels of airborne fungi inside the house with those found outdoors may provide a method for determining the moldiness of a home, according to a study found in the September 2004 Journal of Allergy and Clinical Immunology (JACI). The JACI is the peer-reviewed scientific journal of the American Academy of Allergy, Asthma and Immunology (AAAAI).

As part of the Inner-City Asthma Study, George T. O'Connor, MD, MS, Boston University School of Medicine, and colleagues measured the concentrations of airborne fungi inside and outside the homes of 414 mold-sensitive children with moderate to severe asthma in seven low-income urban communities across the United States. Researchers analyzed the relation of the concentration of fungi in indoor air to home characteristics and to the outdoor concentration on the day of the measurement. The research was done as part of the Inner-City Asthma Study.

Previous studies have shown that the most common types of airborne fungi, *Alternaria*, *Cladosporium*, *Penicillium*, and *Aspergillus*, are present in outdoor air and in many indoor environments. The current study found that the levels of these fungi found indoors actually matched those found outdoors across all seven cities, suggesting that the outdoor concentration is an important determinant of the indoor concentration.

### ■ Researchers noted:

- Higher levels of fungi were significantly more likely to be found in homes with reported water damage, dampness, or leaks in the past 12 months. This supports the belief that fungi play a role in the association between home dampness and respiratory symptoms.

- Evidence of cockroach infestation in the child's bedroom was found in homes with higher levels.

- Higher levels of fungi were also found in homes containing cats. This may be the result of fungal growth in a damp litter box or the large amounts of organic material that cats add to house dust.

- Researchers noted that a higher concentration of fungi was less likely in homes with forced air heating and in homes with higher bedroom temperatures.

Exposure to airborne fungi may lead to allergic sensitization and provoke allergy and asthma symptoms. This is the first study to report on the exposure to airborne fungi in asthmatic children living in U.S. inner cities, a group with high morbidity and frequent sensitization to mold. The results of the JACI study may provide a valuable metric for future epidemiologic investigations of the role of fungal exposure as a risk factor for disease.

The AAAAI is the largest professional medical specialty organization in the United States representing allergists, asthma specialists, clinical immunologists, allied health professionals and others with a special interest in the research and treatment of allergic disease. Established in 1943, the AAAAI has nearly 6,000 members in the United States, Canada and 60 other countries. The AAAAI serves as an advocate to the public by providing educational information through its Web site at [www.aaaai.org](http://www.aaaai.org) or the toll-free physician referral and information line at 1(800) 822-2762.

**EDITOR'S NOTE:** This study was published in the peer-reviewed, scientific journal of the American Academy of Allergy, Asthma & Immunology, but does not necessarily reflect the policies or the opinions of the Academy. To receive a copy of the study, please contact John Gardner ([jgardner@aaaai.org](mailto:jgardner@aaaai.org)) at (414) 272-6071. For more information and access to the archive of past JACI news releases, visit the Media Center of the AAAAI Web site, [www.aaaai.org](http://www.aaaai.org).