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Title Page

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Solar urticaria - An Australian case series of 83 patients

Abstract: Solar urticaria (SU) is a rare form of urticaria with a pathogenesis that is poorly understood. It affects all skin types, can be difficult to diagnose, and is challenging to manage effectively. We conducted a retrospective review of patients with SU in our institution. A total of 83 patients were identified as having SU. There were 25 males and 56 females with a mean age of 32 years (7-74) at first development of symptoms/signs of SU. Pruritus was the most common symptom reported (79%). Of the sixty patients who underwent monochromator testing at least once, 35 had SU confirmed with most reacting to visible light and UVA, or to UVA alone. Antihistamines and sun avoidance remain the mainstay treatment for SU but other treatments, including omalizumab, are of potential interest in treating patients with recalcitrant SU. The characterisation of this large case series of patients may help dermatologists recognise and manage this rare disorder appropriately.

Key Words: Solar urticaria, phototesting, photodermatosis, omalizumab, urticaria

Learning Points:

- Solar urticaria is a rare disorder with specific clinical features and diagnosis is aided through the use of phototesting.
- Omalizumab is a potentially exciting new treatment for this difficult to manage condition.

Introduction:

Photodermatoses are a group of dermatological conditions associated with an abnormal reaction to UV radiation, infra-red radiation, visible light or a combination of these. Solar urticaria (SU) is a rare photodermatosis, reported as representing only 4-8% of all photodermatosis presentations [1] and estimated to account for only approximately 0.4% of all urticarias [2]. Current theories about its cause are centered around the idea of an as yet to be elucidated chromophore which is activated by light and which, in turn, induces mast cell degranulation [3]. Patients are a diverse

group. They can present at any age including infancy [2, 4, 5], with any skin phototype, reporting signs of wheals, pruritus, swelling, burning, stinging, and erythema usually within minutes of exposure to sunlight and/or fluorescent light. They may also suffer systemic symptoms of dizziness, nausea, fatigue, headache and flushing. The severity of the symptoms and signs depends largely on the amount of exposure and the intensity of irradiation. Symptoms usually resolve within a few hours, but the negative impact on their quality of life should not be underestimated [6]. The disease course is variable.

Currently, there is no cure for SU and management is primarily symptomatic, consisting of high doses of antihistamines, sun avoidance, sunscreens, and protective clothing. Other treatments have been tried with varying success and some treatments currently recommended for chronic idiopathic/spontaneous urticaria have also been suggested for use in SU: H2-blockers, phototherapy, immunosuppression, intravenous immunoglobulins, plasmapheresis, polypodium leucotomos, extracorporeal photo-chemotherapy, alpha-melanocyte stimulating hormone and more recently, omalizumab has shown promise. Clinical resolution has been reported to occur in 12 - 50% of patients at 5 years, 26 - 70% at 10 years and 36% at 15 years [7, 8].

This paper reports the characteristics of a population of 83 patients with clinically confirmed SU and no other photodermatosis in a single tertiary referral centre in Melbourne, Australia. We aim to use this large case series to aid dermatologists in understanding this rare disease, the usefulness of phototesting in this context and the management options currently available.

Methods:

Ethics approval for the study was obtained from the Research Governance Unit of St Vincent's Hospital, Melbourne. This was a retrospective study. All patient files which were coded as potentially having SU were identified, retrieved and reviewed by the primary investigator - this included paper, microfilm and electronic files. All information was stored in a secure database.

Results:

Patient characteristics: (table 1)

A total of 83 patients were identified as having SU between 1992 and 2017. This diagnosis was primarily clinical and was determined by a consultant dermatologist. Blood tests were undertaken

in all patients to rule out other photodermatoses (as described later). Other possible causes such as medications, infections, and exogenous agents were also investigated and ruled out. Phototesting with monochromator and solar simulator was performed in 60 patients. Not all patients consented to testing or were able to be tested due to technical issues with the machine. Thirty-five patients (58%) had positive light tests confirming SU.

Disease characteristics:

Solar urticaria has many symptoms and signs. Seventy-four patients reported signs/symptoms in response to exposure to sunlight and six reported that fluorescent light could also trigger a response. Forty-five patients were triggered by sunlight through glass (which corresponds to a reaction to UVA) and twenty-three through clothing (which is dependent on the type and thickness of the fabric).

Contrary to the general belief that repeated exposure to the sun results in a certain hardening that reduces the symptoms of SU in these areas [9, 10], thirty of our patients (36%) reported signs on their faces, twenty-four (28.9%) on their neck/chest, twenty-five (30%) on their arms, and twelve (14.4%) on their hands. The majority of patients (61.4%) reported signs on any sun-exposed sites.

Of symptoms reported, pruritus was the most common (66 patients - 79.5%), followed by a burning sensation (9.6%), pain (3.6%) and stinging (2.4%). Erythema was the most common sign reported (51 patients - 61.4%), closely followed by wheals (46.9%), papules or patches (26.5%), and swelling (22.8%). All patients reported a combination of symptoms. Only ten patients (12%) reported systemic symptoms with nausea being the most common (4.8%), then headaches (2.4%), fatigue (2.4%), dizziness (1%) and flushing (1%).

As expected, the majority of patients reported a time to signs/symptoms of $\leq$ 5 minutes (55%), followed by 15-30 minutes (13%), 10-15 minutes (10.8%), and 5-10 minutes (9.6%). The time to resolution was mostly within an hour (62%) but was reported up to and later than 4 hours (36%). Twenty-two patients reported symptoms all year, while twenty-six reported symptoms primarily in summer.

Phototesting and Wavelength Sensitivity:

Several lamps can be used for phototesting - slide projectors and fluorescent tubes are inexpensive and readily available. A solar simulator (a xenon lamp) is more expensive but also more accurate if used with a monochromator to determine the action spectrum (AS) at different wavelengths [1, 11].

Sixty patients underwent monochromator phototesting. The right or left mid-back was chosen as these are usually less sun exposed. An Oriel Corporation (Stratford, USA) monochromator, F/0.7 Aspherb Condenser with a high pressure 450-1000W Xenon arc lamp was used. The patients were tested for specific wavelengths in the visible light, UVB and UVA spectrum. An immediate erythema or urticarial reaction, occurring within one hour, was recorded. It was possible to determine the action spectrum (AS) in thirty-five (58%) of the sixty patients who underwent monochromator testing at least once (figure 1). The remaining twenty-five patients (41.6%) had no reaction. Thirty-three patients reacted to the UVB/UVA solar simulator.

Management: (table 2)

Antihistamines were the most prescribed medication used by our patients (85%). Many patients used several of these medications throughout the study period and sometimes more than one at the same time. Other medications that were prescribed are listed in table 2. Sunscreen was documented as being used by only sixty-one patients (73%). Some patients reported having tried sunscreen without effect and therefore discontinued its use.

Unfortunately, due to the nature of the disease or perhaps the lack of efficacy of most of the treatments, many of the patients in our series were lost to follow up or no record of whether their symptoms had resolved was made.

Discussion:

Pathogenesis:

Solar urticaria (SU) is believed to have first been described by Merklen in 1904 but Duke coined the term in 1923 and was also the first to use sun exposure as prophylaxis [10]. There are currently two theories regarding pathogenesis [3]:

1. An abnormal endogenous substance or "chromophore" that occurs only in the patient

2. An abnormal reaction to a normal endogenous substance present in both patients and controls

The chromophore absorbs light of a wavelength corresponding to a triggering action spectrum (AS). This then acts as a photoallergen, triggering the production of specific IgE antibodies which bind to mast cells. Re-exposure to this AS causes the release of histamine resulting in urticaria, erythema and itch. However, to date no photoactive molecule has been identified and there is currently no good animal model for SU.

The pathogenesis theory is further complicated by the observation of an 'inhibition spectrum' first reported by Hasei and Ichihashi in 1982 [12] and confirmed by other authors [9]. They demonstrated that a dose four times a patient's AS would not induce lesions if the test site was promptly irradiated with light of wavelengths longer than this AS [13]. Shortly thereafter an 'augmentation spectrum' was also observed by Horio and Fujigaki in 1988 [14] and then by Horio in 2003 [9]. They showed that irradiation with specific wavelengths before irradiation with the AS enhanced the urticarial reaction in one, then four other patients with SU. The phenomenon of "fixed" SU, where the eruption occurs only in specific areas of the body, adds further intrigue into the pathogenesis of this dermatosis [15-18].

Investigation of a patient with suspected solar urticaria:

Making a diagnosis of SU can be challenging and can sometimes be a diagnosis of exclusion. As shown in our case series, these patients represent a heterogenous population with varying signs/symptoms and histories. Without access to monochromator testing, or even with it, the diagnosis is often a clinical one. Below we have summarised our approach to making the diagnosis.

1. **Exclude the differentials:** These are predominantly: chronic idiopathic/spontaneous urticaria, polymorphic light eruption, connective tissue disease, drug eruption and photo-exacerbated eczema. The distinction is predominantly clinical on history and examination (see Table 3). Important questions include: variation over the seasons, time to, duration and distribution of signs and/or symptoms, spread to non-light exposed skin and time to resolution. Exposure to medications or exogenous triggers is paramount to ruling out a photo-allergic or photo-toxic reaction. The severity and duration of signs/symptoms is influenced by the length of exposure and the intensity of the light. Long exposures are more likely to produce systemic symptoms [19].

2. **Laboratory investigations:** There are no specific laboratory tests for SU and indeed the EAACI/GA2LEN/EDF/WAO guidelines for the definition, classification, diagnosis and management of urticaria (2013 and 2017 revision and updates) strongly recommend against routine diagnostic measures being performed in acute urticaria and recommend only very limited tests in chronic idiopathic/spontaneous urticaria [20, 21]. However, full blood count, biochemistry and ANA can help exclude autoimmune diseases that cause photosensitivity and porphyrins are often ordered to exclude porphyria.

3. **Biopsy:** Biopsy is of limited value in these patients. The histologic features of SU are similar to other forms of urticaria and depend upon the time of exposure. There is endothelial swelling and increased permeability of the vascular endothelium, with early perivascular dermal infiltration by neutrophils and eosinophils [22].

4. **Phototesting:** This can elicit the eruption which in turn can confirm the diagnosis. The AS for each patient can be determined which can guide patients and physicians in selecting management options. Phototesting is performed on the back or forearm. Monochromator testing distinguishes which wavelengths cause the eruption. UVB (280-315nm), UVA (315-400nm) and visible light (>400nm) wavelengths are tested. Patients can react to a combination of the wavelengths and importantly, a negative phototest does not exclude a diagnosis of SU [6]. Indeed, sometimes it is necessary to perform the test several times, as the AS may change [23]. It may be necessary, or helpful, also to use direct sunlight to elicit a response, particularly when phototesting is not available. Although this doesn't clarify the wavelength responsible it can aid the diagnosis. The difficulty in eliciting the AS in some patients may imply the "existence of several photoactive molecules" which then react to differing wavelengths [13]. Figure 2 shows a graphical representation of the phototesting results of all the case series which included their AS results published in the literature to date which the authors could find on a search of Ovid Medline. This shows a preponderance for reaction to visible light and that up to half of patients may have no reaction. Figure 1 shows our results. We had a similar number of patients with no reaction, however, we had more patients with a reaction to UVA than to visible light.

Treatment Options:

There is currently no cure for SU. Treatment options are directed primarily at symptom control with the aim of allowing patients to lead normal lives. See table 2 for a list of treatment options we used in our patients and table 4 for a list of treatment options reported in the literature. These treatments can be used alone or in combination.

Antihistamines

Continuous second-generation antihistamines, taken at the lowest necessary dose, are first line in treating SU [20]. Histamine is believed to be an important mediator of SU but it is likely other mediators are also involved and this may explain why antihistamines are sometimes ineffective [22] with one study showing only a third of patients had complete suppression of symptoms, another third had a partial response and the rest were unresponsive [24]. Antihistamines act on the H1 receptor and have been shown to reduce urticaria [25]. In many patients however, much higher doses than the conventional dosage are usually needed (up to fourfold) and many patients will try a variety of different formulations over the duration of their disease [20]. This trend was observed in our patients with an average of 2.7 antihistamines used by each patient (range 1-8). Variation in efficacy, price and side effects may explain this. Regular use of antihistamines may not only reduce the discomfort of SU but may also allow the patient to expose themselves to sunlight more often, thus giving them a chance to make their skin more tolerant with time [26]. Treatment with a combination of different antihistamines concurrently has been shown to increase the chance of successful remission [27].

H2 Blockers

While H2 blockers are primarily used in the treatment of gastritis due to hyperacidaemia, it has been observed that the combination of H1 and H2 blockers can suppress the histamine-induced wheal of urticaria in general whilst not in SU specifically [28]. Fifteen of our patients were prescribed Ranitidine.

Phototherapy

Phototherapy, where wavelengths of the AS are administered 2-4 times per week starting with short exposure times and gradually increasing exposure time, can lead to symptomatic relief of SU through an effect called "hardening" [29]. Only 18% of our patients received this therapy. Unfortunately this usually results in short-lived remission (only up to 6 months) [30] and is very time-

intensive making it difficult for most patients to access. Photo-chemotherapy (PUVA), can be used for those patients sensitive to UVA and provides longer-lasting results (weeks to months) but has the increased risk of developing skin cancers and unpleasant side-effects caused by the psoralen [30]. Using wavelengths of the 'inhibition' spectrum as discussed earlier, may also be used to induce tolerance [31].

The mechanism by which these modalities work remains elusive. Leenutaphong *et al* [32] and Keahey *et al* [33], cast doubt on the theory of histamine depletion by showing that mast cells retain their integrity with photo-irradiation. Instead, Leenutaphong *et al* proposed that "it is likely that binding sites of IgE on mast cells remain occupied by the photoallergen during the state of tolerance, and that histamine release from mast cells is blocked." Another theory is that repeated exposure leads to epidermal thickening and increased melanin production which may reduce the intensity of radiation transmitted to the chromophore [34].

Immunosuppression:

The use of these medications in SU lacks evidence. The best that can be determined is that as they have been shown to be useful in chronic urticaria (CU), there may be some use in some patients with SU.

1. Methotrexate: A study of 8 patients with recalcitrant CU [35] showed an 87% complete response rate. However, a randomised placebo-controlled double-blind pilot study of methotrexate in the treatment of antihistamine resistant CU (14 patients) [36] concluded that there was no additional benefit in using methotrexate as compared to H1 antihistamines. Only one of our patients was prescribed this medication.
2. Cyclosporin: Randomised double-blind studies have shown efficacy in approximately two-thirds of patients with CU and 25% of these report long-term improvement [37, 38]. Its use has also been shown to be effective and safe in a small cohort of children [39]. However, Hurabielle *et al* [40] looking at reports of 11 patients in France with severe refractory SU didn't show as strong a benefit from cyclosporin use in this condition. Only one of our patients was prescribed this medication.
3. Leukotriene receptor antagonists (montelukast) - A combination treatment of antihistamine and montelukast has been shown in a small study of eleven patients with SU to result in either complete remission (63%) or partial remission (9%) [41]. This small study also included three

patients who received no treatment and two of these showed complete remission. We included 4 patients who received this treatment.

Omalizumab

Omalizumab is a recombinant humanised monoclonal anti-IgE antibody indicated for the treatment of asthma and CU. Several case reports of SU treated by omalizumab have been reported and results are variable but potentially promising. Aubin *et al* [42] reported a phase II multi-centre study of 10 patients in France in 2016 with severe SU refractory to antihistamines treated with the same regimen of omalizumab as for CU (300mg subcutaneously at intervals of 4 weeks for a total of 8 weeks with a baseline dose). Phototesting, performed at weeks 12 and 20, were performed to determine any change in their minimum urticarial dose (MUD). They were also assessed on changes in the Dermatology Life Quality Index (DLQI) score. Only 2 patients (20%) reached the primary end point of a response rate defined as no SU after exposure to an ultraviolet dose greater than 10-fold the baseline MUD at 12 weeks. No patients achieved this result at 20 weeks suggesting a short time to relapse. Furthermore, only 40% reported a DLQI score of < 6 at 12 weeks, meaning more than half did not see a reduction in symptoms.

More recently, Snast *et al* [43] have reported a case series of 5 patients with SU treated with monthly doses of omalizumab resulting in clinical improvement in all patients with 4 patients experiencing complete remission. Their systematic review of the literature reported that 79% of patients treated with omalizumab showed clinical improvement and 11% had mild adverse effects including "gastrointestinal intolerance, periorbital oedema, local reaction, and short-term asthenia". Also Morgado-Carrasco *et al* [44] reported use of omalizumab in 8 patients with 89% showing improvement. UVA exposure was implicated in the majority of their patients and phototesting was normal in 42.8% after treatment. While these studies are promising, their small patient numbers are a limitation and further studies are needed, however we recognise the difficulty in obtaining larger numbers due to the rarity of this disorder.

IV Immunoglobulins

Intravenous immunoglobulin (IVIG) is a blood product containing polyvalent immunoglobulin G. IVIG has been demonstrated to be effective in the treatment of various types of recalcitrant urticarias. Aubin *et al* [45] showed a response rate of 22.2% in a multi-centre phase II trial of 9 patients with severe SU treated with a single course of IVIG (2g/kg). This was maintained for a varia-

ble length of time (24-48 weeks). They concluded that "a single course was insufficient to obtain prolonged significant control of SU." Adamski *et al* [46] retrospectively reviewed 7 patients with SU treated with IVIG of varying courses and found a "beneficial effect of IVIG in severe SU" but were unable to specify the optimal administration of this product. IVIG is relatively safe but there are potential side effects such as headache, myalgia, flushing, fever, chills, fatigue, nausea or vomiting, low back pain, chest discomfort, hypotension and hypertension, tachycardia and skin eruptions [45]. It is expensive and difficult to obtain in Australia.

Plasmapheresis

Plasmapheresis has only been reported in case studies to date and results have varied from no effect to complete remission, furthermore most results have been short-lived. Leenutaphong *et al* [47] reported three patients with SU treated with plasmapheresis with complete remission in one, transient improvement in the second but no effect in the third.

Other Therapies reported in the Literature:

1. Polypodium leucotomos extract at 480mg/day orally was tested in 57 patients with idiopathic photodermatoses (4 with SU) and the authors saw a benefit in 73.68% of all patients with no side effects [48]. They did not report on the SU patients specifically.

2. Extracorporeal photochemotherapy has been reported as successful in one case of SU after 9 treatment cycles [49].

3. Alpha-melanocyte stimulating hormone (α-MSH) analogue, afamelanotide, is a super-potent agonist of the melanocortin-1 receptor resulting in melanogenesis. A study by Haylett *et al* [50] in 5 patients with SU who received a single dose of 16mg through a subcutaneous implant in winter showed an increased mean melanin density, peaking at day 15. They demonstrated a reduction in wheal induction with a "greater than twofold overall increase in MUD". It is not yet approved for use in SU, and is still awaiting FDA and TGA approval.

Conclusion:

The characterisation of this large case series of patients has been performed with the aim of aiding dermatologists in recognising and managing SU in an appropriate and realistic fashion given what we know about the pathogenesis and management strategies available today. More re-

search into SU is warranted, particularly in regards to the promising new anti-IgE therapies such as omalizumab.

Bibliography

1. Crouch, R.B., P.A. Foley, and C.S. Baker, Analysis of patients with suspected photosensitivity referred for investigation to an Australian photodermatology clinic. Journal of the American Academy of Dermatology, 2003. **48**(5): p. 714-20.

2. Hochstadter, E.F. and M. Ben-Shoshan, Solar urticaria in a 1-year-old infant: diagnosis and management. BMJ Case Rep, 2014. **2014**.

3. Leenutaphong, V.H., E.; Plewig, G., Pathogenesis and classification of solar urticaria- A new concept. J Am Acad Dermatol, 1989: p. 237-240.

4. Harris, A., S.M. Burge, and S.A. George, *Solar urticaria in an infant.* British Journal of Dermatology, 1997. **136**(1): p. 105-7.

5. Fityan, A., et al., Paediatric solar urticaria: a case series. British Journal of Dermatology, 2018. **178**(6): p. 1453-1454.

6. Haylett, A.K., D. Koumaki, and L.E. Rhodes, Solar urticaria in 145 patients: Assessment of action spectra and impact on quality of life in adults and children. Photodermatology, Photoimmunology & Photomedicine, 2018: p. 13.

7. Beattie, P.E.D., R.S.; Ibbotson, S.H.; Ferguson, J., Characteristics and Prognosis of Idiopathic Solar Urticaria - A Cohort of 87 Cases. Arch Dermatol, 2003. **139**: p. 1149-1154.

8. Perez-Ferriols, A., et al., Solar urticaria: Epidemiology and clinical phenotypes in a Spanish series of 224 patients. Actas Dermo-Sifiliograficas, 2017. **108**(2): p. 132-139.

9. Horio, T., *Solar urticaria - idiopathic?* Photodermatol Photoimmunol Photomed, 2003. **19**: p. 147-154.

10. Goetze, S. and P. Elsner, *Solar urticaria.* J Dtsch Dermatol Ges, 2015. **13**(12): p. 1250-3.

11. Ryckaert, S.R., R., Solar Urticaria - A report of 25 cases and difficulties in phototesting. Arch Dermatol, 1998. **134**: p. 71-74.

12. Hasei, K. and M. Ichihashi, Solar urticaria. Determinations of action and inhibition spectra. Archives of Dermatology, 1982. **118**(5): p. 346-50.

13. Armstrong, R.B., *Solar urticaria.* Dermatologic Clinics, 1986. **4**(2): p. 253-9.

14. Horio, T.F., K., Augmentation spectrum in solar urticaria. J Am Acad Dermatol, 1988. **18**: p. 1189-93.

15. Reinauer, S., V. Leenutaphong, and E. Holzle, *Fixed solar urticaria.* Journal of the American Academy of Dermatology, 1993. **29**(2 Pt 1): p. 161-5.

16. Schwarze, H.P., et al., Fixed solar urticaria to visible light successfully treated with fexofenadine. Photodermatology, Photoimmunology & Photomedicine, 2001. **17**(1): p. 39-41.

17. Tuchinda, C.L., V.; Sudtim, S.; Lim, H.W., Fixed solar urticaria induced by UVA and visible light- a report of a case. Photodermatol Photoimmunol Photomed, 2005. **21**: p. 97-99.

18. Wessendorf, U., et al., Fixed solar urticaria with delayed onset. J Am Acad Dermatol, 2009. **60**(4): p. 695-7.

19. Botto, N.C. and E.M. Warshaw, *Solar urticaria.* J Am Acad Dermatol, 2008. **59**(6): p. 909-20; quiz 921-2.

20. Zuberbier, T., et al., The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy, 2014. **69**(7): p. 868-87.

21. Zuberbier, T., et al., The EAACI/GA2LEN/EDF/WAO Guideline for the Definition, Classification, Diagnosis and Management of Urticaria. The 2017 Revision and Update. Allergy, 2018: p. 15.

22. Roelandts, R.R., S., Solar urticaria: the annoying photodermatosis. International Journal of Dermatology, 1999. **38**: p. 411-418.

23. Ng, J.C.H.F., P.A.; Crouch, R.B.; Baker, C.S., Changes of photosensitivity and action spectrum with time in solar urticaria. Photodermatol Photoimmunol Photomed, 2002. **18**: p. 191-195.

24. Diffey, B.L. and P.M. Farr, Treatment of solar urticaria with terfenadine. Photo-Dermatology, 1988. **5**(1): p. 25-9.

25. Faurschou, A.W., H.C., Synergistic effect of broad-spectrum sunscreens and antihistamines in the control of idiopathic solar urticaria. Arch Dermatol, 2008. **144**: p. 765-769.

26. Roelandts, R., Diagnosis and treatment of solar urticaria. Dermatologic Therapy, 2003. **16**: p. 52-56.

27. Grundmann, S.A., et al., Antihistamine combination treatment for solar urticaria. Br J Dermatol, 2008. **158**(6): p. 1384-6.

28. Dhanya, N.B., R. Rai, and C.R. Srinivas, Histamine 2 blocker potentiates the effects of histamine 1 blocker in suppressing histamine-induced wheal. Indian Journal of Dermatology, Venereology & Leprology, 2008. **74**(5): p. 475-7.

29. Addo, H.A. and S.C. Sharma, UVB phototherapy and photochemotherapy (PUVA) in the treatment of polymorphic light eruption and solar urticaria. British Journal of Dermatology, 1987. **116**(4): p. 539-47.

30. Dawe, R.S. and J. Ferguson, Prolonged benefit following ultraviolet A phototherapy for solar urticaria. British Journal of Dermatology, 1997. **137**(1): p. 144-8.

31. Nitiyarom, R. and C. Wongpraparut, Hydroa vacciniforme and solar urticaria. Dermatol Clin, 2014. **32**(3): p. 345-53, viii.

32. Leenutaphong, V.H., E.; Plewig, G., Solar urticaria- studies on mechanisms of tolerance. Br J Dermatol, 1990. **122**: p. 601-606.

33. Keahey, T.M., et al., Studies on the mechanism of clinical tolerance in solar urticaria. British Journal of Dermatology, 1984. **110**(3): p. 327-38.

34. Gambichler, T., R. Al-Muhammadi, and S. Boms, Immunologically mediated photodermatoses: diagnosis and treatment. American Journal of Clinical Dermatology, 2009. **10**(3): p. 169-80.

35. Sagi, L., et al., Evidence for methotrexate as a useful treatment for steroid-dependent chronic urticaria. Acta Dermato-Venereologica, 2011. **91**(3): p. 303-6.

36. Sharma, V.K., et al., A randomized placebo-controlled double-blind pilot study of methotrexate in the treatment of H1 antihistamine-resistant chronic spontaneous urticaria. Indian Journal of Dermatology, Venereology & Leprology, 2014. **80**(2): p. 122-8.

37. Grattan, C.E., et al., Randomized double-blind study of cyclosporin in chronic 'idiopathic' urticaria. British Journal of Dermatology, 2000. **143**(2): p. 365-72.

38. Vena, G.A., et al., Cyclosporine in chronic idiopathic urticaria: a double-blind, randomized, placebo-controlled trial. Journal of the American Academy of Dermatology, 2006. **55**(4): p. 705-9.

39. Doshi, D.R. and M.M. Weinberger, Experience with cyclosporine in children with chronic idiopathic urticaria. Pediatric Dermatology, 2009. **26**(4): p. 409-13.

40. Hurabielle, C., et al., No major effect of cyclosporin A in patients with severe solar urticaria: a french retrospective case series. Acta Derm Venereol, 2015. **95**(8): p. 1030-1.

41. Levi, A. and C.D. Enk, Treatment of solar urticaria using antihistamine and leukotriene receptor antagonist combinations tailored to disease severity. Photodermatol Photoimmunol Photomed, 2015. **31**(6): p. 302-6.

42. Aubin, F., et al., Omalizumab in patients with severe and refractory solar urticaria: A phase II multicentric study. J Am Acad Dermatol, 2016. **74**(3): p. 574-5.

43. Snast, I., et al., Omalizumab for the Treatment of Solar Urticaria: Case Series and Systematic Review of the Literature. The Journal of Allergy & Clinical Immunology in Practice, 2018: p. 20.

44. Morgado-Carrasco, D., et al., Clinical and photobiological response in eight patients with solar urticaria under treatment with omalizumab, and review of the literature. Photodermatology, Photoimmunology & Photomedicine, 2017: p. 24.

45. Aubin, F., et al., Severe and refractory solar urticaria treated with intravenous immunoglobulins: a phase II multicenter study. J Am Acad Dermatol, 2014. **71**(5): p. 948-953 e1.

46. Adamski, H., et al., Solar urticaria treated with intravenous immunoglobulins. J Am Acad Dermatol, 2011. **65**(2): p. 336-40.

47. Leenutaphong, V., et al., Plasmapheresis in solar urticaria. Dermatologica, 1991. **182**(1): p. 35-8.

48. Caccialanza, M., S. Recalcati, and R. Piccinno, Oral polypodium leucotomos extract photoprotective activity in 57 patients with idiopathic photodermatoses. Giornale Italiano di Dermatologia e Venereologia, 2011. **146**(2): p. 85-7.

49. Mang, R.S., H.; Budde, M-A.; Ruzicka, T.; Krutmann, J., Successful treatment of solar urticaria by extracorporeal photochemotherapy (photopheresis) - a case report. Photodermatol Photoimmunol Photomed, 2002. **18**: p. 196-198.

50. Haylett, A.K., et al., Systemic photoprotection in solar urticaria with alpha-melanocyte-stimulating hormone analogue [Nle4-D-Phe7]-alpha-MSH. Br J Dermatol, 2011. **164**(2): p. 407-14.

Figure Legend:

Figure 1: This graph shows the phototesting action spectra results from our case series

Figure 2: This graph shows the percentage of patients with positive phototesting results reported in the literature per the categories of visible light (VL), ultraviolet A (UVA), ultraviolet B (UVB) and combinations of these.

Table 1: Patient Demographics and Characteristics
Total number of patients = 83 Males = 25 Females = 56 Mean Total Age = 32 years (range 7-74) Fitzpatrick phototypes Type I = 10% Type II = 20% Type III = 24% Type IV = 38% Type V = 3% Type VI = 3% Background of atopy found in 32 patients (38.5%)

Table 2: Medications/Treatments used in our patients
Antihistamines - 71 patients (85%) • Cetirizine 46% • Loratidine 40% • Fexofenifidine 39% • Cyproheptadine 17% • Less than 5% (Astemizole, Teldane, Cimetidine, Desloratidine, Ketotifen, Fabahistin, Methdilazine)
Sunscreen - 61 patients (73%)
H2-inhibitor Ranitidine - 15 patients (18%)
Hydroxychloroquine - 6 patients (7%)
Phototherapy • Narrow-band UVB 18% • PUVA 2%
Systemic immunosuppressants • Prednisolone 11% • Methotrexate 1% • Cyclosporin 1% • Mycophenolate mofetil 1%
Topical steroid preparations - 10 patients (12%) Calcineurin inhibitors - 4 patients (5%)
Montelukast - 4 patients (5%)
Anti-anxiolytics • Atarax 8% • Doxepin 8%
Intravenous therapies • Plasmapheresis 3% • IV Immunoglobulins 1%

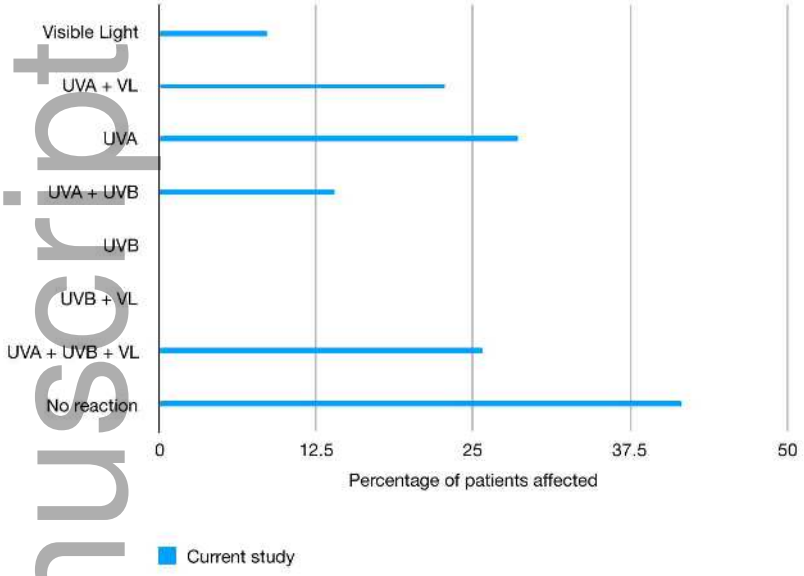
Photodermatosis	Time to symptoms/signs	Time to resolution	Distinguishing feature(s)	Most common age group
Immune-mediated Photodermatoses				
Idiopathic Solar urticaria	Minutes	Within 24 hours	Pruritus, urticarial wheals	Any age
Chronic actinic dermatitis	~30 seconds	chronic	Usually men >50 years old; can occur through glass and with fluorescent light; scaling and lichenification	Mainly older men; younger adult atopics
Polymorphic Light Eruption	2 hours to 3 days	2 to 6 days	Time course, pruritus, papules; V area of the neck, arms, legs; usually spares the face	Any age
Juvenile spring eruption	2 hours to 3 days	2 to 6 days	Superior helices, occurs in Spring; pruritic papule that may evolve into blisters and crusts with no scarring; Localised form of PMLE	Boys and Young Men
Cholinergic (Heat) Urticaria	within minutes	30 minutes to 1 hour	Precipitated by the heat of the sun rather than the irradiation so also affects non-exposed areas; often exacerbated by sweating	Adult
Actinic prurigo	hours to days	chronic	Intensely pruritic papules; Face (lips, nose, eyelids), hands and arms in 60-70%	Any age
Hydroa vacciniforme	30 minutes to 2 hours	years	Associated with EBV infection and UVA exposure; symmetric distribution, ophthalmic and oral involvement; fluid-filled blisters 'hydroa' that heal with pox-like 'vacciniform' scars	Paediatric
Photoaggravated Dermatoses				
Systemic Lupus Erythematosus	minutes to hours	several weeks	Lesions are not urticarial or pruritic, ANA +ve, Skin immunofluoresence +ve	Any age
Exogenous Photodermatoses				
Photo-toxic Reactions	minutes to hours	hours to days	Exogenous agent + UVA; transient painful erythema/oedema; caused by direct tissue damage	Any age
Photo-allergic Reactions	24-72 hours (in presensitised individuals)	2 to 6 days	Exogenous agent: UVA; Immune-mediated. Eczematous changes, papular, vesicular	Any age

Pseudoporphyria	minutes to hours	several weeks	Induced by drugs and/or renal insufficiency; skin fragility, blisters and erosions on hands and feet	Adult
Metabolic Photodermatoses				
Erythropoietic Protoporphyria	</= 5 minutes	chronic	Skin pain, red blood cell protoporphyrin levels are high due to ferrochelatase deficiency; pitted scarring particularly over cheeks, nose and knuckles	Lifelong
Porphyria cutanea tarda	immediate	chronic	Elevated uroporphyrinogen; increased fragility of the skin on the dorsum of hands and forearms with blisters, milia and erosions; scarring	Adult

Table 3 - Distinguishing between the differential diagnoses

Table 4 : Treatment options in solar urticaria
1. Avoidance of their action spectrum & using physical barriers such as dark coloured, densely woven clothing, hats, sunglasses and staying indoors. 2. Chemical barriers such as sunscreens 3. Antihistamines & H2 Blockers 4. Phototherapy (NBUVB, PUVA) 5. Immunosuppression (methotrexate, cyclosporin) 6. Omalizumab 7. IV Immunoglobulins 8. Plasmapharesis 9. Polypodium leucotomos, 10. Extracorporeal photochemotherapy 11. Alpha-Melanocyte stimulating hormone (α-MSH)

Figure 1: Phototesting Action Spectra results from our case series



Action Spectrum	Number of cases
Visible light	3 (8.5%)
UVA + Visible light	8 (22.8%)
UVA	10 (28.5%)
UVA + UVB	5 (14%)
UVA + UVB + Visible Light	9 (25.7%)
Total	35

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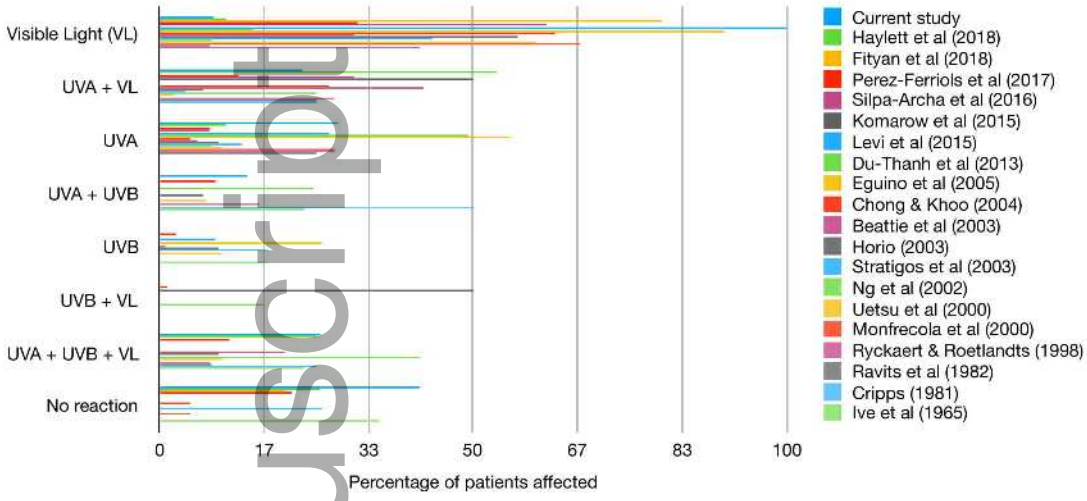
Figure 2: Phototesting action spectra results in published case series



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