Photopatch Testing

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24.1 Introduction

The photocontact reaction is a delayed type hypersensitivity in response to the synergical presence of an exogenous contact agent (photoallergen) and ultraviolet/visible irradiation. A positive reaction may result from a combination of an irritant or contact allergen with irradiation or, much less commonly, be due to photocontact allergy [1].

Photopatch testing (PPT) should be used in patients clinically suspectful for photocontact allergy, with erythematous/eczematous dermatitis involving only photo-exposed body areas. This is a relatively simple technique which is not standardized to the same extent as patch testing. Patients with a positive history for photoexposed site dermatitis, precipitation or aggravation by sunlight exposure or an adverse reaction to a sunscreen –containing product, should be investigated with this technique. PPT should also be considered in a photosensitive patient who deteriorates without identifiable cause.

The method involves the application of duplicate series of allergens and, after 24–48 hrs, one set of allergens is irradiated with a suberythemal dose of UVA. The results are assessed 48 hrs following irradiation, although several centers do additional readings at other time points.

Considerable difficulty may be encountered in interpretation of the PPT results as phototoxicity, photoallergy and photoaugmentation of either irritancy or contact allergy may complicate the clinical morphology.

It is clear that with higher doses of irradiation, irrelevant phototoxic reactions can be induced in the normal population further emphasizing the difficulties in distinguishing between toxicity and true allergy. Chemical sunscreens are currently the main photoallergens of relevance and despite the problems with methodology, the incidence of photocontact allergy to sunscreens appears to be low although clinically significant [2].

Photocontact allergy has been reported to most of the chemical sunscreens available in commercial products. However, frequent review of the agents is required in order to define the

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scale of the problem and to account for changes in exposure pattern.

In 2012 a consensus PPT series was established on the basis of the results of a European multicenter study that was conducted in 30 different centers between 2008 and 2011. Twenty substances were chosen to be part of the European photopatch test baseline series and additional 15 substances were recommended to be included for a selected population of patients [3, 4].

24.2 Prevalence

Photoallergies prevalence in the general population remains still elusive. Remarkably, patients with photodermatoses are frequently misdiagnosed as photoallergic, due to the large use of sunscreens among photosensitive patients. This clinical behavior might be explained considering the big amount of sunscreens applied on the skin by photosensitive patients. Filters applied on a damaged and chronically inflamed skin tend to easily penetrate through the epidermal barrier. This is the main reason why until 10 years ago, most reports of PPT series suggested that 7–10% of tested patients had at least one photoallergic reaction [5, 6].

24.3 UV Filters/Photoallergens

Many substances have been described as photoallergens, including halogenated salicylanilides and sulfonamides. They caused many cases of photosensitivity until they were excluded from the marketplace and they were replaced by other substances in several industrial products (cosmetics, pharmaceuticals). Musk ambrette use was also diffused in high concentrations in toiletries, aftershaves, soaps and hair sprays. Its fragrance caused eczema localized to the application area or a more widespread dermatitis. The concentration of this fragrance was gradually reduced and the incidence of this kind of eczema dramatically decreased.

In the last 30 years, a great increase in the use of sunscreens has been recorded in response to several educational campaigns on photoageing and skin cancer. Moreover, ultraviolet (UV) filters are often contained in cosmetics and day care skin products in order to prevent photoageing. The presence of UV filters in cosmetic products is responsible to an increase in the incidence of photoallergy to these compounds and in some cases substances like isopropyl dibenzoylmethane were definitively removed from the market.

Recently, evidence point out that a correct sunscreen strategy should employ filters capable to stop both UVA and UVB, since UVA play a pivotal role either in photocarcinogenesis or in photoageing processes. UV filters can be divided in organic and physical agents. The physical agents (zinc and titanium oxide) usually do not induce sensitization since they act reflecting UV without undergoing photochemical reactions. They also reflect visible light so they tend to confer a white appearance. This cosmetically unpleasant characteristic has been reduced introducing the use of microfine titanium dioxide. Even in this case sensitization does not occur and the microfine form might be used in high concentrations without percutaneous absorption. Microfine particles tend to aggregate and the aggregation leads to a decreased effectiveness. In order to prevent this, they are coated with dimethicone, thus reducing free radical formation and increasing photostability [7, 8].

Organic filters absorb UV through a chemical transformation that confers the potential to be photoallergenic.

Organic filters can be divided in the following groups:

- Benzophenones: it is mainly a UVB absorber but it also absorbs a small part of the UVA range (UVA II) and it augments UVB protection. During UV exposure oxybenzone becomes highly unstable and generates oxygen radicals. This compound is one of the most commonly used but it has been regarded as the most allergic agent and it has been proved to determine the highest incidence of contact and photoallergic dermatitis.
- Para-aminobenzoic acid (PABA): it is the first UVB filter having a peak of absorption at 283 nm. PABA is not soluble and binds

keratinocytes via hydrogen bond. This property allows to withstand water immersion and perspiration determining in the meantime skin staining. Many reports of contact allergies to PABA exist and there are also concerns regarding the carcinogenic potential of this agent. PABA has been recently replaced by less effective PABA derivatives including Padimate O that do not stain skin and it is combined with other UV filters in order to increase the overall SPF

- Cinnamates: After PABA, Cinnamates (octinoxate and cinoxate) are the most potent UVB absorbers and unlike PABA and its derivatives they do not stain and rarely cause irritation. Sunscreens containing cinnamates require frequent reapplication since they are less potent and have a decreased water resistance as compared to Padimate O.
- Salycilates: The Salicylates group includes octisalate, homosalate and tolamine salycilate. They are considered as the weakest UVB absorbers and high concentrations of these compounds are required to obtain a proper SPF. Salicylates are usually used to augment the UVB protection in a sunscreen. Octisalate and homosalate are highly photostable agents and they both have a good safety profile. They are commonly used to stabilize other sunscreen ingredients [9–11].

In about 65% of patients photoallergic reactions are due to organic filters (in particular benzophenone-3 and benzophenone-10) [12].

Photoallergens other than UV filters include in the majority of cases topical non steroidal anti-inflammatory drugs (NSAIDs), a category of drugs commonly used in Europe. Also chlorpromazine may induce photoallergic reactions [13–15].

24.4 Methodological Issues

The major indication for PPT is the onset of eczema affecting UV exposesed areas. In some cases patients use substances potentially photoallergenic and cutaneous manifestations exacerbate following sun exposure.

False negative results can be obtained in patients treated with immunosuppressive drugs either applied topically or given systemically and antihistamines. When programming PPT it is suggested to stop immunosuppressive drugs at least 1 week before performing the test.

When programming PPT, substances which frequently cause phototoxic reactions should be avoided. The list of agent tested varies greatly among different centres. There is agreement that substances of historical interest including antibacterial salicylanilides, sulphonamides should be omitted. In the last period PPT investigated reactions to organic sunscreens. In Europe, also reactions to NSADs agents should be considered.

The best choice of site corresponds to the mid upper back skin, avoiding 3–5 cm on either side of the vertebrae. It has been suggested to apply maximum 30 agents using the Finn Chamber technique. It has been recommended that duplicate sets should be placed in the standard position for either 24 or 48 hours after which both they can be removed. Afterwards, one set should be shielded by a UV opaque material while the other set is irradiated with a broad spectrum UVA source [3].

24.5 UVA Source

The source is always UVA because it is more relevant than UVB or visible light to photoallergy.

Fluorescent UVA lamps of the kind used for PUVA therapy are commonly used since they have an output across all the UVA region. Moreover, different types of these tubes have similar spectra standardizing the output between different centers.

The dose of UVA usually ranges between 5 and 15 Joules/cm^2 since the dose should be low in order not to induce sunburn. In case of patients very sensitive to UVA and potentially carrying the risk of a severe reaction, the suggested dose may be decreased to 2.5 J/cm^2 [16].

24.6 Photopatch Reading

Results should be evaluated using the International Contact Dermatitis Research Group scoring system immediately after irradiation, post irradiation and 48 post irradiation. Further readings at 72 and 96 hours are not mandatory and are aimed to distinguish allergic from non allergic reactions. False positive PPT can be detected as a result of a weak irritant/allergic response [17, 18].

A peak of the reaction within the first 24 hours indicate phototoxicity whereas a reaction becoming stronger after 24 hours usually indicates photoallergy [18].

24.7 Interpretation of Results

Possible reactions to PPT are the following listed above:

- Negative
- Photoallergic
- Phototoxic
- Irritant
- Photo augmented irritant
- Photo suppressed irritant
- Allergic
- Photoaugmented allergic
- Photo suppressed allergic

No reaction at non irradiated site but a reaction at irradiated site: photoallergy

Equal reaction in both sites: ordinary allergy [19].

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