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ORIGINAL ARTICLE

Photopatch testing: a consensus methodology for Europe

The European Taskforce for Photopatch Testing: †Members of the panel: D.P. Bruynzeel, the Netherlands; J. Ferguson, Scotland, UK; K. Andersen, Denmark; M. Gonçalo, Portugal; John English, UK; A. Goossens, Belgium; E. Holzle, Germany; S.H. Ibbotson, Scotland, UK; M. Lecha, Spain; P. Lehmann, Germany; F. Leonard, France; Harry Moseley, Scotland, UK; P. Pigatto, Italy; A. Tanew, Austria
*Photobiology Unit, Ninewells Hospital, Medical School, Dundee DD19SY, UK. *Corresponding author, Photobiology Unit, Ninewells Hospital, Medical School, Dundee DD19SY, UK, tel. +044 01382632240; fax +044 01382646047; E-mail: j.ferguson@dundee.ac.uk*

ABSTRACT

A group of interested European Contact Dermatologists/Photobiologists met to produce a consensus statement on methodology, test materials and interpretation of photopatch testing. While it is recognized that a range of local variables operate throughout Europe, the underlying purpose of the work is to act as an essential preamble to a Pan European Photopatch Test Study focusing particularly on sunscreen chemicals.
Key words: consensus, Europe, Photoallergy, photopatch testing, sunscreens

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In May 2002, a panel† representing Contact Dermatology/Photobiology/Photophysics, with a special interest in photopatch testing (PPT) (on behalf of the European Society of Contact Dermatitis and European Photodermatology Society), met in Amsterdam. They came together to discuss and, if feasible, establish a consensus methodology, a list of recommended test agents, and interpretation guidelines for photopatch testing.

It is believed that PPT, which is the clinical investigation of choice for suspected photocontact dermatitis/photoallergy, is significantly underused in Europe and probably world-wide. This is due to a number of reasons, not least of which is the fact that responsibility for PPT has fallen between two areas of dermatology subspecialization, the 'photodermatologists' who have light-related, but lack contact experience, and vice versa for 'contact dermatologists'. This in part may explain the lack of standardization throughout Europe, although there have been local attempts at uniformity in the past.[1–7] Despite these, even the most recent literature shows significant differences in methodology,[8–10] the agents used, test concentration and the interpretation of results, which illustrates a level of uncertainty has discouraged general dermatologists from using the technique.

At the meeting it was recognized that the variation in technique also related to a lack of published comparative data and also that a degree of compromise would be required in contentious areas and that an agreed methodology would need to be flexible to take into account local service constraints and geographical photoallergen exposure patterns.

Who should be tested?

It was agreed that the primary indication should be dermatitis predominantly affecting exposed sites with or without a history of a sunscreen reaction and that PPT should also be considered in patients with chronic actinic dermatitis and any individual with a photosensitive eruption for which there is no obvious diagnosis. As with patch testing, this investigation should not be undertaken when the skin test area is active. To avoid the effects of the angry back syndrome it is recommended that testing be conducted on skin that has been clinically normal for the previous 2 weeks.

Patients need to be informed of the possible risk of sensitization as recognized in routine patch testing. It is also important that they be aware of the possibility of strong provocation test results as outlined in a patient information sheet. Most centres do not yet routinely seek written consent for the procedure.

What type of units currently conduct photopatch testing?

From a survey that took place in 2001 (P. Lehmann, personal communication, 2002) of 49 known PPT centres in Europe, 34 replied. From the 34 centres, 21 had separate photoirradiation and contact allergy services. In those centres, patch tests were applied in the allergy unit and the irradiation conducted in the photo unit. The readings were performed by photo unit staff in 14. In 13 centres, the allergy and photo units were combined with

all readings performed by the allergy unit. The test was performed relatively infrequently with only two of the centres conducting > 50 PPT/year with a mean number of tests across the group of 16. It appears that few office dermatologists conduct PPT, an overall picture that suggests PPT is an underused investigation within Europe. It currently appears that PPT is best reserved for major investigation centres either in contact or photodermatology units.

What agents should be tested?

The list of PPT agents used varies greatly between centres. Some traditional agents now felt to be of only historical interest included antibacterial salicylanilides, sulphonamides and the major tranquillizers. There was agreement that these should now be omitted from routine PPT. Over the past decade, PPT has focused on organic sunscreens to include testing with each patient's own suspected products.[11–13] In parts of Continental Europe where topical non-steroidal anti-inflammatory agents are routinely used and are associated with photosensitivity, these and other less commonly reported agents should be considered.[12] Most photopatch test agents are available through Hermal or Chemotechnique (Table 1).

Methodology

It was agreed that mid upper back skin, avoiding 3–5 cm on either side of the vertebrae (the paravertebral groove area) is the best choice of site for application of PPT agents. It was suggested, for reasons of limited back space, that a maximum of 30 agents be applied using the Finn Chamber technique (Table 2). It was recommended that duplicate sets be in position for either 24 or 48 h, after which both are removed. At this point, one set should be covered with a ultraviolet (UV) opaque material and the other irradiated with a calibrated metered broad-spectrum UVA source. The type of lamp used for testing should be noted as this may affect results.[14] Psoralen plus UVA fluorescent lamps are preferred[4] because of their widespread availability, reproducible spectrum and beam uniformity, even though they do contain a small percentage of UVB. Although metal halide lamps may be used, they have differences in spectra emission depending on the type used and also have poor beam uniformity and thus are less suitable. Although UVA is recommended, it was recognized that our knowledge of photoallergen wavelength dependency is incomplete. Mercury vapour, monochromator and solar simulator sources are not recommended for routine PPT.

Choice of ultraviolet dose

The published UVA dose has varied. It requires to be sufficient to trigger the photoallergy response, yet not at such a level to produce a false-positive or phototoxic response. Although we cannot generalize for all patients and all test agents, work conducted with promethazine suggests 5 J/cm^2 is preferable to 10 J/cm^2. In the absence of the required data, it was felt reasonable to recommend 5 J/cm^2 for routine PPT.[3,15–18]

Timing of readings?

Readings should be recorded using the International Contact Dermatitis Research Group (ICDRG) scoring system (Table 2), pre-irradiation, immediately postirradiation and 48 h postirradiation. Further readings at 72 and 96 h postirradiation are desirable to enable detection of crescendo or decrescendo scoring

Table 1 Photopatch test agents (applied in duplicate, one set irradiated)

	Chemical Abstract Service (CAS) no.
Sunscreen agents* Temp. [International Nomenclature of Cosmetic Ingredients (INCI)]	
Petrolatum (control)	800274-2
Octyl Methoxycinnamate(2-Ethylhexyl-p-methoxycinnamate, Parsol MCX, Eusolex 2292) 10%	5466-77-3
Benzophenone-3 (2-Hydroxy-4-methoxy benzophenone, Oxybenzone, Eusolex 4360) 10%	131-57-7
Octyl Dimethyl PABA (2-Ethylhexyl-p-dimethyl-aminobenzoate, Escalol 507, Eusolex 6007) 10%	21245-02-3
PABA (4 Aminobenzoic Acid) 10%	150-13-0
Butyl Methoxydibenzoylmethane (Parsol 1789, Eusolex 9020) 10%	70356-09-1
4-Methylbenzylidene Camphor (Eusolex 6300, Mexoryl SD) 10%	36861-47-9
Benzophenone-4 (2-Hydroxy-4-methoxy-benzophenone-5-sulphonic acid, Uvenyl MS-40) 10%	4065-45-6
Isoamyl p-methoxycinnamate (Neoheliopan, E1000) 10%	71617-10-2
Phenylbenzimidazole Sulphonic Acid (2-Phenyl-5-benzimidazolsulphonic acid, Eusolex 232) 10%	27503-81-7
Non-steroidal anti-inflammatory agents (require to be prepared 'inhouse')	
Naproxen 5%	
Ibuprofen 5%	
Diclofenac 1%	
Ketoprofen 2.5%	

NB: All agents in petrolatum. *Available through Hermal (Trolab Patch Test Allergens) D-21462 Reinbek, Germany or Chemotechnique Diagnostics P.P. Box 80 S320 Malmo, Sweden.

Table 2 Recommended photopatch testing methodology

Application of duplicate patch series for 24 or 48 h	Irradiate UVA 5 J/cm²	Readings				
		Day 0 immediately after irradiation	Day 1	Day 2	Day 3	Day 4 after irradiation
Readings		X	X	X	±	±

X, essential readings; ±, desirable readings. ICDRG readings:[21] ?+, doubtful reaction (faint erythema only); +, weak positive reaction (erythema, infiltration, possibly papules); ++, strong positive reaction (erythema, infiltration, papules, vesicles); +++, extreme positive reaction (intense erythema and infiltration and coalescing vesicles or a bulla); IR, irritant reaction; NT, Not tested.

patterns suggesting allergic and non-allergic mechanisms, respectively.[5,19] The panel recognized that false-positive photopatch tests can be produced as a result of weak irritant/allergic responses combined with a subclinical UVA effect. It was agreed that a positive reaction to a photoallergen and light in the presence of negative 'contact' and 'irradiation' controls strongly supported a photoallergic mechanism, particularly where a strengthening response over the reading time points was recorded.

At the same time, it was felt important to recognize that non-irradiated, test site results due to irritancy/allergy or photoaggravation (at the irradiated site) of an irritant/allergic reaction, phototoxicity and awareness of the possibility of technical error, should all be identified and recorded.

Relevance of readings

In addition, it was felt important to record the relevance of the result using a system such as COADEX. This classifies clinical relevance of positive allergic patch test reactions as:

- current relevance (the patient has been exposed to allergen during current episode of dermatitis and improves when the exposure ceases);
- old or past relevance (past episode of dermatitis from exposure to allergen);
- actively sensitized [patient presents with a sensitization (late) reaction];
- relevance not known (not sure if exposure is current or old);
- cross-reaction (the positive test is due to cross-reaction with another allergen);
- exposed (a history of exposure but not resulting in dermatitis from that exposure or no history of exposure but a definite positive allergic patch test).

(C = current; O = old; A actively sensitized; D = do not know; EX = exposed).[20]

Testing the ultraviolet A photosensitive or immunosuppressed patient

When PPT a patient who has an abnormal UVA sensitivity, it is advisable to establish the UVA minimal erythema dose (MED) prior to PPT. Although there is a lack of recommended dose series data, it is important to test up to and including 5 J/cm² with the same UVA source as used for PPT. If the MED detected at 24 h is less than the lowest dose, it is advisable to use 50% of this value with an awareness of the increased possibility of photoaggravated irritant and contact reactions.

Although concomitant systemic or topical immunosuppression/antihistaminic action may result in a false-negative result, a positive response will be valid. In the absence of published data on the duration/degree of immunosuppressive effect, the panel recommends, when clinically feasible, that such therapy be stopped for at least 2 weeks prior to PPT investigation.

Conclusions

The current differences in PPT methodology that exist within Europe, not only send a confusing message to would-be users of this technique, but also make it difficult to compare published data between studies. Individual photoallergy patients and industry need to know which agents are responsible. The safer design of future products requires such information to be accurate.

With this background, the panel has made a number of simple suggestions to standardize the technique throughout Europe. As further information becomes available, new test agents and alterations in methodology will be appropriate. It is felt that a European Photopatch Test Study using such a methodology is desirable.

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