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นิพนธ์ต้นฉบับ *Original Article*

The Significance of Photopatch Testing and Photoallergic Contact Dermatitis: 10-years experience

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Abstract Photopatch testing (PPT) is a standard tool to help making and confirming diagnosis of photoallergic contact dermatitis (PACD) that should correlate to patients' history and clinical manifestation. This retrospective study reports the significance of PPT and PACD, conducted for 10 years between 2000 and 2009 at the Institute of Dermatology. Among 270 patients who completed PPT, 72 patients (26.67%) had PPT positive, but only 14/72 (19.4%) had relevant to the patients' history and skin lesions which could make definite diagnosis as PACD. Among them, oxybenzone, a sunscreen substance was the most common causative agent (35.7%) which was corresponded with other reports, followed by promethazine hydrochloride, chlorpromazine hydrochloride, fragrance mix, triclocarban and fenticlor. Oxybenzone also caused allergic reaction in 6 cases. Data from this study would be useful for providing information relevant to the improvement of the use of PPT in the diagnosis and management of PACD and other related skin diseases, as well as the future use of data for the development of commercial products that are less harmful to the people.

Key words: **photoallergic contact dermatitis, photopatch test, sunscreen, oxybenzone**

Introduction

Photoallergic contact dermatitis (PACD) is a rare clinical condition caused by skin sensitivity to photoallergen when interacts with ultraviolet (UV) irradiation. There are 2 hypothesis concerning the action of UVA (the long wavelength UV radiation or ultraviolet type A) and photoallergen: first, UVA changes the chemical structure of photoallergen; and second, it induces cross-reaction and turns to a hapten or antigen and stimulate type IV hypersensitivity reaction.[1] PACD generally affects photo-distributed areas and spares the anatomically shadowed portions of the body.[2] The incidents of PACD seems to gradually increase due to increasing use of sunscreen.[3-8] The pattern of PACD has changed over time according to the popularity of sunscreen products. A photopatch test (PPT) procedure was introduced to help finding the etiology of PACD.[1]

A recent prospective multicenter study on the incidence of PACD and common photoallergens in Europe reported by Kerr, et al.[3] showed that 200 out of 1,031 patients (19.4%) had positive photoallergic commonly caused by the topical non-steroidal anti-inflammatory drugs, ketoprofen (128

subjects). A report from North American study in 2010 showed a PACD incidence of 39.5% with relevant photoallergic reactions in 11.2%; and the most common photoallergens were sunscreen ingredients and antimicrobials.[5] In 2013, a report from Singapore showed 5-year experience of PACD and PPT results with 45.5% (10/22 patients) obtained positive PPT. There were 20 positive PPT reactions found in these 10 patients and all of them were relevant to their histories and clinical manifestations.[7]

Most PACD and PPT studies were conducted in Europe and North America. There was minimal information from Asia except a few reports from India[9] and Singapore.[7] In this study, we conducted the first review of 10-year experience, from 2000-2009, of PPT result in PACD of Thai population at the Institute of Dermatology (IOD) that could give a baseline figure and pattern as well as the significance of PPT and PACD in Thailand.

Materials and Methods

After approved by the ethics committee of the Institute of Dermatology, we reviewed medical records of patients who were sent for photopatch test (PPT) from general skin OPD or referred cases from other hospitals in the 10-year period (2000 - 2009). The patients in this group were suspicious cases of PACD such as those who had dermatitis or another form of skin lesions at a sun-exposed site or other photosensitive skin conditions with history of applying some topical agents before lesion occurred. Even though IOD served as an academic center for residency training and one of the highest referral centers in the service system in the field of dermatology; and preferred to conduct PPT investigation as clinicians' request but the exclusion criteria were set as any patient (1) with history of applying a potent topical steroid to the PPT site within the 7 days prior to the PPT; (2) with active skin disease activity at all possible test sites; (3) taking systemic immunosuppressant medication (i.e. prednisolone, methotrexate, azathioprine, ciclosporin); (4) taking photoactive oral medicine such as thiazides, NSAIDS, quinine); or (5) unable to attend 5-day protocol of the PPT.

The PPT test was conducted according to IOD protocol. The twenty selected standard photoallergens (Chemotechnique Diagnostics®, Vellinge, Sweden) (Table 1) were applied on the upper back of patients in duplicated set by using Finn Chambers (Epitest Ltd Oy, Tuusula Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway). In case a patient was using a skin product, he or she was requested to provide small sample of the product to be added to both sets of the tested, in addition to the 20 standard photoallergens,

In case a patient had skin lesions at the upper back and not suitable for PPT procedure, the lower back, buttock or anterior surface of upper thighs was used. The PPT protocol (Figure 1) began by attaching two photoallergen sets on the skin and then covered by black paper for 24 hours. One set was then opened and evaluated as a patch test (PT) reaction, followed by a single dose of 10 J/cm^2 of UVA (Daavlin SL3000®, Halogen lamp, with an irradiance of 85 mW/cm^2 at 35 cm distance) irradiated to that set which would serve as a PPT site. In case a patient had an evidence of photosensitive to UVA by phototest investigation, a reducing single dose of 5 J/cm^2 UVA was applied. After irradiation, the photopatch test site was covered with black paper again. On the third to fifth day both irradiated and non-irradiated sites were evaluated.. The skin reac-

tions at both non-irradiated and irradiated sites which represented patch test (PT) at 24 - 48 -72 - 96 hours and PPT at 24 - 48 - 72 hours respectively were subsequently evaluated using a pre-set criteria (Table 2).

As shown in the Table 2, the term allergic contact dermatitis (ACD) was applied when the PT and PPT sites showed the same degree of reaction; and and PACD was considered if the positive result was only observed on the PPT site. The term ACD and PACD was considered if the PPT site showed stronger reaction than the PT site in corresponding area. If the control site (PT site) had positive reaction but negative reaction was observed at the PPT site of the corresponding area we classified as technical error.

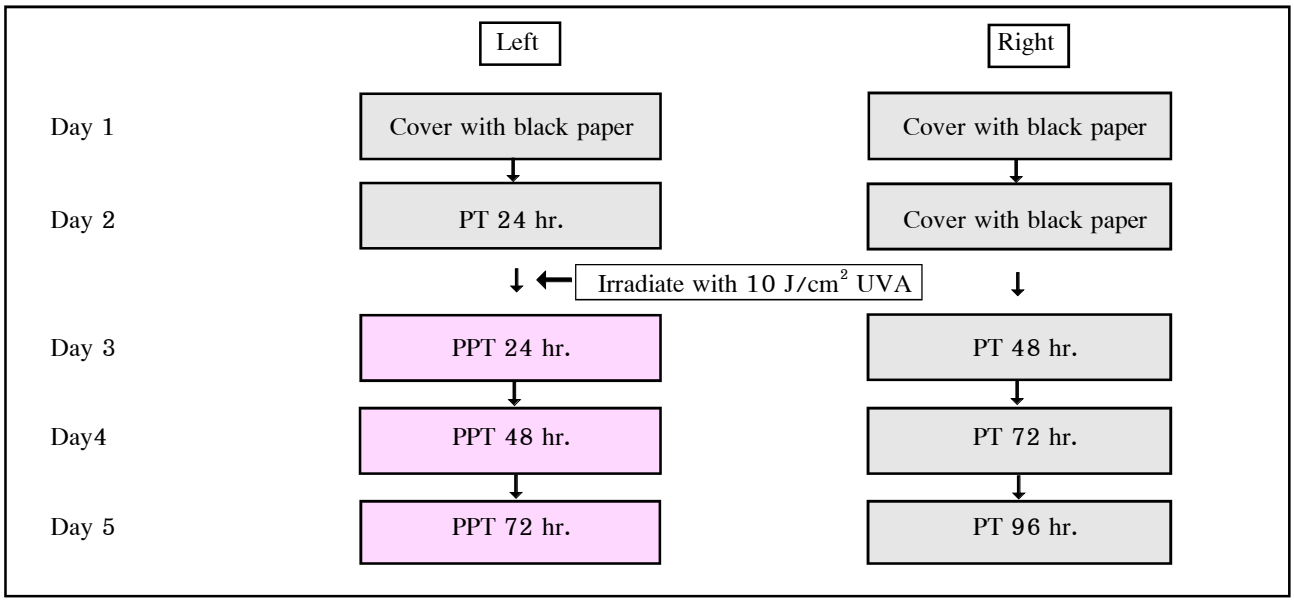
Results

During the year 2000 - 2009, there were 270 patients who completed PPT procedure at IOD, Bangkok. The male to female percentage was 51.0:49.0 (Figure 2). The majority ages were 40 - 50 years old, 25.6% (Figure 3), range from 14 -

Table 1 Photoallergens set for PPT at IOD during 2000-2009

No.	Test substances
1	Octyldimethyl-PABA
2	Oxybenzone
3	Benzophenone-4 10%
4	Octyl methoxycinnamate 10%
5	Methoxy-Dibenzoylmethane 2
6	4-Methylbenzylidene Camphor 10%
7	Phenylbenzimidazole sulfonic acid
8	Fenticlor (Multifungin)
9	Tetrachlor salicylanilide
10	Bithionol 1%
11	Triclosan
12	Hexachlorophene
13	Balsum of Peru
14	Fragrance mix
15	Promethazine Hydrochloride
16	Chlorpromazine Hydrochloride
17	Chlorhexidine diacetate
18	6-Methylcoumarin
19	Musk Ambrette
20	Tribromsalicylanilide

Figure 1 The 5-day protocol of photopatch test (PPT) procedure at IOD



Remark: PT = patch test

Table 2 Interpretation criteria of the results of PPT procedure

Patch test site	Photopatch test site	Interpretation
-	-	Negative result
+	+	Allergic contact dermatitis
-	+	PACD
+	++	Allergic contact dermatitis and PACD
+	-	Technical error

84 years old and 217 patients (80.4%) had skin type IV. The majority of patient were company employee (30.1%), work at home (21.9%), and government officer (17.8%) (Table 3).

The pre-PPT provisional diagnoses were comprised of 8 major diagnostic groups with the leading groups were: polymorphous light eruption (PMLE) 36.3%, photosensitive dermatitis 18.5%, photoallergic contact dermatitis 15.2%, chronic actinic dermatitis 11.1% (Table 4).

Among 270 patients undergoing the PPT test, 72 (26.67%) were found positive (Figure 4). There

Table 3 Occupations of patients

Occupations	Number	%
Company employee	81	30.1
Work at home	59	21.9
Government officer	48	17.8
Agriculture and laborer	41	15.1
street vendor	26	9.6
Student	15	5.5

Figure 2 Number of patients who complete photopatch test, 2000-2009

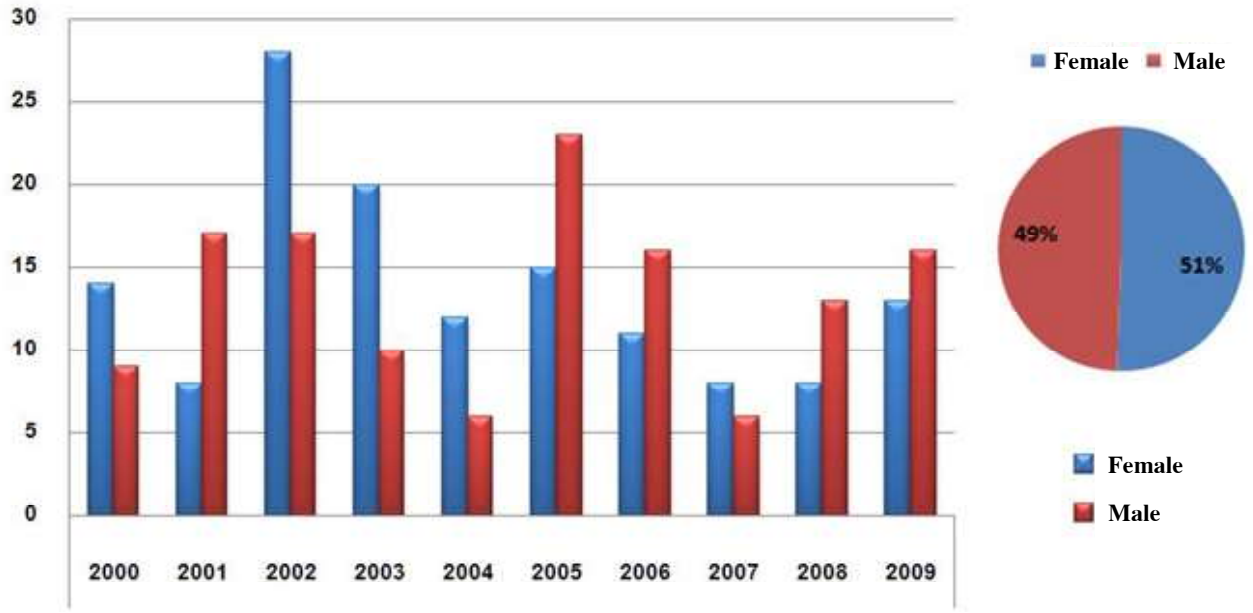


Figure 3 Age group of the patients

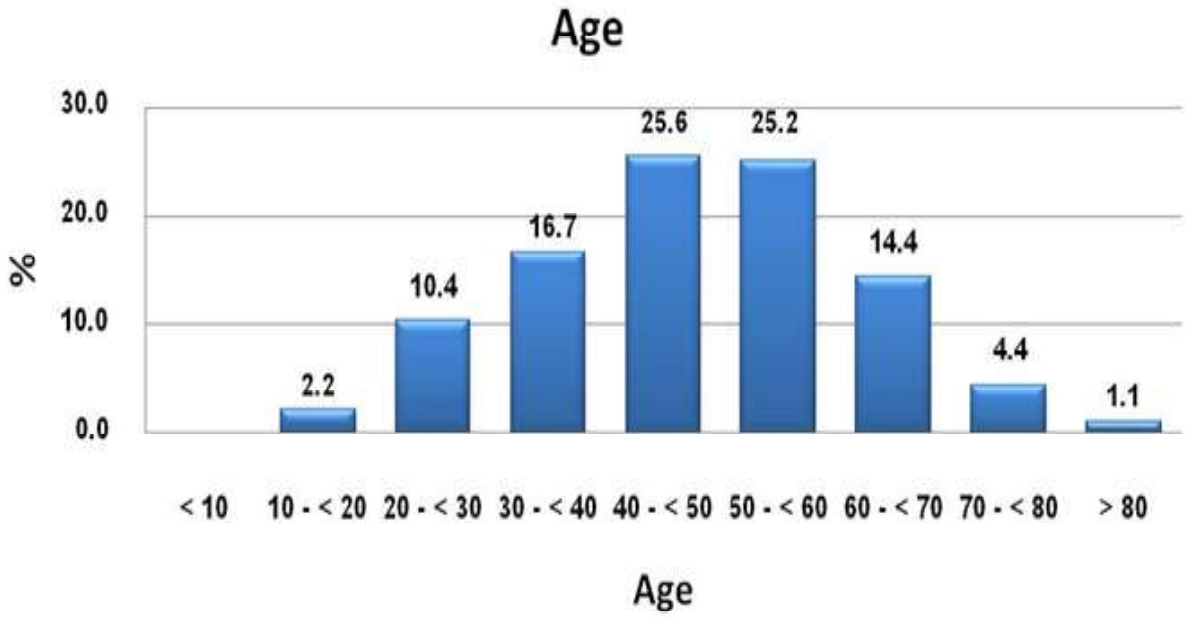
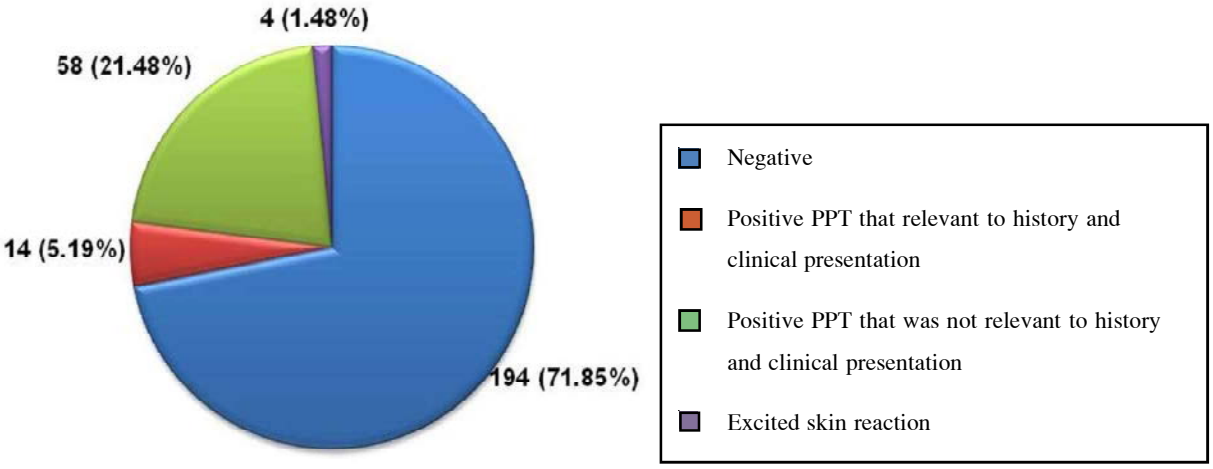


Table 4 Provisional diagnosis before the photopatch test procedure

Disease / Conditions	Number	%
Polymorphous light eruption (PMLE)	98	36.3
Photosensitive dermatitis	50	18.5
Photoallergic contact dermatitis	41	15.2
Chronic actinic dermatitis	30	11.1
Eczematous dermatitis	16	5.9
Other photodermatosis	16	5.9
Allergic contact dermatitis	11	4.1
Lupus erythematosus or related diseases	8	3.0

Figure 4 : Results PPT procedure (total number of patients = 270)



were 4 cases who had "Excite Skin Reaction" that interfered with the interpretation of the test. Among those 72 cases with positive PPT, 14/72 patients (19.4%) had history and clinical manifestation relevant to the diagnosis of PACD. In these 14 patients, there were 17 positive photoallergen test sites. Two patients had multiple photoallergens, one with positive reaction to promethazine hydrochloride, chlorpromazine hydrochloride and fenticlor and the other with positive reaction to promethazine hydrochloride and chlorpromazine hydrochloride. Among 14 PACD patients, 5 cases (35.7%) were PPT positive to oxybenzone, 3 cases (21.4%) to promethazine hydrochloride, and 3 cases to their own products (table 5).

There were 194 patients (71.8%) who had negative PPT results of whom 49.0% (95 cases) had final diagnosis of PMLE. There were 48 patients considered in the group of allergic contact dermatitis (ACD). Among them, fragrance mix was the most common allergen (8 cases), followed by oxybenzone (6 cases), balsum of Peru and triclosan (5 cases).

Disscusion

In our series, PPT was conducted in 270 patients during the 10-year period. We found that most of them did not realize that sun light and/or some topical agents especially sunscreen might be the factors that caused their skin problems. They worked as company employees, government officials or work at home; and most of their workplaces were in the building that they thought it safe from sunlight. Some of them applied sunscreen before going outdoor.

After complete the test, 72 of 270 patients (26.7%) had positive result of PPT; but only 14/72 patients (19.4%) had PPT result correlated with their present history and skin manifestation. The relevance rate of PPT varied from center to center according to various factors such as patient selection, test methodology, test allergens and criteria of interpretation. The relevance rate between PACD and PPT was reported to range from 1% to 40%.[10-17]

Even though PACD should be the main reason to send patients for PPT but it was the third rank of the list of provisional diagnosis of our patients, (15.2%)

Table 5 Photoallergen in patients with positive PPT (14 cases)

Photoallergen	Number of cases	%
Oxybenzone	5	35.7
Promethazine Hydrochloride	3	21.4
Patient's own topical product	3	21.4
Chlorpromazine Hydrochloride	2	14.3
Fragrance mix	2	14.3
Triclocarban	1	7.1
Fenticlor	1	7.1

Remark: some patients were positive to more than one photoallergen

following PMLE (36.3%) and photosensitive dermatitis (18.5%). This implied that the PPT procedure was conducted as a method both to confirm the diagnosis of PACD and to exclude other photodermatoses or other skin diseases. In our study, the portion of the later reason was much higher. Another reason to send patients to do PPT was to complete the line of investigation as the IOD has been serving as an academic center for residency training. If we preserved PPT solely for patients who were highly suspicious of PACD, the relevance rate of PPT would have been much higher.

We selected 20 photoallergens from a standard commercial company that had optimal concentration to create allergic or photoallergic reaction in susceptible cases. There has been no consensus about UVA dose in PPT procedure yet[3,7], and we preferred 10 J/cm^2. We irradiated UVA only 24 hours after patching the allergens because the hot and humid condition might interfere with the procedure. Some researchers suggest that it is better to take UVA after 48 hours patched for more positive results[18]. Furthermore the IOD protocol does not read delayed reactions which may occur in 2-3 weeks after the PPT procedure.

When a positive reaction was detected on the PPT site, the particular photoallergen could be the cause of PACD although it was not necessary to cause the skin problem in that present episode. For the definite diagnosis of PACD, the PPT result should be correlated to patient's present history and clinical manifestation. In case there was no correlation observed, the particular photoallergen should not be considered as the causative agent in that episode; but it could have been the cause of the reaction in the past, or it could be in the future. It is also possible that the patient might have other skin problems or has PACD caused by other photoallergen(s) that were not included in our standard photoallergen set.

Out of the 14 PACD patients, oxybenzone (benzophenone-3), sun screen ingredient, was the most common photoallergen. This result was similar to many reports.[5,6,7,19] Oxybenzone also gained positive reaction in PT group, 6 cases (second in the rank). Because Thai people have recently more health conscious about environmental harshness; and thus many sunscreen products were introduced into the market aiming for sun protection, prevention of pigmentary disorder, anti-aging and skin cancer protection. There were 7 sunscreen active ingredients in our PPT set trying to monitor cases of sunscreen-caused PACD and ACD. Promethazine hydrochloride and chlorpromazine hydrochloride were the second and third most common photoallergen respectively. These results followed the same trends as many previous studies.[5,19] The group of perfume, fragrance mix and balsum of Peru were still the leading cause of ACD and PACD but more in ACD group. There were 3 patients who had positive reaction to their own products which were "day cream" that might contain sunscreen agent, fragrance or other chemical that we could not indentify. In our study, the incidence of ACD (by positive PT) was higher than PACD, which was similar to other reports.[6,19]

This study was limits by its retrospective nature. It is, however, the first report of the relevance of PPT and PACD in Thai population. Because this is a single-center study, it could be a good basic data for multi-center study in the future. For photoallergens, there is a need to provide feedback on the adverse effects of sunscreen products to manufacturers regarding the clinical safety of their product(s) in order to enable safer product development. As PACD to sunscreen

chemicals evolves with the use of new UV filters, continuing clinical surveillance as well as PPT studies on suspected commercial products by clinical experts using standardized PPT procedure together with updated photoallergens should be useful for the protection of the population from harmful products in the market. Thus, standardized PPT methodology and interpretation are essential to facilitate our understanding of photocontact allergy, its nature and the incidence.

References

1. Kerr A, Ferquson J. Photoallergic contact dermatitis. Photodermatol Photoimmunol Photomed 2010;26:56-65.
2. Goossens A. Photoallergic contact dermatitis. Photodermatol Photoimmunol Photomed 2004;20:121-5.
3. European Multicentre Photopatch Test Study (EMCPPTS) Taskforce. A European multicentre photopatch test study. Br J Dermatol 2012;166:1002-9.
4. Scalf LA, Davis MD, Rohlinger AL, Connolly SM. Photopatch testing of 182 patients: a 6-year experience at the Mayo Clinic. Dermatitis 2009;20:44-52.
5. Victor FC, Cohen DE, Soter NA. A 20-year analysis of previous and emerging allergens that elicit photoallergic contact dermatitis. J Am Acad Dermatol 2010;62:605-10.
6. Bryden AM[1], Moseley H, Ibbotson SH, Chowdhury MM, Beck MH, Bourke J, English J, Farr P, Foulds IS, Gawkrodger DJ, George S, Orton DI, Shaw S, McFadden J, Norris P, Podmore P, Powell S, Rhodes LE, Sansom J, Wilkinson M, van Weelden H, Ferguson J. Photopatch testing of 1155 patients: results of the U.K. multicentre photopatch study group. Br J Dermatol 2006;155:737-47.
7. Chuah SY, Leow YH, Goon AT. Theng CT, Chong WS. Photopatch testing in Asians: a 5-year experience in Singapore. Photodermatol Photoimmunol Photomed 2013;29:116-20.
8. Victor FC, Cohen DE, Soter NA. A 20-year analysis of previous and emerging allergens that elicit photoallergic contact dermatitis. J Am Acad Dermatol 2010;62:605-10.
9. Jindal N, Sharma NL, Mahajan VK, Shanker V, Tegta GR, Verma GK. Evaluation of photopatch test allergens for Indian patients of photodermatitis: preliminary results. Indian J Dermatol Venereol Leprol 2011;77:148-55.
10. Darvay A, White IR, Rycroft RJ, Jones AB, Hawk JL, McFadden JP. Photoallergic contact dermatitis is uncommon. Br J Dermatol 2001;145:597-601.
11. Bakkum RS, Heule F. Results of photopatch testing in Rotterdam during a 10-year period. Br J Dermatol 2002;146:275-9.
12. English JS, White IR, Cronin E. Sensitivity to sunscreens. Contact Dermatitis 1987;17:159-62.
13. Lee PA, Freeman S. Photosensitivity: the 9-year experience at a Sydney contact dermatitis clinic. Australas J Dermatol 2002;43:289-92.
14. Schauder S, Ippen H. Contact and photocontact sensitivity to sunscreens. Review of a 15-year experience and of the literature. Contact Dermatitis 1997;37:221-32.
15. DeLeo VA, Suarez SM, Maso MJ. Photoallergic contact dermatitis. Results of photopatch testing in New York, 1985 to 1990. Arch Dermatol 1992;128:1513-8.
16. Berne B, Ros AM. 7 years experience of photopatch testing with sunscreen allergens in Sweden. Contact Dermatitis 1998;38:61-4.
17. Neumann NJ, Lehmann P. The photopatch test procedure of the German, Austrian, and Swiss photopatch test group. Photodermatol Photoimmunol Photomed 2003;19:8-10.
18. Batchelor RJ, Wilkinson SM. Photopatch testing— a retrospective review using the 1 day and 2 day irradiation protocols. Contact Dermatitis 2006;54:75-8.
19. Greenspoon J, Ahluwalia R, Juma N, Rosen CF. Allergic and photoallergic contact dermatitis: a 10-year experience. Dermatitis 2013;24:29-32.

บทคัดย่อ: นัยสำคัญของ Photopatch Test และโรค Photoallergic Contact Dermatitis - ประสบการณ์ 10 ปี

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วารสารวิชาการสาธารณสุข 2557;23:753-61

Photopatch test (PPT) เป็นวิธีทดสอบมาตรฐานในการยืนยันและวินิจฉัยโรค photoallergic contact dermatitis (PACD) ซึ่งต้องสอดคล้องกับประวัติผู้ป่วยและลักษณะทางคลินิก การศึกษานี้เป็นการศึกษาย้อนหลังเพื่อศึกษานัยสำคัญของ PPT และโรค PACD ในช่วงเวลา 10 ปีระหว่าง พ.ศ. 2543 - 2552 ที่สถาบันโรคผิวหนัง ในผู้ป่วยทั้งหมด 270 รายที่ทำทดสอบ PPT ครบ พบว่ามีผู้ป่วย 72 ราย (ร้อยละ 26.7) ที่มี PPT เป็นผลบวกแต่พบว่ามีเพียง 14 รายจาก 72 ราย (ร้อยละ 19.4) ที่มีความสัมพันธ์อย่างมีนัยสำคัญกับประวัติและลักษณะทางคลินิกของผู้ป่วยและสามารถช่วยวินิจฉัยโรค PACD ได้อย่างชัดเจน สำหรับสารที่ก่อโรคพบว่า oxybenzone ซึ่งเป็นสารกันแดดชนิดหนึ่งพบเป็นสาเหตุมากที่สุดเช่นเดียวกับรายงานอื่น ๆ นอกจากนี้ สารอื่นที่พบบ่อยคือ promethazine hydrochloride, chlorpromazine hydrochloride, fragrance mix, triclocarban และ fenticlor และยังพบว่า oxybenzone เป็นสาเหตุของ allergic reaction ในผู้ป่วย 6 ราย การศึกษานี้เป็นรายงานผลการทำ PPT รายงานแรกในประเทศไทย ซึ่งเป็นประโยชน์ในการอ้างอิงเป็นข้อมูลพื้นฐานของประเทศ แม้ว่าผลการรายงานจะแสดงนัยสำคัญของการทำ PPT ในการวินิจฉัยโรค PACD ที่ต่ำ ซึ่งหากมีการคัดกรองผู้ป่วยในการทำ PPT เฉพาะรายที่มีแนวโน้มสนับสนุนจากประวัติและลักษณะทางคลินิกที่เข้าได้กับ PACD เท่านั้น คาดว่าจะทำให้ได้ผลลัพธ์ที่มีนัยสำคัญสูงขึ้น รวมทั้งควรต้องมีการทบทวนรายการสารทดสอบมาตรฐาน (photoallergen) ที่ใช้ให้มีความทันสมัยสอดคล้องกับความนิยมที่มีการใช้จริงในช่วงเวลานั้น ๆ จะทำให้การทำ PPT เกิดประโยชน์ในทางคลินิกและช่วยในการวางแผนในการรักษาได้ดียิ่งขึ้น

คำสำคัญ: **โรค photoallergic contact dermatitis, การทดสอบทางผิวหนังด้วย photopatch test, สารกันแดด, สาร oxybenzone**