A 30-year Patch Testing Experience at Siriraj Dermatology

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ABSTRACT

Objective: To identify trends of contact allergy and patch testing amendments at the Contact Dermatitis Clinic, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University.

Materials and Methods: Medical records of 6,862 patients referred to our clinic between January 1992 and December 2021 for patch testing were reviewed.

Results: The number of patients patch tested increased and reached a peak of 600 patients/year in 2019 before the COVID-19 pandemic. The most frequently used series was baseline, while the most used specific series was cosmetics. The overall positivity rate was 69%. The highest positivity rate was in the cosmetics series (70.2%). Nickel sulfate was the most common contact allergen found (24.2%).

Conclusion: Our patch test service has been growing in the last 30 years. The series of allergens used for patch testing has been amended every few years to be up-to-date with current global trends of contact allergies. Continual surveillance of contact prevalence and periodic updating of those series are necessary to enhance our ability to detect culprit contact allergens, which could help us improve care of our patients.

Keywords: Patch test; contact dermatitis; Siriraj; contact allergens; skin allergy; Thailand (Siriraj Med J 2023; 75: 62-69)

INTRODUCTION

Allergic contact dermatitis (ACD) is a common skin disease caused by immunological hypersensitivity to particular substances. Patch testing is considered the gold standard diagnostic procedure for identifying specific allergens that cause contact skin allergies. The baseline allergens, which contain common contact allergens found in certain populations is recommended for patch testing in every patient.[1] Furthermore, additional series are selected and used in testing based on a patient's rash and exposure history.[2] Specific allergens in each patch test series are updated, depending on the current trends of allergenicity at that time.[3]

History

Patch tests were introduced as a diagnostic tool for ACD in the late nineteenth century by German physician Joseph Jadassohn.[4] Contact Dermatitis Clinic, at Siriraj Hospital was established by Clinical Professor Emeritus Patcharee Sunthonpalin, M.D., who wrote the first and only *Contact Dermatitis* textbook in Thai. The clinic has been in operation since 1972 under the Department of Medicine, Faculty of Medicine Siriraj Hospital. The clinic started with six allergen series, including baseline, cosmetic, fragrance & botanical, textile, photoallergen & sunscreen, and the hair series. In 2010, our clinic hired more staff and expanded its services. In 2013, the name

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of clinic was changed to the Occupational and Contact Dermatitis Clinic to broaden the range of disease focus. Since this time, many studies have been published in various international academic journals. There has also been improvement in our services, such as the creation of a own Nickel spot test (dimethylglyoxime),[5] cobalt test,[5] skin marking pen, Thai mite allergen for patch testing and a Thai database of Contact Allergen Avoidance Program or CAAP,[5,6] in accordance with Mahidol University's "Wisdom of the Land" to promote higher education and help society achieve a better quality of life. Currently, we have over 30 years of experience providing patch testing and treating contact and occupational-related dermatitis. Nowadays, we are the standard referral center for patch testing, and seventeen kinds of allergen series are available.[7]

As this year is the 30th anniversary of the founding of the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, we aimed to publish the outcomes and trends of patch testing in our clinic over its history to celebrate this memorable achievement.

MATERIALS AND METHODS

Study design and participants

Retrospective charts between January 1992 and December 2021 were reviewed at the Occupational and Contact Dermatitis Clinic, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand. Patients' characteristics and patch test results were collected. This study was approved by the Siriraj Institutional Review Board (COA no. Si 808/2021).

Patch testing was carried out according to guidelines by the International Contact Dermatitis Research Group.[8] The allergens (Chemotechnique Diagnostics, Vellinge, Sweden) in aluminium Finn Chambers (SmartPractice, Phoenix, Arizona) were applied on the patients' upper back for 48 hours. The dermatologists measured the readings on day 2, 4 and 7, and the reaction was scored according to the guideline. Siriraj baseline series were adapted from the International standard and European baseline series.[7,9] Some patients were tested with additional series such as the cosmetics series, and hairdressing series, depending on patients' clinical histories.

Some series were not universally available at that period of time such as pigmented series that composed of 24 allergens; 13 allergens are allergen from baseline series such as paraphenylenediamine, fragrance etc. plus 11 particular allergens were jasmine oil, Ylang-ylang oil, benzyl salicylate, ammonium mercury, sudan I, disperse orange 3, disperse yellow 3, hydroquinone, coal tar, tricosan, and tretinoin. These allergens had been reported causing hyperpigmentation.

Statistical analysis

PASW Statistics for Windows, version 18 (SPSS Inc., Chicago, IL, USA), was used for data analysis. Categorical data was described using frequency and percentage. Continuous data was reported using mean and standard deviation for data with normal distribution or median and interquartile range for data with non-normal distribution.

RESULTS

Our clinic performed patch tests on a total 6,862 patients over a 30-year period. Most patients were female (78.6%), and the median age was 40 (29.0, 52.0) years old. Also, most patients were 18 – 59, or of working-age. Personal and family history of atopy was found in 42% and 32% of cases, respectively. Almost 40% of patients had a history of metal allergy, while only 15% had history of cosmetic allergy (Table 1).

The average number of patients who underwent patch testing was 229 (±158) patients/year. Between 1992 and 2006, the number of patients tested was approximately 100 patients/year, before it rose to almost 600 patients/year in 2019 (Fig 1). However, the number of patients tested decreased in 2020 and 2021 due to the COVID-19 pandemic. The positivity rate was 69%, and it ranged between 60% and 90% each year. Table 2 shows all positivity rates of each series in five-year intervals over the 30-year study period.

The most frequent additional allergen series used besides the baseline over the 30-year period were cosmetics, cheilitis and hairdressing in 1,203 (17.5%), 493 (7.2%) and 292 (4.3%) patients, respectively. The positivity rate varied in each series over time (Table 2). The cosmetic series had the highest positivity rate of 70.2%, and at times reached as high as 80%, followed by melasma (66.7%), baseline (66.5%) and pigmented cosmetic series (65.1%).

Regarding allergens in the baseline series, the one with the highest positivity rate over 30 years was nickel sulfate (24.2%), followed by gold sodium thiosulfate (19.9%), linalool hydroperoxide (13.0%) and fragrance mix I (12.95%). The top three most common allergens during each five-year period were three metals (nickel, gold sodium thiosulfate, potassium dichromate), two fragrances (fragrance mixed I, linalool hydroperoxide) and two preservatives (paraben mix, methylisothiazolinone) as displayed in Fig 2. Common sensitizers throughout the course of the study are summarized in Fig 2. The constant rate of nickel was approximately 20-30%, with the highest clinical relevance rate at 83.23% over the past 30 years. Fragrance allergens, including fragrance mix I, mix II and balsum of Peru gradually decreased after

TABLE 1. Demographic data.

Demographic data	n	(%)
Gender, n = 6,862		
Male	1,466	(21.4)
Female	5,396	(78.6)
Age, years (median; IQR), n= 6,851	40.0 (29.0 – 52.0)	
< 18 years, n (%)	221	(3.2)
18-59 years, n (%)	5,072	(83.1)
≥ 60 years, n (%)	928	(13.5)
Occupation, n= 6,702		
Blue collar workers*	1,470	21.9
White collar workersᵀ	3,792	56.6
Unemployed/retired	752	11.2
Student	688	10.3
Median duration of symptoms (months) (IQR)	12.0 (4.0 – 36.0)	
Personal history of atopy, n=6,859	2,908	(42.4)
Familial history of atopy, n=6,390	2,040	(31.9)
History of metal allergy, n=6,515	2,429	(37.3)
History of cosmetic allergy, n= 6,350	923	(14.5)
Positive for at least one allergen, n=6,862	4,738	(69.0)

*, Blue-collar worker refers to workers who engage in hard manual labor, typically agriculture, manufacturing, construction, homemaker, mechanic, maintenance, or another physically exhausting task that implies belonging to a lower social class.
ᵀ,White-collar workers are known as suit-and-tie workers who often avoid physical labor which implies belonging to a higher social class

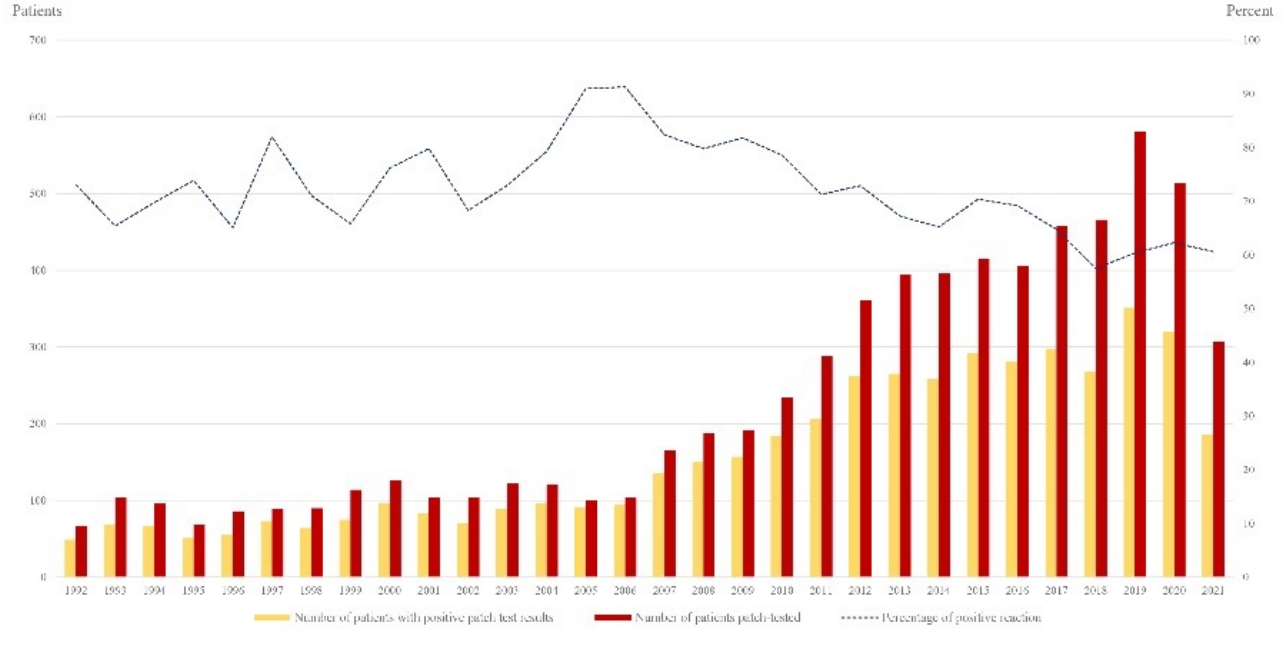


Fig 1. Number of patients referred for patch testing and percentage of positive reactions between 1992 and 2021.

TABLE 2. Positive patch test results in each patch test series.

Patch test series	Positive patch test results Total Number of patients tested	Number of patients with positive reaction n (%)	Year 1992-1996 n (%)	Year 1997-2001 n (%)	Year 2002-2006 n (%)	Year 2007-2011 n (%)	Year 2012-2016 n (%)	Year 2017-2021 n (%)
Baseline	5527	3673(66.5)	261/377(69.2)	289/371(77.9)	303/359(84.4)	553/701(78.9)	957/1427(67.1)	1310/2292(57.2)
Cosmetic	1203	845(70.2)	37/60(61.7)	91/121(75.2)	69/95(72.6)	147/176(83.5)	263/328(80.2)	238/423(56.3)
Cheilitis	493	292(59.2)	0/0(0.0)	0/0(0.0)	38/47(80.9)	64/94(68.1)	90/145(62.1)	100/207(48.3)
Hair dressing	292	125(42.8)	4/9(44.4)	15/22(68.2)	8/17(47.1)	21/25(84.0)	30/72(41.7)	47/147(32.0)
Photoallergen	207	27(13.0)	0/2(0.0)	6/39(15.4)	5/32(15.6)	2/23(8.7)	6/72(8.3)	8/39(20.5)
Eyelid	152	73(48.0)	0/0(0.0)	0/0(0.0)	1/1(100.0)	20/23(87.0)	32/59(54.2)	20/69(29.0)
Corticosteroids	151	10(6.6)	0/0(0.0)	4/46(8.7)	2/10(20.0)	1/26(3.8)	2/29(6.9)	1/40(2.5)
Plastic & Glue	144	27(18.8)	2/24(8.3)	5/13(38.5)	1/9(11.1)	10/23(43.5)	7/35(20.0)	2/40(5.0)
Textile	138	24(17.4)	0/15(0.0)	1/25(4.0)	6/19(31.6)	7/14(50.0)	6/30(20.0)	4/35(11.4)
Dental	128	72(56.3)	0/0(0.0)	0/0(0.0)	10/12 (83.3)	19/29(65.5)	27/52(51.9)	16/35(45.7)
Pigmented	126	82(65.1)	0/0(0.0)	0/0(0.0)	13/14(92.9)	18/26(69.2)	36/53(67.9)	15/33(45.5)
Fragrance & Botanical	61	31(50.8)	2/4(50.0)	0/3(0.0)	3/3(100.0)	7/10(70.0)	8/15(53.3)	11/29(37.9)
Prosthesis	14	7(50.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	3/7(42.9)	4/7(57.1)
Oil and cooling	13	2(15.4)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/6(0.0)	2/7(28.6%)
Melasma	12	8(66.7)	0/0(0.0)	0/0(0.0)	8/12(66.7)	0/0(0.0)	0/0(0.0)	0/0(0.0)
Shoes	9	1(11.1)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	1/9(11.1)
Bakery	9	0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/0(0.0)	0/9(0.0)
Overall	6862	4738(69.0)	291/422(69.0)	391/523(74.8)	442/551(80.2)	833/1068(78.0)	1359/1972(68.9)	1422/2326(61.1)

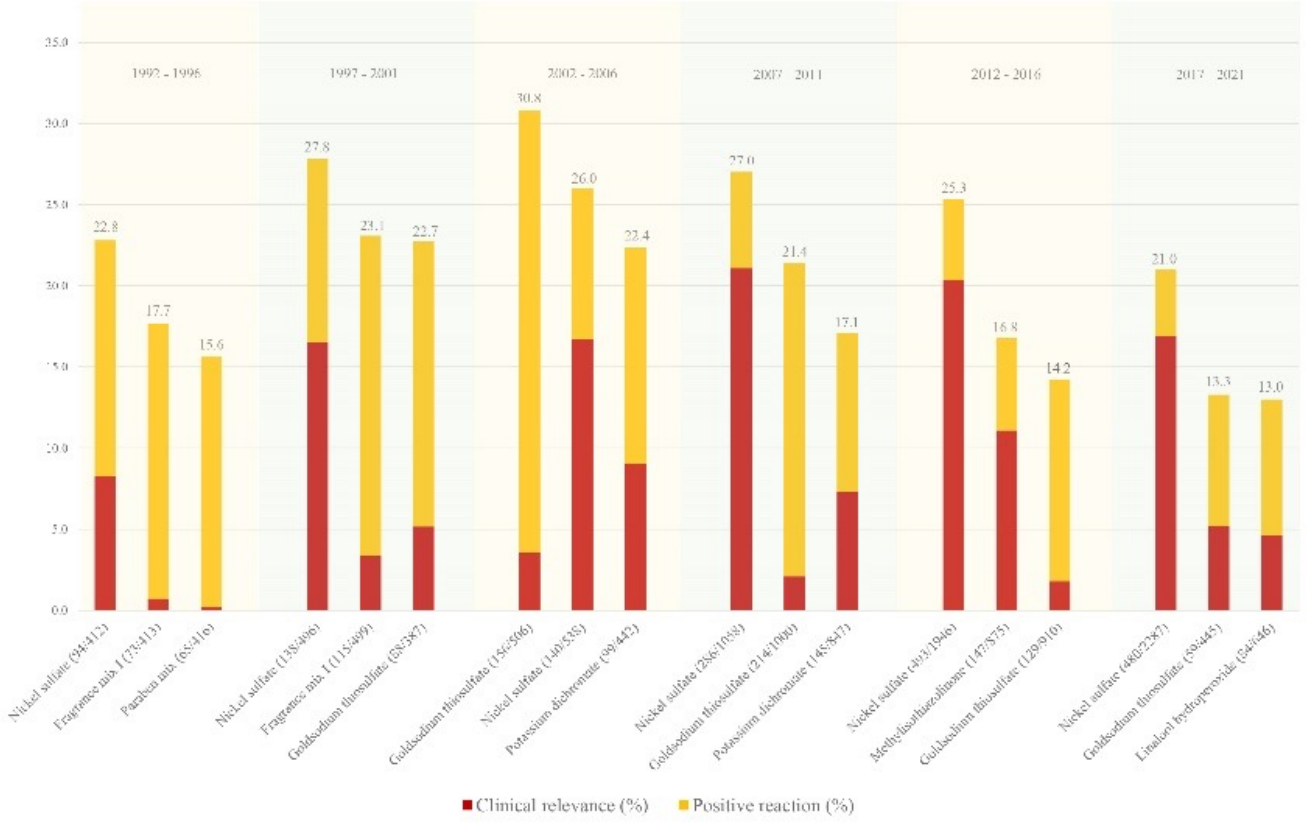


Fig 2. Common allergens in baseline series between 1992 and 2021.

2002, however, linalool hydroperoxide, a new fragrance allergen, had a high percentage of positive reactions and was a top three most common allergen in the last five years. Regarding preservative allergens, the paraben mix showed a high positivity rate in the early period of the study period (1992-1997), but it later declined. In contrast, isothiazolinone, including methylchloroisothiazolinone/methylisothiazolinone (MCI/MI) and methylisothiazolinone (MI), saw a gradual rise in positive reactive rate, and a slight decrease after 2016.

DISCUSSION

This retrospective study uncovered big changes in the patch testing process, and allergen series over a 30-year period at the Occupational and Contact Dermatitis Clinic, Siriraj Hospital. We noticed growth in patch testing services along with changes in contact sensitizers over time. The number of patients referred for patch testing per year has progressively increased year-on-year, with a remarkable rise since 2006, and a five to six-fold increase in 2019. We believe the growth of our clinic is the result of several support systems such as our departments and faculties, along with ongoing encouragement of referring patients suspected of having ACD for patch testing. However, patch testing numbers decreased abruptly due to the COVID-19 outbreak from early 2020, like the rest of the world.[10]

The rate of positive patch test results in the baseline series, which are the standard set of allergens used in almost every patients suspected of having ACD in our clinic, was 66.5%, which is consistent with studies from the United states and Saudi Arabia as well as our previous study covering 2006-2018.[11-13] We also noticed a decline in the percentage of reactions after 2006, which coincided with an increase in the number of patients tested. This could be due to the fact that there were more patients interested in getting tested and that we were less stringent on which patients to include. There are discrepancies in patch testing positivity worldwide, ranging from 22%-55%.[14-16] This variation in positivity may be due to different exposures linked to local culture, industries, and regulations in each country. Furthermore, individual factors and the patch testing method are influential factors on the outcome as well.[17]

A chronological change in our contact allergen series was established around the world. Sensitizing allergens

in each patch test series were updated based on the current trends in allergenicity at that time.[3] Many sets of allergens are available in our clinic, and each series differs in number of substances. The cosmetic series is the second most common, after following baseline series, but it generated the highest yield. In addition, the percentage of positive results from the cosmetic series has been gradually rising. Despite a slightly downward trend in the last five years, it is worth using in patients suspected of having ACD because ninety percent of cosmetic products in the Thai market contain at least one allergen.[18] High rates of sensitization also reflect the growth of the cosmetic business and wide use of cosmetic products in our country. The melasma series was second, but it was only used between 2002-2004. Later, its allergens were merged into the cosmetic and pigmented series. Although reactions to the pigmented series have been declining, it remains the series with the fourth highest positivity rate. These findings suggest that although the baseline series already include common allergens from a specific time period, the addition of specialty allergen series relating to personal history or work products is still necessary for a complete evaluation, to increase the success rate of identifying the culprit, and to improve management of patients' allergic contact dermatitis.[11,19] However, the other series, such as, photoallergen, corticosteroid, plastic & glue, textile, oil & cooling and shoe, which have a small positivity rate, are more of a concern. This may indicate an inadequate set of allergens, which warrants a review.

Regarding individual allergens, nickel sulfate is known as the most common allergen worldwide.[11,20-22] Its prevalence in this study was steady over the time and comparable with a previous study from Thailand (24.0% in 2006-2018 vs 27.6% in 2000-2009).[9,21] However, the current study revealed a much higher share of positive reactions (24.2%) to nickel sulfate than studies from other Asian and European countries (13.9-20.4%).[11,14,22-24] A declining trend was noted in European countries following nickel regulations and introduction of novel substitute metals,[24] which contradicts results from our Thai study where there are no regulations on the specific amount of nickel allowed in nickel-containing accessories in the market.[5] The allergens, which displayed a downward trend in our study, include cobalt, gold sodium thiosulfate, fragrance mix I and II, *Myroxylon pereirae* and parabens, which were potent sensitizers in the past. This can potentially be explained by a decline in exposures to these sensitizers. Furthermore, many industries have substitutes to avoid this problem, resulting in relatively less prevalence.

For allergens showing more prevalence, hydroperoxide of linalool has been an emerging allergen since 2020. Linalool is the most common fragrance material in cosmetic products sold in the European market and has been increasingly responsible for contact allergy in Europe.[25] Our data showed that a positive reaction occurred in 13% of cases, compared to prior reports which reported a positivity rate ranging from 1.7-20%.[11,26,27] The variation depends on the exposure rate of the individual country, the popularity of the allergen in the environment, regional legislation, and the population tested. An increase in MCI/MI was also noted. MI is isothiazolinone preservative mainly used in cosmetic and personal care products. High concentrations of MCI/MI and MI caused a global epidemic in the mid-2010s.[21,28-30] Consequently, for leave-on cosmetics, the use of MCI/MI and MI as an ingredient in Europe has been banned since 2016 and 2017,[31,32] respectively, and the concentration of MI in rinse-off cosmetics has reduced since 2018 by the European Commission.[33] According to the legislation, the prevalence of isothiazolinone allergy considerably decreased after 2016. The change in MCI/MI and MI allergies in our study will likely follow global data as the Thai FDA usually takes a few years to adopt EU regulations.[34,35]

Limitation of our study was incomplete data due to long retrospective nature of study design e.g. clinical relevance of positive reaction information. Moreover, the study originated from single tertiary centre in Bangkok, Thailand, leading to lack of regional generality.

Siriraj Contact Dermatitis Clinic has been in operation for 30 years. This study reviewed 30-year outcomes at the clinic. Our patch testing service has grown over this period. The series of allergens used for patch testing is amended every few years to update it to the latest global trends of contact allergies. Continual surveillance of contact prevalence and periodic updates are necessary to enhance our ability to detect culprit contact allergens, and improve care of our patients.

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