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# Hyposensitization to urushiol among Japanese lacquer craftsmen: results of patch tests on students learning the art of lacquerware

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8 subjects learning the art of lacquerware were patch tested to urushiol before and after contact with lacquer, in order to document whether hyposensitization to urushiol occurred among Japanese lacquer craftsmen. Simultaneously, we performed patch tests on 2 urushiol-sensitized controls who had no contact with lacquer during the investigation. Lacquer is made from the sap of the Japanese lacquer tree and raw lacquer is composed of 60–65% urushiol and its oligomer. 5 of the 8 subjects showed positive reactions to urushiol 1 month after their first contact. They became negative or less positive after prolonged (9 or 10 months) exposure to lacquer. As reactions to urushiol decreased, dermatitis became less severe. Controls showed consistently high reactions. However, 1 subject showed persistently strong reactions to urushiol. Unlike the other 7 subjects, he was previously sensitized to urushiol before the first contact with lacquer. The remaining 2 subjects showed no reaction throughout our investigation. These results strongly suggest that hyposensitization to urushiol does occur among Japanese lacquer craftsmen.

*Key words:* hyposensitization; urushiol; allergic contact dermatitis; Japanese lacquer craftsmen; hardening; occupational; continued exposure; patch test study.

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The art of lacquerware was introduced to Japan from China via Korea, along with Buddhism, in the 6th century (1). Since then, lacquerware has been a traditional Japanese art and has supported an important industry. Lacquer is made from the sap of the Japanese lacquer tree (*Rhus verniciflua*), a member of the Anacardiaceae family of trees, which has been recognized in Japan and China as the cause of dermatitis for more than 1000 years (1). Urushiol, the major component of the sap, is an antigenic chemical that causes lacquer dermatitis (2). As raw lacquer is composed of 60–65% urushiol and its oligomer (1), lacquer craftsmen sometimes suffer from severe contact dermatitis. Even when dried, the lacquer can produce dermatitis, as it still contains unpolymerized urushiol. In fact, Toyama (2) reported that dermatitis was produced by lacquer taken from an antique jar which had been buried in a Japanese ruin for about 1000 years.

It has been said that Japanese lacquer craftsmen become hardened to lacquer by chewing raw lacquer. The term "hardening" in industrial dermatitis was introduced by Jadassohn. Hardening indicates a condition in which allergic contact dermatitis (ACD) in sensitized persons disappears or fails to reappear on repeated exposure to the sensitizing chemical, i.e., the subject becomes less sensitive (hypo-

sensitive) to the antigen. On the other hand, it is a common belief that contact allergy in humans, once acquired, is usually a lifelong state, and the phenomenon of "hardening" occurs only in rare instances.

In order to document whether Japanese lacquer craftsmen became hardened to lacquer, we previously investigated 232 craftsmen by questionnaire (4). The results showed that 189 had experienced lacquer dermatitis while 43 never developed it. Among the 189 sensitized persons, there were 158 who had shown spontaneous improvement after continuous prolonged exposure to lacquer. Thus, they had become hardened (hyposensitive) to lacquer (urushiol). While they usually showed no symptoms of dermatitis, occasionally mild dermatitis did occur when the raw lacquer was not properly washed off after working. Among the sensitized persons, 3 suffered serious lacquer dermatitis continuously. These 3 persons worked less than 2 h per day, while the craftsmen in this study worked about 6 h on average. From these data, we inferered that hyposensitization to urushiol occurred among lacquer craftsmen as a result of repeated exposure to lacquer.

Reginella et al. (5) have recently reported that workers at a cashew nut shell oil (CNSO) processing plant developed hyposensitization to urushiol through their exposure to CNSO, which contains similar chemicals to urushiol. They also pointed out that a majority of the new workers showed clearing of their dermatitis several weeks after starting work, while approximately 10% continued to suffer dermatitis and quit their jobs.

In contrast, according to Fisher & Adams (3), hardening or hyposensitization occurs only in rare instances, and scientific proof of specific hardening (hyposensitization) would be established when the following criteria have been satisfied.

(i) The subject has had an ACD due to a specific chemical that caused a strongly positive patch test reaction.

(ii) The ACD produced by the chemical clears and remains clear in spite of exposure to the chemical that caused the positive patch test reaction.

(iii) The previously strongly positive patch test reaction to the chemical becomes negative or weakly positive.

Our results from the questionnaire were not sufficient to satisfy these criteria. To confirm clinically our earlier hypothesis that hyposensitization to urushiol occurs among lacquer craftsmen, we performed repeated patch tests to urushiol on subjects learning the art of lacquerware, before and after contact with lacquer, and clinically observed their dermatitis history during a 10-month period.

### Subjects and Methods

Patch tests were carried out on 8 healthy subjects (3 male and 5 female), between 19 and 21 years old. They had no previous history of urushiol sensitivity. The 1st patch test (PT1) was performed in May, a few days before their first contact with lacquer. The 2nd patch test (PT2) was performed in June, about 1 month after their first contact. At this time, they were in contact with lacquer for an average of 2 h per day. During the summer vacation (July and August), they had no contact with lacquer. Contact with lacquer resumed in September and the hours of contact per day increased through December. The 3rd patch test (PT3) was performed in December when the subjects were in contact with lacquer for a minimum of 5 h per day in preparation for an exhibition. The 4th patch test (PT4) was performed in February, just before their exhibition, when they were in contact with lacquer for more than 10 h per day. All subjects continued to have contact with raw lacquer regardless of the existence of dermatitis.

Contact with lacquer was not only external. As the process of manufacturing lacquerware involves sanding, they may inhale fumes and ingest particles of lacquer.

Patch tests were also performed on a 44-year-old man and a 42-year-old woman as con-

*Table 1.* The results of urushiol patch tests

| Subject no. | Sex | Age (years) | Urushiol (pet.) concentration 0.01% PT1 | 0.01% PT2 | 0.01% PT3 | 0.01% PT4 | 0.002% PT1 | 0.002% PT2 | 0.002% PT3 | 0.002% PT4 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 20 | − | ++ | − | − | − | + | − | − |
| 2 | M | 21 | − | + | − | − | − | +? | − | − |
| 3 | M | 21 | ++ | ++ | ++ | ++ | +? | ++ | ++ | + |
| 4 | F | 21 | − | − | − | − | − | − | − | − |
| 5 | F | 19 | − | ++ | NT | + | − | ++ | NT | + |
| 6 | F | 20 | − | ++ | +? | +? | − | + | +? | +? |
| 7 | F | 20 | − | +? | +? | − | − | − | +? | − |
| 8 | F | 19 | − | − | NT | − | − | − | NT | − |
| Scoring system | | | | | | | | | | |
| 0 | | | 7 | 2 | 3 | 5 | 7 | 3 | 3 | 5 |
| 0.5 | | | − | 1 | 2 | 1 | 1 | 1 | 2 | 1 |
| 1 | | | − | 1 | − | 1 | 0 | 2 | 0 | 2 |
| 2 | | | 1 | 4 | 1 | 1 | 0 | 2 | 1 | 0 |
| total score | | | 2.0 | 9.5 | 3.0 | 3.5 | 0.5 | 5.5 | 3.0 | 2.5 |
| average score | | | 0.25 | 1.19 | 0.50 | 0.48 | 0.06 | 0.81 | 0.50 | 0.31 |

The results of patch tests were read according to the ICDRG classification and were scored as follows: 0=(−), 0.5=(+?), 1=(+), 2=(++). NT: not tested.

trols at PT2 and PT4. Both had previously been sensitized to urushiol, but they had no contact with lacquer during our investigation.

Urushiol, diluted in white petrolatum at concentrations of 0.01% and 0.002% was applied as closed patch tests on the backs of the subjects, using Finn Chambers and Scanpor tape, and removed after 2 days. The reactions were read at 3 days according to the ICDRG classification. The results were scored as follows: 0=(−), 0.5=(+?), 1=(+), 2=(++). Urushiol for the tests was purchased from Torii & Co., Ltd.

## Results

Results are shown in Tables 1, 2 and Fig. 1.

The reactions to urushiol of 5 subjects (nos. 1, 2, 5, 6, 7) became negative or weakly positive at PT3 and PT4. Previously they had showed positive reactions to urushiol at PT2 (Table 1). On the other hand, the reactions of the controls were consistently high at PT2 and PT4 (Table 2).

Although these 5 subjects were not sensitized before contact with lacquer, they experienced dermatitis mainly on exposed areas of their bodies at PT2, 1 month after the 1st contact. Their dermatitis became less severe, as the reaction to urushiol decreased. At the time of PT3 and PT4, mild dermatitis occurred. This dermatitis occurred only when the raw lacquer was not properly washed off, and it subsided within few days without any medical treatment. These subjects had developed hyposensitization to urushiol. Moreover, the average score calculated from the patch test results continued to decline after PT2, in spite of prolonged contact with lacquer (Fig. 1).

*Table 2.* The results of the controls' patch tests

| Subject no. | Sex | Age (years) | Urushiol (pet.) concentration 0.01% PT2 | 0.01% PT4 | 0.002% PT2 | 0.002% PT4 |
|---|---|---|---|---|---|---|
| 9 | M | 44 | ++ | ++ | ++ | ++ |
| 10 | F | 42 | ++ | ++ | ++ | ++ |

However, 1 subject (no. 3) had consistently strong reactions to urushiol. Before the 1st contact with lacquer, he was positive to urushiol at PT1. He had no known previous history of urushiol sensitivity. He experienced dermatitis on the face, arms and hands several days after the 1st contact with lacquer. He suffered dermatitis continuously, but, at PT3 and PT4, the area of his dermatitis became limited to his hands, which had direct contact with the raw lacquer.

The remaining 2 subjects (nos. 4, 8) showed no positive reaction throughout our investigation. They experienced dermatitis between PT2 and PT3, but it cleared by the time of PT3.

## Discussion

Our results in this study confirmed our previous results based on questionnaires. Hyposensitization to urushiol occurred among Japanese lacquer craftsmen, as a result of repeated exposure to lacquer.

Of the 8 subjects studied, at least 5 (nos. 1, 2, 5, 6, 7) satisfied the Fisher & Adams (3) criteria. They experienced lacquer dermatitis within 1 month after their 1st contact and showed positive reactions to urushiol at that time. Their dermatitis improved after repeated exposure in spite of a prolonged increase in contact with lacquer. The patch test reaction to urushiol became negative or weakly positive 10 months after their 1st contact, while the controls who did not have contact with lacquer during the course of the tests showed consistently strong reactions to urushiol. However, 1 subject (no. 3) showed consistently strong reactions to urushiol throughout the course of patch tests. Although his dermatitis improved clinically, his improvement might not have been due to the development of hyposensitization, but due to a decrease in contact with lacquer as a result of careful handling. Hardening does not occur in all individuals (6), and thus he did not become hardened to lacquer. The remaining 2 subjects (nos. 4, 8) showed no

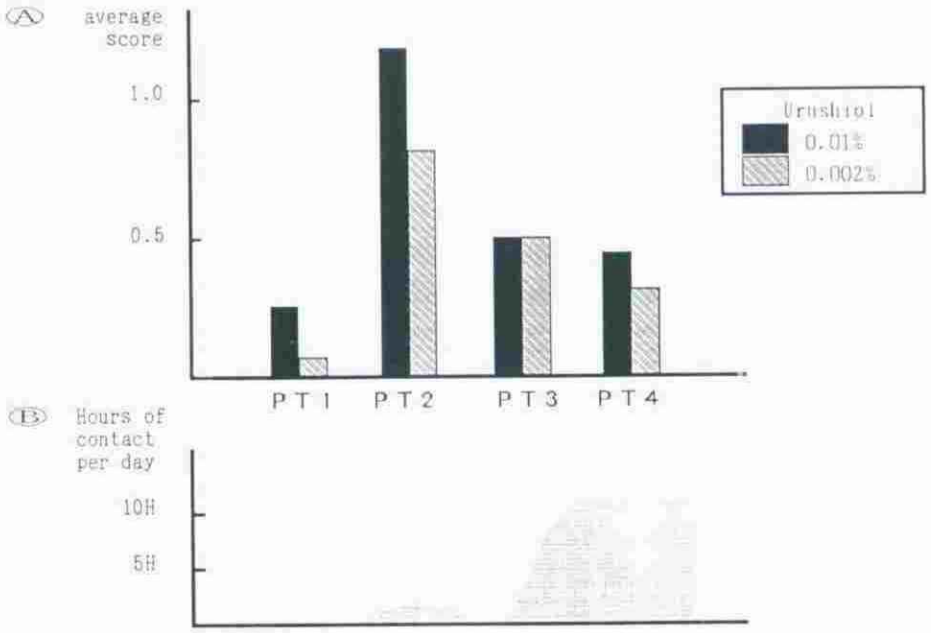


*Fig. 1.* (A) Reactions to urushiol before (PT1) and 1 month (PT2), 8 months (PT3), and 10 months (PT4) after exposure to lacquer. (b) Hours of contact with lacquer per day.

positive reaction throughout our investigation, although both experienced dermatitis about 2 months after their 1st contact. Their dermatitis was less severe than the other 6 subjects. There are 2 possible explanations why they had dermatitis in spite of a negative patch test reaction. One, they were sensitized to urushiol between PT2 and PT3, and they had developed hyposensitization by the time of PT3. Two, they were tolerant to urushiol and merely had irritant contact dermatitis.

The mechanism of hyposensitization remains unknown. Several explanations have been proposed, including induction of suppressor cells (7), depletion of specifically reactive lymphocytes (8), serum suppressive factors (9, 10) and macrophage (Langerhans cell) inactivation (11). Recently, Stampf et al. (9) showed that a serum IgG fraction from human subjects hyposensitized to poison ivy/oak by oral administration of urushiol suppressed the induction of delayed-type hypersensitivity (DTH) responses in mice to urushiol. Dunn et al. (10) also showed that serum suppressive factors induced hyposensitivity in mice. Both suggested that anti-idiotypic antibodies were involved in reducing DTH reactions. This mechanism may have occurred in the subjects studied. Currently, we are conducting an in vitro study using hapten-specific lymphocytes and IgG from hyposensitized subjects in order to verify this mechanism.

Boerrigter & Scheper (12) showed that repeated epicutaneous DNCB application induced hyposensitization in the guinea pig. They also suggested that the mechanism of local (site of ACD) and systemic (total body) hyposensitization are not the same. According to their hypothesis, local hyposensitization is due to the accumulation of T-suppressor cells at the hyposensitized skin sites, while systemic hyposensitization is due to the sequestration of circulating effector cells to the draining lymph nodes. We observed no lymph node enlargement of our subjects during the investigation, and we performed patch tests on the medial aspect of the forearm that often had contact with lacquer, and on the back that had no contact with lacquer at the time of PT3. The reactions to urushiol at both sites were similar. Local hyposensitization may not have occurred in our subjects.

The route by which hyposensitization developed is unclear. The antigen may bypass the Langerhans cells and exert a direct action on suppressor T cells or may cause receptor blockade (13). Kligman (14) reported that hyposensitization could be accomplished by either the oral or the intramuscular route. Inhalation of the antigen was also considered to be a route of hyposensitization (6). The subjects studied possibly ingested or inhaled urushiol, since they breathe fumes and particles produced by sanding lacquer.

In summary, we performed urushiol patch tests on subjects learning the art of lacquerware before and after contact with lacquer, and confirmed the hypothesis from our questionnaire that Japanese lacquer craftsmen developed hyposensitization to urushiol after prolonged continued exposure to lacquer. At present, the exact mechanism of hyposensitization is unknown. To pursue the mechanisms of this phenomenon is very meaningful, since it may be utilized in the treatment of ACD.

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