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# Contact Urticaria from Rubber Gloves

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Contact urticaria was considered rare in dermatological practice until recently, when increases in knowledge of the eliciting agents and the pathomechanism made it possible to classify contact urticaria into two main types: immunological and nonimmunological.<sup>13</sup> The most common immunological urticaria is that mediated by IgE. In particular, allergens of animal and plant origin penetrating intact or diseased skin can evoke local and even systemic urticarial reactions in previously sensitized individuals.<sup>4, 8, 9, 12, 15, 17</sup> The diagnosis may easily be missed because many affected persons mention recurrent immediate symptoms on the hands such as itching, tingling, and redness but paradoxically present with chronic hand eczema. Therefore, the terms "contact urticaria syndrome"<sup>17</sup> or "protein contact dermatitis"<sup>9</sup> have been generally accepted for these cases. The increasing number of eliciting environmental agents includes such food proteins as egg, flour, meat, vegetables, fruits, and spices and such allergens from animals as hair, saliva, and placenta.<sup>13</sup> In agreement with this finding, occupational contact urticaria seems to be fairly common in kitchen personnel handling various foods<sup>9</sup> and in veterinary surgeons working with cattle or pigs.<sup>10, 21, 22</sup>

A new potential contact urticaria agent emerged in 1979, when Nutter described a housewife who experienced skin irritation from rubber cleaning gloves and who was shown by skin testing to have contact urticaria.<sup>20</sup> The case of a female nurse with contact urticaria from surgical rubber (latex) gloves, observed by

Förström<sup>6</sup> called attention to the occupational problems elicited by this allergy. Several similar cases have since been reported, and it can be expected that increasing awareness and better diagnostic facilities will reveal many new cases. The supposition that the immediate allergen in rubber gloves is a protein derived from the rubber tree *Hevea brasiliensis* that persists after glove manufacture seems obvious but has not yet been proved.<sup>2, 18, 25</sup> The present report summarizes the available clinical findings on rubber-glove contact urticaria and presents data on its prevalence and diagnostic evaluation.

## FREQUENCY

Table 1 lists the first reported cases of rubber-glove contact urticaria. The list includes cases associated with both cleaning and surgical gloves, and therefore the persons at risk seem to be those using rubber gloves for personal protection in cleaning work or medical personnel using surgical gloves.<sup>1-3, 5, 14, 16, 23, 24</sup> The increasing number of medical employees allergic to surgical gloves indicates that the incidence is higher than previously suggested. Frosch and associates described three operating-room instrument nurses,<sup>5</sup> Carillo and co-workers one physician<sup>2</sup> and Wrangsjö and associates one surgeon<sup>25</sup> with immediate allergy to surgical gloves.

In order to examine the frequency of immediate surgical-glove allergy and to identify the risk groups in our hospital, we performed skin

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This study was supported by a grant from the University Central Hospital, Tampere, Finland.

Table 1. *Reported Cases of Rubber-Glove Contact Urticaria*

| AUTHOR                              | PROFESSION     | GLOVE TYPE | HAND SYMPTOMS           |                |
|-------------------------------------|----------------|------------|-------------------------|----------------|
|                                     |                |            | <i>Acute</i>            | <i>Chronic</i> |
| Nutter <sup>20</sup>                | Housewife      | Cleaning   | Itching<br>No urticaria | Eczema*        |
| Förström <sup>6</sup>               | Instr. nurse   | Surgical   | Urticaria               | None           |
| Galinsky and Kleinhans <sup>7</sup> | Housewife      | Cleaning   | Urticaria               | Eczema*        |
| Meding and Fregert <sup>15</sup>    | Orderly        | N.g.†      | Urticaria               | Eczema*        |
|                                     | Lab. assistant | Surgical   | Urticaria               | None           |
|                                     | Cleaning woman | N.g.       | Urticaria               | None           |
|                                     | Surgeon        | Surgical   | Urticaria               | None           |
| Ketel <sup>11</sup>                 | Instr. nurse   | Surgical   | Urticaria               | Eczema*        |
| Turjanmaa et al <sup>21</sup>       | Nurse          | Surgical   | Urticaria               | None           |
|                                     | Nurse          | Surgical   | Urticaria               | None           |

\*Preceding contact urticaria

†N.g. = glove type not given

tests on 512 employees who used either rubber or vinyl gloves.<sup>23</sup> Twenty-three employees were suspected, and fifteen (2.9 per cent) were confirmed with prick tests, to be allergic to surgical rubber gloves (Table 2). The highest prevalence was found in operating units, where 6 per cent of the employees tested were allergic; the frequency was lower in nonoperating units and laboratories. In the main surgery unit, two of the 31 physicians (6.5 per cent) and three of the 23 instrument nurses (12.5 per cent) were allergic (Table 3). In contrast, none of the 14 nurse anesthetists or 19 other employees in this unit were allergic to surgical gloves. Interestingly, among 44 medical students examined with skin tests, we found one (2.3 per cent) who had a relevant history of immediate glove allergy, and among 130 controls we found one person (0.8 per cent) with a similar history (Table 2). These prevalences show that the immediate rubber-glove allergy frequency can be 6 per cent in a selected group of hospital personnel using surgical gloves and as high as 1 per cent in a group of individuals suspected

for atopy and admitted for routine prick testing.

In agreement with our data from Finland, Nilsson found four cases of rubber-glove contact urticaria among 142 selected hospital employees in Sweden (2.8 per cent).<sup>19</sup> Rubber-glove contact urticaria can also be detected incidentally among patients suspected of contact dermatitis and admitted for patch testing. During a 10-year period in an occupational outpatient clinic, Estlander and coworkers observed 68 patients with a delayed type of rubber-glove allergy and two patients who had contact urticaria from these gloves.<sup>3</sup>

## SYMPTOMS

Most patients with rubber-glove contact urticaria experience itching, redness, and wheal and flare reactions at the site of glove contact (Table 1). These symptoms appear very soon, 5 to 20 minutes after putting on the gloves, and disappear without any treatment in 1 to 2 hours. The symptoms are similar for cleaning and surgical gloves, and patients may have symptoms from both kinds of glove. The patients are soon aware of the skin irritation from the gloves, but they frequently suspect that glove powder or hand washing, not the rubber, causes the symptoms.<sup>1, 23</sup> Rubber-glove contact urticaria may also easily escape diagnosis because many patients exhibit signs of hand eczema (Table 1). It is not known whether this eczema is a consequence of repeated urticarial lesions being rubbed and scratched, whether it is a separate irritant hand eczema, or whether both mechanisms are involved. However, two of the present five employees suffered from hand eczema before urticaria appeared (Table 3), indicating

Table 2. *Frequency of Surgical-Glove Allergy Among Hospital Personnel,\* Medical Students, and Controls*

|                        | SCRATCH-<br>CHAMBER<br>TEST POSITIVE<br>(%) | PRICK TEST<br>POSITIVE<br>(%)† | USE TEST<br>POSITIVE<br>(%) |
|------------------------|---------------------------------------------|--------------------------------|-----------------------------|
| Employees<br>(n = 512) | 23 (4.5)                                    | 15 (2.9)                       | 14 (2.7)                    |
| Students<br>(n = 44)   | 2 (4.5)                                     | 1 (2.3)                        | 1 (2.3)                     |
| Controls<br>(n = 130)  | 2 (1.5)                                     | 1 (0.8)                        | 1 (0.8)                     |

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†Regarded as true positives

Table 3. *Clinical and Laboratory Findings in Surgical-Glove Allergic Patients Working in the Operating Unit of Main Surgery*

| CASE         | AGE/SEX | YEARS IN PROFESSION | DURATION OF SYMPTOMS      |                             | LATEX GLOVE TEST* |     |     | PRICK TEST WITH 20 COMMON INHALANT ALLERGENS |
|--------------|---------|---------------------|---------------------------|-----------------------------|-------------------|-----|-----|----------------------------------------------|
|              |         |                     | Contact Urticaria (years) | Chronic Hand Eczema (years) | P                 | U   | R   |                                              |
| Surgeon      | 50/M    | 23                  | 10                        | 10                          | Pos               | Pos | Pos | Pos                                          |
| Anesthetist  | 41/M    | 15                  | 3                         | 20                          | Pos               | Pos | Pos | Pos                                          |
| Instr. nurse | 43/F    | 22                  | 8                         | 17                          | Pos               | Pos | Neg | Neg                                          |
| Instr. nurse | 48/F    | 20                  | 8                         | 8                           | Pos               | Pos | Neg | Neg                                          |
| Instr. nurse | 43/F    | 22                  | 17                        | 17                          | Pos               | Pos | Neg | Neg                                          |

\*P = Prick test, U = Use test, R = RAST test

that glove-contact urticaria may develop on eczematous hands.

The contact urticaria syndrome includes a broad symptom spectrum with cutaneous and extracutaneous reactions.<sup>13</sup> The patients may also have generalized urticaria, facial edema, rhinitis, and respiratory symptoms including dyspnea and asthmatic attack. One atopic woman among the 44 medical students we examined had a severe attack of laryngeal edema with dyspnea less than 5 minutes after rubbing her face with surgical latex gloves following the completion of a surgical procedure (Table 4).

Immediate rubber-glove allergic patients may be at serious risk if the allergy has passed undiagnosed and the sensitized individuals are examined or operated on by persons wearing these gloves. We have seen two nurses without previously diagnosed allergy who during cesarean section or delivery with a vacuum extraction developed anaphylactic reactions from surgical gloves worn by the obstetricians.<sup>24</sup> Moreover, Axelsson and associates described a dentist, examined by a gynecologist wearing surgical latex gloves, who immediately got generalized urticaria and dyspnea and lost consciousness.<sup>1</sup> She recovered with conventional treatment and was later confirmed to be allergic to rubber gloves.

## DIAGNOSIS

Only a few patients with rubber-glove contact urticaria present a typical history of immediate localized urticarial response; many merely complain of noncharacteristic sensations such as itching and burning or give a history of recurrent hand eczema. Therefore, the clinical history may not be very helpful in indicating whether the patient has contact urticaria. The alerted physician may use patch tests to exclude

contact dermatitis caused by rubber chemicals in the gloves but also needs tests to confirm immediate rubber allergy. Commercial skin and blood tests are becoming available but have not been evaluated in larger patient series.<sup>1, 5, 25</sup>

The diagnosis of contact urticaria can be confirmed in several different ways,<sup>12</sup> many of which have been used to examine for immediate hypersensitivity in rubber-glove allergic patients. However, care should be taken to interpret the results correctly and to avoid harmful, even life-threatening, test reactions.

## Skin Tests

The diagnosis of rubber contact urticaria has been established by open or occlusive application of glove pieces to either intact or slightly affected skin.<sup>5, 7, 11, 20</sup> In these tests, the glove pieces or skin should be moistened to permit the allergen to dissolve from the glove into the skin. False-negative as well as false-positive reactions may occur. If the test is negative, it should be repeated with a closed system.

To improve the penetration of the glove allergen into the skin, a scratch-chamber test can be performed. We found Finn Chambers<sup>26</sup> and moistened glove pieces placed over scratches made on the volar side of the forearm a convenient test procedure when screening hospital employees for the allergy.<sup>23</sup> However,

Table 4. *Generalized Symptoms Reported in Rubber-Glove Contact Urticaria*

| SYMPTOMS                     | REFERENCES     |
|------------------------------|----------------|
| Eyelid and facial edema      | 1, 3, 5-7, 18  |
| Rhinitis                     | 2, 3, 5, 6, 18 |
| Generalized urticaria        | 1, 5, 24       |
| Laryngeal edema              | Present report |
| Dyspnea and asthmatic attack | 1, 2, 24       |
| Anaphylactic reaction        | 1, 24          |

the test gave several false-positive reactions, and prick tests were needed to confirm the diagnosis (Table 2). We incubated both sterile and nonsterile glove pieces in saline at room temperature to dissolve allergen from the glove. The solution, which we then used in prick testing, was more reliable than the scratch-chamber test with glove pieces and as good as the use test with whole glove.<sup>23</sup>

The advantage of prick testing over scratch or open testing with glove material is that the test solution can be diluted, permitting the reactions to be observed in a dose-dependent way (K Turjanmaa, T Reunala; unpublished observations). Prick testing with diluted allergen solution also has a clear advantage if the patient has severe allergy; we have never observed generalized reactions during prick testing even if the patients had anaphylactic reactions from surgical gloves. In contrast, the use test with the whole glove on the hand may be dangerous. For example, we carried out the use test on an atopic kitchen worker suspected of glove allergy, who wore two different latex surgical gloves on her hands at the same time. The latex glove prick test responses were of the size of the histamine response and were followed by the use test. Because of intense itching, the gloves were removed from the patient's hands after 1 minute, whereupon severe local wheal and flare was seen. In 10 minutes, she developed generalized urticaria, facial edema, and dyspnea. She was conscious, but the systolic blood pressure was only 90 mm Hg. Epinephrine and intravenous cortisone were given, after which the patient recovered quickly, but the urticarial reaction on the skin lasted for 12 hours. Therefore, when a use test is performed, one should initially expose only one finger,<sup>1</sup> not a whole hand.

#### RAST and Prausnitz-Kustner Tests

The contact-urticaria allergen in rubber gloves is obviously a protein that causes a specific IgE-antibody response. We demonstrated IgE antibodies with the RAST technique in the serum of our two patients with anaphylactic reactions.<sup>24</sup> In agreement with a previous report,<sup>14</sup> a Prausnitz-Kustner test was positive with both of our patients' sera. The latex RAST test has also been used by other investigators: all three contact urticaria patients examined by Frosch and associates<sup>5</sup> and five patients studied by Axelsson and coworkers<sup>1</sup> had positive results with RAST. In contrast, Wrangsjö and

colleagues<sup>25</sup> found only three positive cases among 15 patients suspected of having contact urticaria and only two of our five allergic patients had a positive result with latex RAST (Table 3). This suggests that the RAST test is not as sensitive as the prick test, but larger series are needed to confirm this finding. We have used freshly prepared discs made from either the glove incubation solution or the sap or leaf of the rubber tree. All these RAST discs seem to function similarly. The commercial RAST test now available (Latex, k82; Pharmacia Diagnostics, Uppsala, Sweden) gave comparable results in our patients with contact urticaria (K Turjanmaa, F Björkstén, T Reunala; unpublished observations).

Carillo and associates have tried to characterize the glove allergen. They found that the molecular weight is greater than 30,000 daltons, that the allergen is trypsin sensitive, and that the histamine release assay detects IgE antibodies in patient serum.<sup>2</sup>

#### PREDISPOSING FACTORS AND PROPHYLAXIS

Atopy seems to be a predisposing factor for rubber-glove contact urticaria. Many of the patients reported in the literature suffered from atopic diseases, and in our series of 15 hospital employees allergic to rubber gloves, ten (67 per cent) were atopic, a significantly higher prevalence than the 24 per cent observed in nonallergic employees.<sup>23</sup> The allergic employees also had history of hand eczema more often than did the controls, suggesting that this also, may predispose to rubber contact urticaria.

It seems clear that cleaning and surgical work are risk occupations for rubber-glove contact urticaria. Interestingly, we found no correlation between the duration of glove use and occurrence of allergy in our hospital employees;<sup>23</sup> some were sensitized during the first years of employment, whereas others observed glove irritation only after several years at work (Table 3). We also found one allergic medical student who had only briefly been exposed to surgical gloves (Table 2). However, she had a persisting atopic hand eczema, which could have contributed to early sensitization. A concomitant delayed allergy to rubber chemicals has been found in only a few cases of contact urticaria. Two patch-tested patients were allergic to thiuram mix<sup>11, 23</sup> and one to PPDA,<sup>25</sup> suggesting that no close relation exists between immediate and delayed rubber-glove allergy.

The need for prophylaxis of rubber-glove contact urticaria reactions depends on the profession and the sensitivity of the allergic person. Six of the 14 surgical-glove allergic employees in our hospital found latex gloves that produced no reaction, and eight had begun using plastic or cotton undergloves to avoid local symptoms.<sup>23</sup> These employees included one surgeon and three instrument nurses who, with these prophylactic measures, could continue their work in the operating theater. People doing nonsurgical or cleaning work can easily switch to vinyl gloves, which hardly ever cause any problem more serious than skin irritation.<sup>3</sup> In laboratories, the demand for protection against human immunodeficiency virus infection by employees handling blood samples increases glove consumption, and for such purposes, nonsensitizing vinyl gloves also can be recommended.

The reported frequent occurrence of immediate rubber-glove allergy among hospital personnel focuses attention especially on the manufacture of better surgical rubber gloves. To our knowledge, all of these gloves are made from natural rubber latex, and all brands we have tested have caused allergic symptoms, at least in some sensitized individuals. One brand may naturally give fewer symptoms than another, and, in agreement with this view, several of our allergic employees could tolerate one glove brand but not others. Better characterization of the sensitizing allergen in the gloves and knowledge of its persistence after manufacture is required before recommendations can be made about which gloves should be worn for surgical work.

#### ACKNOWLEDGMENT

The authors thank Mrs. Leena Petman for her skillful assistance in allergological testing.

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