STUDY

A Topical Cream Containing a Zinc Gel (Allergy Guard) as a Prophylactic against Latex Glove–Related Contact Dermatitis

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Background: Many health care workers are sensitized to the proteins in natural rubber latex and get contact dermatitis as a result of wearing latex gloves.

Objective: The aim of the study was to evaluate a topical formulation containing a zinc gel (Allergy Guard) as a prophylactic against latex glove–related contact dermatitis.

Methods: The study was carried out with volunteers who exhibited mild to moderate contact dermatitis (type IV) after wearing latex gloves as per the protocol.

Results: Allergy Guard significantly reduced skin irritation in volunteers who exhibited type IV hypersensitivity when exposed to latex gloves. Allergy Guard also exhibited a barrier effect as shown by the permeation of chlorophyllin dye into the skin of volunteers. Allergy Guard prevented dermal irritation induced by sodium lauryl sulfate.

Conclusion: Topical formulations containing a zinc gel may be used to delay or prevent latex sensitivity, especially among health care professionals.

WIDESPREAD USE OF LATEX GLOVES by health care workers has resulted in an increase in the incidence of dermal irritant reactions and sensitization to latex among these workers. It has been reported that up to 17% of health care workers are sensitized to natural rubber latex allergens.[1–9] Two types of irritant reactions to latex products are known: type I (immediate hypersensitivity) and type IV (delayed hypersensitivity). Type I is immunoglobulin E (IgE) mediated and includes localized urticaria (stage 1), angioedema (stage 2), asthma (stage 3) and anaphylaxis (stage 4). Immediate itching and urticarial wheals are the most common manifestations of a dermal response to natural proteins from latex gloves.[10–12] Type IV hypersensitivity reactions are mainly due to the chemicals added to the gloves during manufacturing.[13,14] However, type IV reactions can also occur from raw latex without added chemicals.[15–17] This may be due to direct skin contact with latex protein.[16] Type IV hypersensitivity is not usually a serious condition since it resolves when the person stops wearing the gloves. However, there have been reports of anaphylactic reactions to latex in persons who previously had experienced only contact dermatitis.[10]

Skin breakdown secondary to the contact dermatitis during surgical procedures may allow latex antigen to enter the systemic circulation, leading to the development of latex-specific IgE.[14,17] More than half of latex-sensitive health care workers in one study reported a history of hand dermatitis before the development of contact urticaria and systemic reactions[18]; hence, prevention of the initial onset of irritant contact dermatitis from exposure to latex gloves is critical.

One method of preventing contact dermatitis is avoiding repeated contact with the protein and chemicals in the glove that can cause skin sensitization.[15,16] Skin protectant creams are frequently applied by health care workers when latex gloves are used. However, the protective effect of such creams has not been thoroughly investigated. In fact, a study conducted by Baur and colleagues[15] showed that skin protectant creams may favor the uptake of irritants from gloves, thus increasing dermal reactions.[10]

Zinc salts have been shown to have antiinflammatory and antiirritant properties and to affect skin integrity.[19–22] We have developed a zinc gel (consisting of zinc gluconate, other zinc salts, and a hydrogel) for use in topical formulations. Allergy Guard (VSP Technologies, Inc.,

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Ossining, NY), a topical cream containing the zinc gel, was prepared and evaluated for its antiirritant effectiveness. In our preliminary evaluation in a small number of volunteers, Allergy Guard significantly reduced latex glove–related irritant dermatitis.[23] In this study, we evaluated the protective effect of the zinc gel, incorporated in Allergy Guard, in a large number of volunteers who exhibited latex glove–related contact dermatitis when not using the zinc gel. We also studied the efficacy of Allergy Guard in preventing the permeation of irritants through the skin and in preventing irritant contact dermatitis induced by sodium lauryl sulfate (SLS).

Materials and Methods

Allergy Guard and the placebo cream were supplied by VSP Technologies, Inc., Ossining, NY. Allergy Guard contains 5.2% of the zinc gel in a hydrophilic base. The placebo cream was the same as Allergy Guard except that it did not contain the zinc gel. The zinc gel is a complex of zinc gluconate, other zinc salts, and a hydrogel in water.

Derma-Safe Barrier Cream (General Physiotherapy, Inc., St. Louis, MO), Uni Salve Protective Barrier (Smith & Nephew, Largo, FL), and Proguard Protective Hand Cream (Curtin Matheson Scientific Inc., Houston, TX) were the commercial barrier creams used. Powdered latex gloves and powder-free gloves were obtained from Baxter Health Care Corporation, Valencia, CA.

Test of Prophylactic Effect of Allergy Guard against Latex Glove-Related Contact Dermatitis

A total of 22 volunteers participated in this study. Individuals who exhibited mild to moderate irritant contact dermatitis after wearing powdered or powder-free latex gloves were recruited for this study after personal interviews. Health care workers who are more likely to have direct skin contact with gloves can develop irritant contact dermatitis or itchy scaly skin, which is a delayed type IV reaction to latex.[17] These individuals have no other symptoms of latex allergy, and their dermatitis resolves when they stop wearing gloves. The volunteers selected for this study belonged to this group. Individuals with type I hypersensitivity were not included in this study because such a reaction may result in serious injury.

Study Protocol

The evaluation of Allergy Guard was performed in the Department of Surgery, Columbia University, under the approval of the Institutional Review Board of Columbia Presbyterian Medical Center. The study was carried out among volunteers at their own work sites or in one of the laboratories of the Department of Surgery. The gloves were worn until there was a skin reaction or for 3 to 4 hours, depending on the volunteer's activity.

Group A (Allergy Guard on the right hand and placebo cream on the left hand) consisted of 10 volunteers who used powdered gloves. Each volunteer applied 3 cc of the Allergy Guard on the right hand and 3 cc of the placebo cream on the left hand and waited until the cream dried (30–60 seconds) before donning gloves. To apply the cream to both hands up to the wrists, the volunteer wore a vinyl glove on the left hand and used this gloved hand to rub Allergy Guard onto the right hand. A latex glove was then put on the right hand, and the vinyl glove on the left hand was removed and discarded. Because two creams were being tested on the volunteer at the same time, the volunteer placed a vinyl glove on top of the latex glove on the right hand, to which Allergy Guard had been applied. This vinyl-gloved right hand was then used to apply placebo cream to the left hand. The left hand was then covered with a latex glove, and the vinyl glove on the right hand was removed and discarded. The latex gloves were worn until the volunteer felt a noticeable reaction occurring on the skin surface under the glove or until up to 3 to 4 hours had passed. The glove was then removed, and one or more of the investigators examined the hand and noted the reaction.

Group B (Allergy Guard on the left hand and no cream on the right hand) consisted of 10 volunteers who used powdered gloves. Each volunteer applied Allergy Guard to the left hand and no cream to the right hand. The same procedure used by study Group A was used for applying the cream and examining the reactions.

Group C (Allergy Guard on the left hand, no cream on the right hand, and powder-free gloves on both hands) consisted of two volunteers. The procedure for the application of cream and examination of the skin was the same as that described for Group A.

The following scoring system was used for the evaluation of skin reactions from contact with latex gloves: 0 = no visible reaction; 1 = mild itching and redness on more than 1 cm^2 within 30 minutes; 2 = moderate itching and redness on more than 1 cm^2 with or without papules within 30 minutes; 3 = severe itching, redness, and papules all over the hand within 30 minutes.

Test of the Effect of Allergy Guard on the Inactivation of Latex Proteins

Latex gloves were chopped into small pieces. To remove soluble latex proteins, 10 g of latex pieces were suspended

in 100 mL of distilled water and the proteins extracted over a span of 2 hours at 37°C. The extract was then centrifuged, and the supernatant was separated and treated with ammonium sulfate to a saturation of 40% salt. At this saturation, the additives in the latex rubber coagulated and separated as a solid mass. The supernatant that contained the soluble protein was separated from the solid mass. Six aliquots of 5 mL (equivalent to 0.5 g of glove) of this supernatant protein extract were removed. To three of these aliquot portions, 5 mL of water was added; to the other three aliquot portions, 5 mL of aqueous solution containing 1.0 g of Allergy Guard was added. The control used was 10 mL of water containing 1 g of Allergy Guard. These samples were held at 37°C for 2 hours. All the solutions were then centrifuged, and the clear supernatants were removed. The protein concentration in the supernatant was measured at 280 nm with a Hitachi U-2000 ultraviolet (UV) spectrophotometer (Hitachi High Technologies America, San José, CA). Albumin solution was used as the standard.

The ratio of glove extract to Allergy Guard is based on the recommended use of 3 g of Allergy Guard applied to the hands. In clinical use, only a small amount of soluble protein will be released from the inner surface of a glove (0.05 mg of protein per gram of glove). This protein will come into contact with the Allergy Guard applied to the hand (0.2 g of cream per gram of glove). The soluble protein release from an intact glove was measured in a previous study, during which 30 mL of saline was added to a glove and incubated at 37°C for 2 hours. In the current study, 10 g of a glove was chopped into small pieces and extracted at 37°C for 2 hours.

Since both surfaces and the chopped edges of the glove were extracted, the amount of soluble protein released may be significantly larger than that released in the normal wearing of gloves. Therefore, a greater proportion of cream to glove extract was used (2 g of cream per gram of glove).

Test of the Barrier Effect of Allergy Guard and Other Creams

This test was carried out as a model to determine the efficacy of various creams in preventing the permeation of irritants into the skin. Six volunteers participated in this study. Placebo cream (control), Allergy Guard, and three commercially available barrier creams were evaluated on each volunteer.

The volunteers washed their forearms with plain soap and water and dried them thoroughly before applying the cream; 0.1 cc of each test product was then spread over a 4 × 4 cm area and allowed to dry for 5 minutes. A 3 × 3 cm piece of paper towel dipped in a 1.5% solution of chlorophyllin was placed centrally on the 4 × 4 cm area treated with the creams and was occluded with plastic wrap and taped in place at the edges. All the test and control cream groups were tested on each volunteer (two test groups on the left forearm and two test groups and 1 control group on the right forearm).

After 4 hours, the occluding plastic and the paper towel square were removed, and the site was wiped with a dry paper towel to completely remove the cream. The skin was then observed for the presence of staining by the chlorophyllin. Staining would indicate that permeation through the cream had occurred. The coloration of the skin was scored as follows: 0 = no color (no permeation); 1 = slight coloration; 2 = moderate coloration; 3 = heavy coloration.

Test of Allergy Guard's Effect against SLS-Induced Dermal Irritation

This test was carried out in an independent laboratory. A total of 14 volunteers participated. Allergy Guard (1.0 cc) was applied randomly to the forearms of volunteers at two locations, so as to cover an area of 4 × 4 cm, and was allowed to dry for 15 minutes. Wet absorbent occlusive dressings wetted with SLS solution were applied over one of the areas covered with Allergy Guard and over a control area (bare skin without any cream applied). One area where Allergy Guard was applied was left untreated with the SLS solution. The reaction (if any) on the skin was scored after 24 and 48 hours. Occlusive dressings were used for worst-case conditions.

The following scoring system was used for the evaluation of the skin reactions: 0 denoted no visible reaction; ± denoted barely perceptive erythema; 1+ indicated mild erythema; 2+ indicated well-defined erythema; and 3+ indicated erythema and edema.

Results

Prophylactic Effect

Table 1 shows the scores of the skin reactions on the hands of volunteers in the various groups. Twenty-one of the 22 volunteers who applied Allergy Guard had no reaction whereas 1 volunteer had a mild reaction. In the control group, 10 volunteers used placebo cream and 12 volunteers used no cream under the glove. One person in each control group had no reaction; all the other 20 volunteers had mild to moderate reactions (scores of 1–2).

Table 1. Skin Reaction Scores of Volunteers Wearing Latex Gloves with and without Allergy Guard

Volunteer Group and Glove Type (N)	*Cream (Hand)*	*Skin Reaction Score**†		
		2	*1*	*0*
A, powdered glove (10)	Placebo‡ (left)	3	6	1
	Allergy Guard§ (right)	0	1	9
B, powdered glove (10)	Allergy Guard§ (left)	0	0	10
	None‡ (right)	5	4	1
C, powder-free glove (2)	Allergy Guard§ (left)	0	0	2
	None‡ (right)	1	1	0

N = number of volunteers.
*Column values represent the number of volunteers with each skin reaction score.
†Skin reaction scoring system: 0 = no visible reaction; 1 = mild itching and redness on > 1 cm^2 within 30 minutes; 2 = moderate itching and redness on > 1 cm^2 with or without papules within 30 minutes.
‡Reaction within 5 to 30 minutes.
§No reaction for 3 to 4 hours after glove was removed.

Inactivation of Latex Proteins

The effect of Allergy Guard in regard to the inactivation of proteins is shown in Table 2. The untreated latex glove protein extract had a protein content of 1.14 mg per gram whereas the latex protein extract from a glove treated with Allergy Guard had a protein content of 0.28 mg per gram. Allergy Guard reduced the latex protein in the extract by about 74.7%.

Barrier Effect

The color intensity of the dye penetrating through the various creams is indicated in Table 3. The color intensity score of the skin where Proguard and Derma-Safe were applied was the same as that for the control (2.5) whereas that for the Uni Salve group was 1.0. The skin where Allergy Guard was applied showed no coloration.

Table 2. Protein Content of Latex Glove Extract Untreated and Treated with Allergy Guard

Latex Glove Extract	*Protein Concentration (mg/g of Glove)*			
	Aliquot 1	*Aliquot 2*	*Aliquot 3*	*Mean*
Untreated	1.16	1.00	1.24	1.14
Treated with Allergy Guard	0.26	0.24	0.36	0.28

Table 3. Effect of Various Creams in Preventing Penetration of Chlorophyllin Dye

Test Product	*Mean Color Intensity Score* (N = 6)*
Allergy Guard	0
Derma-Safe	2.5
Uni Salve	1.0
Proguard	2.5
Control (no cream)	2.5

N = number of volunteers.
*Scoring system: 0 = no color (no permeation); 1 = slight coloration; 2 = moderate coloration; 3 = heavy coloration.

Effect against SLS-Induced Dermal Irritation (SLS Challenge Test)

In the group that applied SLS alone, skin reactions were seen in 92.9% of the volunteers in 24 hours and 100% of the volunteers in 48 hours. In the group treated with SLS over Allergy Guard, 100% of the volunteers had no reaction in 24 hours, and 28.6% of the volunteers had a mild reaction after 48 hours. No volunteers in the group that used Allergy Guard alone had a reaction (Table 4).

Discussion

The topical cream containing zinc gel (ie, Allergy Guard) was found to prevent skin reactions resulting from SLS contact (see Table 4). This result indicates that Allergy Guard may reduce irritation caused by surfactant/foaming agents used in the gloves' manufacture, similar to the reduction seen against SLS.

It was also demonstrated that Allergy Guard inactivates the latex proteins (see Table 2). In this experiment, 1.0 g of Allergy Guard cream was added to the extract from 0.5 g of chopped glove (2.0 g of cream per gram of glove), which is 10 times more than the ratio of cream to glove weight that would normally be used. As shown in Table 2, the extract of an untreated chopped glove contained 1.14 mg of protein per gram of glove, which is about 23-fold higher than the amount of protein expected to be released when a glove is worn (0.05 mg of protein per gram of glove). Even at this ratio of protein to Allergy Guard, a 74.7% reduction in protein was noted (see Table 2). Therefore, the amount of Allergy Guard applied to the hands may be sufficient to produce a similar inactivation of the proteins and reduce latex protein–related skin reactions in clinical situations. Most

Table 4. Effect of Allergy Guard against Sodium Lauryl Sulfate–Induced Dermal Irritation (Percentages of Volunteers with Each Dermal Score)

		Dermal Score (N = 14)*				
Tested Cream	*Test Hours*	*0*	*±*	*1+*	*2+*	*3+*
SLS challenge alone	24	7.1%	28.6%	28.6%	35.7%	0%
	48	0%	14.3%	21.4%	50.0%	14.3%
Allergy Guard with SLS challenge	24	100%	0%	0%	0%	0%
	48	71.4%	14.3%	14.3%	0%	0%
Allergy Guard alone	24	100%	0%	0%	0%	0%
	48	100%	0%	0%	0%	0%

N = number of volunteers; SLS = sodium lauryl sulfate.
*Scoring system: 0 = no visible skin reaction; ± = barely perceptive erythema; 1+ = mild erythema; 2+ = well-defined erythema; 3+ = erythema and edema.

important, Allergy Guard appears to reduce latex glove–associated contact dermatitis when used prophylactically (see Table 1).

The irritant dermatitis resulting from skin contact with latex gloves may be due to soluble latex proteins leached from the glove as well as to other chemicals used in the gloves' manufacture. It has been reported that approximately 5% of the finished glove's weight represents chemicals added during manufacturing, and these chemicals may be responsible for some delayed type IV reactions.[10]

In addition to interacting with the soluble protein, the zinc gel in the Allergy Guard cream may also act as a barrier to other chemicals in latex gloves. An experiment using chlorophyllin dye as a marker to determine the barrier effect of Allergy Guard as compared with other barrier creams was carried out. Evaluation of the degree of penetration of chlorophyllin dye to the skin through various barrier creams showed that only Allergy Guard prevented the permeation of the dye, indicating a barrier effect of the zinc gel between the irritants and the skin.

To reduce the risk of irritant dermal reactions from latex proteins adsorbed on starch powder, powder-free gloves have been manufactured and are being increasingly used. However, these gloves do not provide a safe alternative for people who are sensitive to latex proteins and glove chemicals.[10] Another option is the use of vinyl gloves, which are not as effective a barrier as latex gloves.

While topical formulations containing antihistamines or corticosteroids are used to treat dermal irritation, the routine use of these compounds as prophylaxis or as treatments of latex or starch allergies is not recommended.

Zinc oxide and zinc acetate are used in topical skin formulations. For example, creams containing zinc oxide at high concentrations (20–40%) are used as skin protectants. Compositions containing readily soluble zinc acetate (1–2%) combined with antihistamines have been used to treat local itching topically (eg, Benadryl Itch Relief cream [Pfizer, New York, NY]). Zinc salts are known to bind proteins and prevent skin irritation.[18,23]

Since glove-related contact dermatitis is the manifestation of skin sensitivity to natural proteins and other ingredients associated with latex gloves,[10–12] we investigated the effect of lower concentrations of various zinc salts, either alone or in combination, for efficacy in preventing irritant dermatitis when used prior to donning latex gloves. Several organic and inorganic zinc salts were evaluated.

It was found that zinc gluconate (which forms a gel under certain conditions) in combination with small amounts of soluble zinc salts (zinc gel) appears to exhibit antiirritant properties. The zinc gel contains minimum concentrations of zinc salts that are needed to render Allergy Guard a prophylactic cream against latex glove–related dermatitis. This zinc gel composition was incorporated into a cream base containing special emollients (Allergy Guard) and was evaluated on volunteers who exhibited mild to moderate skin irritation after wearing latex gloves. In our study on the prophylactic effect of Allergy Guard, 19 of 20 volunteers who used either placebo or no cream under the glove showed mild to moderate skin irritation whereas only 1 of 22 volunteers who used Allergy Guard prior to donning the gloves exhibited skin irritation. The protective effect of Allergy Guard does not appear to be a mere barrier effect since the placebo group did not show any protective effect. It appears that upon application, Allergy Guard forms a protective gel matrix that prevents contact between the skin and the irritants when the gloves are donned. Furthermore, the small amount of zinc ions released from the zinc salts present in Allergy Guard may bind the soluble latex proteins and other irritants, thus preventing their contact

and reaction with the skin. Allergy Guard appears to reduce glove-related dermatitis either from the soluble latex protein leached from the glove or from the chemicals added to the glove during manufacture.

Irritant contact dermatitis has been reported to result from the direct local cytotoxic effect on the cells of the epidermis and a subsequent inflammatory response in the dermis.[17,24,25] It appears that the chemicals used in the gloves, as well as the soluble latex proteins, acted as irritants and produced irritant contact dermatitis in the volunteers. Small amounts of zinc from Allergy Guard may bind to the epidermis or penetrate into the dermis, preventing these reactions. Furthermore, by preventing the interaction between the skin and the chemical and protein irritants leaching from the gloves, both simple cytotoxic and the more complex dermal responses to these irritants may be significantly reduced.

Conclusions

The results of this study indicate that the use of Allergy Guard may reduce latex glove–induced dermatitis or other chemical-related contact dermatitis. Our studies have also shown that Allergy Guard does not interfere with the action of antiseptic scrubs (unpublished data). It needs to be emphasized that Allergy Guard is not indicated for use as prophylaxis against immediate type I hypersensitivity. However, the prophylactic use of Allergy Guard may delay or prevent the onset of latex sensitivity, especially among health care workers who are continually exposed to latex.

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