

CONTACT DERMATITIS

ENVIRONMENTAL AND OCCUPATIONAL DERMATITIS

THE OFFICIAL PUBLICATION OF THE EUROPEAN SOCIETY OF CONTACT DERMATITIS



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VOL. 55 | NO. 1 | JULY 2006 BLACKWELL MUNKSGAARD

A randomized, controlled, double-blind study of the effect of wearing coated pH 5.5 latex gloves compared with standard powder-free latex gloves on skin pH, transepidermal water loss and skin irritation

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Hand dermatitis is a common occupational disease. Altered skin pH plays an important role in the development of skin irritation. A glove that maintains tight control over skin pH may reduce hand dermatitis in glove users. The purpose of the study was to characterize the effect of glove wearing on skin pH, investigate the impact of study glove on skin pH compared with standard gloves and determine whether wearing study gloves reduced irritation. 20 healthy volunteers enrolled in a 4-week double-blind comparison of study and control gloves and served as their own controls. Gloves were worn 8 hr per day for 5 days per week. Skin pH and transepidermal water loss were measured during and 2 days after the glove-wearing period. The subject and an observer assessed the skin for irritation. The study glove maintained lower skin pH than the control glove ($P < 0.05$) and trended towards having less irritation. Observers noted increases in dryness and scale in both hands after 4 weeks but significantly less dryness in the study hand at week 4 ($P = 0.006$). Glove wearing increased skin pH and dryness. The pH 5.5 glove maintained lower skin pH levels than the control glove and may reduce irritation in long-term glove wearers.

Key words: acid mantle; gloves; hand dermatitis; irritation; latex; pH. © 2006 The Authors. Journal compilation © 2006 Blackwell Munksgaard.

Accepted for publication 15 January 2006

Hand dermatitis remains one of the most common occupational diseases seen by dermatologists. The use of disposable gloves serves to protect the skin from potentially noxious agents; however, prolonged glove use has been linked to an increase in hand dermatitis (1, 2). While latex allergy plays an important role in glove-associated morbidity, the allergic component of contact dermatitis accounts for a small fraction of all clinical presentations of hand dermatitis secondary to latex glove use.

The majority of glove-induced clinical presentations of hand dermatitis are thought to be irritant type contact dermatitis. Previous studies have estimated irritant contact dermatitis occurrence to account for 93.2% of all presentations of hand dermatoses secondary to latex exposure, followed by contact urticaria (4.4%), and contact dermatitis associated with contact urticaria (2.4%) (3).

Gloves create an occlusive environment that may damage the skin barrier function and delay epidermal repair activities (4–6). Several factors of an occlusive environment contribute to the development of irritant contact dermatitis including altered temperature, increased sweating leading to skin maceration, damage to the stratum corneum and alkalization of the glove environment (7–10). Occlusion, independent of other factors, has also been shown to increase the pH of the skin (11, 12). In a study by Aly et al. (11) the pH of skin shifted gradually from 4.38 before occlusion to 7.05 after 4 days. The number of hours spent wearing gloves plays an important role in the occurrence of skin irritation, further suggesting a cumulative effect (6).

One of the integral mechanisms of skin protection, the acidic milieu of the stratum corneum, maintains skin surface at a relatively constant pH of 5.4–5.9 but can vary from 4 to 6 (13).

The compounds that help maintain the acidic environment of the skin surface are known as the natural moisturizing factors. In fact, the acid pH of skin is so important in skin protection that it has been termed the 'acid mantle'. Disruptions in the acid mantle contribute to irritant contact dermatitis (14). Therefore, variation in glove pH may be a highly responsible factor for skin irritation due to gloves (9).

Skin pH is affected by several factors including age, race, sebum, moisture, sweat, cosmetic products, soaps and detergents (15–18).

Changes in skin surface pH are closely related to surface barrier protection (17). It has frequently been shown *in vitro* that low extracellular pH is required to create the necessary environment for the processing of certain precursors to the non-polar lipids involved in formation and maintenance of the stratum corneum layer. Many of the enzymes involved in skin barrier formation, such as β -glucocerebrosidase, ceramides, acid lipases, phosphatases, phospholipases and stratum corneum gelatinase, are pH-dependent enzymes which are active in an acidic milieu (19). Several studies have shown that stripping the skin thereby damaging of the superficial layers of the skin results in increased surface pH (10, 11). It has been demonstrated *in vivo*, in both hairless mice and later in human skin, that the recovery of barrier function proceeds significantly faster when exposed to pH 5.5 buffer solutions than when exposed to a pH of 7.4 (19).

These changes are believed to contribute to the development of irritant contact dermatitis and possibly play a role in other conditions such as atopic dermatitis. Elevated pH plays a pathogenic role in primary irritant diaper dermatitis and has been significantly correlated with both its incidence and severity in infants (19). In adults, Wilhelm and Maibach demonstrated a significant correlation between skin surface pH and the severity of sodium lauryl sulphate-induced dermatitis (20). The observed correlation may be explained by lower lipid concentration, which occurs with rising pH, and a more hydrated stratum corneum, both of which would weaken the skin barrier.

The purpose of the study was to determine the effectiveness of the study glove in maintaining hand skin pH within physiological limits and the degree to which changes in skin pH affect skin irritation and damage in occluded hands.

Materials and Methods

20 healthy volunteers were included in the study (10 men and 10 women, mean age 36 years [range 23–53 years]). Subjects with known allergy to latex,

evidence of pre-existing hand dermatitis or other skin conditions affecting the hands were not included in the study. The volunteers were recruited from the general population. Many were graduate students or healthcare employees of Stanford University who used gloves regularly in their work. Informed consent was obtained from all participants prior to enrolment, and the Stanford University Administrative Panel on Human Subjects in Medical Research approved the study.

The study glove was a non-powdered natural rubber latex (NRL) glove, coated with chemicals designed to keep skin pH at 5.5. The study glove coating was comprised of citric acid and sodium citrate. A regular non-powdered NRL glove was used as the control.

Subjects were randomized to one of two groups at baseline. Both the subject and the physician grader were blinded as to which hand wore the study glove. Group 1 wore the study glove on the right hand and the control glove on the left hand. Group 2 wore the study glove on the left hand and the control glove on the right hand. Participants wore the gloves 8 hr daily, 5 days per week over a 4-week period. Subjects were instructed to wash their hands with a standardized gentle hand wash every 45 min to 2 h and subsequently wore new gloves after each washing. Subjects were not allowed to use moisturizers during the 8-hr period of glove use. Participants recorded the times and frequency of glove substitution in an individual compliance log collected at the completion of the study.

Evaluation was performed at 4 time-points, by means of transepidermal water loss (TEWL) and pH measurements, physician skin assessment and subject skin assessment. Measurements were taken prior to glove use (baseline), at week 2, week 4 and 2 days following discontinuation of glove use (end of study). 19 of the 20 subjects completed the study. 1 subject withdrew due to difficulty in scheduling appointments. The study was performed in the months of March and April 2005. Median ambient temperature was 22°C [range 20–25], and the relative humidity varied between 25 and 60%. Evaluation was performed with the following non-invasive methods.

pH

Skin surface pH was recorded with a flat surface electrode connected to a pH meter (SENTRON pH meter, ARGUS type, Roden, the Netherlands). The use of a planar electrode allowed for better contact between the probe and the skin surface. The pH meter was calibrated daily prior to measurement

with pH 4.0 and 7.0 standard buffers and stored in distilled water between measurements.

Two test sites were chosen for measurement of skin surface pH. The thenar eminence on the palmar surface of the hand and 1 cm proximal to the 3rd metacarpophalangeal joint on the dorsal surface of the hand were selected due to the observation that well-fitting occlusive gloves are often tightest at these sites, resulting in greater contact with the skin surface. A study of occlusive glove use by Held and Jorgensen (15) supports this observation. Measurements were taken by the same physician for all subjects throughout the duration of the study. A first reading was taken on each hand immediately following the removal of the gloves; a second reading was taken after a relaxation period of 15 min.

TEWL

TEWL is the passive diffusion of water through the stratum corneum and a useful indication of the effective barrier function of this layer. A VapoMeter (SWL₃ type, Delfin Technologies Ltd, Kuopio, Finland) was used to measure TEWL. Measurements were taken proximal to the 3rd metacarpophalangeal joint on the dorsal surface and the thenar eminence on the palmar surface as for pH. The probe was held on the skin for 10 seconds and the evaporation rate value given in grams per square meter per hour (g/m²/hr). TEWL readings were taken immediately after glove removal and following a 15-min relaxation period.

Physician assessment

Clinical assessment of skin irritation was made with respect to the predominant observable characteristics of chronic irritant contact dermatitis: erythema, roughness, dryness, scale and overall irritation (9). A score of 0–5 was given for each parameter (0 = none, 1 = trace, 2 = mild, 3 = moderate, 4 = severe and 5 = very severe).

Subject assessment

Subjects assessed each hand separately on a 0–5 scale with respect to the following parameters: redness, roughness, dryness, scale, itch and overall irritation. A score of 0–5 was given for each parameter (0 = none, 1 = trace, 2 = mild, 3 = moderate, 4 = severe and 5 = very severe).

Statistics

Data were tabulated using Microsoft Excel 2003 (Microsoft Corp., Redmond, WA, USA), and statistical analyses were carried out using SAS (SAS Institute Inc. Cary, NC, USA) and Analyse-it version 1.71 (Analyse-it Software Ltd, Leeds, UK).

Non-parametric tests were used to accommodate for a relatively small sample size. Mean pH values were calculated for the study and control arms at each time-point and location. The study glove pH values were compared with control values using the Wilcoxon signed rank test at each time-point and location. The Wald statistical test for paired observations was used to compare the experimental hand with the control hand for each participant across the entire range of values. Finally, a linear logistic model was created to determine the association of various factors with the pH measurements. A significance level of $P < 0.05$ was chosen.

Results

pH

At baseline, there was a significant difference between palmar pH (mean = 4.88) and dorsal pH (mean = 5.18). In both study and control groups, pH measurements were consistently higher on the dorsal surface of the hand than on the palmar surface ($P < 0.0001$) (Fig. 1).

Glove wearing led to a significant increase in pH in study and control groups and at all time-points when compared with baseline levels ($P < 0.0001$). In the control group, at week 2, mean pH reached 5.58 on the palmar surface and 5.66 on the dorsum. At week 4, mean pH values remained elevated, at pH 5.37 and pH 5.65, on palmar and dorsal surfaces, respectively. The study glove demonstrated protective qualities (Figs 2 and 3). Despite an increase in pH values in both hands, skin surface pH of the study hand was significantly less alkaline and thus closer to physiological levels than control hand at both week 2 and week 4 ($P < 0.005$).

Cutaneous pH was re-measured 15 min after removal of the gloves. The changes in pH seen in the control group began to normalize after 15 min ($P < 0.001$), while study hand pH values remained constant (Fig. 4). These changes were seen at both week 2 and week 4 and were consistent between palmar and dorsal readings (Table 1). At

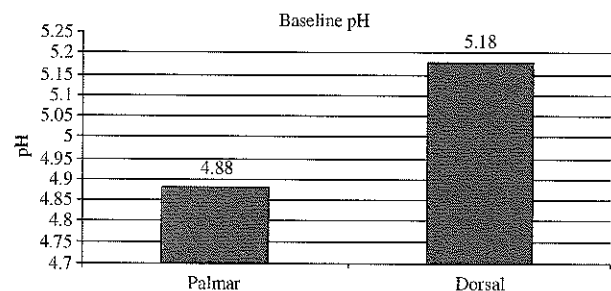


Fig. 1. Mean pH measurements taken prior to glove wearing as measured on palmar and dorsal hands.

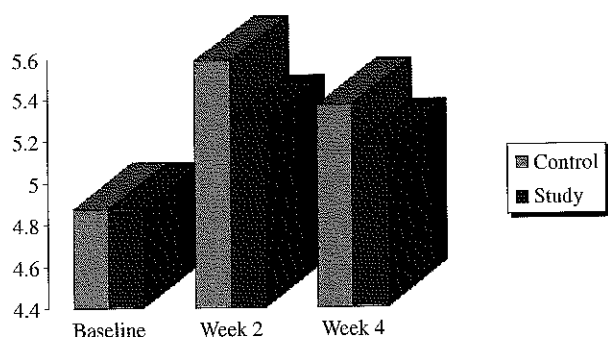


Fig. 2. Mean pH measurements taken from palmar hand at baseline, week 2, and week 4 visits for hand wearing control versus study glove.

the end of study, 2 days after wearing gloves, the pH of both groups remained elevated compared with baseline. At this time-point, no significant difference was seen between study and control groups.

TEWL

TEWL increased from baseline with glove use. In both control and study hands, TEWL values increased at week 2 and week 4 to a statistically significant level ($P < 0.0001$). This increase in TEWL was not maintained at 2 days following discontinuation of glove use, with values dropping to baseline levels by the end of study visit. Palmar TEWL was significantly higher than water loss from the dorsum of the hand in both study and control groups ($P < 0.0001$) (Table 2). As with pH, no significant difference in TEWL was appreciable between left and right hands.

Physician assessment

Physician assessed scores of dryness increased from baseline to week 4 in both groups ($P < 0.05$). Notably, at week 4, dryness scores in the study hand were significantly lower than the control ($P = 0.006$). Additionally, an expected increase in scale was seen in both groups ($P < 0.05$), corresponding to increased dryness (Tables 3 and 4).

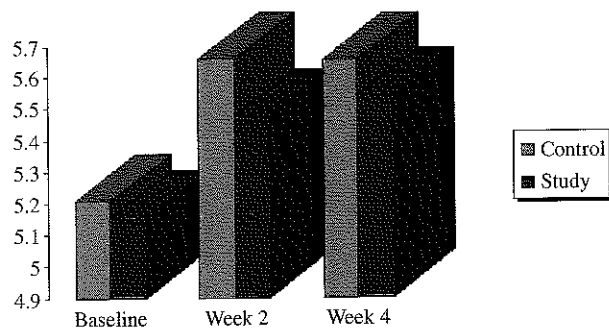


Fig. 3. Mean pH measurements taken from dorsal hand at baseline, week 2, and week 4 visits for hand wearing control versus study glove.

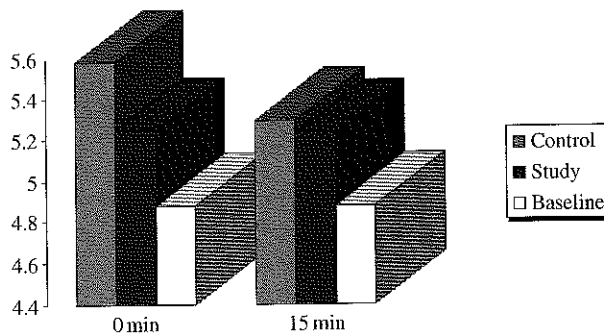


Fig. 4. Changes in mean skin pH measurements in palmar hand from immediately after removal of glove to 15 minutes after glove removal, and compared to mean pre-glove wearing baseline pH measurements.

There was no sizeable difference from baseline or study and control groups in physician-assessed levels of erythema, roughness or scale at weeks 2 and 4.

Scores for scale, dryness and roughness were consistently higher on the right hand than the left ($P = 0.003$, $P = 0.002$, $P = 0.007$, respectively).

Subject assessment

No significant difference was reported in the subject self-assessment with respect to dryness, itch, roughness, redness, scale or overall irritation between study hand and control hand. Additionally, there were no significant changes in any of these parameters in either group over the course of the study (Tables 5 and 6).

Discussion

The study illustrates that use of pH 5.5 gloves helped maintain skin surface pH nearer to physiological acidic levels than the control glove over a 4-week period. Standard glove use resulted in significant increases in skin pH and was associated with physician-assessed increases in skin dryness. Wearing the study gloves significantly lowered these adverse effects. The changes in

Table 1. Mean skin pH as measured on subject's hand comparing palmar with dorsal hands as well as control glove to pH 5.5 glove

	Palmar aspect		Dorsal aspect	
	pH 5.5 glove	Standard glove	pH 5.5 glove	Standard glove
Baseline	4.875	4.88	5.16	5.21
Week 2: T = 0 min	5.29	5.58	5.48	5.66
Week 2: T = 15 min	5.23	5.25	5.48	5.51
Week 4: T = 0 min	5.17	5.39	5.54	5.65
Week 4: T = 15 min	5.16	5.2	5.41	5.6
End of study	5.3	5.27	5.52	5.53

Skin pH at weeks 2 and 4 were measured immediately after glove removal (T = 0 min) and again 15 min after glove removal (T = 15 min).

Table 2. Mean transepidermal water loss as measured on subject's hand comparing palmar with dorsal hands and pH 5.5 glove to standard glove

	Palmar hand		Dorsal hand	
	pH 5.5 glove	Standard glove	pH 5.5 glove	Standard glove
Baseline	72.19	65.95	17.71	17.53
Week 2	112.24	103.48	40.71	37.06
Week 4	113.98	110.41	35.55	34.66
End of study	97.17	87.83	20.63	24.01

pH were by 2 weeks and persisted through the full 4 weeks of the study. They were most notable immediately after removal of the glove and then normalized somewhat during the first 15 min after the gloves were removed.

Past studies have shown elevated pH of the skin to cause irritation and may ultimately result in the development of dermatitis. This effect of increasing skin pH is thought to be caused by an increase in stratum corneum ion permeability allowing a neutralizing effect on the normally acidic skin surface. Thus, lower pH in study hand compared with control may signify less damage to the stratum corneum during glove usage. Impaired barrier function is one of the chief factors contributing to cutaneous sensitivity; thus, by maintaining stratum corneum integrity, the pH 5.5 glove may minimize irritant contact dermatitis associated with long-term latex glove use. Because many glove users wash their hands immediately after removing their gloves, there may be an increased sensitivity to irritation from soaps and detergents during this time period before the skin pH has had an opportunity to normalize.

TEWL measurements were higher than baseline in both study group and control group at week 2 and week 4. At the end of study visit, when gloves had not been worn for 2 days, TEWL measurements had returned to baseline values. These results may reflect an initial evaporation of sweat as a result of the hands being kept in an occlusive environment for an extended period of time. Previous studies have demonstrated that TEWL measurements after glove removal tend to be high during the first 2 min, regardless of other conditions. Subsequently, these values stabilize and are more representative of

Table 3. Mean grader assessment of control glove hands on a scale of 0-4

	Erythema	Roughness	Scale	Dryness	Overall irritation
Baseline	0.05	0.65	0.2	0.55	0.4
Week 2	0	0.47	0.39	0.74	0.47
Week 4	0	0.42	0.53	0.95	0.47
End of study	0	0.63	0.58	0.95	0.58

Table 4. Mean grader assessment of study glove hands on a scale of 0-4

	Erythema	Roughness	Scale	Dryness	Overall irritation
Baseline	0.05	0.55	0.15	0.6	0.4
Week 2	0.05	0.39	0.26	0.63	0.39
Week 4	0	0.42	0.42	0.68	0.42
End of study	0.05	0.63	0.58	0.79	0.53

skin barrier function (5). In this study, TEWL measurements were taken within the first 5 min of glove removal, and may have been effected by this period of rapid vapourization.

In physician assessment of irritation, dryness scores in study hands were less than control hands at the week 4. This may be indicative of long-term benefits of wearing of the pH 5.5 gloves in reducing dryness and possibly other parameters of irritation. A significant difference in dryness scores was not present between study and control groups at the end of study visit due to an improvement in control hand scores. The length of the study may not be adequate to demonstrate a statistically significant difference in other clinical parameters such as erythema, scaling and roughness. The difference noted between the left and right hands on physician scores may be attributable to effects of hand dominance and increased frequency of friction-causing activities such as writing; however, subjects were not queried as to hand dominance in this study.

In subject-assessed scores, subjects reported no significant differences between the gloves with respect to dryness, scale, roughness or erythema. One reason for this lack of difference may be that the subjects who enrolled in this study self-reported as having non-sensitive skin. It has been established in other studies that individuals with sensitive skin are more prone to symptoms of irritation with latex glove use than the general population and that the large majority of subjects who are self-diagnosed with latex allergy have more accurately experienced irritant contact dermatitis.

None of the participants developed clinical hand eczema during the course of the study. All of the subjects enrolled in this study were coincidentally self-assessed as non-sensitive at baseline, and those who believed themselves to have latex allergy were excluded from the study. This occurrence could have lowered the likelihood of seeing irritation, clinical eczema and differences in reported irritation between the two groups.

Prolonged glove use is often combined with frequent hand washing in wet work occupations. Rinsing of the skin with water alone produces a transient increase in skin pH (19). Work type was

Table 5. Mean subject self-assessment of skin irritation after wearing control glove on a scale of 0-5

	Dryness	Itching	Roughness	Redness	Scaling	Irritation
Week 2	2.37	0.84	1.47	0.21	0.68	0.79
Week 4	2.11	0.32	1.47	0.26	0.74	0.58
End of study	2	0.63	1.58	0.37	0.79	1.05

Table 6. Mean subject self-assessment of skin irritation after wearing study glove on a scale of 0-5

	Dryness	Itching	Roughness	Redness	Scaling	Irritation
Week 2	2.37	0.53	1.37	0.32	0.74	0.68
Week 4	1.95	0.63	1.47	0.26	0.74	0.68
End of study	1.9	0.47	1.21	0.26	0.58	0.63

not controlled for in this study; however, the majority of subjects were self-reported routine glove wearers. Furthermore, having subjects change gloves and wash their hands at a standard interval of 45 min to 2 h minimized variations in hand washing frequency. Another limitation of the study was that varying degrees of sweating were not controlled for when measuring TEWL.

In conclusion, the pH 5.5 gloves helped maintain lower levels of pH than the control glove and may contribute to reduced irritation in long-term glove wearers. We propose that further studies be done to establish the clinical effects of wearing pH 5.5 gloves including evaluating the use of these gloves in subjects with known hand dermatitis and sensitive skin.

Acknowledgement

Financial support for this study was provided by Shen Wei, Inc.

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