



Dermatologic Effects and Management of Urine and Feces on Infant and Adult Skin

**Miranda A. Farage^{1*}, Ghebre Tzeghai¹, Kenneth W. Miller¹, Bruce Tepper¹,
Rob O'Connor¹, Wendy Qin¹ and Mauricio Odio¹**

¹*The Procter and Gamble Company, Winton Hill Business Center, Cincinnati, OH, USA.*

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Original Research Article

Received 11th March 2014
Accepted 13th April 2014
Published 28th April 2014

ABSTRACT

The effect of urine and feces on the skin is a contributing factor to the development of incontinent and diaper dermatitis. The objective of this research was to evaluate skin effects of a given urine or fecal sample on the donor child and/or an adult caregiver, both of whom would be exposed to the biological material in course of daily life.

Methods: Urine was evaluated under a variety of experimental skin conditions: normal (N), compromised by tape stripping (C), hydrated by prolonged exposure to water via occlusive patch (H), and hydrated/compromised (H/C). After pre-treatment, sites were patched (3 times of 24-h each) with 0.5 ml infant urine, saline (negative control) or 0.3% sodium lauryl sulfate (SLS, positive control). Fecal material was evaluated using a 4-h patch followed by tape stripping of selected sites.

Results: In the urine study, a single 24-h patch produced a significant elevation of pH compared to both the negative (saline) and positive (sodium lauryl sulfate) controls for all experimental skin conditions. Erythema produced by urine was intermediate between the negative and positive controls, and significantly different from the negative control on the N and C skin test sites. All three materials produced an increase in hydration of the skin. The single 4-h patch of fecal material produced significant erythema, a significant elevation of pH, and a significant increase in TEWL. Recovery to pre-treatment levels was observed by the next day on sites that received no further treatment. However, on sites patched with fecal material, then further compromised by tape stripping, recovery to pre-treatment levels for erythema and TEWL were delayed.

Conclusion: These studies indicate that urine appears to have an inherent low level

*Corresponding author: Email: farage.m@pg.com;

irritant property when in continuous contact with skin for 24 to 48 hours. With relatively short exposures of 4 hours fecal material causes visible erythema, increases in pH and TEWL, and decreases in stratum corneum resilience to the subsequent insult of tape stripping. Results re-inforce the utility of modern diapers and incontinent products, utilizing superabsorbent materials, to effectively absorb wetness, keeping skin dryer and minimizing adverse skin effects.

Keywords: *Diaper dermatitis; incontinent dermatitis; fecal incontinence; urinary incontinence; urine; feces; skin pH; TEWL, chemical composition, occlusion.*

1. INTRODUCTION

It has long been recognized that contact with urine and feces in the perineal area can have adverse dermatologic effects on the skin. Any physical barrier designed to contain moisture can result in prolonged exposure of the skin to these substances. Among infants diaper dermatitis is considered the most common dermatologic problem. Parent-reported prevalence among infants in the USA was more than 60%, and in the UK was 25% [1]. Among adults suffering from incontinence, Incontinence associated dermatitis (IAD) is reported to affect 5.7% to 50% of patients [2]. In a recent study by Rohwer et al. [3], an incidence of IAD of 52.5% was reported among 189 community-living individuals with fecal incontinence. Therefore, dermatitis in the perineal area affects both adults with incontinence and the very young.

The etiology of incontinent or pediatric dermatitis is related to a number of factors, including: a) the presence of urine, b) the presence of feces and fecal enzymes, c) a moist, occluded environment resulting in hydration of the skin, d) friction resulting in damage to the skin barrier, and e) the presence of microorganisms [4,5]. These factors are all inter-related [6]. The presence of urine establishes an environment conducive to the development of dermatitis. Urine creates a moist environment that hydrates the skin and compromises the skin barrier function [1,4]. In addition, urine contributes to an alkaline pH that promotes activity of digestive enzymes in feces [1,4]. The use of containment systems (i.e., diapers or incontinence products) can promote an environment where friction and/or prolonged contact with feces/urine mixtures contribute to epidermal barrier damage. Thus, defining the relative contributions of each of these factors can be difficult since all are likely to be present.

Composition and other characteristics of human urine can vary due to a number of factors, such as ethnicity [7], diet, time of day, and the presence of certain disease states. However, that of typical human urine was reported in detail by Putman in 1971 [8]. Human urine consists primarily of water (over 95%) Table 1. The solutes that comprise the remaining 3.5-5% consist of over 150 different chemical constituents; about 70 are present at concentrations over 10 ng/ml. The most abundant material is urea at 9.3-23.3 g/L. The remaining constituents can be classified into inorganic salts, organic compounds resulting from protein metabolism, and organic ammonium salts. Typically, adult humans produce about 1.5-2L of urine in a 24-h period. The pH is around 6 and the specific gravity is similar to that of water [7,9].

Human feces consists of about 75% water [10] Table 1. Of the remaining 25%, about a third is made up of undigested food residue and substances released from the intestines, and about a third is dead bacteria from the normal microflora of the intestines. The rest consists of fats, salts and inorganic matter, and protein. Cell debris shed from the intestinal tract, bile

pigments (bilirubin) and dead leukocytes are also present. Adult humans excrete about 100-250 g of feces per day.

Table 1. Characteristics of human excreta

Representative composition of adult urine (Adapted from (8))	
Water	>950 g/L
Urea	9.3-23.3 g/L
Inorganic Salts (sodium chloride, potassium chloride, potassium sulfate, magnesium sulfate, magnesium carbonate, potassium bicarbonate, potassium phosphate and calcium phosphate)	~15 g/L
Organic compounds (creatinine, tyrosine, creatine, glycine)	~5 g/L
Organic ammonium salts (ammonium hippurate, ammonium citrate and ammonium glucuronate)	~4 g/L
Typical adult daily volume	1.5-2.0 L
Typical pH	~ 6
Density range of urine (g/ml)	1-1.4 g/ml
Representative composition of adult feces (10)	
Water	75%
Undigested fiber and solidified components of digestive juices	7.5%
Bacteria	7.5%
Fat	2.5-5%
Salts and inorganic matter	2.5-5%
Protein	0.25-0.5%
Cell debris, bile pigments (bilirubin)	~5%
Typical adult daily excretion	100-250 g

There are limited data on the direct irritant effects of human urine and feces. In a study to evaluate the irritant properties of urine, Berg et al. [11] exposed hairless mice to infant urine for 48-h and found no appreciable irritation. However, with a continuous exposure for 10 days sites exposed to urine showed a significant level of irritation, as assessed by visual scoring of erythema and edema, compared to sites exposed to water or 2% urea. Feces produced a low level of irritation when tested on hairless mice, however, when the two materials were combined, the level of irritation increased dramatically.

Andersen et al. [12] investigated the irritant properties of proteolytic and lipolytic digestive enzymes in bile salt mixtures at fecal concentrations via 21-day cumulative irritation patch testing. Test sites were treated daily with freshly prepared bile salt and enzyme mixtures at pH 6.5 and pH 8, and evaluated on days 5, 12 and 19 by visual assessment of erythema and objective measures (transepidermal water loss or TEWL, skin pH, and skin reflectance spectrophotometry). Skin sites were not significantly altered by test substances after 5 days of exposure. However, after 12 and 19 days increases in visually assessed and objective measures were observed.

Our objective was to further evaluate the direct irritant effects of urine and feces on skin. We investigated the irritation potential of urine itself on normal, adult skin, and on skin where the stratum corneum had been compromised by tape stripping, and/or hydrated by pre-treatment with water. The irritant effects of feces were evaluated by applying short-term (4-h) patch tests of children's own fecal material to buttock sites, and to each child's mothers' forearms. The strategy was to evaluate skin effects of a given urine or fecal sample on the child and/or an adult caregiver, both of whom would be exposed to the biological material in course of daily life.

2. MATERIALS AND METHODS

2.1 Subjects

Subjects were healthy, adult volunteers who had signed an informed consent. Participation was completely voluntary. Subjects were excluded from participation if they had certain skin abnormalities or health conditions that could adversely impact the test. All protocols involving human testing were conducted in accordance with the Declaration of Helsinki [13] and were approved by the test facility's Institutional Review Board.

For the study on urine subjects consisted of healthy adult volunteers (male and/or female) between the ages of 18 and 65 who had children or grandchildren. For the study on fecal material, subjects consisted of children between 9 and 27 months of age (approximately 16 - 35 lbs.) with a Fitzpatrick skin grade \leq III and the female parent who was the primary care giver.

2.2 Test Materials

In the urine studies each panelist was patched with the sample of urine collected from his/her own child or grandchild. On the day of sample collection, parents were asked to keep a diary of the child's diet. Panelists were instructed on collecting urine from their own children or grandchildren using pediatric collector units placed inside the diaper (Abco 556760) or sample jars for older children. After collection the urine was frozen. Patch tests were conducted within 24-h of collection. In the preliminary study, urine was passed through a 0.45 μ m filter prior to testing. This step was eliminated in subsequent studies since filtering did not impact the results, as discussed in the results section. The negative and positive irritant controls were isotonic saline and sodium lauryl sulfate (SLS), respectively. Materials were applied via occlusive patches (Webril® patch, Kendall LTP, Chicopee, MA, USA) covered with medical tape (Blenderm®, 3M Health Care, MN, USA).

In the studies on fecal material each panelist was patched with the sample of his/her own feces (in the case of the children) or a sample of the feces collected from her own child (in the case of the mothers). For the 3 days prior to the sample collection, parents were asked to keep a diary of the child's diet. Children were brought to a clinical facility where they waited until a bowel movement occurred. The fecal material (FM) was collected immediately after defecation for use in the studies. Materials were applied as occlusive patches (25 mm diameter, Hill Top Chamber patches) covered with medical tape (Blenderm®, 3M Health Care, MN, USA).

2.3 Urine Exposure Studies

In the preliminary study, a single, 24-h patch test was conducted on 10 volunteer panelists patched with both unfiltered and filtered biological urine collected from his/her own child/grandchild. Sites were scored for erythema approximately 30 minutes after patch removal by visual assessment conducted by an expert grader under a 100-watt incandescent daylight blue bulb. Scoring for erythema was done using a numerical scale previously described [14] where '0' indicates no apparent cutaneous involvement and '4' indicates a severe reaction.

A 3-application repeated patch test study was conducted on 8 subjects, with a pre-treatment phase to produce 4 different experimental skin conditions: normal (N), compromised (C),

hydrated (H), and hydrated/compromised (H/C). For each subject 12 test sites were chosen; 4 on the upper left arm, 4 on the upper right arm, and 4 on the upper back. Each of the 4 sites at each body location was subjected to a different pretreatment Table 2a. The skin barrier function of 2 test sites on each body region was left intact. Barrier function at the other 2 sites was compromised by tape stripping using medical tape applied 10 times (Blenderm surgical tape, 3M). One non-compromised and one compromised site were identified for further pretreatment, e.g., hydration. Hydration during pretreatment was achieved using distilled water applied via occluded patches for 24-h on the first pretreatment day, and 72-h in the second pretreatment day. Remaining sites were selected as non-hydrated test sites and were patched with dry patches using the same regimen. After the pretreatment phase 0.5 ml patches of either isotonic saline, 0.3% SLS, or biological urine (non-filtered) were applied to different designated test sites. Each volunteer panelist was patched with urine collected from his/her own child. Treatment with test substances consisted of patches for 24-h per day for 3 days.

Evaluation of skin test sites consisted of measurements of skin pH (Skin-pH-Meter® pH 900, Courage + Khazaka electronic GmbH, Cologne, Germany) and skin hydration (Novameter DPM 9003, NOVA Technology Corporation, Portsmouth, NH), and visual scoring of erythema as described above. These were conducted prior to any treatment and one-half hour after removal of each pretreatment and treatment patch. The same grader was used throughout an experiment. Statistical analyses consisted of Analysis of Variance (ANOVA), Generalized Linear Mixed Model (GLM) were conducted to compare test materials for all skin conditions (SAS®, SAS Institute Inc., Cary, NC).

2.4 Fecal Material Exposure Studies

During the specified time period, 16 children had bowel movements of adequate amount. These children and their mothers were included in the study outlined in Table 2b. The areas of the test sites on both mother and child were cleaned by wiping 5 times with standard baby wipes. Using a skin marker, 4 test sites were chosen on each child (contralaterally on the lower portion of the child's buttocks) and each mother (on the forearm). On each subject (child and mother) 2 sites were patched with 0.3 g of collected fecal material, and 2 sites were patched with dry patches as control sites. Materials were applied via occlusive patches (Hill Top Chamber®, Hill Top Research, <http://www.hill-top.com/hill-top-chambers.html>) covered with medical tape. Patches were left in place for 4-h. After patch removal the sites were cleansed for evaluation. Subsequently, one test and one control site on each mother and child were tape-stripped using 5 consecutive applications of D-Squame tape (Cu-Derm, Dallas, TX).

Table 2. Exposure protocols

a. Urine study: 3 application patch test under different experimental skin conditions

Skin condition	Code	Pretreatment		Treatment: 24-h patches for 3 consecutive days		
		Tape stripping	Hydration	Upper left arm	Upper right arm	Upper back
Normal	N	None	Dry patch	0.5 ml Saline	0.5 ml SLS	0.5 ml Urine
Compromised	C	10 applications	Dry patch	0.5 ml Saline	0.5 ml SLS	0.5 ml Urine
Hydrated	H	None	0.5 ml Dist. water	0.5 ml Saline	0.5 ml SLS	0.5 ml Urine
Hydrated / Compromised	H/C	10 applications	0.5 ml Dist. water	0.5 ml Saline	0.5 ml SLS	0.5 ml Urine

b. Fecal material study: single 4-h patch test

Test sites	Treatment: Single 4-h patch	Post treatment tape-stripping
A	0.3 g of collected fecal material	5 applications
B	Dry patch	5 applications
C	0.3 g of collected fecal material	None
D	Dry patch	None

Skin condition assessments consisted of TEWL (Dermalab Evaporimeter), skin pH (Skin-pH-Meter® pH 900, Courage + Khazaka electronic GmbH, Cologne, Germany), and visual scoring for erythema. TEWL and pH measurements were taken after an undiapered acclimation period of at least 20 minutes in a temperature and humidity controlled room (approximately 20-25°C and 40%±5% RH). Assessments were conducted prior to any treatment (baseline) and approximately 30 minutes after patch removal. When tape stripping was used to compromise the skin barrier, measurements were taken after tape stripping with an acclimation period of no less than 5±1 minutes and no greater than 10±1 minutes. Clinical measurements were also taken the day following the patch applications, i.e., approximately 24-h after patch treatment, or 20-h after patch removal. ANOVA was conducted to compare group mean responses (SAS®, SAS Institute Inc., Cary, NC).

3. RESULTS**3.1 Effects of Urine**

In the preliminary study using a single, 24-h occlusive patch on normal skin, the irritation potential of biological urine was similar to the negative control (saline), with no statistical difference between two different test volumes (0.1 and 0.3 ml) Fig. 1. Further, there was no difference between filtered and non-filtered urine, therefore, the filtering step was eliminated in subsequent testing. Based on this result, the program proceeded to the repeated exposure protocol.

The effect of urine on skin in different conditions was evaluated using a 3-application patch test after pretreatment (tape stripping and/or hydration). As expected, SLS produced significantly ($p<0.05$) higher mean erythema scores than either urine or saline for all 4 skin conditions Fig. 2. Hydrated skin, whether non-compromised or compromised, (i.e., H or H/C) appeared to be more susceptible to the irritant effects of SLS, with significantly higher overall mean erythema scores compared to normal skin (N) or skin that had been compromised but not hydrated (C) (data not shown). Urine produced erythema that was intermediate between saline and SLS. For two skin conditions the difference in erythema scores between urine and the negative control achieved significance at some time points: after the second and third patch for normal (N) skin and after the second patch for compromised (C) skin.

Urine produced a significantly higher pH than either SLS or saline Fig. 3. Skin condition was not an important factor in the increased pH, with significant differences ($p<0.05$) for all skin conditions (N, C, H and H/C). None of the skin conditions appeared to be more susceptible to the pH effects of urine.

Novameter readings increased similarly as a result of all treatment regimens Fig. 4. The SLS patch on hydrated skin produced significantly higher mean readings than the urine or saline patches. There were no other significant differences between treatment materials.

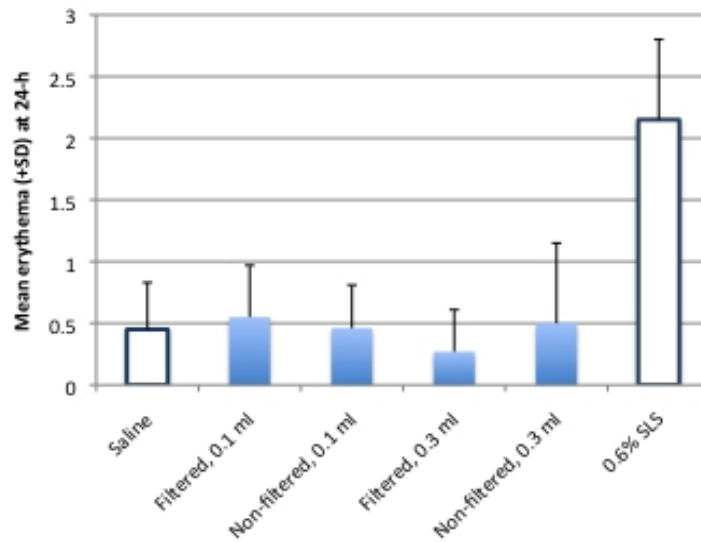


Fig. 1. Irritant potential of biological urine in a standard 24-h patch test

Subjects (N=10) were patched with 0.1 ml and 0.3 ml of both unfiltered and filtered biological urine collected from his/her own child/grandchild. After a single 24-h occlusive patch, test sites were visually graded for erythema. Isotonic saline and SLS served as negative and positive irritant controls, respectively. There was no significant difference between mean erythema scores for filtered and unfiltered urine

3.2 Effects of Feces

A 4-h patch with fecal material (Fig. 5a and 5b, patch sites A and C) produced significantly higher mean erythema scores than a dry patch (patch sites B and D) on both children and mothers. The mean erythema increased further at those test sites subjected to tape stripping after patch removal (patch sites A and B), and sites patched with fecal material (patch sites A) remained significantly higher than sites patched with dry patches (patch site B). Skin sites had recovered to levels approaching pre-patch scores at all patch sites at 24-h after patching, however, at the tape stripped sites on the mothers' skin patched with fecal material (Fig. 5b patch site A), the mean erythema was still significantly higher than the dry patched control sites (patch site B).

Compared to the dry patch control sites, fecal material produced an elevation of skin pH after a 4-hour patch Fig. 6. On the children's skin (Fig. 6a), this elevation was significant at patch site A, but did not reach significance at patch site C. On the mothers' skin (Fig. 6b), this elevation was significant at patch sites A and C. Tape stripping did not produce a further increase in pH. At 24-h after patching, skin sites had recovered to levels approaching pre-patch scores at all patch sites.

A 4-h patch with fecal material produced a significantly elevated TEWL compared to a 4-h dry patch Fig. 7a and 7b. This elevation appeared unaffected by tape stripping when TEWL was measured immediately after tape stripping (patch sites A), however, after 24 hours the TEWL at the tape stripped sites had not recovered to baseline levels. TEWL at the non-tape stripped sites had recovered to baseline by 24 hours (patch sites C).

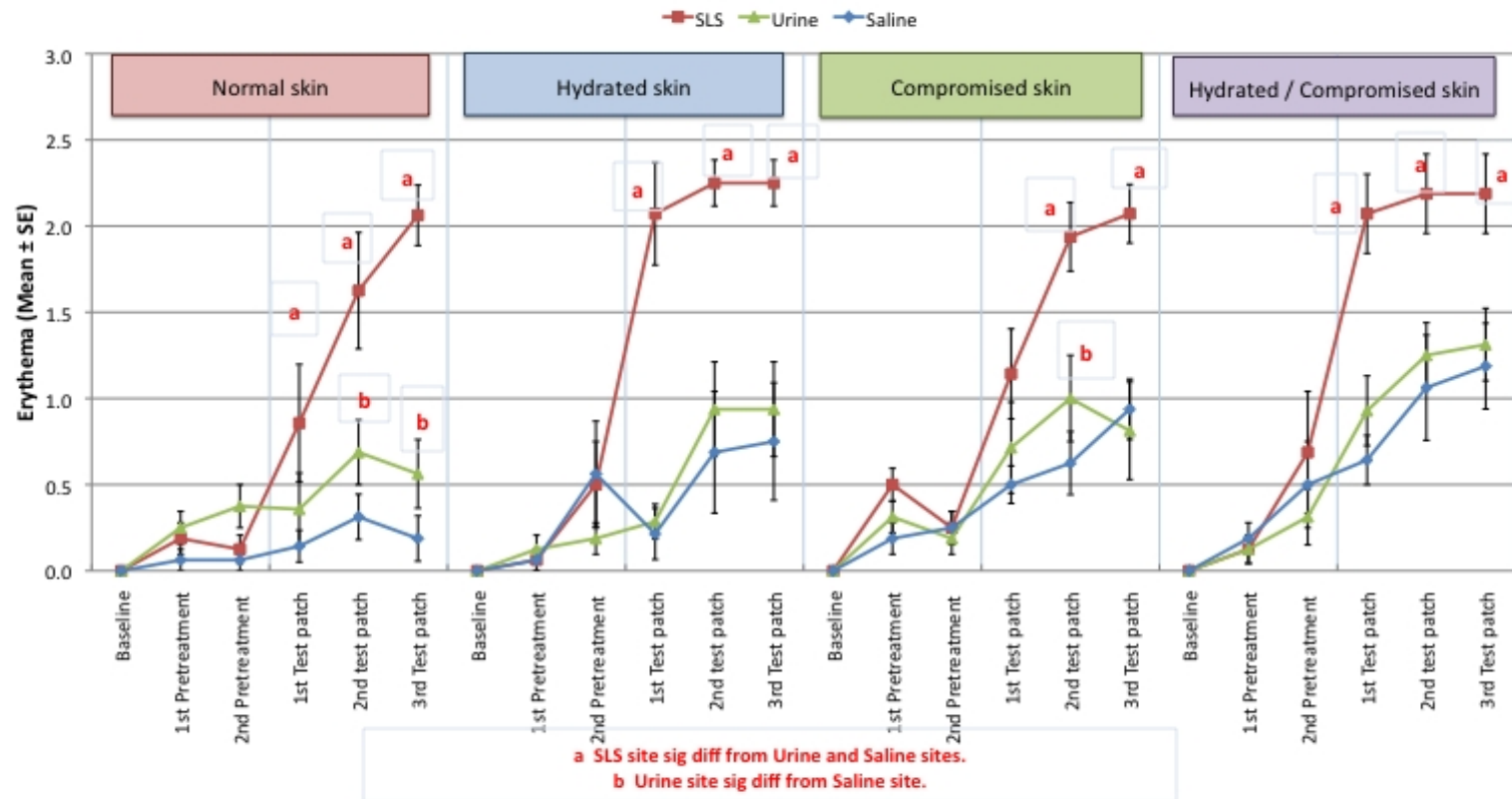


Fig. 2. Irritant potential of biological urine in 3-application patch test under different experimental skin conditions
 Skin sites on volunteer subjects (N=8) were pretreated as described in the methods section to produce 4 experimental skin conditions: Normal (N), Compromised (C), Hydrated (H) and Hydrated/Compromised (H/C). After pretreatment, 0.5 ml patches were applied to designated test sites for 24-h per day for 3 days. Patches contained either 0.3% SLS, biological urine, or isotonic saline. Irritation was evaluated by visual scoring of erythema 30 minutes after removal of each patch. Significant differences ($p < 0.05$) in mean responses were determined by ANOVA.
 a SLS site significantly different ($p < 0.05$) from Urine and Saline sites.
 b Urine site significantly different ($p < 0.05$) from Saline site

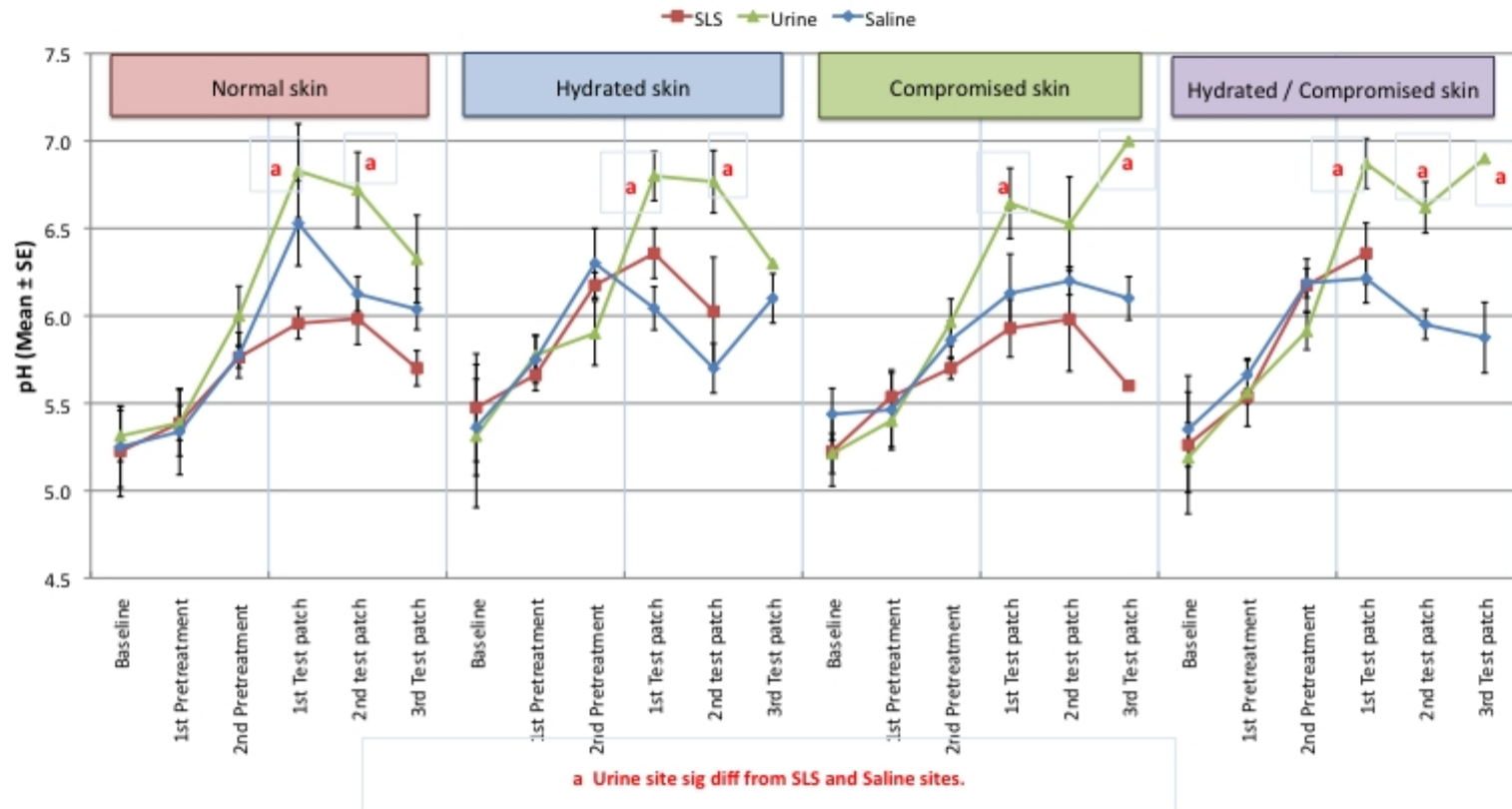


Fig. 3. Change in pH caused by biological urine in 3-application patch test under different experimental skin conditions
 Experimental conditions were as described in the previous caption (Figure 2). Skin pH was measured 30 minutes after removal of each patch.
 Significant differences ($p < 0.05$) in mean responses were determined by ANOVA.
 a Urine site significantly different ($p < 0.05$) from SLS and Saline sites.

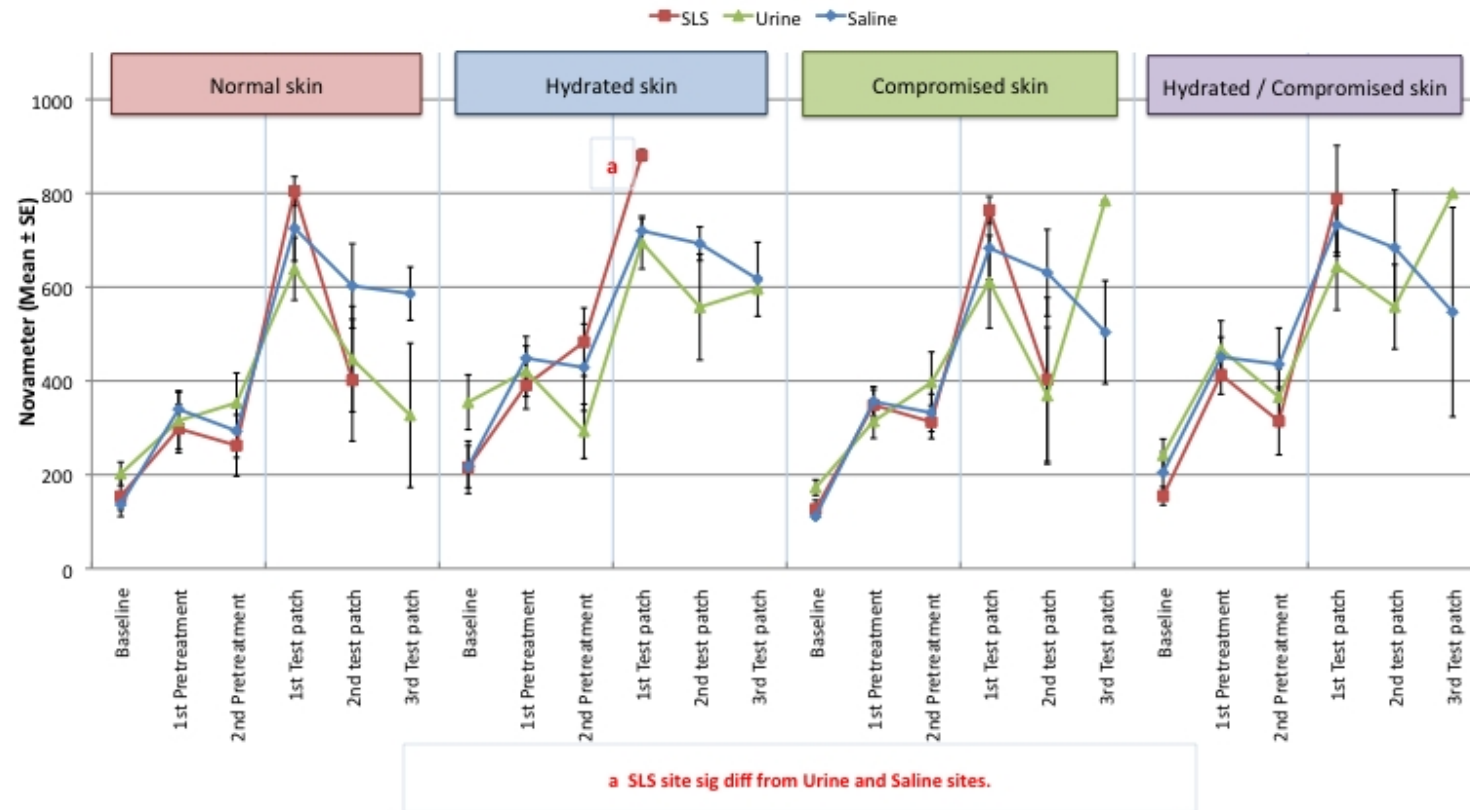


Fig. 4. Change in skin hydration caused by biological urine in 3-application patch test under different experimental skin conditions

Experimental conditions were as described in a previous caption (Figure 2). Skin moisture was measured 30 minutes after removal of each patch. Significant differences ($p < 0.05$) in mean responses were determined by ANOVA. There were no significant differences between treatments.

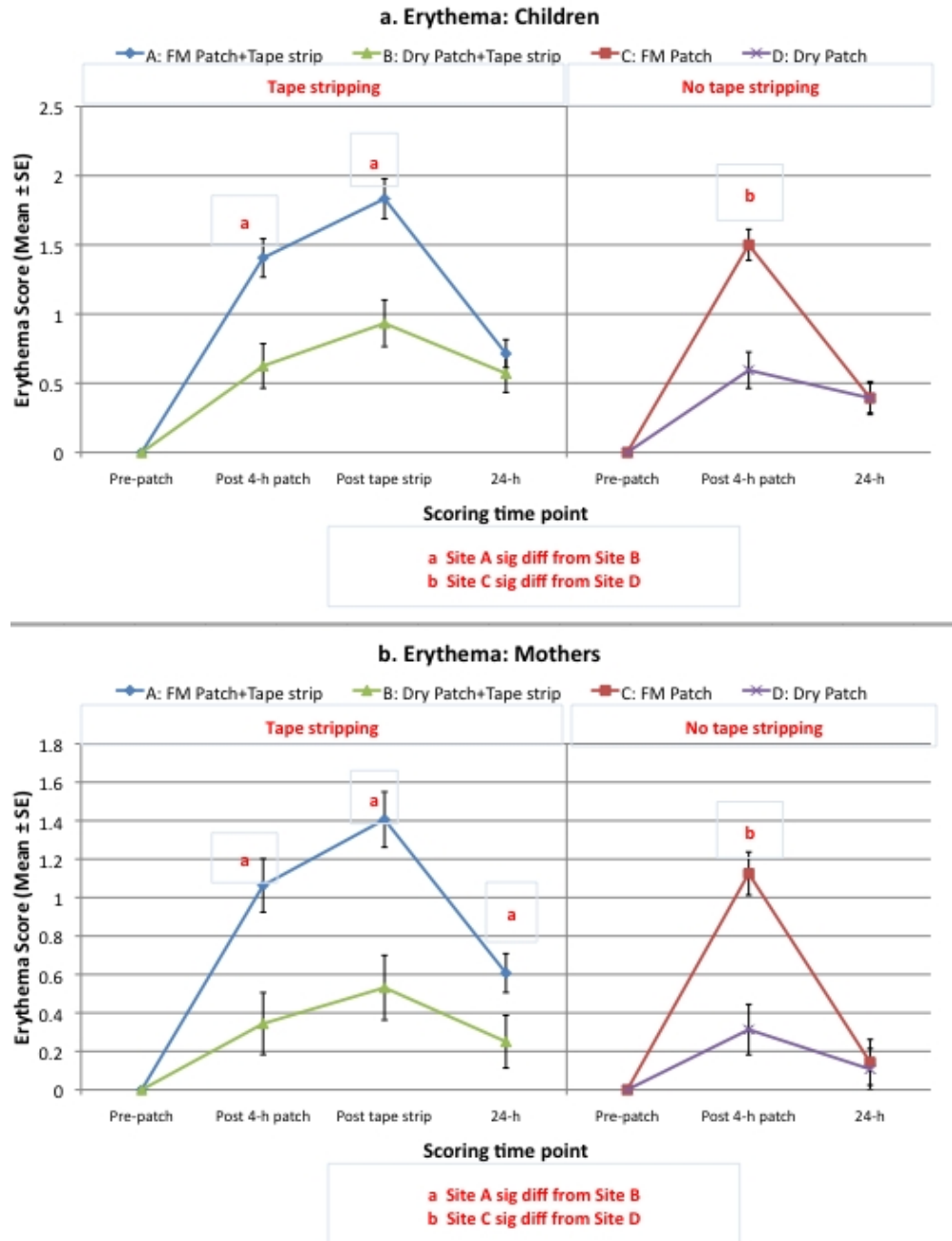


Fig. 5. Irritant potential of fecal material after a 4-h patch test under different experimental skin conditions

On the morning of the study, fecal material (FM) was collected from 16 children used for patch testing on each donor child (a) and that child's mother (b). The collected material was used for 4-h patch tests on designated sites (A and C). Dry patches were applied to designated control sites (B and D). Selected sites were then subjected to tape stripping as described in the methods section (patch sites A and B). Irritation was evaluated by visual scoring of erythema prior to any treatment (i.e., pre-patch), 30 minutes after removal of each patch (i.e., post 4-h patch), after tape stripping (i.e., post tape strip), and after 24-h of recovery (i.e., 24-h). Significant differences ($p < 0.05$) in mean responses were determined by ANOVA. a Site A (patch of fecal material + tape stripped) significantly different ($p < 0.05$) from Site B (dry patch + tape stripped). b Site C (patch of fecal material) significantly different ($p < 0.05$) from Site D (dry patch).

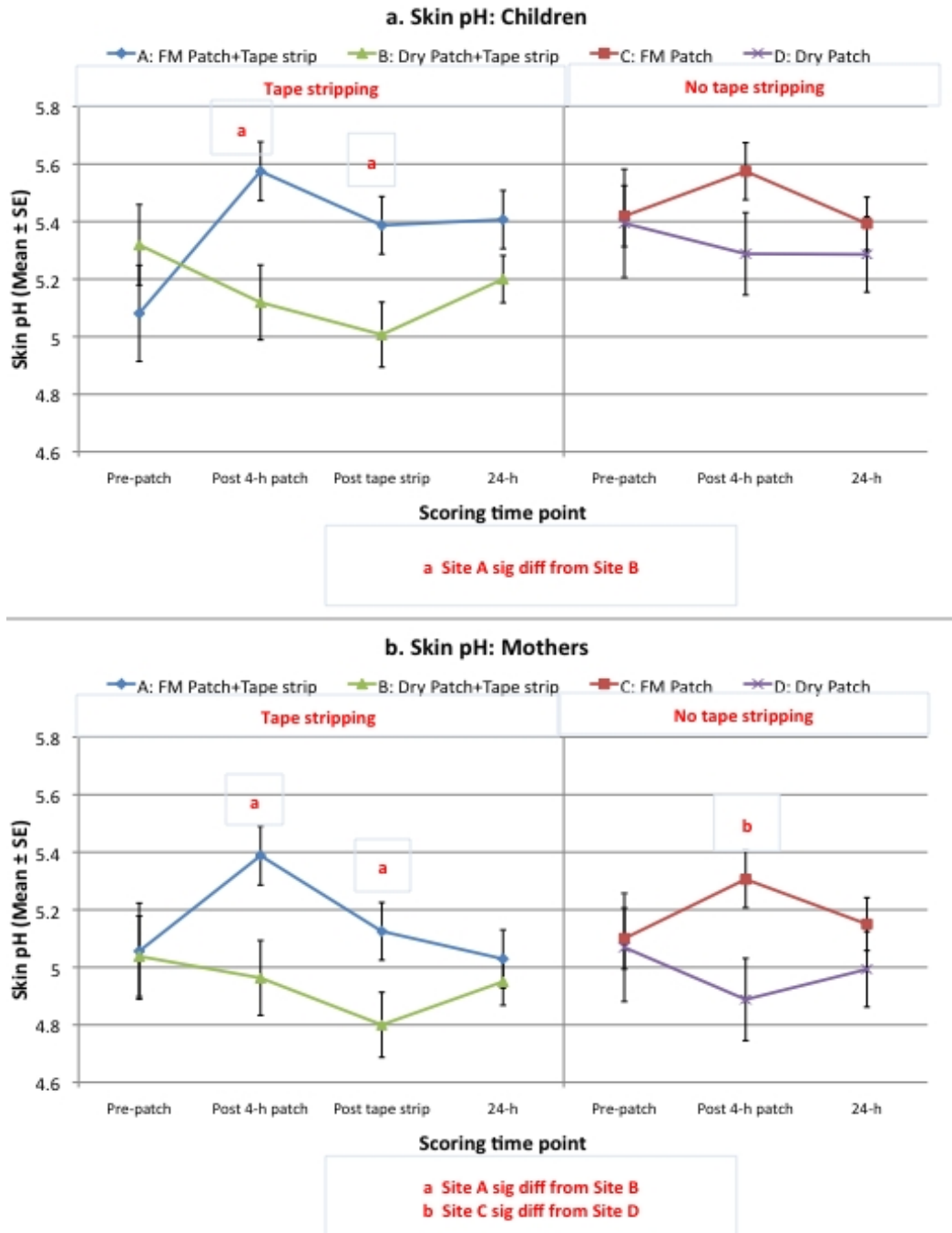


Fig. 6. Change in pH caused by fecal material after a 4-h patch test under different experimental skin conditions

Experimental conditions are as described in a previous caption (Figure 5). Skin pH was measured pre-patch, post 4-h patch, post tape strip, and after 24-h. Significant differences ($p < 0.05$) in mean responses were determined by ANOVA. a Site A (patch of fecal material + tape stripped) significantly different ($p < 0.05$) from Site B (dry patch + tape stripped). b Site C (patch of fecal material) significantly different ($p < 0.05$) from Site D (dry patch).

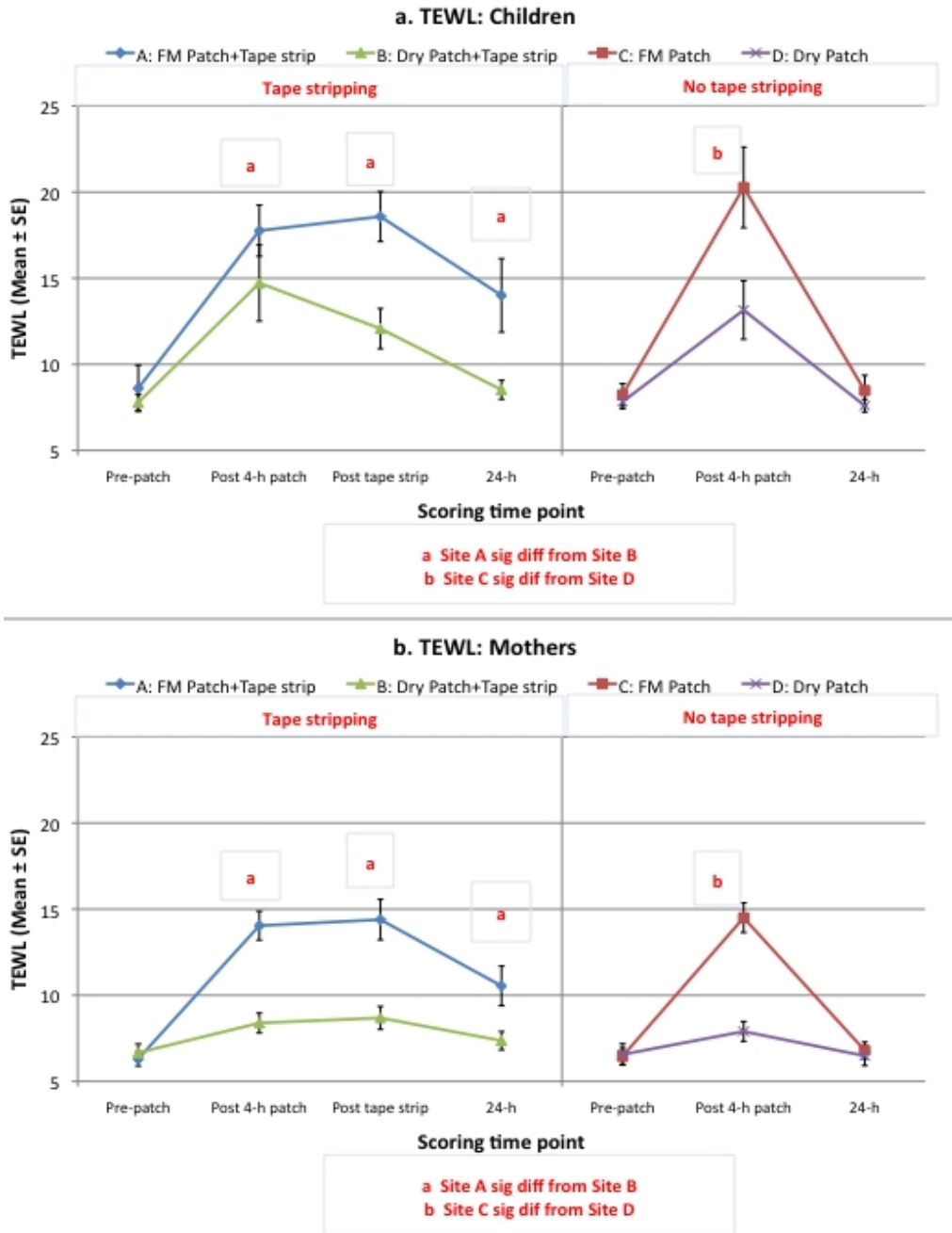


Fig. 7. Change in TEWL caused by fecal material after a 4-h patch test under different experimental skin conditions

Experimental conditions are as described in a previous caption (Figure 5). TEWL was measured pre-patch, post 4-h patch, post tape strip, and after 24-h. Significant differences ($p < 0.05$) in mean responses were determined by ANOVA

a Site A (patch of fecal material + tape stripped) significantly different ($p < 0.05$) from Site B (dry patch + tape stripped).

b Site C (patch of fecal material) significantly different ($p < 0.05$) from Site D (dry patch).

4. DISCUSSION

In this current investigation, short-term exposures to urine do not appear to cause discernable irritation, as assessed by visual scoring of erythema. With a single 24 h patch, there was no difference between erythema caused by urine and saline in the single exposure patch study on normal skin (Fig. 1) and in the study under different experimental skin conditions (Fig. 2, all skin conditions after the first patch). However, after 48-h exposures, low levels of erythema became apparent, with significant differences between urine and saline on normal and compromised skin (Fig. 2, after the second test patch). These observations are consistent with the investigation of Berg et al [11] using hairless mice who reported that 48 hours of exposure to urine produced no irritation when compared to the saline control. With longer-term exposures of 10 days, irritant effects of urine became apparent.

A single 24-h exposure to urine produced a significant increase in skin pH compared to an irritant control (SLS) and a saline control (Fig. 3). The pH of individual samples was not evaluated prior to use in the patch testing, but it is likely that samples with a higher pH produced a greater increase in skin pH elevation compared to lower pH samples. Prolonged exposure to urine has been described by other investigators as causing an increase in the pH of the skin. Stamatas reported that the pH of non-diapered skin of infants was 5.02 [1]. Normal, diapered skin had a pH of 5.7, and skin sites with active diaper dermatitis were at pH 6.13. This elevated pH can, in turn, increase the irritancy of fecal lipases and proteases [15]. Maintaining the pH of the skin is critical in avoiding and treating incontinence dermatitis [16] and in the case of infant diaper dermatitis [11].

Fecal material in the absence of urine caused discernable erythema indicative of irritation after a single 4-h patch (Fig. 5), and an elevation in the skin pH (Fig. 6) and TEWL (Fig. 7). Such rapid effects are in contrast to the findings of Andersen et al. [12] who evaluated the irritant potential of physiological concentrations of proteolytic and lipolytic enzymes found in fecal material. These investigators found significant elevations in TEWL, pH and visual irritation, after 12 days of exposure. Five days of exposure did not produce significant elevations over control materials. Our results may indicate that other components of feces in addition to the enzymes may contribute to the irritant properties of fecal material.

Our results show that the effects of exposure to fecal material on the skin may result in an increase in susceptibility to subsequent insults. Sites receiving exposure to both the fecal material patch and subsequent mild tape stripping demonstrated a prolonged recovery in irritation assessed by visual erythema and TEWL (Figs. 5 and 7, respectively) compared to sites treated with only the fecal material patch or the tape stripping (i.e., dry patch). While the mechanism underlying this effect cannot be discerned from the present experimental design, an explanatory possibility may be that FM can reduce corneocyte-to-corneocyte cohesion, hence, facilitating removal by tape strip.

Test models of skin effects using adult volunteers are often used by the consumer products industry as a screen of potential effects on baby skin. In this study on fecal material, baby and adult skin gave similar patterns of responses for erythema, skin pH, and TEWL (Figs. 5-7). The observation lends support to the use of adult skin responses as a screening tool in the development of diaper area products intended for use by babies.

In our investigation we observed directional (non-significant) increases in erythema scores, pH, and hydration for all four experimental skin conditions during the pretreatment phase

Figs. 2-4 that likely reflect the effects of occlusion. A review by Zhai and Maibach [17] indicated that occlusion alone increases stratum corneum hydration, alters skin pH, and effects microbial flora. Aly et al. [18] demonstrated that occlusion alone increased the pH of skin on the arms from 4.4 to 7 after 4 days. An increase in TEWL was also observed, indicating some compromise of barrier function. Hartmann reported the results of 3 days of occlusion on adult forearms [19]. Relative skin-moisture increased significantly, as did the skin pH.

Pediatric and incontinence dermatitis have similar etiologies (reviewed in [4,20,21]). Elevated skin wetness results in hydrated skin that is more susceptible to mechanical forces. Elevated pH induced by urinary ammonia alters skin barrier function and activates fecal enzymes that compromise skin integrity. If the individual is elderly, the skin is more susceptible to damage (as reviewed in [22]). Increase in cutaneous pH as well as impairment of immune function can increase susceptibility to infection. Elderly skin shows diminished circulation and a slowing of wound repair and re-epithelization putting this individual at an increased risk for dermatitis.

Moisture and occlusion that invariably accompanies incontinence can contribute to physiologic changes in the skin. However, it is apparent that urine and feces contain substances that further contribute to irritation. In a recent publication by Ichikawa-Shigata et al. [23], the physiological characteristics of skin were examined among 69 elderly women at a longterm medical facility in Japan. These individuals suffered from severe urinary and/or fecal incontinence. The investigators identified individuals with macerated skin, characterized by a whitened appearance and swelling, and demonstrated that hydration of the stratum corneum and dermis, TEWL, and skin pH, were significantly increased on the anatomical regions that are normally exposed to excreta (i.e., the area of the buttocks), but not on the subumbilical region that is occluded but not typically exposed to excreta (i.e., the subumbilical region). The authors concluded that skin maceration caused by urine and feces containing irritants may be more severe than that caused by moisture alone in elderly individuals.

Treatment and prevention of pediatric and incontinence dermatitis require an overall strategy to restore and maintain natural skin physiology and normal microflora. It involves a multifaceted approach that includes: keeping the skin dry, maintaining a healthy skin pH, avoiding mechanical forces, and minimizing contact with urine and feces [2]. Specially formulated perineal disposable wipes using gentle, pH-balanced cleansers and soft substrate materials can remove excreta without causing further skin damage from friction [4,24,25]. Diapers and incontinent products constructed of high quality, super-absorbent materials sequester urine and other moisture quickly, minimizing skin contact and, therefore, adverse skin effects from wetness and alkaline materials [26]. Barrier creams provide a physical barrier on the skin surface that protects from irritant materials in excreta and prevents excessive moisture loss. In addition, lipids in the barrier creams penetrate the skin surface to replace lipids that may be lost from the stratum corneum, and partially restore function [4,27,28].

A limitation in both of our studies was that each panelist was patched with a different specific biological sample, e.g., the care giver with his/her own child's urine, the child's own fecal material, or the mother with her own child's fecal material. We felt this was a necessary precaution in order to avoid exposing panelists to biologic material that they wouldn't be exposed to in their normal lives. Further, the samples were not examined with regard to composition or pH, and the urine and fecal samples from different individuals would

necessarily differ in these respects. Clearly, this introduced additional variables in the studies. It is noteworthy that significant differences were observed despite these variables, and despite relatively small sample sizes for group comparisons. In addition, during the treatment phase of the urine study, each test material was patched at a different anatomic site; SLS on right arm, saline on left arm, and urine on upper back. Ideally, samples would have been randomized. However, due to the complexity of the pretreatment and patch test protocols, and the increased likelihood of errors in execution over a multiple exposure experiment, the decision was made to patch consistent sites with test and control materials.

5. CONCLUSION

Both urine and fecal material have inherent irritant properties to skin. Urine significantly increased the skin pH of all 4 experimental skin conditions (normal, hydrated, compromised and hydrated/compromised) after a single 24-h exposure. With a longer exposure (48-h) urine caused a low level of irritation for 2 of 4 experimental skin conditions (normal and compromised). Fecal material caused a significant increase in erythema, pH and TEWL after only a single 4-h exposure, and recovery of skin was delayed with subsequent compromise via tape stripping. Results re-inforce the utility of modern diapers and incontinent products utilize superabsorbent materials to effectively absorb wetness keeping skin dryer and minimizing adverse skin effects.

CONSENT

A consent to publish is not applicable for these investigations. All studies were conducted on healthy volunteers, and no personal information, medical or otherwise, was released on any of the subjects. The author declares that each study participant read and signed an informed consent document prior to study commencement regarding the study design and any potential adverse effects.

ETHICAL APPROVAL

All study protocols were conducted in accordance with the Declaration of Helsinki, and were reviewed and accepted by the Institutional Review Board of the research facility (13).

ACKNOWLEDGEMENTS

The authors are grateful to Howard Maibach, M.D. for his technical review, and to Terresa L. Nusair, Ph.D., of the Health and Environmental Safety Alliance (Cincinnati, Ohio) for technical input.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Stamatias GN, Zerweck C, Grove G, Martin KM. Documentation of impaired epidermal barrier in mild and moderate diaper dermatitis in vivo using noninvasive methods. *Pediatr Dermatol.* 2011;28(2):99–107. [PMID:21504443 DOI:10.1111/j.1525-1470.2011.01308.x]

2. Gray M, Beeckman D, Bliss DZ, Fader M, Logan S, Junkin J et al. Incontinence-associated dermatitis: a comprehensive review and update. *J Wound Ostomy Continence Nurs.* 2012;39(1):61–74. [PMID:22193141 DOI:10.1097/WON.0b013e31823fe246]
3. Rohwer K, Bliss DZ, Savik K. Incontinence-associated dermatitis in community-dwelling individuals with fecal incontinence. *J Wound Ostomy Continence Nurs.* 2013;40(2):181–84. [PMID:23442827 DOI:10.1097/WON.0b013e31827e8b3d]
4. Stamatias GN, Tierney NK. Diaper dermatitis: etiology, manifestations, prevention, and management. *Pediatr Dermatol.* 2014;31(1):1–7. [PMID:24224482 DOI:10.1111/pde.12245]
5. Scheinfeld N. Diaper dermatitis: a review and brief survey of eruptions of the diaper area. *Am J Clin Dermatol.* 2005;6(5):273–81. [PMID:16252927]
6. Runeman B. Skin interaction with absorbent hygiene products. *Clin Dermatol.* 2008;26(1):45–51. [PMID:18280904 DOI:10.1016/j.clindermatol.2007.10.002]
7. Taylor EN, Curhan GC. Differences in 24-hour urine composition between black and white women. *J Am Soc Nephrol.* 2007;18(2):654–59. [PMID:17215441 DOI:10.1681/ASN.2006080854]
8. Putnam DF. Composition and concentrative properties of human urine. NASA Contractor Report No NASA CR-1802. 1971
9. Curhan GC, Willett WC, Speizer FE, Stampfer MJ. Twenty-four-hour urine chemistries and the risk of kidney stones among women and men. *Kidney Int.* 2001;59(6):2290–98. [PMID:11380833 DOI:10.1046/j.1523-1755.2001.00746.x]
10. Britannica E. Available: <http://www.britannica.com/>.
11. Berg RW, Buckingham KW, Stewart RL. Etiologic factors in diaper dermatitis: the role of urine. *Pediatr Dermatol.* 1986;3(2):102–06. [PMID:3952026]
12. Andersen PH, Bucher AP, Saeed I, Lee PC, Davis JA, Maibach HI. Faecal enzymes: in vivo human skin irritation. *Contact Dermatitis.* 1994;30(3):152–58. [PMID:8187514]
13. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA.* 2000;284(23):3043–45. [PMID:12432198 DOI:doi:10.1001/jama.284.23.3043]
14. Farage MA, Gilpin DA, Enane NA, Baldwin S. Development of a new test for mechanical irritation: behind the knee as a test site. *Skin Res Technol.* 2001;7(3):193–203. [PMID:11554707 DOI:10.1034/j.1600-0846.2001.70309.x]
15. Berg RW. Etiology and pathophysiology of diaper dermatitis. *Adv Dermatol.* 1988;3(75–98). [PMID:3152829]
16. Beguin AM, Malaquin-Pavan E, Guihaire C, Hallet-Lezy AM, Souchon S, Homann V et al. Improving diaper design to address incontinence associated dermatitis. *BMC Geriatr.* 2010;10(86). [PMID:21092161 DOI:10.1186/1471-2318-10-86]
17. Zhai H, Maibach HI. Skin occlusion and irritant and allergic contact dermatitis: an overview. *Contact Dermatitis.* 2001;44(4):201–06. [PMID:11260234]
18. Aly R, Shirley C, Cunico B, Maibach HI. Effect of prolonged occlusion on the microbial flora, pH, carbon dioxide and transepidermal water loss on human skin. *J Invest Dermatol.* 1978;71(6):378–81. [PMID:31403]
19. Hartmann AA. Effect of occlusion on resident flora, skin-moisture and skin-pH. *Arch Dermatol Res.* 1983;275(4):251–54. [PMID:6625652]
20. Farage MA, Bramante M. Genital hygiene: culture, practices, health impact. In: Farage MA, Maibach HI, editors. *The Vulva: Anatomy, Physiology and Pathology*, 1st edition. New York: Informa Healthcare; 2006.
21. Farage MA, Miller KW, Berardesca E, Maibach HI. Incontinence in the aged: contact dermatitis and other cutaneous consequences. *Contact Dermatitis.* 2007;57(4):211–17. [PMID:17868212 DOI:10.1111/j.1600-0536.2007.01199.x]

22. Farage MA, Miller KW, Elsner P, Maibach HI. Functional and physiological characteristics of the aging skin. *Aging Clin Exp Res*. 2008;20(3):195–200. [PMID:18594185].
23. Ichikawa-Shigeta Y, Sugama J, Sanada H, Nakatani T, Konya C, Nakagami G, et al. Physiological and appearance characteristics of skin maceration in elderly women with incontinence. *J Wound Care*. 2014;23(1):18–9, 22-23, 26 passim. [PMID:24520581]
24. Visscher M, Odio M, Taylor T, White T, Sargent S, Sluder L et al. Skin care in the NICU patient: effects of wipes versus cloth and water on stratum corneum integrity. *Neonatology*. 2009;96(4):226–34. [PMID:19407468 DOI:10.1159/000215593]
25. Beeckman D, Verhaeghe S, Defloor T, Schoonhoven L, Vanderwee K. A 3-in-1 perineal care washcloth impregnated with dimethicone 3% versus water and pH neutral soap to prevent and treat incontinence-associated dermatitis: a randomized, controlled clinical trial. *J Wound Ostomy Continence Nurs*. 2011;38(6):627–34. [PMID:21952346 DOI:10.1097/WON.0b013e31822efe52]
26. Odio M, Friedlander SF. Diaper dermatitis and advances in diaper technology. *Curr Opin Pediatr*. 2000;12(4):342–46. [PMID:10943814]
27. Odio MR, O'Connor RJ, Sarbaugh F, Baldwin S. Continuous topical administration of a petrolatum formulation by a novel disposable diaper. 2. Effect on skin condition. *Dermatology*. 2000;200(3):238–43. [PMID:10828633 DOI:18366]
28. Baldwin S, Odio MR, Haines SL, O'Connor RJ, Englehart JS, Lane AT. Skin benefits from continuous topical administration of a zinc oxide/petrolatum formulation by a novel disposable diaper. *J Eur Acad Dermatol Venereol*. 2001;15 Suppl 1(5–11). [PMID:11720074].

© 2014 Farage et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sciencedomain.org/review-history.php?iid=496&id=12&aid=4386>