

Review Article

Is atopic dermatitis a predisposing factor for experimental acute irritant contact dermatitis?

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Proclivity to acute irritant contact dermatitis has been reviewed by comparing the response in patients with atopic dermatitis to controls. Although several controlled studies demonstrate such a proclivity, others do not, suggesting that the mechanisms involved are complex.

Key words: acute irritant contact dermatitis; irritation; atopy; experimental; atopic dermatitis; sodium lauryl sulfate; transepidermal water loss. © Munksgaard, 1998.

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Patients with atopic dermatitis (AD) are alleged to have defective skin barrier function in their irritated and clinically normal skin. Epidemiologic data (1, 2) and several controlled experiments (5–14, 22) suggest they may be more prone to acute irritation than a normal population. For this reason, atopic patients, on the threshold of their choice of occupation, are sometimes advised to avoid industries with an increased risk of irritant contact dermatitis (3). We review the controlled experiments (5–14, 22) to ascertain their integrity as relates to this assumption. We searched Medline (1975–1997), *Contact Dermatitis* (1975–1997) and refs. (15) to (21). Key experiments are summarized in Tables 1, 2, 3.

Kinunnen & Hannuksela (5) demonstrated that, in non-occluded application, transepidermal water loss (TEWL) was greatly increased by propylene glycol (PG) in patients with atopic dermatitis, but less so in non-atopic normal controls; hexylene glycol (HG) did not increase TEWL in either group, suggesting that its effect on keratin is less than PG's in atopics and controls.

Agner (6) showed that the response to sodium lauryl sulfate (SLS) was statistically significantly increased in atopics compared to controls, when evaluated by visual scoring and skin thickness, but not TEWL. This dichotomy requires clarification. Baseline TEWL, measured on normal-looking

skin, revealed higher values in atopics than controls.

Tabata et al. (10) demonstrated, that after exposure to 1% SLS, patients with atopic dermatitis had greater and longer lasting TEWL elevation than controls. Biopsy revealed spongiosis, exocytosis of mononuclear cells and perivenular infiltrate containing eosinophils (Eo), that suggest atopic dermatitis in the atopics but not the controls.

Basketter et al. (7) noted a statistically higher reaction of atopic skin to 20% sodium dodecyl sulfate compared to controls. The other 2 chemicals [35% cocotrimethyl ammonium chloride and 10% hydrochloric acid (HCl)] failed to provoke significantly different irritation in atopics compared to controls.

Hannuksela & Hannuksela data (8) suggested that different methods of application of a detergent may produce dichotomous results; statistical differences in TEWL were seen between atopics and controls when applied in a plastic chamber, but not in an open (non-occluded) application.

Nassif et al. (12) observed a higher % of positive results to SLS in the AD group than in controls at all SLS concentrations tested (from 0.06% to 4.0%); the same result was demonstrated in atopic allergic rhinitis patients without dermatitis. They concluded that atopic dermatitis patients, as well

Table 1. Experiments with atopic dermatitis patients

Author	Kinnunen and Hannuksela (5)				
no. atopics	823	423	400	8	
no. controls		no details		11	
authors' criteria		present eczema		present atopy	
irritant	30% PG in H ₂ O	50% HG in H ₂ O	30% HG in H ₂ O	50% in H ₂ O	50% HG in H ₂ O
site		healthy back skin		mid-back skin	
time of application		48 h		atopics 2×daily, 5 days	
method		routine patch test		controls 2×daily, 7 days	
criteria for irritancy		visual scoring (0–3 scale)		non-occluded application	
results	3.8%+ve	2.8%+ve	2.8%+ve	TEWL (g/m ² h)	A – 5.0 NA – 0.9
Author	Agner (6)				Agner (6)
no. atopics		28			28
no. controls		28			28
authors' criteria		criteria of Hanifin & Rajka (4)			criteria of Hanifin & Rajka (4)
irritant		0.50% sodium lauryl sulfate (SLS)			no irritant added
site		flexor side of upper arm			upper arm
time of application		results, 1 h after removal			N/A
method		closed patch test			N/A
criteria for irritancy	visual scoring	TEWL (g/m ² h)	skin thickness		TEWL (g/m ² h) –
	(0–3 scale)	DTEWL (g/m ² h)	D skin thickness		basal value
results	A – (1–2)	A – 18.7 – A – 10.7	A – 1.42 – A – 0.36		A – 9.5
	NA – (0.5–1)	NA – 17.0 NA 9.0	NA – 1.17 NA 0.20		NA – 5.3

PG: propylene glycol; HG: hexylene glycol; AD: atopic dermatitis; A: atopics; NA: non-atopics.

Table 2. Experiments with atopic diathesis patients

Author	Basketter et al. (7)			Hannuksela & Hannuksela (8)	
no. atopics		30			10
no. controls		28			11
author's criteria		elevated IgE in blood		history of rhinoconjunctivitis, asthma, or AD	
irritant	20% SDS	10% HCI	35% Coco TAC	40 µl of 10% aqueous solution of detergent	
site		upper arm		upper back skin	
time of application		4 h		48 h	
method		4 h patch test		chamber test	
criteria for irritancy		visual scoring (0–3 scale)		TEWL (g/m ² h)	
results	A – 53%+ve	A – 17%+ve	A – 24%+ve	A – 13	
	NA – 36%+ve	NA – 18%+ve	NA – 18%+ve	NA – 5	
Author	Hannuksela & Hannuksela (8)			Nassif et al. (12)	
no. atopics		10			21
no. controls		11			20
author's criteria		history of rhinoconjunctivitis, asthma, or AD		history of rhinoconjunctivitis, asthma, or AD	
irritant		40 µl of 10% aqueous solution of detergent		SLS – graded dilutions	
site		upper arm		upper back	
time of application		2×daily for 1 week		48 h	
method		use test		Finn Chamber test	
criteria for irritancy		TEWL (g/m ² h)		visual scoring	
results		A – 25 NA – 26		In 0.25% SLS: A – 60%+ve, NA – 25%+ve	

PG: propylene glycol; HG: hexylene glycol; AD: atopic dermatitis; A: atopics; NA: non-atopics; SLS: sodium lauryl; CocoTAC: cocotrimethyl.

as those with a history of allergic rhinitis, had a lower irritant threshold than controls. A significantly greater intensity of response in the atopics, compared to controls, was also observed.

Seidenari (13) studied 34 nickel-sensitive patients: 1/2 of the sites patched with 0.05% aqueous NiSO₄ were pretreated with 5% SLS. SLS-pretreated nickel sites' mean clinical scores and values

of sonographic parameters of inflammation were higher in atopics.

Tupker et al. (14) failed to detect a significant difference in skin hydration between atopic and control groups throughout a 15-day exposure. However, the TEWL values for apparently normal atopic skin were higher than controls for each irritant used (0.1% SLS, 2.3% di-sodium lauryl 3-

Table 3. Experiments with atopic dermatitis patients

Author	Tabata et al. (10)	Tabata et al. (10)	Nassif et al. (12)	Seidenari (13)*	Tupker et al. (14)
no. atopics	6	13	21	14 AD	20
no. controls	5	13	20	20 ACD	18
author's criteria	Hanifin & Rajka criteria	Hanifin & Rajka criteria	Hanifin & Rajka criteria	Hanifin & Rajka criteria	Hanifin & Rajka criteria
irritant	1% SLS in water	1% SLS in water	SLS graded dilutions	SLS + NiSO ₄ : NiSO ₄	0.1% SLS; 2.3% SUC; 2.0% SOL
site	mid-forearm	mid-forearm	7 – upper arm, 14 – upper back	volar forearm	volar forearm
time of application	24 h	24 h	48 h	24 h	2 × 45 min for 3 weeks
method	24 h patch test	24 h patch test	Finn chamber test	Finn chamber test	22 mm chamber test
criteria for irritancy	histopathology	TEWL (g/m ² /h)	visual scoring	clinical evaluation (score)	TEWL (g/m ² /h)
results	A: spongiosis; LY: exocytosis; perivascular mononuclear infiltrate + Eo; NA: absent	In 30 min – A – 7, NA – 3 In 7 days – A – 27, NA – 13	In 0.5% SLS: A – 85% + ve, NA – 45% + ve	sonography AD: SLS + Ni – 5.14, Ni 1.99 ACD: SLS + Ni – 3.90, Ni 1.55	hydration A – 14; 13: 11 NA – 10; 9: 7

AD: atopic dermatitis; A: atopics; NA: non-atopics; ACD: allergic contact dermatitis; SLS: sodium lauryl sulfate; SUC: di-sodium lauryl 3-ethoxysulfosuccinate; SOL: Shellsol K.
* All the patients are nickel-sensitive.

ethoxysulphosuccinate, SUC, 2% Shellsol K, SOL).

Tanaka et al. (22), comparing the recovery of barrier function of stratum corneum measured by TEWL after its tape stripping in patients with atopic dermatitis and controls, did not find a difference in the response to mechanical irritation in atopic skin compared to controls.

Goh (23) compared skin irritability to sodium lauryl sulfate (1% aq.) and benzalkonium chloride (0.5%) on atopic and non-atopic skin after 48 h occlusion. The tests were performed on apparently normal skin. The TEWL values for sodium lauryl sulfate irritated skin in non-atopics were significantly lower than atopics (31.9 versus 47.7 g water/m²/h, respectively). In contrast, the TEWL values of benzalkonium chloride treated skin in atopics were significantly higher than non atopics (33.5 versus 237 g water/m²/h, respectively).

Discussion

The interpretation of these results is far from obvious: much of the data appears contradictory. Some studies show an increased susceptibility of atopics to irritation, while others do not.

Several facts may explain the conflict:

Several investigations (5, 8, 10, 12–14) document increased baseline TEWL in AD patients with apparently normal skin. However, TEWL values undergo changes in different phases of the disease: Agner (6) reports normal TEWL in patients with an atopic history in childhood without any atopic manifestations in adult life other than hand eczema.

Patient populations varied from an atopic diathesis, as defined by RAST and IgE levels (7), to patients with a present (5, 6, 10) or past (8) history of AD. Most authors used the criteria of Hanifin and Rajka (4) as well as those recently defined by Diepgen (11).

The visual scoring scale may be less discriminating than bioengineering measurements.

Few chemicals have been studied: even within the same class (propylene glycol & hexylene glycol), each exhibited specific effects (5, 23).

Most studies were performed on the forearm, upper back or thigh with little information on the hand, the prototypical site of occupational irritant contact dermatitis.

Most authors utilized only patch testing; yet, Hannuksela et al. (5, 8) found significant differences in the results after patch testing and open (non-occluded) application. They documented equal irritancy in atopics and controls in a detergent use test, whereas in a chamber test with 10% aqueous detergent, TEWL increase was significantly higher in atopics than controls.

Table 4. Key parameters in experimental studies

Subject	Methods	Types of chemicals	Measurement
definition of atopic dermatitis	patch testing (size, type, composition)	molecular weight	visual scoring
definition of normals	open testing, etc.	hydrophilic	appropriate statistics
sex		hydrophobis	bioengineering methods
race		anionic	
age (years)		cationic	
anatomic site etc.		amphoteric	
		non-ionic etc.	

Conclusion

We do not suggest that experimental irritancy replaces epidemiology; however, it may be a tool to better understand the relationship between atopy and acute irritant contact dermatitis and should provide fewer confounding variables influencing study interpretation. Future studies might benefit from a standard format (Table 4) that should facilitate more meaningful comparisons between investigations. These complex findings demonstrate the challenges for those investigating mechanisms and interventions. Until more experimental cumulative irritation data become available, we can only question whether this data will be as perplexing in future as it is today. In any instance, trials, utilizing parameters listed in Table 4, will hopefully produce the basis of a theoretical approach to more efficient interventions.

Note added in proof

Since submission of the article, Stolz et al. (*Contact Dermatitis* 1997: 36: 281–284) describe 205 trainees who had been examined and then the 3 model irritants applied. They noted no increased experimental skin irritability in the atopic group.

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