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New Aspects of Itch Pathophysiology: Component Analysis of Atopic Itch Using the 'Eppendorf Itch Questionnaire'

U. Darsow[a] E. Scharein[b] D. Simon[c] G. Walter[c] B. Bromm[b] J. Ring[a]

[a]Department of Dermatology and Allergy Biederstein, Technical University Munich, Munich,
[b]Institute of Physiology, University Hospital Eppendorf, Hamburg, Germany;
[c]Department of Dermatology and Allergy, Alexanderhausklinik, Davos, Switzerland

Key Words

Itch · Pruritus · Atopic eczema · Multidimensional questionnaire · Eppendorf Itch Questionnaire

Abstract

Itch represents a leading symptom in dermatological practice with many psychophysiological aspects. Instruments for qualitative registration of these central nervous factors and evaluation of therapeutic measures are still missing. We analyzed in detail the subjective itch sensation in 108 patients with acute atopic eczema with a new questionnaire developed in analogy to the McGill pain questionnaire. The descriptors with the highest load in atopic itch and the most frequent reaction patterns in atopic eczema patients were identified. Itch intensity (mean VAS 62%) and eczema severity (SCORAD mean 41 points) showed a different frequency distribution pattern with a correlation of $r = 0.33$ ($p < 0.05$). Principal component analysis of the itch questionnaire data was performed and compared with the standardized SCORAD severity index for the patients with atopic eczema. Three main factors of atopic itch explained 58% of the total variance: (1) 'suffering' (correlation with SCORAD, $r = 0.6$); (2) 'phasic intensity' (correlation with SCORAD, $r = 0.4$), and (3) 'ecstatic' component (associated with certain active reaction patterns). In conclusion, the complete description of itch has to consider different factors, which may be described on a more general level by three main components. Two of these are correlated with objective criteria of disease activity.

Introduction

In many dermatologic patients, itch is the major therapeutic problem; it may often be more difficult to treat than pain. Whereas pain may be controlled by a multitude of specifically acting pharmacological compounds, similar effective and well-directed relief is missing for itch. In contrary to many precisely controllable and quantifiable experimental pain models [for a review, see ref. 1], even the precise description of itch sensations is a difficult matter. The lack of an appropriate animal model hampers investigations into the pathophysiology of pruritus [2]. Itch intensity may be quantified by the use of visual analog scales [for a review, see ref. 3]. Nocturnal measurement of scratch activity [4, 5] may give more objective covariates. Central nervous components must be considered in human itch models; in analogy to pain, investigations of sensory physiology suggest that the subjective perception of itch is a complex emotional experience influenced by many factors. Our studies [6, 7] with volun-

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Correspondence to: Priv.-Doz. Dr. med. U. Darsow
Klinik und Poliklinik für Dermatologie und Allergologie am Biederstein
Technische Universität München, Biedersteiner Strasse 29
D–80802 München (Germany)
Tel. +49 89 4140 3170, Fax +49 89 4140 3171

teers under highly controlled experimental conditions using a standardized histamine stimulus showed significant correlations between the peripheral axonal reflex (representing the intensity of afferent C fiber activation) and the continuously recorded subjective intensity of perception as measured by a computerized visual analog scale. Correlation coefficients of around r = 0.5 point to further, as yet unknown variables modulating itch perception.

Atopic eczema is one of the most pruritic skin diseases. In fact, itch is an essential diagnostic feature of atopic eczema (in association with the markedly better-characterized criteria age-related eczematous appearance and localization, history and clinical signs of atopy and IgE-mediated sensitization). Severity scoring of this disease may be performed using the SCORAD index of the European Task Force on Atopic Dermatitis [8]. SCORAD includes objective variable parameters of the extent and intensity of inflammatory skin lesions and a visual analog scale for subjective quantification of itch. In 340 patients with atopic eczema who were scored with this device in a multicenter study [unpubl. data], a significant correlation between itch intensity (visual analog scale) and several eczema intensity parameters was obtained, with correlation coefficients of between 0.4 and 0.5.

In pain research, the McGill pain index is well established for evaluating psychophysiological aspects of perception. This questionnaire may be used in addition to visual analog scale ratings and evoked potentials [9–11]. The McGill pain questionnaire comprises affective (e.g. 'cruel') as well as purely sensory descriptive (e.g. 'stinging') items and may on a higher level also give information about quality of life parameters. A comparable instrument for the detailed investigation of itch perception is still missing [12].

We present the English version of a multidimensional itch questionnaire (Eppendorf Itch Questionnaire [13]) which was developed in Germany in cooperation between dermatology and neurophysiology as a modified analogon to the McGill index. This German version ('Eppendorfer Juckreizfragebogen') was used to evaluate different dimensions of the itch sensation in a group of 108 patients with acute exacerbation of atopic eczema.

Patients and Methods

Patients and SCORAD Index

One hundred and eight patients with atopic eczema [65 female, 43 male; age 33.4 ± 11.4 years (range 17–70 years)] were enrolled in the study. The diagnostic criteria for atopic eczema were fulfilled if at least four of the following six features were diagnosed: eczematous skin lesions, itch, typical localization (age related), at least one sign of atopy [8], history of atopy and IgE-mediated sensitization confirmed by skin prick test or RAST. After giving informed consent, the patients were asked to fill in both forms of the itch questionnaire.

The SCORAD index was developed for severity scoring of atopic dermatitis, and its evaluation is described elsewhere [8]. The index considers three main components: intensity, extent and subjective discomfort (visual analog scales for itch intensity and sleep loss). Due to different weighting of these factors, a maximum score of 103 can be achieved with the SCORAD index.

Itch Questionnaire

The first version of the itch questionnaire was composed using items of the McGill pain questionnaire [10] and items used in a previous study on clinical itch [14]. A file of descriptive adjectives was obtained by open patient interviews. Further items were added with regard to common dermatological observations (time course, scratch behavior, topographic information). The first version of the itch questionnaire was presented to 30 patients of the Dermatology Department of the University Hospital Eppendorf. This led to the elimination of several descriptors derived from the McGill pain questionnaire, highlighting different perceptional components of pain and itch.

A cover sheet (not shown) is filled in by the investigator. It comprises patient identification data, relevant medication, other diseases and description of skin lesions (if necessary). The questionnaire consists of two pages, which are filled in by the patient (fig. 1a, b). Form 1 presents 80 randomized descriptors. Sensory items are grouped on the left side and more affective or emotional items of different intensity values are found on the right side. Every item is scored as in previous evaluations of different versions of the McGill index [10, 11], within the range of 0 ('not true') to 4 ('describes exactly my itch sensation'). Statistically evaluable intensities can be derived from form 1 for every item. Form 2 deals with temporary and topographic aspects. Anti-itch ('pruritofensive') measures are grouped here and itch intensity is rated on a visual analog scale. It takes about 30 min to fill in both forms.

Statistical Analysis

The data from the multidimensional itch questionnaire and the SCORAD index (132 items) were subjected to a frequency and principal component analysis with Varimax rotation. Normal distribution was tested with the Kolmogorov-Smirnov test. SPSS and Excel for Windows were used for statistical calculations. A p value of 0.05 or lower described a significant result.

Results

The distribution of itch intensity as measured by the questionnaire's visual analog scale (fig. 2) is skewed to higher intensities compared to the objective SCORAD eczema severity index (fig. 2). The Spearman correlation coefficient of SCORAD and pruritus on the questionnaire's visual analog scale was $r = 0.33$ ($p < 0.05$). The descriptors with the most and/or highest ratings by the 108 patients (arbitrary cutoff was a descriptor total of

a EPPENDORF ITCH QUESTIONNAIRE — Patient Form 1

Name: Date: ID No:

The following descriptions apply: *Please check for every item from 0 to 4.*

	No 0	1	2	3	Yes 4
painful					
pulsating					
throbbing					
pricking					
piercing					
hurting					
dragging					
ticking					
biting					
stinging					
warm					
penetrating					
burning					
cold					
feels ant-like					
acute					
more when cold					
less when cold					
more when warm					
less when warm					
palpable					
dull					
soft					
sharp					
tingling					
comes in waves					
pointed					
sore					
high-pitched					
pinprick-like					
hot					
itching					
like sunburn					
pinching					
prickling					
stroking					
vibrating					
squeezing					
mosquito bite-like					
goes right through me					

	No 0	1	2	3	Yes 4
unbearable					
annoying					
physical urge to scratch					
awful					
rumbling					
terrible					
cruel					
bothersome					
no room for other feelings					
torturing					
merciless					
exciting					
inflaming					
excruciating					
numbing					
tormenting					
wearing					
unpleasant					
pleasurable					
disgusting					
confusing					
tiresome					
tiring					
pleasant					
restricting my life					
disturbing my sleep					
dreadful					
churning up					
bothering					
grim					
unmanageable					
I only feel the itch					
My only desire: no itch					
stubborn					
frightful					
oppressive					
insistent					
severe					
uncontrollable					
compulsive					

Fig. 1. The Eppendorf Itch Questionnaire. Emotional descriptors are found on the right side of form 1 (**a**). Form 2 comprises topographical, diurnal and reaction items and the visual analog scale (**b**).

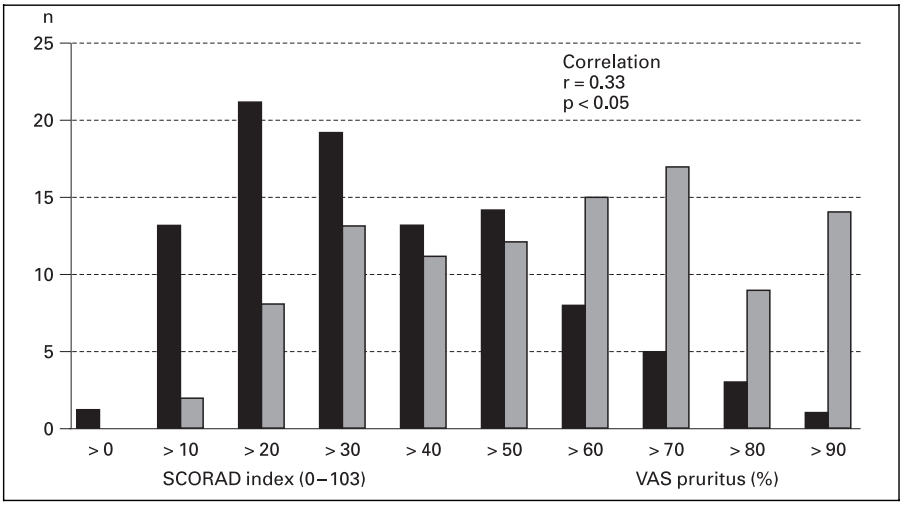
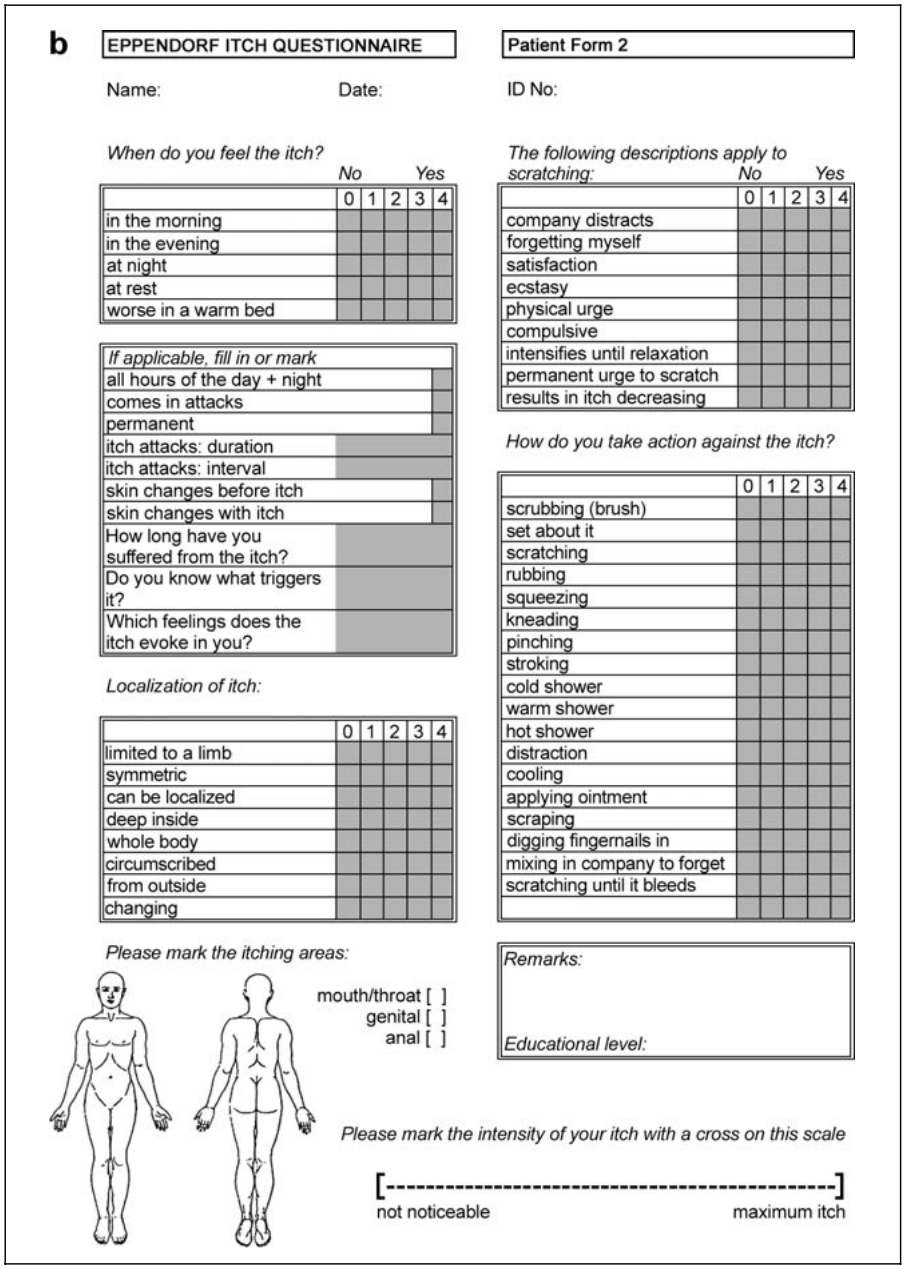


Fig. 2. Frequency distribution of atopic eczema intensity (SCORAD, filled bars) and itch intensity [visual analog scale (VAS), open bars]. The SCORAD and visual analog scale from the Eppendorf Itch Questionnaire are not equally distributed, but are significantly correlated (Spearman correlation coefficient, 0.33). The mean ± SD for SCORAD and the itch visual analog scale were 41.4 ± 19.8 ($p < 0.05$, Kolmogorov-Smirnov test) and 61.9 ± 23.2 ($p > 0.05$, Kolmogorov-Smirnov test), respectively.



b EPPENDORF ITCH QUESTIONNAIRE — Patient Form 2

Name: Date: ID No:

When do you feel the itch?

	No 0	1	2	3	Yes 4
in the morning					
in the evening					
at night					
at rest					
worse in a warm bed					

If applicable, fill in or mark	
all hours of the day + night	
comes in attacks	
permanent	
itch attacks: duration	
itch attacks: interval	
skin changes before itch	
skin changes with itch	
How long have you suffered from the itch?	
Do you know what triggers it?	
Which feelings does the itch evoke in you?	

Localization of itch:

	0	1	2	3	4
limited to a limb					
symmetric					
can be localized					
deep inside					
whole body					
circumscribed					
from outside					
changing					

Please mark the itching areas:

mouth/throat [ ]
genital [ ]
anal [ ]

The following descriptions apply to scratching:

	No 0	1	2	3	Yes 4
company distracts					
forgetting myself					
satisfaction					
ecstasy					
physical urge					
compulsive					
intensifies until relaxation					
permanent urge to scratch					
results in itch decreasing					

How do you take action against the itch?

	0	1	2	3	4
scrubbing (brush)					
set about it					
scratching					
rubbing					
squeezing					
kneading					
pinching					
stroking					
cold shower					
warm shower					
hot shower					
distraction					
cooling					
applying ointment					
scraping					
digging fingernails in					
mixing in company to forget					
scratching until it bleeds					

Remarks:

Educational level:

Please mark the intensity of your itch with a cross on this scale

[----------]
not noticeable maximum itch

200, lowest total was 11 for 'cold') are listed in table 1. Comparing the mean and median values gives an estimate of skewed distribution. Thus, for several descriptors, marked differences between the mean and median were noted (e. g. 'painful' has a high median and low mean value). In addition to a sensory and emotional definition of atopic eczema itch, the most frequent itch-relieving reaction patterns of the patients can be taken from the table.

The principal component analysis of the itch questionnaire data from 108 patients with atopic eczema revealed 12 common factors on a lower level, explaining 75% of the total variance. The most specific of these factors are given below: (1) a group of sensory quality descriptors including the items soft, dull, pulsating, throbbing and wave-like; (2) certain reactive patterns like pinching, rubbing and kneading; (3) a component of temperature describing the influence of cold or warmth; (4) the topo-

Table 1. Most frequent questionnaire items chosen by 108 patients with atopic eczema

Descriptor item		Total	Mean	SD	Median
Sensory					
1	Itching	352	3.26	1.3	4
2	More when warm	291	2.75	1.5	3
3	Can be localized	261	2.44	1.7	3
4	Tingling	239	2.25	1.5	2
5	Hot	235	2.22	1.7	3
6	Burning	234	2.21	1.6	3
7	Less when cold	223	2.1	1.7	2
8	Painful	209	1.94	1.5	3.5
Emotional/affective					
1	Unpleasant	358	3.31	1.1	4
2	Bothersome	355	3.29	1.2	3
3	My only desire: no itch	342	3.2	1.3	3
4	Tiresome	340	3.18	1.3	3
5	Unbearable	311	2.91	1.4	4
6	Bothering	310	2.9	1.4	3
7	Disturbing my sleep	309	2.89	1.4	4
8	Restricting my life	281	2.63	1.5	4
9	Uncontrollable	276	2.58	1.4	4
10	Excruciating	270	2.52	1.4	3
11	Unrulable	267	2.52	1.4	2
12	Stubborn	259	2.42	1.4	2
13	Annoying	255	2.36	1.6	1
14	Wearing	248	2.32	1.6	3
15	Torturing	240	2.24	1.6	4
16	Severe	227	2.14	1.5	1
17	Churning up	224	2.09	1.5	3
18	Terrible	223	2.08	1.6	2
19	Compulsive	217	2.05	1.6	4
20	No room for other feelings	205	1.95	1.61	0
21	Hideous	206	1.93	1.6	3
22	Awful	206	1.93	1.7	2
23	I only feel the itch	204	1.92	1.5	1.5
Prurifensive/scratch behavior					
1	Scratching	367	3.4	1	4
2	Applying ointment	295	2.73	1.4	3.5
3	Scratching results in itch decrease	267	2.47	1.4	2.5
4	Scratching until it bleeds	253	2.34	1.5	1
5	Rubbing	247	2.29	1.4	4
6	Cooling	237	2.19	1.5	1.5
7	Company distracts from scratching	217	2.05	1.4	2.5
8	Distraction	214	1.98	1.4	2
9	Scrubbing	205	1.9	1.5	3.5

Skewed distribution of descriptors is seen by differences between mean values and medians.

graphic factor, with the main emphasis on arm involvement; (5) a specific sharp sensory group of items: sharp, pricking and stinging; (6) a psychosocial factor involving the influence of company and distraction, and (7) scratching as a separate behavior pattern.

On a more general level, these components could be organized into three main factors still explaining 58.1% of the total variance:

Component A: 'suffering', derived from the corresponding items of the right side of form 1, and also associated with decreased quality of life and sleep loss.

Component B: 'phasic intensity factor'. This involved a group of items describing a sharp, stinging and burning quality of sensation.

Component C: 'active reaction' and 'compulsive, ecstatic' component. This included items of pleasure, loss of control, pulsating and a warm sensation in association with taking action against the itch by pinching or setting about it.

The SCORAD index and its components were used in this study as 'standard' criteria of disease activity. Several associations between the main components of atopic eczema itch and the severity scales in the SCORAD were seen in a correlation analysis. Component A was significantly correlated with the SCORAD index ($r = 0.59$) and with the visual analog scale of itch intensity contained within the SCORAD ($r = 0.52$). There was also a correlation between this component and the extent of eczema ($r = 0.47$). Component B was also associated with SCORAD ($r = 0.38$). In contrast, component C was statistically independent from objective eczema severity (SCORAD) and the subjective visual analog scale itch intensity (no significant correlation coefficient).

Discussion

A complete description of the itch sensation has to consider a large number of factors. These may be subject to variation, depending on the course of the pruritic sensation (e.g. laboratory setting in volunteers, different skin disorders). It has been shown that itch and objective atopic eczema severity scores are not equally distributed but are nevertheless related to each other to a certain degree. In this study, the SCORAD index was used to evaluate the patients' overall eczema severity, whereas the Eppendorf Itch Questionnaire was aimed at a differentiated analysis of the main subjective symptom, pruritus. Factor analysis was used to reduce the large number of items to a few meaningful factors: atopic eczema itch sensations could be charac-

terized by three main components, and these were also partially correlated with objective clinical criteria (SCORAD). The psychosocial significance of suffering from itch due to pruritic skin diseases is highlighted by the results of the study. A disease-related emotional component may lead to an intensification of the sensation with subsequently higher visual analog scale ratings. The individual intensity of such components, which are usually not separately measured for the itch sensation, can be assessed with the Eppendorf Itch Questionnaire. This may be of interest for quality of life and therapeutical studies, in analogy to the methods in pain research. However, using the multidimensional questionnaire in other pruritic states and diseases may lead to further group-specific standards. For this reason, the number of items was not reduced after this study, which involved only atopic eczema patients. Results of an experimental evaluation of the itch questionnaire with standardized histamine stimuli have been previously published [7].

Whereas the main components A ('suffering') and B ('phasic intensity') may represent more direct perceptional and emotional aspects for the patient affected by atopic eczema, and could be correlated with disease severity, the reaction to the itch as described by component C ('compulsive') was not directly associated with the disease activity. The association of anti-itch reactions and compulsive feelings described as 'pleasurable' deserves further attention as an important component of the itch-scratch cycle, which is of pathophysiological relevance.

A multidimensional itch questionnaire may be more suitable to fulfill the criteria of the complexity of itch perception as compared with the usual visual analog scales used for itch quantification. This is underscored by experimental evidence that within the poorly defined element of itch intensity (described by a visual analog scale), the quantity and quality of the sensations are influenced by each other [7]. Apart from descriptive and emotional factors, a high number of clinically relevant (e.g. topographic) elements were included in this multidimensional questionnaire. This may be universally useful in physiological laboratory settings (short-term volunteer trials) as well as in clinical or pharmacological research (documentation of antipruritic therapy). Form 1 may be used independently from form 2 to save time. The influence of educational level on filling in the questionnaire is possible, of course, and remains to be evaluated. The same holds true for the intraindividual repeatability of results in repeated investigations in the same patients. We suggest that the English version of the Eppendorf Itch Questionnaire be further evaluated in itch and chemoreceptor trials.

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