Observational Study

Medicine®

OPEN

Classification and possible bacterial infection in outpatients with eczema and dermatitis in China

A cross-sectional and multicenter study

Xin Wang, MD[a,b], Xiao-Dong Shi, PhD[c], Lin-Feng Li, MD, PhD[b,*], Ping Zhou, MD[a], Yi-Wei Shen, MD[a]

Abstract

Little is known about the classification and bacterial infection in outpatients with eczema and dermatitis in China.

To investigate the prevalence of eczema and dermatitis in outpatients of dermatology clinics in China, examine classification and proportion of common types of dermatitis and the possible bacterial infection, and analyze the possible related factors.

Outpatients with eczema or dermatitis from 39 tertiary hospitals of 15 provinces in mainland China from July 1 to September 30, 2014, were enrolled in this cross-sectional and multicenter study. Among 9393 enrolled outpatients, 636 patients (6.7%) were excluded because of incomplete information.

The leading subtypes of dermatitis were unclassified eczema (35.5%), atopic dermatitis (13.4%), irritant dermatitis (9.2%), and widespread eczema (8.7%). Total bacterial infection rate was 52.3%, with widespread eczema, stasis dermatitis, and atopic dermatitis being the leading three (65.7%, 61.8%, and 61.4%, respectively). Clinically very likely bacterial infection has a significant positive correlation with disease duration, history of allergic disease, history of flexion dermatitis, and severe itching.

Atopic dermatitis has become a common subtype of dermatitis in China. Secondary bacterial infection is common in all patients with dermatitis, and more attentions should be paid on this issue in other type of dermatitis apart from atopic dermatitis.

Abbreviations: ACD = allergic contact dermatitis, AD = atopic dermatitis, HE = hand eczema, ICD = International Classification of Diseases, ICD = irritant contact dermatitis, *S aureus* = *Staphylococcus aureus*, UE = unclassified eczema.

Keywords: atopic dermatitis, bacterial infection, dermatitis, eczema, epidemiology

1. Introduction

Eczema is a common disease characterized by erythema, edema, vesicles, and pruritus.[1–3] The related histopathological changes include intercellular edema of the epidermis and dermal inflammatory infiltrate of predominantly lymphocytes and macrophages.[4] Eczema is a specific inflammatory reaction of the skin that comprises a set of highly etiologically heterogeneous clinical conditions.[5,6] The classification of eczema is largely empirical, and in most circumstances, the diagnosis is only based on clinical findings.[7] In clinical practice, eczema is divided into unclassified eczema (UE) and many subtypes of specified eczema.

The incidence of eczema is increasing annually worldwide. A systematic review of 69 cross-sectional and cohort studies confirmed that atopic dermatitis (AD) is now a worldwide phenomenon with a lifetime prevalence of well over 20% in many affluent country settings.[8,9] Also, the prevalence of current eczema in a Swedish study was 13.5%.[10] It is well-known that eczema and dermatitis are very common in dermatological clinics in China, but we still do not know about its classification and bacterial infection, which has not been reported to date. This survey may have greater significance in clinical practice.

Staphylococcus aureus (*S aureus*) colonization/infection is a very common and important factor in the pathophysiology of AD.[11] The *S aureus* colonization rate was higher in AD patients, which might be due to the skin barrier defects[12] and imbalance of immune function. This phenomenon may be not limited to AD, because it has been reported that *S aureus* colonization rate was higher in non-AD patients.[13] However, the bacterial infection in other types of dermatitis and eczema has not been fully studied. Putting all these together, the purpose of this study was to: investigate the classification and proportion of common type of dermatitis in outpatients of dermatology clinics in China; and to examine possible bacterial infection in these patients and analyze the possible related factors.

2. Methods

2.1. Study design and subjects

This cross-sectional study was conducted from July 1 to September 30, 2014. The information of outpatients diagnosed with eczema or dermatitis in the dermatology department were collected and analyzed from 39 tertiary hospitals of 15 provinces

Editor: Fateh Rahimi.

Funding: This work was supported by Dermatology Committee and Chinese Association of Integrative Medicine.

The authors report no conflicts of interest.

[a] Department of Dermatology, Beijing Shijitan Hospital, Capital Medical University, [b] Department of Dermatology, Beijing Friendship Hospital, Capital Medical University, [c] Market Research Department, China Telecom Corporation Limited, Beijing Research Institute, Beijing, China.

[*] Correspondence: Lin-Feng Li, Department of Dermatology, Beijing Friendship Hospital, Capital Medical University, 95 Yong An Road, Xicheng District, Beijing 100050, China (e-mail: zoonli@sina.com).

Medicine (2017) 96:35(e7955)

Received: 5 March 2017 / Received in final form: 6 August 2017 / Accepted: 8 August 2017

http://dx.doi.org/10.1097/MD.0000000000007955

and municipalities in mainland China, including Guangdong, Chongqing, Hunan, Jiangxi, Henan, Zhejiang, Shanghai, Hubei, Jiangsu, Anhui, Shanxi, Beijing, Tianjin, Shandong, and Liaoning Province, which covered most areas of China (Fig. 1). All participants provided oral informed consent. This study was approved by the ethics committee of the respective hospitals.

2.2. Specific research content

All enrolled patients had completed a specific survey containing questionnaires regarding their general demographic characteristics, disease duration, severity of itching, lesion's distribution, type of skin lesion, and medical history before treatment. Itch was evaluated and divided into 4 levels: no itching; mild itching that interrupted neither daily activities nor sleep of the participant; moderate itching that interrupted daily activities, but not affected sleep; and severe itching that affected both daily activities and sleep of the participant. History of allergic disease, dry skin, infantile eczema, and flexion dermatitis was also recorded. Then the investigators examined the patients and made the clinical diagnosis. Eczema was classified based on International Classification of Diseases (ICD)-10[14] and diagnosed accordingly based on standard textbooks.[5,15] Specific types of dermatitis including AD, ICD, widespread eczema, hand eczema, allergic contact dermatitis (ACD), neurodermatitis, seborrheic dermatitis, nummular eczema, asteatotic eczema, photo-contact dermatitis, autosensitization eczema, dyshidrotic eczema, and stasis dermatitis were clinically diagnosed accordingly. The remaining unspecified eczema was diagnosed as UE.[7]

2.3. Secondary bacterial infection criterion

Possible secondary bacterial infection of dermatitis was evaluated clinically. Very likely bacterial infection was considered if pustules, prudent exudation, or yellow colored crust was detected. Bacterial infection was suspected if multiple scratches, oozing, erosion, or ulceration was found. The combination of very likely bacterial infection and suspected bacterial infection is called total bacterial infection or bacterial infection. Our previous study demonstrated that the clinical diagnosis of bacterial infection was correlated well with the laboratory bacterial culture results. In eczema patients with clinical diagnosed very likely bacterial infection, *S aureus* was isolated in 92.9% patients.[13] No laboratory test was performed for dermatologists to make the diagnosis.

2.4. Statistical analysis

Statistical analyses were processed by SPSS software (17.0 version). For continuous variables, the mean ± standard deviation (SD) was used according to the data distribution. The statistical methods included *t* test, chi-square test, and a correlation analysis. In the correlation analysis, the dependent variable was "total bacterial infection" and the independent variables included

Figure 1. Geographic distribution of the investigated hospitals. The shaded parts indicate the provinces investigated in this study.

characteristics such as age, disease course, sex (male/female), history of allergic disease (yes/no), history of dry skin (yes/no), itching (mild/moderate/severe), skin lesion distribution, and geographical location (20–25°N/25°01′–30°N/30°01′–35°N/35°01′–40°N/40°01′–45°N). In the multivariable analysis logistic regression, the dependent variable was "very likely bacterial infection" and the independent variables included characteristics such as age, disease duration, sex, history of allergic disease, history of flexion dermatitis, history of dry skin, history of infantile eczema, and itching. The multicategorical variables were bringing into regression model as dummy variables. Missing data were excluded from the analyses. All the analyses were 2-tailed tests with the significant level of .05.

3. Results

3.1. Demographic characteristics

In all, 9393 patients were screened, of whom 636 cases (6.7%) were excluded because of incomplete information. So, 8758 patients were recruited in the final analysis, including 4435 men (50.6%) and 4323 women (49.4%). The age ranged from 1 day to 91 years (average 33.99 years; SD 16.84 years). The course of disease ranged from 1 day to 54 years (median 1.667 years).

3.2. Classification and proportion of each type of dermatitis

Table 1 shows the classification and proportion of each type of dermatitis. The leading subtypes of specified eczema were AD, which was up to 1174 cases (13.4%), followed by irritant dermatitis and widespread eczema (810 cases [9.2%] and 765 cases [8.7%], respectively).

3.3. Prevalence of bacterial infection

Bacterial infection was found in 52.3% of patients, 17.2% being very likely infection and 35.1% being suspected infection. The bacterial infection rates in each type of eczema and dermatitis are summarized in Table 1. The 3 leading subtypes with high bacterial infection were widespread eczema (65.7%), stasis dermatitis (61.8%), and AD (61.4%).

The 3 leading subtypes of dermatitis with high suspected bacterial infection were AD (50.1%), widespread eczema (47.3%), and asteatotic eczema (43.5%), and the suspected bacterial infection in AD was the highest compared with other type of dermatitis ($P < .05$, chi-square test), but no difference with that of widespread eczema ($P > .05$, chi-square test). The 3 leading subtypes of dermatitis with very likely bacterial infection were autosensitization dermatitis (34.8%), seborrheic dermatitis (23.7%), and stasis dermatitis (23.6%), and the very likely bacterial infection in autosensitization dermatitis was the highest compared with other type of dermatitis ($P < .05$, chi-square test).

Bacterial infection rate was 71.5% in patients with acute eczema, which was much higher than that of patients with chronic eczema (38.6%) ($P < .05$, chi-square test), but no difference with those of subacute eczema ($P > .05$, chi-square test). The very likely bacterial infection rate in acute eczema was also higher than that in subacute eczema and chronic eczema (45.9% vs 36.5; 45.9% vs 8.3%, both $P < .05$, chi-square test). The very likely, suspected, and total bacterial infection rates in men were significantly higher than that in women (35.3% vs 32.7%, 17.5% vs 15.6%, and 52.8% vs 48.3%, respectively; all $P < .05$, chi-square test). Age was not associated with the bacterial infection rate. There was also a positive correlation between disease course and bacterial infection rate ($R = 0.316$, Pearson correlation analysis $P < .05$).

The most frequently involved body locations were leg (26.2%), upper limbs (23.6%), thighs (21.6%), hands (20.7%), and face (19.6%). As the number of involved body locations (range 1–10) increased, the bacterial infection rate increased significantly ($R = 0.745$, Pearson correlation analysis $P < .05$) (Fig. 2).

The bacterial infection rates in patients with no itching, mild itching, moderate itching, and severe itching were 29.3%, 35.7%, 53.6%, and 73.8%, respectively. As the itching severity increased, the suspected and total bacterial infection rates increased significantly ($R_{sus} = 0.967$, $R_{tot} = 0.978$, Pearson correlation analysis $P < .05$).

The incidence in patients with disease history of allergic disease, dry skin, infantile eczema, or flexural dermatitis were 14.36% (1285/8758), 21.57% (1889/8758), 9.35% (819/8758), and 10.03% (878/8758), respectively. The patients who had history of allergic disease had higher very likely, suspected, and total bacterial infection rates than those patients without it

Table 1

Classification and proportion of each type of dermatitis (%) and bacterial infection rate (%).

Classification	Proportion (%)	Very likely bacterial infection (%)	Suspected bacterial infection (%)	Total bacterial infection (%)
Unspecified eczema (n = 3109)	35.5	18.5	29.9	48.4
Atopic dermatitis (n = 1174)	13.4	11.3	50.1	61.4
Irritant dermatitis (n = 810)	9.2	18.1	35.3	53.4
Widespread eczema (n = 765)	8.7	18.4	47.3	65.7*
Hand eczema (n = 590)	6.7	12.5	26.8	39.3
Allergic contact dermatitis (n = 513)	5.9	22.6	33.1	55.7
Neuro dermatitis (n = 483)	5.5	9.7	37.7	47.4
Seborrheic dermatitis (n = 447)	5.1	23.7	22.1	45.8
Nummular eczema (n = 400)	4.6	16	39.5	55.5
Asteatotic eczema (n = 301)	3.4	10.6	43.5	54.1
Photosensitive dermatitis (n = 244)	2.8	13.5	39.3	52.8
Auto sensitization dermatitis (n = 221)	2.5	34.8	22.6	57.4
Dyshidrotic eczema (n = 220)	2.5	18.2	18.2	36.4
Stasis dermatitis (n = 123)	1.4	23.6	38.2	61.8*

* Total bacterial infection of widespread eczema and stasis dermatitis are higher than others diseases ($P < .05$, chi-square test).

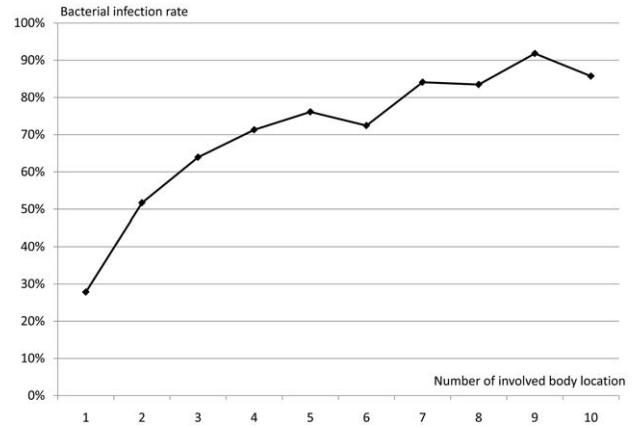

Figure 2. Relationship between number of body locations involved and bacterial infection (%). $R=0.745$, Pearson correlation analysis, $P<.05$ for the comparison between number of body locations involved and bacterial infection.

(21.1% vs 15.8%, 37.7% vs 33.4%, 58.8% vs 49.2%; all $P<.05$). Similarly, the patients who had a history of dry skin had higher suspected or total bacterial infection rates than those patients without it (39.4% vs 32.5%, 56.9% vs 48.8%; both $P<.05$).

Thirty-nine hospitals were divided into 5 groups based on their latitude: those located in latitude 20°01' to 25°N was Guangdong Province; latitude 25°01' to 30°N included Chongqing, Hunan, and Jiangxi Provinces; latitude 30°01' to 35°N included Henan, Zhejiang, Shanghai, Hubei, Jiangsu, Anhui, and Shanxi Provinces; latitude 35°01' to 40°N included Beijing, Tianjin, and Shandong province; and latitude 40°01' to 45°N included Liaoning Province. The bacterial infection rates in the lowest latitude region were higher than that in the highest latitude region (73.3% vs 58.9%; $P<.05$, chi-square test). As latitude decreased and average temperature increased, the suspected bacterial infection increased observably ($R_{sus}=-0.9$, nonparametric correlation analysis $P=.037$). In terms of severity of the infection, the patients in low latitude may be less severe than that in high latitude ($R_{sus/tot}=-0.9$, $R_{ver/tot}=0.9$, nonparametric correlation analysis $P=.037$) (Table 2).

3.4. The multivariable analysis logistic regression of very likely bacterial infection

In multivariable analysis logistic regression of very likely bacterial infection, the independent variables included characteristics: age, disease duration, sex, history of allergic disease, history of flexion dermatitis, history of dry skin, history of infantile eczema, and itching. The probability of very likely bacterial infection in eczema outpatients was 96.9% of those outpatients who were 1 year younger (odds ratio [OR] 0.969, 95% confidence interval [CI] 0.961–0.977, $P<.001$), and in eczema outpatients with history of dry skin, the risk of bacterial infection was 75% of that in eczema outpatients without it (OR 0.750, 95% CI 0.637–0.881, $P<.001$) (Table 3).

After controlling age and history of dry skin, very likely bacterial infection remained associated with disease duration, history of allergic disease, history of flexion dermatitis, especially severe itching, but not with sex, history of infantile eczema, and mild and moderate itching (Table 3). Clinically very likely bacterial infection had a significant positive correlation with disease duration, history of allergic disease, history of flexion dermatitis, and severe itching. The probability of very likely bacterial infection in eczema outpatients with severe itching was 3 times of that in eczema outpatients without it (OR 3.018, 95% CI 2.056–4.429, $P<.001$), and in eczema outpatients with history of flexion dermatitis it is 1.9 times of that in eczema outpatients without it (OR 1.922, 95% CI 1.591–2.322, $P<.001$) (Table 3).

4. Discussion

Eczema and dermatitis are common skin diseases in dermatology clinics. The present study provides the rare outpatient-based prevalence of eczema and bacterial infection analysis in dermatology clinics of Mainland China.

There are several interesting findings about this study. First, unclassified eczema is still the leading type of dermatitis in dermatology clinics. Second, AD has become the most common type of specified dermatitis in China. And finally, secondary bacterial infection is a common clinical finding in all types of dermatitis and eczema. Our results showed that about one-third of all patients were unclassified eczema (3109 cases; Table 1). The first leading subtype of classified eczema was AD (13.4%, 1174/9400), indicating that AD is very common in outpatients visiting dermatologic clinic in China, and more attention should be paid to it. Likewise, AD also was the most common type of eczema (29.8%) among children in a Nigerian study.[16] The incidence of AD varied widely, but the prevalence was increasing worldwide, mainly due to industrialization and living environment change.[9] The prevalence of AD in students aged 6 to 20 years was 0.7% in China in 2000,[17] but in 2012, in Shanghai, it had reached up to 8.3% (95% CI 7.6%–9.1%) in children aged 3 to 6 years.[18] Now, we demonstrated that AD has become the leading type of specified dermatitis in dermatology clinics in China, and a population-based epidemiological study on the prevalence of AD, especially in adults, should be performed to prove it.

Bacterial infection, especially *S aureus* in the eczema, is very common. Our study shows that about half of patients had bacterial infections; this finding is in accordance with the results of our other

Table 2

Correlation between latitude and bacterial infection (%).

Degree of latitude	Average daily temperature (°C)	Very likely bacterial infection (%)	Suspected bacterial infection (%)	Total bacterial infection (%)	Very likely/total bacterial infection (%)	Suspected/total bacterial infection (%)
20–25°N (n=1126)	33.3	12.5	60.8	73.3*	17.1	82.9
25–30°N (n=530)	31.3	8.3	35.8	44.1	18.8	81.2
30–35°N (n=3714)	29.6	17.9	27.6	45.5	39.3	60.7
35–40°N (n=2390)	29.3	12.0	33.8	45.8	26.1	73.9
40–45°N (n=997)	28.3	31.7	27.2	58.9*	53.8	46.2

* Total bacterial infection rate in 20 to 25°N and 40 to 45°N are higher than others diseases ($P<.05$, chi-square test).

Table 3

Multivariable logistic regression of very likely bacterial infection in eczema outpatients.

Variables	OR	OR (95% CI)	P
Age	0.969	0.961–0.977	<.001
Disease duration	1.037	1.023–1.051	<.001
Severe itching	3.018	2.056–4.429	<.001
History of allergic disease	1.182	1.001–1.396	.049
History of dry skin	0.750	0.637–0.881	<.001
History of flexion dermatitis	1.922	1.591–2.322	<.001

CI = confidence interval, OR = odds ratio.

previous study,[19] in which of 54 patients with dermatitis and eczema, the *S aureus* isolation rate in eczema group was similar to the control group of patients with suspected primary *S aureus* infections (44% vs 47%; $P > .05$, chi-square test). Widespread eczema, stasis dermatitis, and AD had the highest bacterial infection rates (65.7%, 61.8%, and 61.4%, respectively; Table 1). This may be related to barrier dysfunction of the skin in these diseases. The skin lesions of widespread eczema, stasis dermatitis, and AD mainly manifest as multiple scratch or exudation, which can lead to more direct damage to the epidermal skin barrier, and *S aureus* can easily penetrate or invade the skin and feed off skin exudates,[12] whereas skin barrier dysfunction and host–microbiome interactions might be primary alterations in AD.[20] Another reason is that these 3 diseases affected areas that are relatively large, which also increases the possibility of bacterial infection. This coincided with our conclusion that as the number of involved body locations increases, the bacterial infection rates increased significantly. Bacterial infection rates of acute eczema (71.5%) is much higher than that of chronic eczema (38.6%) ($P < .05$), but is roughly equal to subacute eczema (68%); this is in agreement with our clinical diagnosis. Another study found that *S aureus* may invade the skin through barrier defects in acute skin lesions, but the colonization in chronic lesions may be orchestrated through many different factors.[12]

Regarding the geographical location, as the latitude became lower and atmosphere warmer, the suspected bacterial infection increased observably ($R_{sus} = -0.9$, correlation analysis $P < .05$). The bacterial infection rate in the lowest latitude was significant higher than that in the highest latitude (73.3% vs 58.9%; $P < .05$, chi-square test). A study from the United States also showed that higher temperature and increased sun exposure were associated with poorly controlled eczema,[21] and they assumed that bacterial infection might make eczema worse. But the bacterial infection rate in latitude 40°01′ to 45°N was higher than that in latitude 35°01 to 40°N, latitude 30°01′ to 35N°, and latitude 25°01′ to 30°N (58.9% vs 45.8%, 45.5%, 44.1%; $P < .05$, chi-square test). This result was in agreement with another study, which revealed that bacterial skin colonization with *S aureus* decreases from a frigid zone to a temperate zone,[22] and the low humidity and low temperatures lead to a general decrease in skin barrier function and increase its susceptibility towards mechanical stress.[23] Also, after analyzing the proportion of bacterial infection, we found the eczema in patients of low latitude was less severe than that in patients of high latitude ($R_{sus/tot} = -0.9$, $R_{ver/tot} = 0.9$, nonparametric correlation analysis $P = .037$; Table 2). There seems to be contradiction, mixed in with effect of some other factors besides temperature. The objective being is better economic condition in latitude 35°01′ to 40°N, latitude 30°01′ to 35N°, and latitude 25°01′ to 30°N than that in latitude 40°01′ to 45°N. It is well-known that the economic and living condition in southern China is better than those in the northern regions[24]; therefore, in addition to temperature, economic condition might contribute to the lower rate of bacterial infection.

To further explore the influence factors of bacterial infection, we conducted the multivariable analysis logistic regression of very likely bacterial infection. The results showed that very likely bacterial infection has a significant positive correlation with disease duration and negative correlation with age (Table 3). It is known that the amounts of *Staphylococcus* species are higher on neonatal skin compared with adult skin.[25] Given that infant skin is more hydrated than adult skin, the skin microbiome of newborns resembles the microbiome of moist skin sites in adults.[25] In addition, infant skin is functionally still developing, and the barrier function of newborn skin makes it more susceptible to chemical irritation and local or systemic infections compared with adults.[26] Namely, the skin immune function will be improved within limits with age. Disease duration and bacterial infection are causal relationship on some level, longer disease duration is more susceptible to bacterial infection, and in turn, the infection will extend disease duration.

An interesting finding is that history of dry skin has a significant negative correlation with very likely bacterial infection (Table 3). Although the normal functioning of the SC can be disturbed in dry, flaky skin conditions, the environment lacking in water and lipid in skin is not easy for bacteria to breed. This result is in agreement with a study that pathogen colonization is limited by the geometry of mature and intact skin layers, low skin water content, low skin pH, resident microflora, antimicrobial surface-deposited free fatty acids, and sphingosine.[27] Beyond that, dry skin makes people uncomfortable and a prompt treatment is required, which may also decrease the chance of infection. This result implies that when we moisturize the uninfected eczema skin, we should be aware of a possible bacterial infection.

Furthermore, our data suggest that severe itching has a significant positive correlation with very likely bacterial infection. Skin integrity and antimicrobial function are both interdependent. The barrier permeability is correlated to the antimicrobial barriers, and most of the defensive skin functions are localized in the stratum corneum.[27] Scratches caused by severe itching directly damage the cuticle, which is bound to increase the risk of infection.

The bacterial infection rates of our study were relatively high, which were associated with our diagnostic criteria, especially the diagnostic criteria of the suspected bacterial infection is very wide. Although we had demonstrated the criteria of very likely bacterial infection were quite reliable,[13] the reliability of our criteria of suspected bacterial infection is still unclear. The other major limitations of this study includes the following: the study was a hospital-based survey, the bacterial infection was only judged by clinical doctors, and bacterial culture was needed to confirm our findings; all of the 15 participating centers were tertiary referral hospitals located in provincial capital or central city, and most patients visiting these hospitals were in a better financial condition and medical insurance than average; and the sample size in the present study was relatively small, considering the total 1.3 billion Chinese population. All these factors may lead to some degree of inevitable selection bias.

5. Conclusions

In conclusion, this research shows that AD has become a common subtype of dermatitis in China. Secondary bacterial

infection is common in many types of eczema and dermatitis. The role of bacterial colonization in these diseases should be studied further.

References

[1] Flohr C, Weinmayr G, Weiland SK, et al. How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two. Br J Dermatol 2009;161:846–53.

[2] Douwes J, Travier N, Huang K, et al. Lifelong farm exposure may strongly reduce the risk of asthma in adults. Allergy 2007;62: 1158–65.

[3] Pekkarinen PT, von Hertzen L, Laatikainen T, et al. A disparity in the association of asthma, rhinitis, and eczema with allergen-specific IgE between Finnish and Russian Karelia. Allergy 2007;62:281–7.

[4] Soter NA. Morphology of atopic eczema. Allergy 1989;44:16–9.

[5] Champion RH, Burton JL, Burns DA, et al. Textbook of Dermatology, Vol 3. 6th ed.1998;England Blackwell Science Ltd, Oxford:629–667.

[6] Johansson SG, Bieber T, Dahl R, et al. Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. J Allergy Clin Immunol 2004;113:832–6.

[7] Li LF, Liu G, Wang J. Prognosis of unclassified eczema: a follow-up study. Arch Dermatol 2008;144:160–4.

[8] Deckers IA, McLean S, Linssen S, et al. Investigating international time trends in the incidence and prevalence of atopic eczema 1990–2010: a systematic review of epidemiological studies. PLoS One 2012;7:e39803.

[9] Flohr1 C, Mann J. New insights into the epidemiology of childhood atopic dermatitis. Allergy 2014;69:3–16.

[10] RÖnmark Erik P, Ekerljung Linda, Mincheva Roxana, et al. Different risk factor patterns for adult asthma, rhinitis and eczema: results from West Sweden Asthma Study. Clin Transl Allergy 2016;6:28–38.

[11] Hon KL, Tsang YC, Lee VW, et al. Efficacy of sodium hypochlorite (bleach) baths to reduce *Staphylococcus aureus* colonization in childhood onset moderate-to-severe eczema: a randomized, placebo-controlled cross-over trial. J Dermatol Treat 2016;27:156–62.

[12] Park HY, Kim CR, Huh IS, et al. *Staphylococcus aureus* colonization in acute and chronic skin lesions of patients with atopic dermatitis. Ann Dermatol 2013;25:410–6.

[13] Li LF, Yuan XY. Detection and analysis of bacteria flora in the skin of the patients with non-atopic eczematous dermatitis. J Clin Dermatol 2003;32:74–5.

[14] International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). World Health Organization. edition 2010: Chapter XII, Dermatitis and eczema (L20-L30).

[15] Richard JGR, Torkil M, Frosch PJ. Textbook of Contact Dermatitis. Berlin, Germany: Springer-Verlag, 1995.

[16] Akinboro AO, Mejiuni AD, Akinlade MO, et al. Spectrum of skin diseases presented at LAUTECH Teaching Hospital, Osogbo, southwest Nigeria. Int J Dermatol 2015;54:443–50.

[17] Gu H, Yan Y, Chen C. Epidemiology of atopic dermatitis in 6–0 year-old population in China. Chinese J Dermatol 2000;33:379–80.

[18] Xu F, Yan S, Li F, et al. Prevalence of childhood atopic dermatitis: an urban and rural community-based study in Shanghai, China. PLoS One 2012;7:e36174.

[19] Li LF, Zhang L. Methicillin-resistant *Staphylococcus aureus* in dermatology outpatients with suspected bacterial infections in a university hospital in Beijing. Clin Exp Dermatol 2010;35:554–5.

[20] Santoro D, Marsella R, Pucheu-Haston CM, et al. Review: Pathogenesis of canine atopic dermatitis: skin barrier and host-micro-organism interaction. Vet Dermatol 2015;26:84–e25.

[21] Sargen MR, Hoffstad O, Margolis DJ. Warm, humid, and high sun exposure climates are associated with poorly controlled eczema: PEER (PediatricEczema Elective Registry) cohort, 2004–2012. J Invest Dermatol 2014;134:51–7.

[22] Byremo G, Rød G, Carlsen KH. Carlsen Effect of climatic change in children with atopic eczema. Allergy 2006;61:1403–10.

[23] Jantsch J, Schatz V, Friedrich D, et al. Cutaneous Na+ storage strengthens the antimicrobial barrier function of the skin and boosts macrophage-driven host defense. Cell Metab 2015;21:493–501.

[24] Wang Huachun , Liu Shuanhu , Liu Qingjie . Analysis of the Determinants and Difference on Financial Decentralization in China-based on the empirical data of different provinces, cities and counties from the year of 2000 to 2007. J Heibei Univ Econ Business 2016;37:79–85.

[25] Oranges T, Dini V, Romanelli M. Skin physiology of the neonate and infant: clinical implications. Adv Wound Care (New Rochelle) 2015;4:587–95.

[26] Eichenfield LF, Hardaway CA. Neonatal dermatology. Curr Opin Pediatr 1999;11:471–4.

[27] Elias PM. The skin barrier as an innate immune element. Semin Immunopathol 2007;29:3–14.