

# Incidence of allergic contact sensitization in central Chinese subjects with chronic urticaria\*

Hao Chen<sup>1</sup>  
Nan Huang<sup>1</sup>  
Xiang Dong<sup>1</sup>

Guanghui Liu<sup>1</sup>  
Wenjing Li<sup>1</sup>  
Rongfei Zhu<sup>1</sup>

DOI: <http://dx.doi.org/10.1590/abd1806-4841.20164606>

**Abstract:** BACKGROUND: Chronic urticaria (CU) can be provoked by a wide variety of causes. Some studies suggest contact sensitization may play a role in the disease.

OBJECTIVE: To investigate the incidence and distribution characteristics of allergic contact sensitization in central Chinese subjects with CU, and assess contact allergen avoidance measures in managing CU.

METHODS: Patch tests were performed, following the recommended standard procedure, with 20 selected allergens, in line with the European baseline series. All subjects with positive results were prescribed appropriate avoidance measures for the sensitizing substances, while subjects with negative results served as the control group. CU severity was assessed daily from week 1 to week 4 and for each subject, applying the Urticaria Activity Score.

RESULTS: 42.9% (233/543) of subjects with CU showed positive reactions to one or more contact allergen(s). Potassium dichromate, benzene mix and carba mix were more common in male patients, while nickel sulfate was more frequent in females. The positive rates for different allergens varied with age and occupation. The median (interquartile range) severity scores at week 1 were 20 (14-21) and 15 (14-27) for the allergen avoidance group and control group, respectively ( $P>0.05$ ); and 12 (7-15) and 14 (12-17) at week 4 ( $P<0.001$ ).

CONCLUSION: The incidence of allergic contact sensitization in CU patients was high, and appropriate contact allergen avoidance measures benefitted CU management. Contact allergens may play a role in the pathogenic mechanism of CU and patch tests are an option for CU patients.

**Keywords:** Allergens; China; Patch tests; Urticaria

## INTRODUCTION

Urticaria is a frequent, mast cell-driven disease, presenting with wheals, angioedema or both. The lifetime prevalence for acute urticaria is approximately 20% and up to 80% of acute urticaria cases are due to allergenic triggers.<sup>1</sup> Recurrent urticaria lasting over 6 weeks is clinically defined as chronic urticaria (CU), which causes a decrease in quality of life and affects academic and professional performance.<sup>2</sup> Multifactorial etiologies including autoimmune processes, intolerance to food or drugs and infectious diseases have been proved to play roles in CU's pathogenesis.<sup>3-5</sup> Etiology is essential to the management of CU. However, in most CU patients, no exogenous cause is deter-

mined even after a detailed diagnostic procedure, and the condition is termed chronic idiopathic urticaria, leading to symptomatic pharmacological treatment, usually antihistamines.<sup>6</sup> Thus, symptoms always relapse rapidly after discontinuance of medications. Although guidelines do not recommend patch testing for contact sensitization in CU patients, some studies have suggested contact sensitization may contribute to the pathogenic mechanism of CU.<sup>7-8</sup> Our study sought to investigate the incidence and distribution characteristics of allergic contact sensitization in central Chinese subjects with CU, and assess contact allergen avoidance measures in managing CU.

Received on 02.04.2015

Approved by the Advisory Board and accepted for publication on 27.06.2015

\* Work performed at the Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology - Wuhan, Hubei, China.

Financial support: None.

Conflict of interest: None.

<sup>1</sup> Huazhong University of Science and Technology - Wuhan, Hubei, China.

## METHODS

**Patient inclusion and exclusion.** CU patients from central China were included in our study at Tongji Hospital, Wuhan, between January 2011 and January 2012. Exclusion criteria were the following: (i) inducible urticaria such as dermatographism, cold urticaria, delayed pressure urticaria, heat urticaria, cholinergic urticaria, etc; (ii) urticaria related to other autoimmune disorders; (iii) abnormal results to routine laboratory measures, including differential blood count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); (iv) symptoms relieved after omission of suspected factors suggested by history, such as drugs and foods; (v) patients with positive reactions to autologous serum skin tests (ASST).

All subjects gave written informed consent and approval was obtained from Tongji hospital ethics committees.

**Patch test procedure.** Patch tests were performed at the first visit with 20 contact allergens from a new European baseline series (IQ Chamber System, Sweden), and each patient was instructed not to bathe, exercise or take drugs like antihistamines or systemic steroids, during the test period. All patches were uncovered carefully one hour after initial application, examining signs of contact urticaria to exclude acute urticaria. Strips were removed 48 hours later, while reactions were checked 72 hours later. Results were evaluated in accordance with the standard scoring system recommended by the International Contact Dermatitis Research Group guidelines.<sup>9</sup>

**Contact allergen avoidance.** Once contact allergen sensitization was diagnosed, patients were informed about how to avoid the revealed allergens, with detailed oral and written instructions (e.g. for nickel sensitization, patients were instructed to avoid contact with nickel items and adopt a low-nickel diet).

**Symptom assessment and treatment.** Urticaria severity was assessed via the UAS, a unified and simple scoring system to evaluate the symptom (pruritus) and sign (wheal) from 0 (none) to 3 (intense).<sup>9</sup> UAS7 is the aggregate score for seven consecutive days, ranging from 0 to 42. For each patient, UAS scores were recorded for 4 weeks following receipt of patch test results.

Patients were prescribed loratadine or cetirizine 10mg daily, but systemic steroids and immunomodulator were forbidden during our study period.

**Statistical analysis.** Continuous measures were expressed as means  $\pm$  standard deviations for normally distributed data, and medians and percentiles for non-normally distributed data. Descriptive statistics was used to describe demographic data. Pearson's chi-squared tests and Fisher's exact tests were employed to evaluate the categorical variables. Non-parametric (Mann-Whitney U) tests were performed to assess

comparability of UAS scores between the allergen avoidance group and control group. A *P* value of under 0.05 was considered statistically significant. All data were analyzed using the SPSS software, version 17.0.

## RESULTS

**Demographic data.** Of the 543 patients in this study, 165 (30.39%) were male and 378 (69.61%) were female. Their ages ranged from 5 to 85 years, with a median age of 39 years (interquartile range, 27-48).

**Positive rates for patch tests in CU.** Two hundred and thirty-three patients (42.9%) had positive reactions to the contact allergens. Positive rates for each contact allergen are displayed in table 1.

Among these patients, 146 (62.66%) had a positive reaction to one allergen, 55 (23.61%) to two allergens, 21 (9.01%) to three allergens, 6 (2.58%) to four allergens, and only 5 (2.14%) to five or more allergens.

**Frequency of contact allergens.** Potassium dichromate was the most common sensitizer (10.5%, n=57), followed by carba mix (9.94%, n=54), nickel sulfate (7.55%, n=41), fragrance mix (7.37%, n=40), formaldehyde (6.45%, n=35) and cobalt chloride (6.26%, n=34) (Table 1).

**TABLE 1:** Positive rates for contact allergens in 543 CU patients

Allergen	Positive reaction rate	
	n	%
Cobalt chloride	34	6.26
Mercapto mix	3	0.55
Imidazolidinyl urea	2	0.37
p-Phenylenediamine	14	2.58
N-cyclohexyl-ylthio phthalocyanine lactone	7	1.29
Potassium dichromate	57	10.5
Ethylenediamine dihydrochloride	8	1.47
Colopony	10	1.84
Formaldehyde	35	6.45
Epoxy resin	4	0.74
Bronopol	8	1.47
Thiuram mix	2	0.37
Benzene mix	18	3.31
Nickel sulfate	41	7.55
Sesquiterpene lactone mix	11	2.03
Fragrance mix	40	7.37
Cl+Me-Isothiazole	18	3.31
Black rubber mix	3	0.55
Carba mix	54	9.94
Quaternium-15	6	1.1

Contact sensitization profile between genders. Positive reactions to nickel sulfate were more common among women than men (9.26% vs. 3.64%,  $P=0.023$ ), while positive reactions to potassium dichromate, benzene mix, and carba mix were more frequent among men than women (14.55% vs. 8.73%,  $P=0.042$ ; 6.67% vs. 1.85%,  $P=0.004$ ; 18.79% vs. 6.08%,  $P<0.001$ ). There was no statistically significant difference between genders regarding other allergens (Table 2).

Contact sensitization among different age groups. Formaldehyde was a common allergen in middle-aged patients (9.93%) ( $P=0.013$ ), while the positive rate for epoxy resin was higher in elderly patients (4.88%) ( $P=0.004$ ). Fragrance mix sensitivity was more frequent in elderly patients (19.51%) than juvenile (4.86%) ( $P=0.001$ ) and middle-aged (8.08%) ones ( $P=0.021$ ) (Table 2).

Contact sensitization among different occupations. Positive reaction rates were as follows: cobalt chloride in office workers (11.50%,  $P=0.009$ ), potassium dichromate in construction workers (19.44%,  $P=0.038$ ), and bronopol and fragrance mix in farmers (11.76% and 32.35%,  $P=0.023$  and  $0.017$ ) (Table 2).

Allergen avoidance and symptoms score. In week 1, the median (interquartile range) severity scores were 20 (14-21) and 15(14-27) in the allergen avoidance group and control group, respectively ( $P>0.05$ ). In week 4, the scores were 12 (7-15) and 14 (12-17), respectively ( $P<0.001$ ) (Figure 1).

TABLE 2: Contact sensitization profile among different genders, age groups and occupations

Allergens	Gender		Age					Occupation						
	M	F	Ch	Ad	Yo	Mi	El	OW	TS	Fa	MS	CW	Sp	UE
	165	378	15	30	185	272	41	113	130	34	42	36	31	157
	Percentage (%)													
Cobalt chloride	6.67	6.08	0.00	3.33	8.65	6.25	0.00	11.50*	6.15	0.00	7.14	8.33	9.68	2.55
Mercapto mix	0.00	0.79	0.00	0.00	0.00	1.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.91
Imidazolidinyl urea	0.00	0.53	0.00	0.00	0.00	0.37	2.44	0.00	0.00	0.00	0.00	0.00	0.00	1.27
p-Phenylenediamine	2.42	2.65	0.00	0.00	0.00	4.41	4.88	1.77	0.00	5.88	0.00	5.56	6.45	3.82
N-cyclohexyl-ylthio phthalocyanine lactone	2.42	0.79	0.00	0.00	0.54	1.47	4.88	0.88	0.77	2.94	0.00	2.78	0.00	1.91
Potassium dichromate	14.55*	8.73	0.00	6.67	11.35	12.50	0.00	17.70	5.38	17.65	9.52	19.44**	0.00	8.28
Ethylenediamine dihydrochloride	0.61	1.85	0.00	0.00	1.62	1.10	4.88	1.77	0.00	0.00	2.38	0.00	3.23	2.55
Colopony	1.21	2.12	0.00	0.00	0.54	3.31	0.00	3.54	0.00	0.00	0.00	2.78	3.23	2.55
Formaldehyde	4.24	7.41	0.00	0.00	4.32	9.93*	0.00	8.85	4.62	0.00	0.00	13.89	12.90	6.37
Epoxy resin	1.21	0.53	0.00	0.00	0.54	0.37	4.88*	0.00	0.00	0.00	0.00	5.56	0.00	1.27
Bronopol	1.82	1.32	0.00	0.00	1.62	1.84	0.00	1.77	0.00	11.76**	0.00	0.00	0.00	1.27
Thiuram mix	1.21	0.00	0.00	0.00	0.00	0.37	2.44	0.00	0.00	2.94	0.00	2.78	0.00	0.00
Benzene mix	6.67**	1.85	26.67	3.33	2.70	2.94	0.00	2.65	5.38	0.00	4.76	8.33	0.00	1.91
Nickel sulfate	3.64	9.26*	0.00	3.33	11.35	6.62	2.44	9.73	4.62	11.76	0.00	11.11	16.13	7.01
Sesquiterpene lactone mix	1.21	2.38	0.00	3.33	1.62	2.21	2.44	0.00	2.31	0.00	4.76	5.56	6.45	1.27
Fragrance mix	6.06	7.94	6.67	0.00	4.86	8.09	19.51*	6.19	0.77	32.35**	4.76	11.11	12.90	7.01
Cl+Me-Isothiazole	1.82	3.97	0.00	3.33	1.62	4.41	4.88	4.42	2.31	0.00	4.76	2.78	0.00	4.46
Black rubber mix	1.21	0.26	6.67	0.00	0.00	0.37	2.44	0.00	1.54	0.00	0.00	2.78	0.00	0.00
Carba mix	18.79**	6.08	0.00	6.67	11.35	8.46	19.51	10.62	8.46	14.71	11.90	19.44	0.00	8.92
Quaternium-15	1.21	1.06	0.00	0.00	1.62	0.74	2.44	1.77	0.00	0.00	0.00	5.56	0.00	1.27

\* $P<0.05$ ; \*\* $P<0.01$ .

M, male; F, female; Ch, children ( $\leq 14$  years); Ad, adolescence (15-18 years); Yo, youth (19-35 years); Mi, middle-aged (36-60 years); El, elderly ( $>60$  years); OW, office worker; TS, teacher or student; Fa, farmer; MS, medical staff; CW, construction worker; Sp, spinner; UE, unemployed.

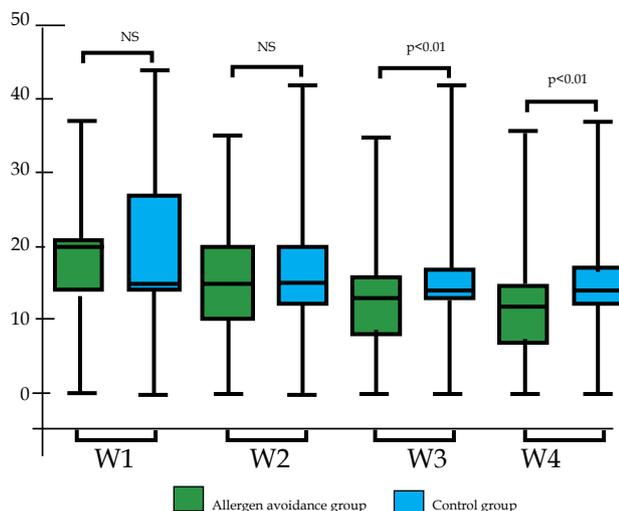


FIGURE 1: The comparison of UAS scores between allergen avoidance group and control group

## DISCUSSION

Worldwide CU prevalence has been estimated to range from 0.5% to 5%.<sup>10</sup> CU severely affects patients' quality of life and can cause disability and distress.<sup>11</sup> However, the cause or pathogenic mechanism of CU cannot be identified in many patients, and symptoms always relapse when symptomatic pharmacological treatments are discontinued. Patch testing is an important diagnostic tool for identifying the responsible allergens in allergic contact dermatitis (ACD), and the incidence of contact sensitization has been well documented.<sup>12</sup> According to current guidelines, patch testing is not recommended for CU. However, in several studies, the prevalence of contact sensitization in CU was high and avoidance measures resulted in remission of symptoms, implying that allergic contact sensitization may play a role in the pathogenic mechanism of CU.<sup>6,7,8</sup> In China, patch testing is not routinely performed for CU. We focused on the incidence and distribution characteristics of allergic contact sensitization in central Chinese subjects with CU, and sought to assess contact allergen avoidance measures in managing CU.

In our study, 42.9% (233/543) of subjects exhibited positive reactions to one or more allergens, which was similar to results in Italy (41%)<sup>7</sup> but lower than those of a previous study conducted in northern China (52.4%).<sup>13</sup> These studies suggested that almost half of the CU patients had contact sensitization. However, given the lack of well-designed intervention studies, previous reports could not determine definitively whether these sensitizations were relevant. Allergic contact sensitization is known to be influenced by environmental, cultural, occupational, individual, genetic, racial or ethnic factors, which may explain why the rates of positive

reactions to each allergen vary across different regions and countries. For example, nickel was the most common contact allergen in Italian CU patients; metals and fragrances were still the most frequent allergens across Europe.<sup>7</sup> In our study, the most frequent allergen was potassium dichromate (10.5%), mostly from cement, perhaps due to the nationwide infrastructure investment programs, especially in Chinese construction in recent years. Carba mix (9.94%), nickel sulfate (7.55%), fragrance mix (7.37%), formaldehyde (6.45%) and cobalt chloride (6.26%), were also common allergens in CU patients in central China, revealing a different sensitization profile compared with Europe.

Our study also demonstrated that the positive reaction rate for allergens varied according to gender, age and occupation. Positive reactions to potassium dichromate, benzene mix and carba mix, were more common among men, while nickel sulfate was more frequent among women. Formaldehyde was a common allergen in middle-aged patients, whereas epoxy resin and fragrance mix sensitivity were more frequent among elderly patients. Construction workers presented higher positive reaction rates to potassium dichromate than workers from other occupations, as is the case in other countries.<sup>14-16</sup> We supposed these differences might be due to the different frequencies and durations of contact allergen exposure among CU patients.

Determining the relevance of positive reactions from patients upon contact sensitization is pivotal. As mentioned above, the role of contact allergens in CU remains a controversial issue. We divided our CU patients into 2 groups: contact allergen positive and negative. Patients with positive reactions were informed about how to avoid the revealed allergens, with detailed oral and written instructions. Results revealed that symptoms had improved significantly in the positive group - compared with the negative group - after 4 weeks' observation, suggesting that contact allergens may play a role in the pathogenic mechanism of CU. Moreover, we noticed that some patients' symptoms subsided dramatically after removing or avoiding contact allergens (e.g. artificial teeth or intrauterine contraceptive rings). However, the exact mechanism by which these allergens cause CU is not yet clear. Since CU is a mast cell-driven disease, we hypothesize that contact allergens can be absorbed into the body and delivered to antigen-presenting cells, leading to mast cell activation. Alternatively, they may activate mast cells directly. Further studies are needed to elucidate the exact mechanism.

Our study has some limitations, including the following: (i) not all CU patients who presented to our hospital agreed to undergo patch testing, which may have affected our contact sensitization profiles; (ii) pa-

tients included in our intervention study were based on the patch testing results, but not in a randomized manner, though randomizing positive reaction patients into allergen avoidance and control groups is preferable; (iii) the data on CU severity reevaluation were acquired by telephone interview, not via re-scheduled follow-up visits to assure patient compliance, while the scores filled out by patients in a print scale directly under the doctors' guide were considered reliable; and (iv) like other trials, some patients may have had poor compliance, likely influencing the final outcome.

## REFERENCES

1. Sharma AD. Use of patch testing for identifying allergen causing chronic urticaria. *Indian J Dermatol Venereol Leprol.* 2008;74:114-7.
2. Baiardini I, Pasquali M, Braidò F, Fumagalli F, Guerra L, Compalati E, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). *Allergy.* 2005;60:1073-8.
3. Di Campli C, Gasbarrini A, Nucera E, Franceschi F, Ojetti V, Sanz Torre E, et al. Beneficial effects of *Helicobacter pylori* eradication on idiopathic chronic urticaria. *Dig Dis Sci.* 1998;43:1226-9.
4. Wedi B, Wagner S, Werfel T, Manns MP, Kapp A. Prevalence of *Helicobacter pylori*-associated gastritis in chronic urticaria. *Int Arch Allergy Immunol.* 1998;116:288-94.
5. Liutu M, Kalimo K, Uksila J, Kalimo H. Etiological aspects of chronic urticaria. *Int J Dermatol.* 1998;37:515-9.
6. Magen E, Mishal J, Menachem S. Impact of contact sensitization in chronic spontaneous urticaria. *Am J Med Sci.* 2011;341:202-6.
7. Guerra L, Rogkakou A, Massacane P, Gamalero C, Compalati E, Zanella C, et al. Role of contact sensitization in chronic urticaria. *J Am Acad Dermatol.* 2007;56:88-90.
8. Abeck D, Traenckner I, Steinkraus V, Vieluf D, Ring J. Chronic urticaria due to nickel intake. *Acta Derm Venereol.* 1993;73:438-9.
9. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, et al. Methods report on the development of the 2013 revision and update of the EAACI/GA2LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy* 2014;69:e1-e29.
10. Bernstein JA, Lang DM, Khan DA, Craig T, Dreyfus D, Hsieh F, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. *J Allergy Clin Immunol.* 2014;133:1270-7.
11. Sabroe RA, Seed PT, Francis DM, Barr RM, Black AK, Greaves MW. Chronic idiopathic urticaria: comparison of the clinical features of patients with and without anti-FcεRI or anti-IgE autoantibodies. *J Am Acad Dermatol.* 1999;40:443-50.
12. Davis MD, Hylwa SA, Allen EM. Basics of patch testing for allergic contact dermatitis. *Semin Cutan Med Surg.* 2013;32:158-68.

## CONCLUSION

Our study outlines the incidence of contact sensitization and distribution profiles in central Chinese subjects CU. Almost half of the CU patients had positive reactions to contact allergens, and allergen avoidance methods can help to relieve CU symptoms. Contact sensitization may play a role in CU, and we suggest that patch testing should be considered in patients with chronic idiopathic urticaria. □

13. Li LF, Wang J. Patch testing and aeroallergen intradermal testing in suspected allergic contact dermatitis, unclassified endogenous eczema and non-atopic chronic urticaria. *Contact Dermatitis.* 2001;45:84-8.
14. Macedo MS, de Avelar Alchorne AO, Costa EB, Montesano FT. Contact allergy in male construction workers in Sao Paulo, Brazil, 2000-2005. *Contact Dermatitis.* 2007;56:232-4.
15. Sijercić N, Hadzigrabić N, Kamberović S, Suljagić E. Frequency of standard and occupational contact allergens in Tuzla area, Bosnia and Herzegovina: retrospective study. *Acta Dermatovenerol Croat.* 2003;11:75-9.
16. Akasya-Hillenbrand E, Ozkaya-Bayazit E. Patch test results in 542 patients with suspected contact dermatitis in Turkey. *Contact Dermatitis.* 2002;46:17-23.

---

### MAILING ADDRESS:

Rongfei Zhu  
No.1095 Jie Fang Avenue, Hankou  
Wuhan, P.R. China  
E-mail: zrf13092@163.com

**How to cite this article:** Chen H, Liu GH, Huang N, Li WJ, Dong X, Zhu RF. Incidence of allergic contact sensitization in Central China subjects with chronic urticaria. *An Bras Dermatol.* 2016;91(2):168-72.