

ACADEMIC EXPLORATION

Allergic Constitution Theory of Chinese Medicine and its Assessment Criterion and Related Studies*

WANG Ji (王 济)[△], WANG Ting (王 婷)[△], LI Ying-shuai (李英帅), LI Ling-ru (李玲孺),
ZHENG Yan-fei (郑燕飞) and WANG Qi (王 琦)

ABSTRACT Constitution factor plays an important role in the occurrence, development, and transformation of diseases. The occurrence of allergic diseases is mainly caused by the disorganized physiological function and suitability regulation of patients, except for their exposure to outside allergens. Moreover, it represents susceptibility and hypersensitivity to allergens. The current study expresses the concept of allergic constitution from the perspective of Chinese medicine (CM) and presents the criterion of allergic constitution. In addition, the distribution of allergic constitution in population, its factors, and its relation to health-related quality of life (HRQOL) were investigated. The HRQOL scores of allergic constitution were found to be lower than those of the Pinghe constitution. After making a study on the gene expression profile of allergic constitution, the characteristics of up-regulated or down-regulated genes were found. Finally, CM drug was researched and developed to improve allergic constitution. Based on clinical trials and animal experiments, CM is found to have good regulatory effects on allergic constitution.

KEYWORDS allergic constitution, criterion, epidemiological survey, gene expression, prevention and cure

Constitution, which plays an important role in the occurrence, development, transformation, and other aspects of diseases, is a comprehensive and relatively stable distinguishing characteristic in the formed morphological structure, physiological function, and state of mind based on the congenital heredity and acquired character in the course of an individual life.⁽¹⁾ The constitutionology of Chinese medicine (CM) divides the constitution of the Chinese population into nine types including allergic constitution. Based on the results of the epidemiological investigation we conducted on 21,948 cases of the general population, the population with allergic constitution accounted for 4.97% of the total population.⁽²⁾

When exposed to certain materials, some people are allergic while others are not, indicating that some allergies only affect particular types of people. We believe this phenomenon presents a disorganized or low physiological function and suitability regulation of allergic patients. Non-allergic patients have normal physiological functions and suitability regulation abilities. Objectively, an allergen that exists in nature is an external factor and a condition that causes diseases. Allergic reaction presents pathological changes caused by internal and external pathogenic factors. The modern medicine approach to allergic diseases is to study changes in the physiological functions and pathological organisms of human bodies with diseases. The constitutionology of

CM regards allergic constitution as a natural state of an organism susceptible to outside allergens. The current study establishes the criterion of susceptible status and performs epidemiological investigations on the factors and the distributional and psychological characteristics of allergic constitution. In addition, the gene expression profile of people with allergic constitution was investigated to develop a CM drug for adjusting and controlling allergic constitution, and consequently, to prevent susceptibility to allergic diseases.

Theoretical Formation of Allergic Constitution and Establishment of Assessment Criterion

In ancient literature of CM, the term "allergic constitution" was not defined clearly, but ancient Chinese did have an initial understanding of allergic constitution. For example, CHAO Yuan-fang clearly expounded the cause of diseases, syndromes, and allergic constitutions to paint in the *General Treatise*

©The Chinese Journal of Integrated Traditional and Western Medicine Press and Springer-Verlag Berlin Heidelberg 2014

*Supported by the National Natural Science Foundation of China (No. 81273611 and No. 81473554)

Center for Studies in Constitution Research of Traditional Chinese Medicine, Basic Medical School, Beijing University of Chinese Medicine, Beijing (100029), China

Correspondence to: Prof. WANG Qi, Tel: 86-10-64286867, E-mail: wangqi710@126.com

[△]These authors contributed equally to this article

DOI: 10.1007/s11655-014-1996-y

on the *Causes and Symptoms of Diseases* (Zhu Bing Yuan Hou Lun). Typically, CM uses dietetic restraints to prevent and treat diseases. Huang Di of the Han Dynasty wrote the *Dietetic Restraint* in seven volumes, which revealed in-depth studies on stimulating foods, dietetic restraints, and clinical observations. Most of the stimulating foods listed in CM induce transformation reactions, in accordance to the principle of avoidance therapy adopted in the treatment of modern allergic diseases.

The formation and development of the constitution theory of CM gradually created a systematic knowledge of allergic constitution. Theoretical research, literature research and clinical investigation were used in the current study. The concept of allergic constitution is expressed as follows: allergic constitution is a kind of special constitution formed based on genetic endowment, which presents disorganized physiological function and suitability regulation, enhancement of reactivity to outside factors, and individual difference and family gathering trend in affinity and reactivity to different allergens. Allergic constitution is one of the eight unbalanced constitutions. Compared with the unbalanced constitutions, Pinghe constitution is a balanced constitution. People with a balanced constitution are fit, full of energy with fine lustrous complexion, shiny hair, bright eyes, get good sleep and have a good appetite. They seldom fall ill and can adapt to their natural and social environment.

Three stages were investigated to draw the criterion of allergic constitution. In the first stage, the allergic constitution library was formed. A literature study was performed to find literature containing allergic constitution, which are regarded as basic data sources for information analysis. Moreover, the expression of allergic constitution was analyzed and concluded from the basic data sources to extract representative issues reflecting allergic constitution and feature information. This enabled informatics treatment to obtain diagnostic entry as the basic content for creating the allergic constitution measuring scale.⁽³⁾

In the second stage, the allergic constitution rating scale was established.⁽⁴⁾ Based on our discussions with multidisciplinary experts in the constitution science of CM, clinical epidemiology, psychometrics, and statistics, 7 items were selected

from the library as bases for determining allergic constitution. The selected items were then compiled into a questionnaire to make each problem easy to understand for an examinee. The entry form in the measuring scale used the Likert Scale, a five-star evaluation formation approved and applied by many international scholars. For example, the question "Did your skin turn red and show traces when you scratched it?" allows the examinee to select an anastomosing answer from the following five evaluations: 1=no, 2=slightly, 3=sometimes, 4=often, and 5=all the time. In making the evaluation, the original score is calculated first (original score = total score of all items), and then the original score is converted into a conversion score [conversion score = [(actual score – lowest possible score of the measuring scale)/(highest score – lowest score)] × 100%. The higher the conversion score is, the more obvious the allergic constitution trend. In light of the created measuring scale, 4 investigations were conducted on 1,000 experts and study subjects to make further amendments on the items.

On the third stage, a performance evaluation was performed on the Constitution Measuring Scale of Traditional Chinese Medicine (CMSTCM).⁽⁵⁾ The amended measuring scale was used to make reliability and validity evaluations in Beijing and other provinces and cities, and to translate the CMSTCM into the Japanese language to make reliability and validity evaluations in Japan. The evaluation results show that the measuring scale has good reliability and validity.⁽⁶⁾ Systematic random sampling was used in the national range to sample 21,948 cases, epidemiological surveys were conducted in a large sample, and verify the criterion of the measuring scale was verified.⁽²⁾ The research group of the current study drew the Classification and Criterion of Constitution of Traditional Chinese Medicine based on systematic random sampling, which was published in 2009 as the formal standard of the China Association of Traditional Chinese Medicine. Moreover, it was the first documentation for guiding and governing studies and applications of constitution in CM, and it provided a practical identification tool for allergic constitution (Table 1).

Epidemiological Survey on the Distribution Characteristics, Factors, and Psychological Characteristics of Allergic Constitution

Based on a national epidemiological survey

Table 1. The Measuring Scale for Allergic Constitution of CM (Score)

Experience/condition in the past year	No	Slightly	Sometimes	Often	All the time
(1) Did you sneeze even when you did not have a cold?	1	2	3	4	5
(2) Did you have runny or stuffy nose even when you did not have a cold?	1	2	3	4	5
(3) Did you cough due to seasonal change, temperature change, or unpleasant odor?	1	2	3	4	5
(4) Did you have allergies? (e.g. medicine, food, odors, pollen, pet dander, or during seasonal or weather change, etc.?)	1	2	3	4	5
(5) Did your skin get hives/urticaria easily?	1	2	3	4	5
(6) Did your skin have purpura (purple spots, ecchymosis) due to allergies?	1	2	3	4	5
(7) Did your skin turn red and show traces when you scratched it?	1	2	3	4	5

Notes: Original scores = sum up each item's score; converted scores = $[(\text{original scores} - \text{items}) / (\text{items} \times 4)] \times 100$; diagnosis of allergic constitution = diagnostic standard: converted scores ≥ 40

on 21,948 cases, allergic constitution accounted for 4.97% of the total population. The investigation on the distribution of allergic constitution in the city and countryside shows that the occurrence in the city was higher than that in the countryside.⁽⁷⁾ Hereditary factors have a special role and effect in the formation of allergic constitutions. The age of the parent at birth, birth method, and feeding patterns within 4 months after birth have certain effects on the formation of allergic constitutions. However, the allergic and Pinghe constitutions have no obvious differences in the ranking of children, blood type, nature, movement, sleep, and other aspects. The research results show that 48.39% of people with allergic constitution had disease histories, indicating that diseases have important effects on the formation of allergic constitutions. The occurrence rates of nasal obstruction and discharge, sternutation, asthma, tetter, and skin scratch were higher among the population with allergic constitution than those with non-allergic constitution.⁽⁸⁾

The health-related quality of life (HRQOL) scores on allergic constitution in the physiological function and emotional function dimensions were relatively low. HRQOL showed that the relative risk of the physiological function dimensions of allergic constitution was the highest, which was 3.38 times that of the Pinghe constitution. Relative risk detracting from HRQOL of allergic constitution of the female population was 3.41, which was higher than that of the male population. The brief health status questionnaire SF-36 was used to make a study on the quality of life of allergic constitution. Allergic constitution had lower scores in the physiological and psychological fields than the Pinghe constitution with obvious difference. Moreover, based on the comparison of eight dimensions, the quality of life of

allergic constitution has lower scores in all items than the Pinghe constitution.

In the psychological characteristics, the occurrence rates of the calm and bright, quiet and introverted, irritable, and sentimental characters were 18.63%, 13.60%, 18.06%, and 18.75%, respectively. All kinds of characters had no significant differences. Meanwhile, the middle type had a higher proportion in the allergic constitution population and was a little more introverted compared with that in the Pinghe constitution.⁽⁷⁾

Study on Gene Expression Profile of Allergic Constitution

After making a comparative study on the expression profiles of the full genes between the allergic constitution and the Pinghe constitution, allergic constitution was found to have a special characteristic gene expression profile. Compared with the Pinghe constitution, the allergic constitution has 86 genes with up-regulated gene expressions and 111 genes with down-regulated expressions in the profile of peripheral blood. Out of all the genes, only the expressions of fructooligosaccharide (FOS) and interleukin-16 (IL-16) genes were up-regulated. Previous studies showed that the FOS gene was closely related to allergic asthma. In allergic constitutions, the FOS gene may be the specific expression gene of allergic constitution, and the differential expression of FOS mainly exists in the central nervous system. Researchers established the relationship between the FOS and psychological condition of experimental subjects, and showed that the differential expression of the FOS gene of people with allergic constitution may affect their psychological conditions. This phenomenon will be one of the directions for further studies on the psychological characteristics of

allergic constitution. IL-16 is a chemotactic and induced molecule of eosinophilic granulocyte (Eos). Some studies found that Eos exists in the nasal tissue and mucilage of patients with chronic tuberculum septum and polypus. IL-16 acts as an immunoregulation in allergic reactions. A previous study showed that the polymorphism of the IL16-295 initiator might be related to its susceptibility to allergens. Moreover, the IL-4 and P38 MAPK signaling pathways covering the bioinformatics pathway in genes with other expression differences are related to allergies. Thus, these pathways may have regulating roles in the occurrence of allergic diseases.⁽⁹⁾

Clinical Control of Allergic Constitution and Prevention of Allergic Diseases

Currently, the treatment methods of Western medicine to allergic diseases mainly include specific therapies for the causes of diseases and nonspecific therapies for the allergic reactions. However, it is difficult to confirm the specific causes of allergic diseases, and there is no way to use some allergens to create injections. Antigen desensitization often can not include all allergic materials and has a number of disadvantages such as being time-consuming and troublesome, having potentially serious side effects, and diminishing effectiveness, which greatly limit its clinical application. We believe that it is not enough to prevent and cure allergic diseases by limiting the exposure of patients to allergens, but rather the most important thing is to regulate the allergic constitution of the patients.⁽¹⁰⁾

Constitution has adjustability and its variability includes natural change in the growth and development and the change caused by acquired man-made factors. Among many kinds of acquired man-made factors that influence constitution, the effect of drug factors can not be ignored. Drug factors not only damage individual constitution, but also build up individual health, reduce occurrence of abnormal constitution, and avoid or ease up worsening the constitution of patients. Therefore, the concept of curing allergic people instead of curing allergic diseases must be established. Preventive treatment of diseases should be used to deal with allergic constitution, and the regulation of allergic constitution must be regarded as the basis in preventing and curing allergic diseases. Nothing aside from the improvement and correction of allergic constitutions, regulation of immune functions, and elimination of pathologic bases for the return

of pathogenic factors can gradually improve the suitability of organisms to external stimuli, which make those sensitive to allergen become non-sensitive. Moreover, bad immunoreactions of organisms to allergens can be reduced to minimum.

Therefore, we developed the Guominkang Capsule with the following efficacies: replenish qi and consolidate the superficial resistance, cool blood for calming endogenous wind, and regulate allergic constitutions. Moreover, Beijing University of Chinese Medicine and Johns Hopkins University worked together to verify the inhibitory action of the Guominkang Capsule to allergic reaction. The current study shows that Guominkang Capsule can inhibit general and intracutaneous rapid hypersensitivities, ease up diosmosis of blood vessel, decrease the IgE specificity level of serum antigen, and block reactions of plasma histamine and mastocyte degranulation to delay the occurrence of allergic diseases.⁽¹¹⁾ Clinical application of this drug can improve the allergic constitutions of patients and prevent allergic diseases. Guominkang II can be applied to cure immune infertility and make the antisperm antibody (AsAb) of patients turn negative with a total effective rate of 83.33%.⁽¹²⁾ In addition, it can decrease the AsAb serum level of experimental animals,⁽¹³⁾ and inhibit the apoptosis of AsAb positive rate of epididymal sperm⁽¹⁴⁾ and expression of apoptosis-related factors Bax, and Bcl-2.⁽¹⁵⁾ Therefore, this drug can be used to regulate allergic constitutions, adjust the disorganized immune functions of organisms for the recovery of the whole functions of organisms, and change their maladaptation into adaptation to natural environments. Allergic reactions can be avoided even in much stronger stimuli. The proposed method fundamentally resolves allergies and may have important influences on the prevention and treatment of allergic diseases.

Acknowledgment

We thank Ms. Donna Wings for the revision of this manuscript.

REFERENCES

1. Wang Q, ed. Constitutionology of Chinese medicine 2008. Beijing: People's Medical Publishing House; 2009:2,44.
2. Wang Q, Zhu YB. Epidemiological investigation of constitutional types of Chinese medicine in general population: base on 21,948 epidemiological investigation data of nine provinces in China. China J Tradit Chin Med

- Pharm (Chin) 2009;24:7-12.
3. Wang Q. Classification and diagnosis basis of nine basic constitutions in Chinese medicine. J Beijing Univ Tradit Chin Med (Chin) 2005;28(4):1-8.
 4. Wang Q, Zhu YB, Xue HS, Li S. Primary compiling of Chinese medicine Constitution Questionnaire. Chin J Clin Rehabil (Chin) 2006;10(3):12-14.
 5. Zhu YB, Wang Q, Xue HS, Quaalude O. Preliminary assessment on Performance of Constitution in Chinese Medicine Questionnaire. Chin J Clin Rehabil (Chin) 2006;10(3):15-17.
 6. Zhu YB, Origasa H, Uebaba K, Xu FH, Wang Q. Development and validation of the Japanese version of the Constitution in Chinese Medicine Questionnaire (CCMQ). Kampo Med 2008;59:783-792.
 7. Su J, Qian HN, Wang Q, Li J, Gong SM. Investigation on distribution of special intrinsic constitution and quality of life. Liaoning J Tradit Chin Med (Chin) 2008;35:167-168.
 8. Qian HN, Su J, Wang Q, Li J, Gong SM, Yang S. Initial study of special intrinsic constitution. Liaoning J Tradit Chin Med (Chin) 2008;35:824-825.
 9. Wang RL. Study of allergic constitution theory and expression profile of its peripheral blood. Beijing University of Chinese Medicine; 2009:48-74.
 10. Wang Q. Similarities and differences in treatment of Chinese and Western medicine of allergic diseases. J Anhui Tradit Chin Med Coll (Chin) 2009;28(1):1-3.
 11. Li XM, Wang QF, Schofield B, Lin J, Huang SK, Wang Q. Modulation of antigen induced anaphylaxis in mice by a traditional Chinese medicine formula, Guo Min Kang. Am J Chin Med 2009;37:1-13.
 12. Wang Q, Luo QF, Zhao HW. Clinical observation on No. 2 Guominkang Capsules for treatment of 42 cases of male immune infertility. J Tradit Chin Med (Chin) 2005;46:119-121.
 13. Luo QF, Wang Q, Niu X. Effects of Guominkang Capsules No. 2 on the serum antisperm antibody in NIH male mice. J Beijing Univ Tradit Chin Med (Chin) 2003;26(3):41-43.
 14. Wu HD, Wang Q, Dong J, Ren XJ. The influence of Capsule Guominkang II on apoptosis rate of spermatozoa of AsAb positive male rat. J Zhejiang Chin Med Univ (Chin) 2011;35:231-233.
 15. Wu HD, Wang Q, Ren XJ, Li YS, Wang RL. The influence of capsule Guominkang II on Bcl-2, Bax expressions in testes of AsAb positive male rat. Chin J Androl (Chin) 2007;21:39-41.
- (Received June 18, 2012)
Edited by YUAN Lin