SYSTEMIC STUDIES ON MOLECULAR MECHANISMS FOR
NON-ALLERGENIC AIR POLLUTANT FORMALDEHYDE-INDUCED
ASTHMA

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ABSTRACT
In past 20 years, the average prevalence of asthma in China has been growing up from 0.9 % to about
3.0 %. We carried out these studies to find out the reasons and relative molecular mechanisms. Data
multiple-regression was used for prevalence and risk factor investigation (1990-2000) and animal
experiments were used for mechanism study. According to multiple-regression, 10 statistical items, in
which some of the items are building related factors, were found to be the asthma risk factors
significantly; in the animal model of formaldehyde induced asthma, vanilloid receptor, thymic
stromal-lymphocytes protein and S-nitrosoglutathione reductase were found to have important roles in
asthma initiation and promotion.

KEYWORDS
Asthma, Prevalence, Formaldehyde, Acquired atopy, Molecular mechanism

INTRODUCTION
In the past 40 years the prevalence of asthma/allergies and unspecific hypersensitivities has been
dramatically increasing worldwide despite intense research focus on the problem [1, 2]. From being a
relatively uncommon disease, a few decades ago, asthma/allergies today, in many regions, are
affecting a large part of the population. The worldwide variations in the prevalence of asthma
symptoms, can indicate causative environmental factors, and have been mapped through the
International Study of Asthma and Allergies (ISAAC) [3] and the European Community Respiratory
Health Survey (ECHRS) [4].

Despite such efforts no causality has been unambiguously established. The role of pollutants in indoor
air for the incidence and prevalence of asthma has recently been reviewed by The Institute of
Medicine, The National Academy of Sciences in USA [1]. They conclude “Asthma research clearly
needs interdisciplinary involvement– not only of clinicians, immunologists, and researchers in related
biologic areas–but also of engineers, architects, material manufacturers and others who are
responsible for design and function of indoor environments”. The American conclusions have been
confirmed in interdisciplinary reviews, of the scientific literature, conducted in Sweden [5, 6], the Nordic
countries [7] and in Europe [8].

In past 20 years, the average prevalence of asthma in China has been growing up from 0.9 % to about
3.0 %. Formaldehyde, the uppermost indoor air pollutant in China at present and concentrations have
been increasing for many years. Formaldehyde as example of adjuvant factors or “atopy stressor”, it
does not induce formaldehyde-specific IgE (more precise term is “specific IgE antibody to
formaldehyde-human serum albumin complex”) in body, but promotes more valbumin specific IgE

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formation [8], makes IL4 long lasting increased in bronchoalveolar lavage of mice [10], and impulses more Dunkin-Hartley guinea-pigs to attack asthma at the same valbumin level [11].

In this study, we wanted to find some of the environmental risk factors that associated with asthma and the statistical relationship between non-allergic air pollutant formaldehyde and asthma.

METHODS

Asthma prevalence investigation

A correlation analysis was taken using SPSS software by Dr. Soron K. K from Danmark with asthma data that published in Chinese medical journals (national wide asthma prevalence in 1990 and 2000) and the nation development data (2000) on website (http://www.stats.gov.cn/) that promulgated by National Bureau of Statistics of China.

Molecular mechanisms of formaldehyde-induced asthma

These studies were undertaken by Prof. Yang Xu and his students with many of molecular toxicological approaches, especially immuno-toxicological methods. For more information, contact Yang Xu by the email address: yangxu@mail.ccnu.edu.cn.

RESULTS AND DISCUSSIONS

Asthma prevalence of the children in China

In the history of China, there were two nationwide asthma surveys, the first one was undertaken in 1990, included 27 cities in 26 provinces (Nanjing City and Changzhou City both come from Jiangsu Province), and the second one was taken in 2000, included 32 cities in 31 provinces. The subjects of the two surveys were the same 0-14 year old urban children. These two surveys were all guided by a same leading committee with ISSAC standard protocol. The city-based results are as below figure 1. Within 10 years, the national average asthma prevalence increased from 0.91 % to 1.50 %

Correlation between asthma data and the nation development data (2000)

According to this analysis, there were some risk factors being found:

1. The birth rate has correlation coefficient -0.444 (p=0.012) with prevalence of asthma ever; -0.439 (p=0.013) with prevalence of current asthma;

2. The population accrual rate has correlation coefficient -0.501 (p=0.004) with prevalence of asthma ever; -0.497 (p=0.004) with prevalence of current asthma;
The average area of housing per family member has correlation coefficient 0.618 (p=0.000) with prevalence of asthma ever; 0.570 (p=0.001) with prevalence of current asthma; the result strongly supports the effect of “crowding” factor in Europe.

The water supply/person-day has correlation coefficient 0.339 (p=0.062) with prevalence of asthma ever; 0.290 (p=0.113) with prevalence of current asthma; the result seems to agree with the effect of “dampness” factor in Europe.

The liquefied petroleum gas supply has correlation coefficient 0.399 (p=0.026) with prevalence of asthma ever; 0.355 (p=0.050) with prevalence of current asthma; If the result means more indoor air pollutants (NO2) generated?

Also the natural gas supply has correlation coefficient 0.393 (p=0.070) with prevalence of asthma ever; 0.386 (p=0.076) with prevalence of current asthma; If the result means more indoor air pollutants (NO2) generated?

The liquefied petroleum gas supply has correlation coefficient 0.378 (p=0.036) with prevalence of asthma ever; 0.356 (p=0.049) with prevalence of current asthma; If the result means more outdoor air pollutants (PM2.5) generated?

The liquefied petroleum gas supply has correlation coefficient 0.499 (p=0.004) with prevalence of asthma ever; 0.449 (p=0.011) with prevalence of current asthma; If the result means more outdoor air pollutants (PM2.5) generated?

The W.C. Station number has correlation coefficient -0.378 (p=0.096) with prevalence of current asthma;

The Urban Greenland has correlation coefficient 0.338 (p=0.063) with prevalence of asthma ever.

Three molecular mechanisms of formaldehyde-induced asthma
Increase in the number of non-allergenic air pollutants considered to be one of the reasons. However, the molecular mechanism has not been convincingly explained. The purpose of this part is to explore the possible relations between non-allergenic air pollutants and asthma and its molecular mechanisms. The primarily results include: (1) Formaldehyde activation of Th2 lymphocytes via the pathway of type II vanilloid receptor signaling system (Fig.2); (2) Formaldehyde activation of Th2 lymphocytes via the pathway of thymic stromal-lymphocytes protein, TSLP (Fig.3); (3) Arrestment of formaldehyde on the protective effect for expedite airway via the pathway of upregulating the expression of S-nitroso-glutathione reductase (Fig.4).

Fig. 2 Activation of Th2 lymphocytes via the pathway of vanilloid receptor signaling system

Fig. 3 Activation of Th2 lymphocytes via the pathway of thymic stromal-lymphocytes protein
CONCLUSIONS
The results showed: as a model compound of "non-allergenic air pollutants" formaldehyde can induce the form of acquired atopy and asthma. One of the major pathways of formaldehyde-induced asthma is that formaldehyde can activate of Th2 lymphocytes system by way of the form of "atopy stressors". Another molecular mechanism for formaldehyde-induced asthma may come from the break of protective effect of S-nitrosoglutathione reductase.

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