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ORIGINAL ARTICLE

Prevalence of Childhood Allergic Diseases in Central Taiwan over the Past 15 Years

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Background: The prevalence of asthma, allergic rhinitis and atopic eczema in children from the developed and developing countries has been increasing.

Methods: Three epidemiological surveys of the prevalence of bronchial asthma, allergic rhinitis and atopic eczema in schoolchildren in Taichung, located in central Taiwan, were conducted in 1987, 1994, and 2002. The first questionnaire was used before the International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire was developed; the last two surveys were modified using ISAAC questionnaires.

Results: A total of 37,801, 75,960, and 11,580 children were studied in 1987, 1994 and 2002, respectively. The prevalence of allergic diseases had increased in the past two decades. Results indicate that the prevalence of bronchial asthma had risen, from 2.19% in 1987, and 3.54% in 1994, to 6.99% in 2002. Regardless of sex, the prevalence of bronchial asthma decreased with increasing age. The prevalence of allergic rhinitis was 5.1% in 1987, 12.46% in 1987, and 27.59% in 2002, and the prevalence of atopic eczema was 1.10% in 1987, 1.88% in 1994, and 3.35% in 2002.

Conclusion: There has been a significant increase in the prevalence of bronchial asthma, allergic rhinitis and atopic dermatitis in Taichung schoolchildren from 1987 to 2002.

1. Introduction

The prevalence of asthma, allergic rhinitis and atopic eczema in children from the developed and developing countries has been increasing.^{1,2} This is much more common in the developed countries than the developing ones,³ though of multiple factors being suggested to be the causes of increased prevalence of allergic diseases today, suggesting the possibility of an increase in sensitivity to environmental allergens. In recent years, the prevalence of asthma in children in Taiwan has increased markedly, too.⁴

In Taiwan, there are three major areas—northern Taiwan (e.g., Taipei and Taoyuan County), central Taiwan (e.g., Taichung), and southern Taiwan (e.g., Tainan City & Kaohsiung). Few studies exist on the prevalence of asthma, allergic rhinitis, and atopic eczema in Taichung, and limited studies are available regarding the prevalence of allergic diseases in northern Taiwan (the area includes Taipei and Taoyuan County) and southern Taiwan (Tainan City & Kaohsiung represents the area).^{4–9} To address these issues, we conducted surveys in 1994 and 2002, using questionnaires modified from the International

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Study of Asthma and Allergy in Childhood (ISAAC) questionnaire, to reevaluate the prevalence of childhood asthma, allergic rhinitis, and atopic eczema in Taichung. The resulting data was measured against the data from 1987 and 1994. We also compared the prevalence of the three allergic diseases in Taichung with the prevalence in two other areas in Taiwan.

2. Subjects and Methods

The study method was comprised of a questionnaire, which included brief descriptions of symptoms, signs of asthma, allergic rhinitis, and atopic eczema, and a video. Bronchial asthma was defined as a disease characterized by at least three attacks of recurrent, paroxysmal wheezing, and dyspnea caused by upper respiratory tract infection (URI); a drastic change in weather; exposure to dust, pollens or pollutants; and also emotional upsets within the past year. Allergic rhinitis was defined as nasal mucosa hypersensitivity, which can be caused by low temperatures, hot air, air pollution, and allergens. It is characterized by nasal itching, obstruction, sneezing, and rhinorrhea; itchy, red eyes; and an itchy throat. Atopic eczema, which may be exacerbated by diet, environment, and weather, is an allergic and pruritic dermal inflammatory response, which characteristically induces a symmetrically distributed skin eruption with predilection sites. It begins in infancy with itchy, dry, scaling skin over the forehead, cheeks, and extensor surface of the extremities. Later, the lesions display a flexural pattern of distribution, such as in the antecubital and popliteal areas, and the neck.

Questionnaires were originally planned to be sent to schoolchildren in four primary schools and six junior high schools randomly selected from every district in Taichung. However, finally, there were only 10 schools (i.e., five primary schools and five junior high schools) randomly selected from five major school districts in Taichung in 2002 from October to December. Also, there were 40 schools evenly distributed from every school district in Taichung in 1994 from October to December (i.e., primary schools and junior high schools were randomly chosen), and 24 schools evenly distributed from every school district in Taichung in 1987 from October to December (i.e., primary schools and junior high schools were also randomly chosen). However, the different sample sizes did not affect the statistical power of the comparisons. The studies and questionnaires used in the schools were almost the same in 1987, 1994, and 2002, although the 1994 and 2002 questionnaires were modified in line with ISAAC questionnaires. The Chinese version of the questionnaire was back-translated as a

validity check according to defined guidelines of allergic diseases. As all schoolchildren and parents speak Mandarin Chinese fluently in Taiwan, they were given a Chinese version of the questionnaire for completion. We added no other questions different from ISAAC, but detailed a description was displayed. The questionnaires were filled out by the students and their parents in the elementary schools, and by the students themselves in junior high school with the aid of videos, after their written informed consent was obtained for performing questionnaires. The parents were not directly asked whether their children had asthma, allergic rhinitis or atopic eczema. Instead, they were first presented with a brief description of typical signs and symptoms of those allergic diseases and then asked to fill out the questionnaires. All questionnaires were screened by pediatricians trained in the Allergy Department.

Of the children revealed by questionnaire to be atopic patients, 20% were randomly invited to visit our pediatric allergic clinic, where a physical examination was undertaken, in addition to recording past history and family history, in order to confirm the correct questionnaires. In addition, total eosinophils of peripheral blood and specific IgE of serum allergen specific test (CAP system, Pharmacia) were checked. Pre- and post- β_2 agonist inhalation of FEV₁ were also carried out, an increase of more than 12–15% was the criterion for a diagnosis of bronchial asthma. This study was approved by the hospital's Institutional Review Board. The results of physical examination, past history, family history, total eosinophils of peripheral blood, specific IgE of serum, pre- and post- β_2 agonist inhalation of FEV₁ having been also carried out and showing an increase of more than 12–15%, were almost completely matched with the questionnaire selection.

For all populations and sex, the positive responses for each asthma, rhinitis and eczema symptom with percentage change over the years of 1987, 1994 and 2002 were analyzed using the chi-squared test. Also, we considered the differences as statistically significant when p was less than 0.05. The results of the data were analyzed by χ^2 or Fisher's exact test. All analyses were performed with the statistical software SPSS 13.0.

3. Results

There were 48,463, 91,518, and 14,296 children aged 7–15 years old enrolled in the study in 1987, 1994, and 2002, respectively. The numbers of participants who completed the studies were as follows: 37,801 (18,056 male and 19,745 female) in 1987; 75,960 (37,349 male and 38,611 female) in 1994; and 11,580 (5857 male and 5723 female) in 2002 (Table 1).

Table 1 Demographics of the survey respondent

	6- to 15-year age group: <i>n</i> (%)		
	1987	1994	2002
Total subjects survey	37,801	75,960	11,580
Total schools sampled	24	40	10
Sex			
Male	18,056 (47.77)	37,349 (49.16)	5857 (50.58)
Female	19,745 (52.23)	38,611 (50.83)	5723 (49.42)
Male:Female	0.91	0.97	1.02

Table 2 Positive response (%) for each asthma, rhinitis, and eczema symptoms with percentage change in the over all population and sex for the 1987, 1994 and 2002

	6- to 15-year age group			<i>p</i> value*
	1987	1994	2002	
Asthma				
Current asthma	1.58	2.62	5.24	<0.001
Male	2.02	3.37	6.17	<0.001
Female	1.17	1.90	4.28	<0.001
Prevalence of asthma [†]	2.19	3.54	6.99	<0.001
Male	2.81	4.55	8.23	<0.001
Female	1.62	2.57	5.71	<0.001
Male:Female	1.73	1.77	1.44	
Rhinitis				
Current rhinitis	4.13	10.34	23.73	<0.001
Male	5.20	12.87	26.65	<0.001
Female	3.16	7.89	20.73	<0.001
Prevalence of rhinitis [†]	5.10	12.46	27.59	<0.001
Male	6.42	15.50	30.99	<0.001
Female	3.90	9.51	24.11	<0.001
Male:Female	1.64	1.63	1.29	
Eczema				
Current eczema	0.88	1.52	2.78	<0.001
Male			2.92	
Female			2.64	
Prevalence of eczema [†]	1.11	1.88	3.35	<0.001
Male			3.52	
Female			3.18	
Male:Female			1.11	

**p* value <0.05, significant difference for the chi-squared test; [†]prevalence—defined as asthma, rhinitis, and eczema respectively.

The respective rates of survey completion were 78%, 83%, and 81%.

Table 2 presents the current (i.e. happened in the last 12 months) and prevalent rates of symptoms of asthma, allergic rhinitis and atopic dermatitis for three studies and their comparison. The prevalence of bronchial asthma in 1987 was only 2.19% (2.81% of males and 1.62% of females). In 1994, the prevalence had increased slightly to 3.54% (4.55% of males and

2.57% of females). By 2002, the prevalence had increased significantly to 6.99% (8.23% of males and 5.71% of females). When current asthma was compared, there were also statistically significant increases among the three studies. The prevalence of bronchial asthma in 2002 represented a 1.97-fold increase from 1994 (male: 1.81-fold; female: 2.22-fold) and a 3.19-fold increase from 1987 (male: 2.92-fold; female: 3.52-fold). From the levels in

1994, there was an apparent 1.6-fold increase during the previous 8 years.

The prevalence of allergic rhinitis was 5.10% (6.42% for boys and 3.9% for girls) in 1987; 12.46% (15.5% for boys and 9.51% for girls) in 1994; and spiked to 27.59% in 2002 (30.99% for boys and 24.11% for girls). In 1994, there was a 2.4-fold increase in the prevalence of allergic rhinitis over the previous 8 years. The prevalence in 2002 was 2.21-fold greater than in 1994 (2.00-fold for boys and 2.53-fold for girls), and was 5.40-fold greater than in 1987 (4.83-fold for boys and 6.18-fold for girls). There were

similar results when the current rhinitis was compared among the three groups.

There was also an increase in the current and prevalence rates of atopic eczema over a period of 15 years. The prevalences of the different periods were 1.11%, 1.88%, and 3.35%, respectively. There was little increase from 1987 to 1994, but there was a 3.05-fold increase from 1987 to 2002.

Tables 3 and 4 compare our study (6–12 and 13–15 years old, respectively) with the survey of asthma, allergic rhinitis and allergic eczema in northern Taiwan (the area includes Taipei and Taoyuan County)

Table 3 Prevalence of asthma and other allergic disorders in our study (6–12 years) compares with other studies (%)

Allergic disorders	Our study: Taichung (central Taiwan)	Northern Taiwan		Southern Taiwan
		Taipei	Taoyuan county	Tainan city
		2002 (6–12 yr) (n=6288)	1997 [†] (6–7 yr) (n=4806)	2002 [‡] (6–8 yr) (n=3079)
Asthma				
Current asthma	5.67	9.6**	7.5*	
Prevalence of asthma	6.90	12.7**	16.8**	8.45*
Allergic rhinitis				
Current allergic rhinitis	20.79		36.3**	
Prevalence of allergic rhinitis	26.11		41.3**	29.83**
Allergic eczema				
Current eczema	2.87		7.8**	
Prevalence of eczema	3.05		9.7**	

* $p < 0.01$, ** $p < 0.001$, the chi-squared test significant differences between our study and other studies in the same allergic disease, respectively; [†]Reference 10; [‡]Reference 7; [§]Reference 5.

Table 4 Prevalence of asthma and other allergic disorders in our study (13–15 years) compared with other studies (%)

Allergic disorders	Our study: Taichung (central Taiwan)	Northern Taiwan	
		Taipei	Taoyuan county
		2002 (13–15 yr) (n=5292)	1994–1995 [†] (13–14 yr) (n=11,400)
Asthma			
Current asthma	4.67	5.2	4.2
Prevalence of asthma	7.09	9.0**	10.8**
Allergic rhinitis			
Current allergic rhinitis	27.23	28.8*	37.8**
Prevalence of allergic rhinitis	29.35	35.1**	47.9**
Allergic eczema			
Current eczema	2.51	1.4**	4.3**
Prevalence of eczema	3.33	11.8**	5.7**

* $p < 0.05$, ** $p < 0.001$, the chi-squared test significant difference between our study and other studies in the same allergic disease, respectively; [†]Reference 8; [‡]Reference 7.

children (6–8 years old and 13–15 years old) and southern Taiwan (Tainan City represents the area) children (6–12 years old) conducted in 1994–1995, 1997 and 2002.^{5,7,8,10} We found that the current and prevalence rates of asthma, allergic rhinitis and atopic eczema were lower in our study than those of the study in Taoyuan County in 2002, except the current asthma group of children aged between 13 and 15 years old.

4. Discussion

Taiwan is a subtropical country with high relative humidity (>80%) levels throughout the year, but there are no differences in relative humidity and temperature among Taichung, northern Taiwan and southern Taiwan. Taichung, a city in central Taiwan, has relative humidity levels ranging from 76% (November and December) to 82% (June), with average temperatures ranging from 15.7°C in January to 28.4°C in July.

In the pridian study, similar questionnaires previously employed to survey the prevalence of allergic diseases were also used as early as 1974 to survey the prevalence of allergic diseases.⁴ We used the questionnaires to compare the prevalence of the allergic diseases in Taichung for three different dates, and compared the current and prevalence rates in Taichung, northern Taiwan (the area included Taipei and Taoyuan County) and southern Taiwan (Tainan City represented the area). The total response rates in our study were 78%, 83%, and 81%, respectively, in 1987, 1994 and 2002. But reviewing other studies in Taiwan, the questionnaire response rates were almost above 90%,^{5,7,9} and for one report from Malta, the questionnaire response rate was almost 90%.¹¹ The validity of the questionnaire is likely to have varied across cultures and languages, thus the difference of the response rates appeared. For example, the equivalent of “wheezing” understood by English speakers may not be understood by Taiwanese. Also, it may be owing to infrequent health education for allergic diseases that lower questionnaire response rates were found in our study. But the randomness of our sample adds strength to the result obtained, thus the questionnaires are a reliable way to differentiate asthmatics from nonasthmatics.⁴

The trend for the prevalence of bronchial asthma, allergic rhinitis and atopic eczema, both in different countries worldwide as well as within distinct countries, is increasing on the whole, despite appearing to vary widely.¹² The rise in the prevalence of allergic diseases can be accounted by changes in the environment, particularly with the advent of new allergens.¹³ It is a valid argument that the interpretation of an increase in the prevalence of allergic diseases could be due to the use of a variety of different

questionnaires and methods used with different criteria. However, in the current study, the same questionnaires, methods and diagnostic criteria were used at three disparate time points. Contributing factors to the increase in the prevalence of allergic diseases include changes in housing structure, interior modification after urbanization, and a probable decrease in breast-feeding practices. There is also a relationship between dampness in the home and childhood asthma. Fungi, dust mites, and cockroaches, which are prevalent in subtropical areas, are found in damp homes; these produce substances that can trigger allergic reactions.¹⁴

The differences in asthma prevalence among different population groups and different time periods are due to differential exposure to environmental factors; genetic variation alone could not account for the sharp rise in the prevalence of asthma.¹⁵ Ninan et al reported that the prevalence of wheezing in Aberdeen (United Kingdom) rose from 4.1% in 1964 to 10.2% in 1989.¹⁶ In Australia, the prevalence of the history of asthma among 7-year-old rose from 19.1% in 1964 to 46% in 1990.¹⁷ In Taiwan, Lee et al reported that physician-diagnosed asthma increased from 4.54% in 1995–1996 to 6.05% in 2001.¹⁸ Questionnaire-determined asthma also increased from 9.5% in 1995–1996 to 11.8% in 2001.⁹ In the current study, the prevalence of asthma in schoolchildren in Taichung rose from 2.19% in 1987 to 3.54% in 1994 and to 6.99% in 2002. In 2002, there was a 3.19-fold increase over the previous 15 years and a 1.97-fold increase from the previous 7 years. The prevalence of asthma in Taipei schoolchildren increased from 1.3% in 1974 to 5.1% in 1985 and to 10.8% in 1994 (unpublished data; KH Hsieh; National Taiwan University Hospital: 1994), indicating a higher prevalence of asthma among schoolchildren in Taipei than in Taichung. Tables 3 and 4 confirm that the current and prevalence rates of asthma, allergic rhinitis and atopic dermatitis were almost lower in the central area than the prevalence in northern and southern areas in Taiwan. According to the ISAAC Steering Committee reported in 1998, the prevalence rates of asthma in Taipei were 9.0% and 12.7%, respectively for the 13–14 years old group and 6–7 years old group; the prevalence rates of asthma in Asia-Pacific area were 9.4% and 10.7%, respectively for the 13–14 years old group and 6–7 years old group; the prevalence rates of asthma in Southeast Asia (India was represented in this area) were 4.5% and 3.7%, respectively for the 13–14 years old group and 6–7 years old group.¹⁰ From the comparison, the increasing trend of asthma is in accordance with the rapid pace of urbanization of lifestyle.

Urban children have a heightened risk of asthma, regardless of race or family income.¹⁹ Our study

and other screening in Taiwan also showed the same results.^{20,21} A series of studies in Seattle, Washington (USA) showed that airborne particulate matter was associated with exacerbation of asthmatic symptoms: the degree of wood smoke correlated with decreased lung function in children.²² Researchers in Finland showed causal relationships among sulfur dioxide (SO₂), PEF, and respiratory symptoms in children with cough; in addition, particulate matter (PM₁₀), black smoke and nitrogen dioxide (NO₂) were associated with a decline in peak flow in asthmatic children.²³ And both Ho et al (2007) and Guo et al (1999) have reported that air pollution factors also interacted with weather parameters when related to asthma attack rate.^{24,25} Elevated concentrations of ozone, which has also been implicated in airway remodeling and chronic inflammation changes²⁶ have been associated with the number of daily emergency cases of asthma in an inner city hospital in Atlanta.²⁷ Hwang et al also observed that long-term exposure to traffic-related outdoor air pollutants such as NO₂, CO, and O₃ increased the risk of asthma in Taiwanese schoolchildren.²⁸ Further more, asthma appears to be a disease of modern civilization such that in utero and early-life environmental exposure leads to increased IgE-dependent hypersensitivity followed by bronchial hyperreactivity and airway inflammation.²⁹ All of the discussed factors may explain why a higher prevalence of childhood asthma exists in Taipei, despite Taipei and Taichung sharing the same climate and weather conditions.

In our study, the prevalence of allergic rhinitis among schoolchildren in Taichung rose from 5.1% in 1987 to 12.46% in 1994, and sharply rose to a high of 27.59% in 2002, exhibiting a 5.40-fold increase over a period of 14 years. The prevalence of hay fever in British children from Aberdeen rose from 3.2% in 1964 to 11.9% in 1989.¹⁶ In addition, there had been a reported 50% increase in prevalence of allergic rhinitis among children 12 years of age in South Wales from 1973 to 1985.³⁰

Atopic dermatitis appears to have increased in prevalence over the past three decades in Western countries, from affecting 2–3% of children before 1960 to 9–12% of those born after 1970. Atopic eczema in children is characterized by a history of itchy skin condition in addition to three or more of the following criteria: (1) history of a rash in the skin creases (fold of elbows, behind the knees, front of ankles, around the neck); (2) history of asthma or hay fever; (3) history of generally dry skin in the past year; (4) onset under the age of 2 years; and (5) visible flexural dermatitis as defined by a photographic protocol.³¹ The prevalence of atopic eczema in the UK has increased from 5.3% in 1964 to 12% in 1989.¹⁶ Current estimates from the UK and

Northern Europe suggest that the prevalence of atopic dermatitis of childhood is 15–23%.^{16,32} The prevalence of atopic dermatitis in our survey of Taiwan was much lower than that reported for other Asian countries: Singapore (20.8% among 7-, 12-, and 16-year-old, 2002),³³ Hong Kong (20.1% among 14-year-old),³⁴ and Japan (19% among 7–9 year-olds).³⁵ However, the prevalence of atopic dermatitis among schoolchildren in Taichung in 2002 was only 3.35%, and there was also an increase of 3.05-fold over the previous 14 years. This increased prevalence of atopic eczema may be due to a decline in breast-feeding, the early introduction of weaning foods and the widespread use of food additives.

Up to now, there have been some studies evaluating the prevalence of asthma, allergic rhinitis and atopic eczema in schoolchildren in the domestic and foreign papers. Chen et al observed that the prevalence of infectious diseases was significantly higher in children with allergic diseases.³⁶ Liao et al reported that the prevalence of asthma diagnosed by a doctor according to the ISAAC, phase III standard written questionnaire administered to 7873 first grade schoolchildren, 6 to 8 years of age from 47 different elementary schools in Changhua County, was 7.0%; the prevalence of rhinitis was 24.6% and the prevalence of eczema was 18.0%.³⁷ Chiang et al also reported that the overall cumulative and 12-month prevalence of wheezing, rhinitis, and eczema were 7.4%, 43.0%, and 7.2%, respectively, using the ISAAC questionnaire administered to 11,874 students from 14 schools in central Taiwan (4167 children aged between 10 and 12 years old and 7677 older children aged between 13 and 15 years).³⁸ It was shown that boys had a significantly higher prevalence of wheezing and rhinitis ($p < 0.001$ and $p = 0.001$) when compared to girls, and the study also found that the prevalence rates among younger children with symptoms of wheezing, rhinitis, and recurrent itchy rash in the past 12 months (8.2%, 44.4%, and 8.8%) were higher than that among older children (6.9%, 42.2%, and 6.3%, respectively).

In 2005, Yan et al reported that there was increasing prevalence of symptoms of asthma, allergic rhinitis, and atopic eczema in the past 12 months in 13- to 14-year-old children in Taipei in a 7-year period (increased by 37%, 51%, and 193%, respectively, compared to the ISAAC phase I study performed in 1994–1995).⁸ The study was performed between 1st December, 2001 and 31st January, 2002. Furthermore, Lau and Karlberg reported that the prevalence of allergic disorders in Hong Kong was comparable to that in Singapore and Great Britain.³⁹ Several potential risk factors, such as parental wheezing, frequent upper respiratory tract infection, born in Hong Kong, male sex and month of birth in girls, were identified.

The prevalence of asthma, allergic rhinitis and atopic eczema in schoolchildren has been gradually increasing in Taiwan. Air pollution caused by Taiwan's rapid industrialization has increased massively throughout the island. In addition, there is a significant correlation between passive smoking, long-term outdoor air pollution (including nitrogen dioxide, ozone, carbon monoxide, airborne dust) and adolescent asthma.⁴⁰ Taichung has become much more affluent in the last 15 years, and the resulting increased traffic fumes are amongst the major atmospheric pollutants. It has been suggested that atopic dermatitis is more prevalent in higher social classes,⁴¹ and that the rapid urbanization of Taichung, including a more westernized lifestyle and a higher standard of living and education, may explain the rapid increase of atopic dermatitis in Taichung children.

5. Conclusion

There has been a significant increase in the prevalence of bronchial asthma, allergic rhinitis and atopic dermatitis in Taichung schoolchildren from 1987 to 2002. This study suggests that further research into the causes of such a significant increase is required.

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References

- Dahl R, Anderson PS, Chiavto T, Valovirta E, de Monchy J. National prevalence of respiratory allergic disorders. *Resp Med* 2004;98:398–403.
- Kivity S, Shochat Z, Bressler R, Weiner M, Lerman Y. The characteristics of bronchial asthma among a young adult population. *Chest* 1995;108:24–7.
- Cookson JB. Prevalence rates of asthma in developing countries and their comparison with those in Europe and North America. *Chest* 1997;91(Suppl):97–103.
- Hsieh KH, Shen JJ. Prevalence of childhood asthma in Taipei, Taiwan, and other Asian Pacific Countries. *J Asthma* 1988;25:73–82.
- Tsuang AHC, Su JHJ, Kao FF, Shih HC. Effects of changing risk factors on increasing asthma prevalence in southern Taiwan. *Paediatr Perinat Epidemiol* 2003;17:3–9.
- Chiang W, Tsai IF, Tsai WC, Chen BH. Effect of age on allergen response of allergic patients in southern Taiwan. *Kaohsiung J Med Sci* 2004;20:323–9.
- Kao CC, Huang JC, Qu LS, See LC. The prevalence, severity and seasonal variation of asthma, rhinitis and eczema in Taiwanese schoolchildren. *Pediatr Allergy Immunol* 2005;16:408–15.
- Yan DC, Ou LS, Tsai TL, Wu WF, Huang JL. Prevalence and severity of symptoms of asthma, rhinitis, and eczema in 13- to 14-year-old children in Taipei, Taiwan. *Ann Allergy Asthma Immunol* 2005;95:579–85.
- Lee YL, Lin YC, Hwang BF, Guo YL. Changing prevalence of asthma in Taiwanese adolescents: two surveys 6 years apart. *Pediatr Allergy Immunol* 2005;16:157–64.
- ISAAC Steering Committee. Worldwide variations in the prevalence of asthma symptoms: the International Study of Asthma and Allergies in Childhood (ISAAC). *Eur Respir J* 1998;12:315–35.
- Montefort S, Lenicker HM, Caruna S, Agius-Muscat H. Asthma, rhinitis and eczema in Maltese 13–15 year-old schoolchildren—prevalence, severity and associated factors [ISAAC]. *Clin Exp Allergy* 1998;28:1089–99.
- Cookson JB. Prevalence rates of asthma in developing countries and their comparison with those in Europe and North America. *Chest* 1987;91:S97–103.
- Hara HJ. Hay fever among Japanese. *Arch Otolaryngol* 1934;20:668–76.
- Korsgaard J. Mite asthma and residency. *Am Rev Respir Dis* 1983;128:231–5.
- Drazen JM, Silverman EK. Genetics of asthma: conference summary. *Am J Respir Crit Care Med* 1997;156:S69–71.
- Ninan TK, Russell G. Respiratory symptoms and atopy in Aberdeen schoolchildren: evidence from two surveys 25 years apart. *BMJ* 1992;304:873–5.
- Roberston CF, Heycock E, Bishop J, Nolan T, Olinsky A, Phelan PD. Prevalence of asthma in Melbourne schoolchildren: changes over 26 years. *BMJ* 1991;302:1116–8.
- Lee YL, Hwang BF, Lin YC, Guo YL and Taiwan ISAAC Study Group. Time trend of asthma prevalence among school children in Taiwan: ISAAC phase I and III surveys. *Pediatr Allergy Immunol* 2007;18:188–95.
- Aligne CA, Auinger P, Byrd RS, Weitzman M. Risk factors for pediatric asthma. Contributions of poverty, race, and urban residence. *Am J Respir Crit Care Med* 2000;162:873–7.
- Yu JH, Lue KH, Lu KH, Sun HL, Lin YH, Chou MC. The relationship of air pollution to the prevalence of allergic diseases in Taichung and Chu-Shan in 2002. *J Microbiol Immunol Infect* 2005;38:123–6.
- Lin RS, Sung FC, Huang SL, et al. Role of urbanization and air pollution in adolescent asthma: a mass screening in Taiwan. *J Formos Med Assoc* 2001;100:649–55.
- Koenig JQ, Laeson TV, Hanley QS, et al. Pulmonary function changes in children associated with fine particulate matter. *Environ Res* 1993;63:26–38.
- Timonen KL, Pekkanen J. Air pollution and respiratory health among children with asthmatic or cough symptoms. *Am J Respir Crit Care Med* 1997;156:546–52.
- Ho WC, Hartley WR, Myers L, et al. Air pollution, weather, and associated risk factors related to asthma prevalence and attack rate. *Environ Res* 2007;104:402–9.
- Guo YL, Lin YC, Sung FC, et al. Climate, traffic-related air pollutants, and asthma prevalence in middle-school children in Taiwan. *Environ Health Perspect* 1999;107:1001–6.
- Bascom R. Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Health effects of outdoor air pollution. *Am J Respir Crit Care Med* 1996;153:3–5.
- White MC, Etzel RA, Wilcox WD, Lloyd C. Exacerbations of childhood asthma and ozone pollution in Atlanta. *Environ Res* 1994;65:56–68.
- Hwang BF, Lee TL, Lin YC, Jaakkola JJK, Guo YL. Traffic related air pollution as a determinant of asthma among Taiwanese school children. *Thorax* 2005;60:467–73.

29. Holgate ST. Asthma and allergy—disorders of civilization? *QJM* 1998;91:171–84.
30. Burr ML, Butland BK, King S, Vaughan-Williams E. Changes in asthma prevalence: two surveys 15 years apart. *Arch Dis Child* 1989;64:1452–6.
31. Larsen FS, Hanifin JM. Secular change in the occurrence of atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)* 1992; 176:7–12.
32. Larsen FS, Diepgen T, Svensson A. The occurrence of atopic dermatitis in North Europe: an international questionnaire study. *J Am Acad Dermatol* 1996;34:760–4.
33. Tay YK, Kong KH, Khoo L, Goh CL, Giam YC. The prevalence and descriptive epidemiology of atopic dermatitis in Singapore school children. *Br J Dermatol* 2002;146:101–6.
34. Leung R, Ho O. Asthma, allergy and atopy in three south-east Asian populations. *Thorax* 1994;49:1205–10.
35. Sugiura H, Umemoto N, Deguchi H, et al. Prevalence of childhood and adolescent atopic dermatitis in Japanese population: comparison with the frequency examined 20 years ago. *Acta Derma Venereol (Stockh)* 1998;78:293–4.
36. Chen CF, Wu KG, Hsu MC, Tang RB. Prevalence and relationship between allergic diseases and infectious diseases. *J Microbiol Immunol Infect* 2001;34:57–62.
37. Liao MF, Huang JL, Chiang LC, Wang FY, Chen CY. Prevalence of asthma, rhinitis, and eczema from ISAAC survey of schoolchildren in central Taiwan. *J Asthma* 2005;42: 833–7.
38. Chiang LC, Chen YH, Hsueh KC, Huang JL. Prevalence and severity of symptoms of asthma, allergic rhinitis, and eczema in 10- to 15-year-old schoolchildren in central Taiwan. *Asian Pac J Allergy Immunol* 2007;25:1–5.
39. Lau YL, Karlberg J. Prevalence and risk factors of childhood asthma, rhinitis and eczema in Hong Kong. *J Paediatr Child Health* 1998;34:47–52.
40. Williams HC, Strachan DP, Hay RJ. Childhood eczema: disease of the advantaged? *BMJ* 1994;308:1132–5.
41. Wang TN, Ko YC, Chao YY, Haung CC, Lin RS. Association between indoor and outdoor air pollution and adolescent asthma from 1995 to 1996 in Taiwan. *Environ Res* 1999; 81:239–47.