

Silk-induced asthma in children: a report of 64 cases

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A total of 64 children less than 15 years of age with asthma caused by silk were studied. The diagnosis was based on a history of wheezing, positive skin tests to silk, positive conjunctival or nasal provocation tests, or serum IgE-Sw (silk waste). The average age of onset was 4 years 2 months. Sex ratio (M:F) was 3.6:1. A positive skin test is essential for the diagnosis. Conjunctival provocation tests were performed in 80% of cases because of reliability, safety, and convenience. The first symptom appeared an average of 10 months after initial exposure to silk. In 61% of patients, asthma was accompanied by allergic rhinitis but in only 14% of cases by conjunctivitis. In most cases, asthma occurred in winter, due to seasonal use of bed quilts or clothes filled with silk. Silk is a highly potent allergen. The average mean wheal diameter elicited by silk in prick testing was larger than two histamine equivalent prick tests. A cross reactivity exists among mulberry silk, and silkworm cocoons, batryticated silkworms, and silkworm chrysalis.

INTRODUCTION

China is the homeland of silk. Sericulture dates back approximately 5,000 years. It was transferred to Japan and other countries later through the Silk Road. China and Japan dominate the world silk production.¹ Allergy to silk products is well-known as an occupational hazard in sericulture.² Allergy to silk often follows exposure to bed quilts or clothes filled with silk waste (Sw) as well as occupational exposure. In this paper, we report clinical and immunologic data on children with asthma induced by silk.

MATERIALS AND METHODS

Children less than 15 years of age with asthma were seen in our clinic from January 1987 to May 1988. The patients were evaluated with complete medical histories, skin tests (intradermal or prick tests), conjunctival and/or nasal provocation tests and laboratory studies including total IgE, IgE-Sw and Sw precipitating antibody measurements.

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Antigens

Silk waste, silkworm cocoons, silkworm chrysalis, and batryticated silkworms³ all are related to mulberry silk. The first three were bought on the open market. The last was bought from a traditional Chinese medicine store. The extracts of these materials and other common inhalant allergens were prepared in our laboratory. The concentration of extracts of Sw was 1:15 wt/vol, protein content was 1.2 mg/mL.

Skin Testing

All the patients were skin tested with Sw by either intradermal or prick testing.

Intradermal tests were done using silk waste antigen 1 in 1,500 wt/vol and a routine battery of 14 common allergens including molds, house dust mite, and pollens. The solvent was used as a negative control. The reaction was read after 15 to 20 minutes. The intensity of the reaction was judged by the size of the wheal and compared with the control reaction. It was graded from 0 to 4+.⁴

Skin prick tests with extracts of silk waste 1:15 wt/vol, cocoons 1:15 wt/vol, batryticated silkworms 1:20 wt/vol, and chrysalis 1:20 wt/vol were performed. Each skin reaction was compared with the positive (1

mg/mL histamine hydrochloride) and negative (phenol solvent) controls. The results were recorded after 15 minutes. The wheal reactions produced by the extracts of allergen or histamine were recorded by measuring the longest diameter (D) and the diameter perpendicular to it (d) to obtain the mean wheal diameter (MWD; $D + d/2$). If the negative control also produced a wheal and flare reaction, it was subtracted from the MWD elicited by extracts of allergen. For the histamine control method the MWD elicited by extracts of allergen were compared with that of histamine hydrochloride as recommended by the Northern Society of Allergology.⁵ The size of a wheal larger than 1 HEP (histamine equivalent prick test)⁶ was considered positive. Patients were requested to observe the test site four to six hours later for the development of any late phase induration.

Intradermal tests to Sw were performed in 50 patients and prick test to Sw in 44 patients.

Conjunctival and Nasal Provocation Test

The conjunctival provocation test was performed on 51 patients by putting a drop of extract of Sw in 1:150 wt/vol into an eye with the other eye used as a negative con-

trol.⁷ The result was observed after 15 minutes and graded as follows: (-) no signs and symptoms; (+) congestion and itching and/or lacrimation; (++) eye symptoms accompanied with nasal manifestations such as sneezing, watery discharge, obstruction, and/or coughing, swelling of eyelids or face.

Only 31 patients received nasal provocation tests because of a lack of sufficient cooperation by many. The nasal provocation test was performed as described elsewhere.⁷ The result was graded as follows: (-), no signs and symptoms; (+), sneezing greater than five bouts, and watery discharge, nose itching, and/or obstruction, mucous membrane of the nose appeared edematous, congested or pale; and (++) coughing, tight chest.

All antihistamines and sympathomimetic drugs were withdrawn at least 24 hours before all tests.

None of the patients was tested by bronchial provocation.

Total Serum IgE and IgE-Sw

Venous blood was obtained from 80% of the patients.

Total serum IgE was measured by enzyme-linked immunosorbent assay (ELISA) in the central laboratory. Measurement of IgE-Sw was performed using ELISA single antibody technique⁸ in a laboratory of our department. The results were scored from 0 to 4 according to the scale.

Precipitins against Sw were determined by the double gel diffusion technique of Ouchterlony.

RESULTS

A total of 64 children were identified as having asthma caused by bed quilts or clothes filled with Sw. One of them had episodes of dry coughing only. The diagnosis was based on the history, positive skin testing, and conjunctival or nasal provocation test to silk waste extract.

Age distribution of onset of symptoms and sex prevalence are shown in Table 1. The age of onset of symptoms ranged from 4 months to

13 years and 5 months with an average age of 4 years and 2 months. The overall sex ratio (M:F) was 50:14, with boys predominating in all age groups. A summary of the clinical characteristics of 64 patients with asthma caused by silk obtained from the questionnaire are listed in Table 2. The patients were considered atopic when they fulfilled two of the following three conditions: (1) and (2) personal and family history of allergic diseases (asthma, allergic rhinitis, atopic dermatitis) and (3) more than two positive skin tests to other common inhalant allergens. Fifty-three percent were graded as severe. There was also rhinitis in 61%, but only 14 % of the patients

had conjunctivitis. Any cutaneous eruption was rare.

The results of skin reactions to intradermal testing with silk waste and the MWD of skin prick test to silk waste, silkworm cocoons, batryticated silkworms and silkworm chrysalis are shown in Tables 3 and 4, respectively. Late phase skin reactions to prick tests appeared in three cases.

The results of conjunctival and nasal provocation tests to Sw are shown in Table 5.

Total serum IgE was elevated to >1,000 IU/mL (normal value = 273 $\pm$ 456) in 31 out of 53 patients (58.5%). A positive (class 1-4) IgE-Sw (ELISA) result was present in 84.4% (38/45) of the cases.

Table 1. Age of Onset of Symptoms by Sex (n = 64)

Age of First Manifestation, yr	Male	Female
<3	29	9
3-5	11	1
6-10	5	4
11-15	5	0
Total	50	14

Table 3. Distribution of Positive Reactions in Intradermal Testing Using Sw

Degree of Positive Reaction	No. of Patients	% of Patients
+	2	4.0
++	16	32.0
>+++	32	64.0
Total	50	100.0

Table 2. Summary of Clinical Manifestations in 64 Silk Waste-Induced Asthmatic Patients from Questionnaire

	No. of Patients	% of Patients
Sensitization time, 10 months (20 day-63 mo)		
Atopy	48	75.0
Severity of asthma*		
Mild	4	6.3
Moderate	26	40.6
Severe	34	53.1
Symptoms		
Sneezing, watery discharge, nose itching	39	60.9
Conjunctival congestion, itching or lacrimation	9	14.1
Fever	8	12.5
Urticaria	1	1.6
Increased density in x-ray	10	15.6
Allergy to batryticated silkworms	3	4.7
Season of symptomatic attacks		
Winter	53	82.8
Perennial	9	14.1
Autumn, summer	2	3.1

* Mild = only wheezing or coughing at night, playing as usual, no school days lost. Moderate = staying in bed most of the day during episodes of asthma. Severe = profuse wheezing, oxygen inhalation.

Table 4. Skin Prick Test Reaction to Silk Waste, Silkworm Cocoons, Batryticated Silkworms, Silkworm Chrysalis, and Histamine Hydrochloride

	Silk Waste	Silkworm Cocoons	Batryticated Silkworms	Silkworm Chrysalis	Histamine
No. of patients	44	56	55	55	56
MWD, mm	14.2	9.4	10.6	7.0	5.8
SD	4.5	4.0	4.7	2.8	1.7
Range	7.5-30	3.5-16.5	3-22.5	0-12.5	3-10.5

Table 5. Results of Conjunctival and Nasal Provocation Testing with Sw

Results of Provocation Test	Conjunctival		Nasal	
	No. of Patients	%	No. of Patients	%
-	2	3.8	7	22.6
+	20	38.5	24	77.4
++	30	57.7	0	0.0
Total	52	100.0	31	100.0

None of 40 patients had demonstrable precipitating antibody against silk waste by the double gel diffusion.

DISCUSSION

Silk in China is mainly divided into two groups, the mulberry silk and wild silk. Both of them have identical allergenicity.^{10,11} Allergy to silk is most frequent with mulberry silk rather than with wild silk in China due to its popularity in use.

In the reeling process, the silk thread is reeled off the cocoon. An unbroken silk thread can be collected as far as one mile from an undamaged cocoon. Severely broken silk threads are only used as a filling for bed quilts or clothes and mattresses and are known as Sw.¹⁰ This is an important source of allergen. Textile products of silk are considered to be practically nonallergenic owing to the complicated processing.

Silk thread consists of two main parts, fibroin and sericin. Sericin is a glue-like substance cementing two fibroin filaments of silk into a single thread. The allergenicity of fibroin is much weaker than that of sericin.¹

In this study, skin testing was found to be very sensitive in the

diagnosis in silk allergy. Disease possibility was correlated with the size of the wheal elicited by skin test. The larger the wheal, the more likely the disease.

An average MWD of skin prick test elicited by silk waste was 14.2 mm, which is apparently larger than 2 HEP. One histamine equivalent prick test is equal to 1,000 biologic units (BU)/mL, which is considered to be of significance in the diagnosis of allergy.⁶ Silk waste extract must therefore contain potent allergens. A MWD smaller than 1 HEP was found to be clinically doubtful or irrelevant. In addition, late reactions to skin prick tests developed at the skin test site three to six hours later in three children; however serum precipitating antibody against silk waste could not be demonstrated in any of them.

The conjunctiva is rich in mast cells and apt to induce an antigen antibody reaction.¹² Conjunctival provocation testing was chosen not only for its safety and convenience, but also for the frequency of induction of obvious symptoms, even though the occurrence of histories of allergic conjunctivitis was rather low. Furthermore, dropping extracts of allergen into the eye is easier and better accepted by the children than injection into the skin. These tests suggested that conjunctival provocation test is an appropriate choice for children with silk allergy.

Serum IgE-Sw in most patients was positive, but negative results did not rule out silk allergy.

Clinically, 64 patients had asthma. The degree of severity is indicated in Table 2. Cyanosis had

occurred in half the patients. In only one patient were symptoms limited to severe dry coughing without wheezing. Although coughing usually accompanies wheezing, occasionally it may be the only symptom of asthma.¹³ Allergic nasal symptoms were not prominent in two younger patients who had no sneezing, watery discharge, or nasal itching except for nasal obstruction. Some patients also had fever and/or opacifications in chest radiographs during asthmatic attacks.

The time required for sensitization from exposure to silk to appearance of first symptoms was an average of 10 months. This is longer than that reported by Johansson,¹⁰ probably because the majority of the children do not use silk-filled bedding or clothing in constant direct contact. Silk waste substances involved in Chinese children's daily life are silk-filled bed quilts or clothes, toys, and mattresses, while Sw curtains and carpets are not popular in China. These children may wear silk-filled clothes or lie under or on silk-filled quilts as the common sources inducing silk allergy in China. Asthma may be caused by other people's clothes filled with Sw or nearby silk bedding in kindergartens. Unfortunately, only rare parents were aware of what their children were allergic to before our evaluation. Once the diagnosis was made, an attentive environmental investigation should be made to identify the sources of silk. In two cases we found the excitant related to their parents' occupations.

Seasonal symptoms correlated with the seasonal exposure to silk. Most patients had used silk-waste filled blankets during the winter. Their symptoms usually occurred in the winter. Often nocturnal asthma occurred in patients exposed to silk-filled bedding.

In three patients urticaria developed immediately after ingestion of batryticated silkworms as a Chinese traditional medicine. In addition, the MWD of skin prick tests for

patients to the extracts of cocoon, batryticated silkworms, and chrysalis were all larger than 1 HEP. Cross reactivity among them is very likely. Patients allergic to silk may be allergic to these substances related to silk.

Batryticated silkworm is a silkworm that died from a mycotic infection caused by *Beauveria bassiana*. These are commonly used in Chinese traditional medicine. This material may contain two antigenic components, silkworm itself and *Beauveria bassiana*. If a patient is allergic to batryticated silkworms, skin tests with both silkworm extracts and the fungal *Beauveria bassiana* extracts is necessary. None of these patients showed a positive reaction to *Beauveria bassiana*.

Most of the children responded favorably to exposure avoidance. Symptoms usually subsided after two or three days. As Sw has been so popular in China, it is very difficult to avoid silk exposure in daily life; therefore, in some highly sensitive patients complete resolution of symptoms is unlikely. Specific Sw immunotherapy has proven to be effective in our experience.

Due to the high potency of silk allergens and frequent exposure to Sw in China, whenever asthma oc-

curs in children in the winter, especially if accompanied by allergic rhinitis, silk products should be considered a possible cause. Any patient with multiple atopic diseases should handle silk waste only with great care.

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