

orally (100 mg/8 h), and she began to receive a tricyclic antidepressant.

In week 4 of the treatment with phenytoin, the patient developed in 24–48 h fever of 39°C combined with generalized erythematous skin rash. The other systemic and neurologic probes were normal. The blood cell count showed leukocytosis with eosinophilia (16 500 leukocytes/mm, 12% eosinophils), and the coagulation study, biochemical and hepatic profile, hemocultures, coprocultures, and urocultures then done, as well as the chest radiography, were normal. Computed tomography of the skull described the continuity to a parietal level without any other important alteration. With the clinical suspicion that there was an adverse reaction to medication, the phenytoin and the tricyclic antidepressant were stopped. During the following week, the patient continued to show fever and eosinophilia, and the skin rash became desquamative. The clinical situation worsened gradually and between days 8 and 10 after stopping the phenytoin, she showed acute hepatic failure with high cytolysis and cholestasis (glucose 57 mg/dl, SGOT 1535 U/l, SGPT 497 U/l, gamma GT 1055 U/l, alkaline phosphatase 662 U/l, cholesterol 110 mg/dl, total bilirubin 17.5 mg/dl, LDH 2862 U/l, albumin 1.7 g/dl), linked to severe coagulopathy (prothrombin Ac. 21%, APTT 53/29).

The analysis then done did not reveal any indication of a possible cause, and the abdominal echography showed only a spleen slightly increased in size. In the following days, the patient developed acute renal failure and pancytopenia with severe neutropenia (2400 leukocytes/mm with 190 neutrophils, 10 000 blood platelets/mm, hemoglobin 8.9 g/dl).

The patient died 15 days after stopping the phenytoin. The autopsy showed submassive hepatic necrosis linked to splenomegaly, and moderate inflammatory infiltrated vascular congestion of the skin. The anatomopathologic diagnosis was phenytoin hypersensitivity syndrome.

Phenytoin is an anticonvulsant affecting hepatic metabolism. Among its more frequent side-effects are gastric intolerance, skin rash, and gingival hyperplasia. Less frequently, cases of hypersensitivity syndrome to DFH have been described.

This syndrome with anticonvulsants was first described in 1950 by Chaiken et al. (1); they called it dilantin hypersensitivity syndrome. Later, cases involving carbamacepine, primidone, and phenobarbital were described.

The hypersensitivity syndrome to phenytoin is of low incidence (1/1000–10 000 treated with DFH), and it usually appears between weeks 1 and 4 of treatment. Risk factors have not been clearly identified when they appeared and their origin is not dose dependent.

Skin signs were the most common in the syndrome in the study by Silverman (2).

Fever, lymphadenopathies, and megalies are common, as well as leukocytosis and eosinophilia. Aplastic marrow and hepatic affection are less common. Those rare signs appear late during the development of the syndrome, and most of the patients who develop them have previous skin alterations. The pathogenic mechanism of this syndrome has not been established. Most of the facts suggest a hypersensitivity phenomenon, although idiosyncratic and toxic mechanisms with enzymatic induction of Cp 450 and the production of intermediary metabolites have also been involved. These metabolites are potentially cytotoxic, and they can alter the lymphocytic function, increasing the hepatocellular necrosis and lymphadenopathies, as described by Haword et al. (3). The diagnosis of this syndrome is clinical and analytic. Studies of lymphocytic stimulation and the patch test can indicate the therapeutic option of withdrawal of DFH, although the patient's condition can alter.

This emphasizes the danger of a premature diagnosis. Steroids are usually used during the treatment, although their indexing is not well established and does not alter the mortality rate. However, they are effective in

the skin symptoms and can shorten their course. Excessive medication taken with DFH can worsen the prognosis. Dreifuss et al. (4) have shown cross-reactivity with other anticonvulsants and interaction with antidepressants.

The mortality rate in this syndrome rises to 30–40% if hepatic damage occurs. Mullick (5), in a clinical pathologic study, has reported 20 cases of hepatic injury associated with diphenylhydantoin; the mortality rate without hepatic affection was 10%. Our patient showed hypersensitivity syndrome to DFH after 4 weeks of treatment. She developed fever, desquamative erythema, and eosinophilia linked to aplastic marrow and severe hepatic failure, which caused her death.

*Section of Allergy, Service of Internal Medicine, Hospital Universitario Marqués de Valdecilla, Av. Valdecilla s/n, 39008 Santander, Spain

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Pattern of food-induced anaphylaxis in children of an Asian community

D. L. M. Goh, Y. N. Lau, F. T. Chew, L. P. C. Shek, B. W. Lee*

Key words: anaphylaxis; children; food allergy.

● THE prevalence of food allergy is estimated to be about 2% in the general population and up to 8% in young children (1). In Singapore, a questionnaire survey in schoolchildren estimated the prevalence to be 4–5% (2). A proportion of IgE-mediated food reactions manifest as anaphylaxis, which is potentially life-threatening. The purpose of this retrospective study was to evaluate the pattern of food allergens inducing anaphylaxis in children seen at a general hospital in Singapore.

As there is no code for the diagnosis of food-induced anaphylaxis in the *International Classification of Diseases* (ICD-9), identification of these cases was made by screening the database of the hospital's information services for the following diagnostic codes: anaphylactic shock (ICD code 995.0), unspecified urticaria (ICD code 708.9), angioneurotic edema (ICD code 995.1), unspecified allergy (ICD code 995.3), dermatitis due to food ingestion (ICD code 693.1), and noninfectious gastroenteritis and colitis (ICD code 55.8). The data for children less than 15 years, seen between January 1992 and December 1996, were evaluated.

Cases of food-induced anaphylaxis were identified and their data collated by review of the patients' medical records. Only cases with a presentation that comprised any combination of angioedema, urticaria, generalized flushing, and/or wheezing were assessed. The trigger, demographic data, and

details on hospitalization were obtained. Procedures of the SAS software package, version 6.08, were used for compilation and analysis (3). Nonparametric comparisons between groups were made by Kruskal-Wallis tests. Multiple comparisons between categories were made by the method described by Siegel & Castellan (4).

The initial screening identified 1054 cases with the list of diagnostic ICD codes, as already described. The case records of 932 patients were available for analysis, as 122 case records were untraceable. Sixty-four patients were excluded, as their primary diagnoses were not allergic reactions (e.g., cellulitis, Stevens-Johnson syndrome, and gingivitis). Of the remaining 868 cases where the reactions resembled acute allergic reactions, a food allergen was suspected by the attending physician in 124 cases (14.3%). This diagnosis was based mainly on history alone, as diagnostic tests were carried out on only four children to confirm egg, milk, fish, and seafood allergies. Besides food, the historical information from case records identified drugs (142 cases, 16.4%), viral infection-induced urticaria (47 cases, 5.4%), insect bites (42

cases, 4.8%), and vaccines and contact with chemicals (25 cases, 3%) as the most likely cause of the reactions. The trigger factor was unknown in 488 (56.2%) cases.

The types of suspected food, the racial and age distribution, and the main symptoms are summarized in Table 1. The most common food-allergen source was the Chinese delicacy bird's nest soup (double-boiled edible nest of swift, *Collocalia* spp.) (34 cases, 27%). This was followed by crustacean seafood (30 cases, 24%), egg and cow's milk (14 cases, 13%), and various traditional Chinese herbs (nine cases, 7%). The Chinese herbs could not be identified, as in all cases they were consumed as soup with a mixture of many herbs (seeds, roots, and bark). The remaining 37 patients (30 cases, 30%) reacted to a variety of other foods that included chicken and duck, ham, fruits (banana, rambutan), cereals (mixture of oats/barley breakfast cereals), gelatin, and spices. There were no recorded reactions to peanuts or tree nuts. Reactions to egg and milk occurred mainly in infants (11/14, 79%), while the remaining food reactions were observed in older children, the oldest group reacting to crustacean seafood ($P<0.001$) (Table 1). Three children had more than one admission for anaphylaxis, and they reacted to the same food allergen.

No deaths were recorded. The overall hospitalization rate was 34%, mainly for moderately severe wheezing or hypotension. None of these patients had a second-phase response.

This study highlights the unique pattern of foods triggering anaphylaxis in our population. The reactions were sufficiently severe to warrant emergency room management. Of particular interest, the food most commonly inducing anaphylaxis was bird's nest soup. This is a Chinese delicacy and frequently consumed as a traditional remedy for asthma and respiratory ailments. This allergy underscores the importance of cultural practices on disease pattern. The nests are made almost entirely from saliva produced by swifts, and composed mainly of glycoproteins. Over 19.9 million nests were recorded to be

The results of this retrospective survey showed a unique pattern of foods triggering anaphylaxis in our community.

Table 1. Foods triggering anaphylaxis in relation to age of presentation

Food allergen	n (%)	Median age (range) (years)	Race Chinese:Malay: Indian	Main symptom
Egg and milk	14 (11)	0.7 ^c (0.1–4.0)	9:3:2	Angioedema
Bird's nest	34 (27)	4.5 ^b (2.0–14.0)	All Chinese	Angioedema
Chinese herbs	9 (7)	5.0 ^b (2.0–11.0)	All Chinese	Angioedema
Others*	37 (30)	7.0 ^{ab} (0–15.0)	32:0:5	Urticaria
Crustacean seafood	30 (24)	11.0 ^a (2.0–15.0)	26:4:0	Urticaria
Total	124 (100)	5.0 (0–15.0)	110:7:7	–

Age refers to age of presentation.
 *Others include wide spectrum of food types, including chicken, duck, ham, fruits (banana, rambutan), cereals, and gelatin (in form of jelly dessert) and spices.
 **Comparison of ages between food allergen groups: median age with same superscript letter is not significantly different ($\alpha=0.05$), as compared by nonparametric multiple comparison method described by Siegel & Castellan (4).

consumed worldwide in 1989, and demand is so high that these swifts are in danger of extinction (5). This form of allergy has not been reported previously. However, our preliminary work using prepared crude extracts for skin prick tests in 13 bird's nest-allergic children showed positive wheal flare reactions, indicating that these reactions are IgE-mediated (unpublished).

There was a notable absence of peanut or tree nuts triggering reactions in our survey. This is stark contrast to reports of food-induced anaphylaxis in the US population (6, 7), where peanuts and tree nuts were responsible for most fatal and near fatal anaphylaxis. Although peanut allergy has been documented in our population (2), this study suggests that this allergy does not produce severe symptoms requiring emergency treatment. Egg, milk, and crustacean seafood appear to be "universal" foods causing anaphylaxis, and are observed in other populations (6, 8). Although crustacean seafood anaphylaxis was found in older children in this study, this form of allergy is not commonly reported in other pediatric populations. Seafood (shrimp) is a common ingredient in Asian cooking. The types of foods triggering anaphylaxis vary between communities. The documentation of these differences will improve our understanding of food allergy as a whole.

*Department of Paediatrics
National University of Singapore
Lower Kent Ridge Road
Singapore 119074
Fax: 65-779 7486
E-mail: paeleebw@nus.sg

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Occupational asthma caused by esparto grass (*Stipa tenacissima*) fibers

G. Baz, M. Hinojosa, S. Quirce, M. Cuevas*

Key words: *Aspergillus fumigatus*; asthma; esparto; hypersensitivity pneumonitis.

● ESPARTO grass (*Stipa tenacissima*), a gramineous plant found widely in Mediterranean countries, has many uses. Hypersensitivity pneumonitis caused by esparto fibers has been recently described (1). We now present the case of a stucco maker who developed bronchial asthma due to inhalation of esparto fibers.

The patient was a 50-year-old stucco maker, who had been exposed to esparto fibers used in his job since he was 14 years old. For the last 6 years, he had developed ocular itching and

rhinorrhea, as well as shortness of breath, cough, and wheeze after exposure to esparto fibers. Absence from work markedly decreased the severity of symptoms. Clinical examination revealed scattered expiratory wheezes on chest auscultation. White blood cell count was 8200/mm³ with 1110 eosinophils/mm³. Spirometry revealed a FEV₁ of 96% and FVC of 106% of predicted. Total serum IgE was 2052 kU/l. Methacholine PC₂₀ was 1.38 mg/ml.

One sample of esparto fibers provided by the patient was cultured to detect the presence of microorganisms.

Rhizopus sp.,
Penicillium sp.,
and *Aspergillus fumigatus* could be identified.

Skin prick and intradermal tests

performed on the patient with a 1:10 w/v aqueous esparto extract (EE) revealed an immediate positive response. The same tests also showed a positive reaction with a 1:5 w/v *A. fumigatus* extract (AFE). No late responses were observed. Skin tests performed with other mold extract (*Rhizopus nigricans* and *Penicillium notatum*), mite, and pollen allergens were negative (Lab. Abelló SA, Madrid, Spain). Specific IgE antibodies against the EE as well as the AFE were demonstrated in the patient's serum by ELISA (2). Esparto activity was markedly inhibited (59%) by AFE in an IgE-inhibition ELISA performed as previously

Esparto fibers cause not only hypersensitivity pneumonitis but also occupational asthma.

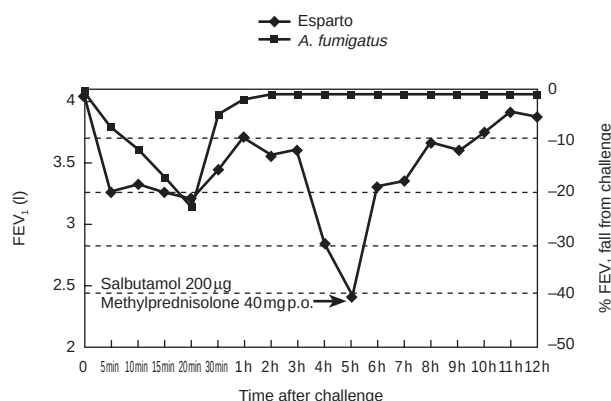


Figure 1.