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Viewpoint

Anaphylactic shock and lethal anaphylaxis caused by food consumption in China

Kunmei Ji^a, Jiajie Chen^a, Meng Li^a, Zhigang Liu^{a,*}, Chunbo Wang^a, Zhengke Zhan^a, Xuli Wu^a and Qingyou Xia^b

^aAllergy and Immunology Institute, Medical School, Shenzhen University, Nanhai Ave 3688 Shenzhen city, Guangdong, PR China 518060 (Tel.: +86 755 2653 5077; fax: +86 755 2653 5065; e-mail: lzg@szu.edu.cn) ^bInstitute of Sericulture and Systems Biology, Southwest University, Chongqing, PR China

A review of case reports of anaphylactic shock and lethal anaphylaxis caused by food consumption occurring in China was conducted. Case reports published in Chinese medical journals from 1980 to 2007 were considered in the review. According to these reports, the most common allergenic offenders were pineapple, soft-shelled turtle and crab.

Anaphylaxis is a life-threatening allergic reaction, and food is one of the most common responsible allergens in the outpatient setting (Wang & Sampson, 2007). As the Chinese economy develops, people in China are consuming an increasing quantity and variety of foods. This has been accompanied by an increase in food allergy incidents, which not only affect the quality of daily life but may be life threatening (Moneret-Vautrin, Morisset, Flabbee, Beaudouin, & Kanny, 2005). We have collected all 141 articles about severe anaphylaxis published in medical journals in China

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from 1980 to 2007. These articles reported 358 episodes of anaphylactic shock and six deaths from anaphylaxis caused by food ingestion (Cao, Deng, & Chen, 1985; Ding, 2001; Ji, Zhan, Chen, & Liu, 2008; Lin, 2000; Zheng & Huang, 1982; Zhou, Pan, & Wang, 2005). All these cases were diagnosed by post-skin testing or food allergy history and the patients showed typical clinical symptoms of anaphylactic shock such as a sudden drop in blood pressure and difficulty breathing.

Of six deaths, two were caused by reactions to peanuts, two by reactions to cashew nuts, one reaction to pineapple and one reaction to milk (Table 1). The victims were 4-36years of age. Timely epinephrine was not available for any of the patients who died. The Case 5 and Case 6 patients (Table 1) had previously suffered severe anaphylaxis after consuming peanut and milk respectively, and were rescued with timely adrenaline treatment. When these two patients had another episode of anaphylactic shock, no treatment was immediately available, and this lack of treatment resulted in their deaths. These fatalities occurred before 1996 (Table 1). The outbreak of severe acute respiratory syndrome (SARS) in 2003 led the Chinese government to build up a national emergency medical rescue system with much faster response times and wider coverage. This may have been a factor in reducing anaphylactic fatalities.

Of the 358 cases of reported anaphylactic shock, the patients' ages ranged from 1 to 83 years; and allergic responses were triggered by 58 foods (Table 2). Sources of allergies included nuts, vegetables, fruits, fish, meat, eggs and insects. The most frequent source of anaphylaxis was pineapple, with 89 cases of anaphylactic shock and one fatality (25%, Fig. 1, Table 2). One case of anaphylactic shock from pineapple consumption was associated with hearing loss, and another was accompanied by acute pancreatitis; both patients recovered without sequelae (Wen, Chen, & Wang, 1992; Zhao & Song, 2008). Pineapples contain a large amount of proteases, which may increase gastrointestinal permeability and allow infiltration of large foreign molecules into the blood, causing allergic reactions (Wang, 1996). Treatment of pineapples with salt may reduce protease activity and prevent food allergy to some extent (Wang, 1996). However, the exact mechanisms of allergic reactions caused by pineapple have not yet been fully understood.

Soft-shelled turtles are very popular in China, as they are believed to keep people strong and healthy in traditional

^{*} Corresponding author.

| Ref. | Patient No. | Age (y), Sex | Occurrence Date | Allergen | Asthma | History of previous allergy | Location | Timely epinephrine | | | |
|-----------------------------------|-------------|--------------|-----------------|------------|--------|--------------------------------|----------|-----------------------|--|--|--|
| Cao, Deng, and Chen (1985) | 1 | 36, M | 6/16/1984 | pineapple | No | No | Home | No | | | |
| Lin (2000) | 2 | 14, M | 6/unk/1996 | cashew nut | Yes | No | Unk | No | | | |
| Sun (1994) | 3 | 35, F | 4/27/1990 | cashew nut | Yes | Yes | Unk | No | | | |
| Ding (2001) | 4 | 4, M | 9/21/1991 | peanut | Unk | No | Home | No | | | |
| Ding (2001) | 5 | 5, F | 8/27/1996 | peanut | Unk | Yes | Home | No | | | |
| Zheng and Huang (1982) | 6 | 25, M | 4/15/1981 | Milk | Yes | Yes | Outdoor | No | | | |
| F, Female; M, Male; Unk, unknown. | | | | | | | | | | | |

Chinese medical view; they were the second most common cause of anaphylaxis, representing 68 cases (19%, Table 2 & Fig. 1). The next highest frequency cause was consumption of crabs, with 33 cases (9%, Table 2 & Fig. 1). In this group, 32 of 33 victims were children, suggesting that children may have increased sensitivity to crabs. Traditional foods unique to China include silkworm pupas, cicada pupas, grasshoppers, locusts and *Clanis bilineata*, which caused 61 reported cases of anaphylaxis totally (Table 2).

A survey of allergen screening with a correlated factor analysis involving 2276 allergic children in Shenzhen City, China cited a variety of food allergens including egg, milk, wheat, shrimp, peanut, soybean, crab and fish. (Liu Wu, Zheng, & Liu, 2008). The most prominant food allergens were egg and milk, which had positive allergenic screening rates of 49.58% and 46.66% in the Shenzhen City allergic child cohort, respectively (Liu et al., 2008). Milk allergy can have grave health effects and in the most severe cases may even lead to death (Zheng & Huang, 1982). Lactic acid bacteria-fermented yogurt, which is commercially available, is reduced allergenic and its consumption may reduce allergic reaction incidence (Cross, Stevenson, & Gill, 2001). Clinical reports have suggested that dietary consumption of fermented foods, such as yogurt, can alleviate allergic hypersensitivity and might also reduce the development of allergies, possibly via a mechanism of immune regulation associated with increased systemic production of Type I and II interferons (Cross, Stevenson, & Gill, 2001). Genetic engineering may provide additional novel strategies to alleviate the problem of peanut allergies from the source. For example, Dodo, Konan, Chen, Egnin, & Viquez (2008) showed that genetic silencing of the immunodominant allergen Ara h 2 reduces peanut allergenicity. Hence, it would be desirable to have more such hypoallergenic foods available in the future.

In China, there is not yet an official database of food allergy cases in the government's bulletins or formal documents. Since it is likely that not all cases of severe anaphylaxis have been reported, the food allergy problems are probably even more severe than reflected by the numbers in these reports. Interestingly, these data still show unique geographic variations. For example, according to the literature, peanuts and other nuts are the major allergen sources for anaphylaxis in Europe and America (Bock, MunozFurlong, & Sampson, 2007). Subjecting peanuts to frying or boiling, as practiced in China, appears to result in a lower allergenicity of peanuts as compared with the dry roasting method of cooking practiced widely in the United States. Roasting uses higher temperatures that may increase the allergenic properties of peanut proteins. This may explain, at least in part, the difference in peanut allergy prevalence observed between China and the United States (Beyer et al., 2001). Geographical differences in food allergy patterns may reflect differences in the varieties of food available, food preferences, food processing, and/or human genetics. Because of its large population and broad geographic area, China has an especially large variety of foods. Distant parts of the country are associated with marked differences in climate, differences in the animals and plants that are cultivated for food, and different traditions among the local populations. There may also exist differences in food allergies. Unfortunately, the data available from the surveyed reports do not show any sign of this geographic diversity. Geographic patterns may emerge as more reports become available.

As more foreigners come to China to study, to work, or for tourism, food allergies may increasingly cause problems, particularly during events with a large influx of foreigners (e.g., the 2008 Beijing Olympics). Large food chains, such as McDonald's, provide food similar to that in other countries, but visitors who choose to try traditional Chinese food may encounter unanticipated allergies. There has been one reported case of anaphylactic shock in a foreign visitor after consuming silkworm in China (Ji, Zhan, & Chen, 2008). It is therefore important that visitors be alerted to the allergenic risks of local foods (Ji, Zhan, & Chen, 2008).

Since anaphylactic shock can lead to death in a matter of minutes in the absence of treatment, immediate effective medical help is critical in such emergency situations. Thus EpiPens should be available in China as soon as possible to help prevent severe allergic incidences in both Chinese citizens and foreign visitors. For the health and safety of athletes and coaches in the 2008 Summer Olympic Games, the government of China passed a specific regulation: food safety for Beijing Olympic Games — food allergen labeling. The accompanying allergen list was generated based on the food allergen labeling experience of the United States and some European countries (Food and Drug Administration (FDA), 2004). However, food allergen

| Food Class | Selected Ref. | Allergen | No. of cases | Sex: age (y) | History of previous allergy |
|------------|---|---------------------|--------------|---|-----------------------------|
| Peanut | Dai and Hou (1985) | peanut | 1 | M: 23 | Yes |
| Nut | Oian (2002) | pistachio nut | 3 | 2 F: 30.42; 1 M:15 | 1 Yes: 2 Unk |
| | Wang, Wang, and Shen (1993) | walnut | 1 | F: 62 | Yes |
| | Li and Zhang (1994) | cashew nut | 17 | 12 F: 18-67: 5 M: 14-46 | 6 Yes: 2 No: 9 Unk |
| | Meng (1996) | hazelnut | 1 | M: 40 | Yes |
| Fruits | Jiao (1988) | pineapple | 89 | 62 F: 4-57; 27 M: 5-56 | 2 Yes; 11 No; 76 Unk |
| | Du, Yan, and Liao (2002) | plum | 4 | 2 F: 21,34; 2 M: 19–23 | 1 No; 3 Unk |
| | Cao and Ma (1992) | mulberry | 1 | M: 22 | Yes |
| | Zang and Li (1992) | kumquat | 1 | M: 36 | Unk |
| | Xu and Di (1996) | litchi | 1 | F: 40 | No |
| | Chen, Zhao, Liu, Xie, and Fan (2007) | apple | 6 | 5 F: 19–38; 1 M: 36 | 5 Yes; 1 No |
| | Si (2001) | kiwifruit | 1 | M: 35 | Yes |
| | Zhang (1984) | shatian pomelo | 1 | M: 10 | Yes |
| | Wang (1991) | banana | 2 | 2 F: 26, 30 | 1 Yes; 1 Unk |
| | Hu and Yu (1988) | pear | 1 | M: 29 | Yes |
| | Zheng (2000) | mango | 2 | 1 F:18; 1 M:24 | 2 Unk |
| | Meng (1996) | peach | 2 | 2 M: 36, 37 | 2 Yes |
| Aquatic | Li Ying and Zhao (2007) | soft shalled turtle | 68 | 21 E. 7_45. 47 M. 7_51 | 3 Voc: 65 Link |
| nyuatic | E, Aing and Zild (2007) Yu and Yu (2000) | son-snelleu turtie | 5 | 2 + 1 + 7 - 43 + 47 + 101 + 7 - 31 2 E+ 18 26+ 1 M+ 24 | |
| products | Chan and Liv (1002) | sinnip | 5 | 2 F: 10,30; 1 M: 34 | |
| | Chen Xu and Yang (2001) | nsn | 2 | 1 F: 35; 1 M: 27 | 2 INO 2 L Ini |
| | Chen, Yu, and Yang (2001) | sea fish | 3 | 2 F: 25,45; 1 M: 48 | 3 Unk |
| | Luo and Wang (2001) | shellfish | 4 | I F: 16; 3 M: 24-62 | 4 Unk |
| | lan (1993) | crab | 33 | 14 F: 7-52; 19 M: 7-15 | 33 Unk |
| Meat | Zhang (1990) | duck meat | 1 | F: 34 | No |
| | Zeng and Li (2003) | venison | 1 | M: 42 | Unk |
| | Xiao (2001) | beef | 1 | M: 32 | No |
| | Liu and Li (2004) | dog meat | 1 | M: 25 | No |
| | Yi, Zheng, and Zhang (2007) | pigeon meat | 1 | F: 17 | No |
| | Gao, LI, Zhang, and Wang (2007) | hoptoad | 1 | M: 21 | No |
| Mill | Tang (1995) | milk | 12 | 8 F. 6-54. 5 M. 6-57 | 5 Voc: 3 No: 5 Link |
| WIIK | Dang and Dang (1992) | milk powder | 1 | F: 4 | No |
| Egg | Zhou <i>et al.</i> (2005) | egg | 2 | 1 F: 5; 1 M: 2 | 2 Yes |
| Other | Xu (1992) | soybean milk | 1 | M: 41 | Yes |
| plants | Zeng, Guan, Hu, and Yang (2006) | millet congee | 1 | M:15 | Unk |
| | Tian and Yi (2006) | pepper | 2 | 1 F: 6: 1 M: 16 | 2 No |
| | Cheng and Oing (2006) | cabbage | 1 | M: 17 | Yes |
| | Li and He (2007) | cilantro | 1 | F: 14 | Yes |
| | Li (1982) | bamboo shoot | 1 | M: 40 | No |
| | Sun (2008) | kidnev bean | 1 | M: 44 | Yes |
| | W_{ang} (2007) | tea | 3 | 3 F: 25-58 | 1 Yes: 2 Link |
| | Tang and Liu (2007) | castor oil | 1 | F: 68 | No |
| | Wang and Li (1982) | castor on | 1 | A4: 41 | Vos |
| | Lizo and Vang (2006) | millot | 1 | M. 41 | Link |
| | The: (10.7) | mushroom | 1 | M.34 E.12 | |
| | Citial (1907) | nushroom | 1 | F:12 F: 41 | Vac |
| | Chara (1000) | ganic | 1 | F: 41 | tes |
| | Chen (1980) | sweet potato | 1 | M: 43 | Unk |
| | Vvang, Guo and Zhang (2003) | corn | 1 | F: 83 | |
| | Guo (2002) | noodle (wheat) | 2 | 1 F: 41; 1 M: 30 | 2 Yes |
| | Wang and Li (2007) | noodle (buckwheat) | 2 | 2 F: 33,45 | 2 Unk |
| Insects | Qiao (1999) | locust | 27 | 3 F: 15-46; 24 M: 15-56; | 3 Yes; 17 No; 7 Unk |
| | Liu (2007) | grasshopper | 27 | 27 M: 22-55 | 1 No; 26 Unk |
| | Wei, Jia, and Wang (1981) | silkworm pupa | 5 | 3 M: 19-21; 2 F: 37,54 | 5 Unk |
| | Pao and Zhao (2003) | cicada pupa | 1 | M: 25 | Unk |
| | Wan and Wei (2003) | bee pupa | 1 | M: 19 | Yes |
| | Wang and Feng (2003) | bee larva | 1 | M: 27 | Unk |
| | Zhang (2007) | Clanis bilineata | 1 | M: 36 | No |
| Othors | M_2 Ly and Li (2005) | honov | 1 | E. 49 | Link |
| Others | $H_{0,1}$ (2001) | duck blood | 1 | 1. 40 E-45 | |
| | 1 IUU (2001) | UUCK DIOOD | I | L.+.) | UTIK |



Fig. 1. Distribution of allergic causes for anaphylactic shock and fatalities in the collected Chinese literature, 1980–2007.

risks that may be specific to China were not taken into consideration in the regulation (Li et al., 2009). The Chinese government is now making a law to address food allergies in which law makers will consider American and European experiences as well as food allergens that may be specific to local Chinese foods, such as soft shell turtle, crab, locust, grasshopper, and silkworm pupa. Hence the present analysis of food allergies is informative to legislators generating a more suitable regulation on food allergen labeling in China. Moreover, education regarding food allergen avoidance is crucial as most of the fatal reactions that occurred were caused by known food allergies. Our findings should stimulate both patients and doctors to recognize the importance of prompt recognition of food anaphylaxis as well as the availability of immediate suitable preventative treatment in order to prevent exacerbated anaphylactic shock and fatality.

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