

Management of Food Allergy: "Food Allergy Management Guideline 2005" by National Food Allergy Research Group Supported by the Ministry of Health, Welfare, and Labor

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In October 2005, we released "Food Allergy Management Guideline 2005". To cover food allergy from infancy to adulthood, the project committee included not only pediatric researchers, but also internists, dermatologists, and otolaryngologists. The guideline concept was to utilize the data accumulated by the National Food Allergy Research Group, to be plain and as short as a pamphlet, and to be released on internet. The most glowing argument was about relation between infantile atopic dermatitis and food allergy, and how it should be treated in the guideline. To avoid neither overvaluation nor undervaluation, fastidious care was given to the denotation. With the definition of "infantile atopic

dermatitis associated with food allergy", both dermatologic and pediatric members of the project committee finally came to agreement, which was a landmark between dermatologists and pediatricians in Japan. The guideline explains fundamentals with the least paragraphs and with tables and figures as many as possible. Flowcharts are made largely as a composition in the parts of diagnosis and treatment. I really hope that this guideline is useful for Korean doctors involved in food allergy and that quality of life of food allergy patients and their parents are improved. (**Korean J Asthma Allergy Clin Immunol 2006;26:177-185**)

Key words: Anaphylaxis, Food allergy, Food provocation test, Referral relationship

INTRODUCTION

In October 2005, we released on internet "Food Allergy Management Guideline 2005",¹⁾ the most important subject we had worked on in the course of "the research on determination of causative agent (allergen) for anaphylaxis caused by food and other factors, and on establishment of its prevention and prognosis" (principal investigator: Motohiro Ebisawa, M.D., Ph.D., 3 years project since 2003), which is the national research project on prevention and treatment of immunological and allergic diseases, supported by the Ministry of Health, Welfare, and Labor by Japanese government.

The guideline was created for general physicians to improve diagnosis and treatment of food allergy and for food-allergy

patients to improve their quality of life. Its concept was decided in 2003 that it should utilize the data accumulated by the Food Allergy Research Group supported by the Ministry of Health, Welfare, and Labor, that it should be plain and as short as a pamphlet, and that it should be released on internet so that anyone is free to download it. In 2004 the draft was written by staffs of the Department of Pediatric Allergy, National Hospital Organization, Sagamihara National Hospital, and then in January 2005 it was discussed for three hours in the public symposium held at the 5th Workshop on Food Allergy, (which was combined with the meeting of the Food Allergy Research Group supported by the Ministry of Health, Welfare, and Labor.) To cover food allergy from infancy to adulthood, the project committee included not only pediatric researchers, but also internists, dermatologists, and otolaryngologists (Table 1). The guideline finally came to completion through three times tough arguments for about 10 hours altogether in June, July and September 2005, and through further communication by e-mail.

The most glowing argument was about relation between infantile atopic dermatitis and food allergy, and how it should be

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Table 1. “Food Allergy Management Guideline 2005” Project Committee

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(Pediatricians)	
Yukou Aihara	Yokohama City University Municipal General Medical Center, Pediatric General Medical Center
Akira Akasawa	General Medical Care Department, National Center for Child Health and Development, Childhood Care Service
Setsuko Ito	Department of Food Studies and Nutrition, Doshisha Women's College of Liberal Arts
Atsuo Urisu	Department of Pediatrics, Fujita Health University Banbuntane Hotokukai Hospital
Naomi Kondo	Department of Pediatrics, Gifu University School of Medicine
Rumiko Shibata	Department of Pediatrics, National Hospital Organization Fukuoka National Hospital
Mitsuhumi Mayumi	Department of Pediatrics, Fukui University School of Medicine
Hiroshi Tachimoto	Department of Pediatrics, National Hospital Organization, Sagamihara National Hospital
Takanori Imai	Department of Pediatrics, National Hospital Organization, Sagamihara National Hospital
(Otolaryngologists)	
Kimihiko Okubo	Department of Otolaryngology, Nippon Medical School
(Internists)	
Kazuo Akiyama	Clinical Research Center for Allergology and Rheumatology, National Hospital Organization, Sagamihara National Hospital
Naohito Suzuki	Department of Allergy and Respiratory Disease, Fraternity Memorial Hospital,
Takemasa Nakagawa	Department of Internal Medicine, St. Marianna University School of Medicine
(Dermatologists)	
Zenro Ikezawa	Department of Environmental Immunopathology and Dermatology, Yokohama City University School of Medicine
Masataka Furue	Department of Dermatology, Kyushu University Graduate School of Medicine
(Collaborator for document preparation)	
Chizuko Sugizaki	Department of Allergym, Clinical Research Center for Allergology and Rheumatology, National Hospital Organization, Sagamihara National Hospital,

treated in the guideline. The point whether to admit dermatitis as a symptom of food allergy or not, was on focus. The committee members of dermatologists insisted that generally eczema can not be developed by the allergic stimuli absorbed through digestive system. In contrast, the committee members of pediatricians insisted that infantile food allergy can be diagnosed in the subjects among infantile atopic dermatitis. The committee members from pediatrics explained the onset situation of infantile food allergy to the members from dermatology in order to achieve agreement.²⁾ The guideline tried to include clinical classifications of types of food allergy as it was thought out to place emphasis basically on comprehensibility.

Another big argument was about definition of “complicated cases of infant atopic dermatitis and food allergy.” To avoid neither overvaluation nor undervaluation, fastidious care was given to the denotation. With the definition of “infantile atopic dermatitis associated with food allergy”, both dermatologic and pediatric members of the project committee finally came to agreement,

which was a landmark between dermatologists and pediatricians in Japan.

The guideline explains fundamentals with the least paragraphs and with tables and figures as many as possible. Flowcharts are made the most of as a composition in the parts of diagnosis and treatment. In the following sections, I explain summary of the guideline using actual tables, figures and flowcharts.

THE GENERAL

1. Definition

It is based on food allergy committee report from the Japanese Pediatric Allergy Society.³⁾ In that report, food allergy is defined as “Phenomenon of harmful symptoms (on skin, in the mucosa, in the digestive system, in the respiratory system or anaphylaxis) triggered by immunologic mechanisms after consuming a causative food. (not including food poisoning, nor response to toxic foods, nor food intolerance; pseudo-allergen, enzyme disorders).”

Table 2. Classifications of clinical types

Clinical type	Age of onset	High frequency food	Tolerance acquisition (Remission)	Possibility of anaphylactic shock	Food-allergy mechanism
Newborn infant's digestive	Neonatal period	Milk (powdered milk for infant)	(+)	(-)	IgE-dependent
Infantile atopic dermatitis associated with food allergy*	Infancy	Hen's eggs, cow's milk, wheat, soybean, etc.	Mostly (+)	(-) to (+)	Mainly IgE-dependent
Immediate type reaction (hives, anaphylaxis, etc.)	Infancy to adulthood	Infancy to early childhood: hen's eggs, cow's milk, wheat, buckwheat, fish, etc. Later childhood to adulthood: shellfish, fish, wheat, fruit, buckwheat, peanut, etc.	(+) Hen's egg, cow's milk, wheat, etc. (-) to (+/-) Most of others	(++)	IgE-dependent
Subtype					
Food-dependent, exercise-induced, anaphylaxis (FEIA/FDEIA)	Later childhood to adulthood	Wheat, shrimp, calamari, etc.	(-) to (+/-)	(+++)	IgE-dependent
Oral allergy syndrome (OAS)	Early childhood to adulthood	Fruit, vegetables, etc.	(-) to (+/-)	(+-) to (+)	IgE-dependent

*There are cases that might develop complications with digestive symptoms, such as chronic diarrhea and hypoproteinaemia. Not all cases of infantile atopic dermatitis are associated with food allergy.

Table 3. Symptoms triggered by food allergy

Symptoms on skin and in mucosa:
Skin symptoms: pruritus, urticaria, angioedema, flushing, eczema
Eye symptoms: Hyperemia in conjunctiva, edema, pruritus, watery eyes, blepharidema
Oral and throat symptoms: Sense of discomfort and edema on oral cavity, lips and tongue, strangalesthesia in throat, laryngeal edema, hoarseness, itchy throat, tickle in throat
Symptoms in the digestive system:
Abdominal pain, nausea, vomiting, diarrhea, bloody stool
Symptoms in the respiratory system:
Upper-airway symptom: Sneezing, rhinorrhea, nasal obstruction
Lower-airway symptom: Dyspnea, cough, wheezing
Generalized symptoms:
Anaphylaxis: Symptoms in multiple organs
Anaphylactic shock: Tachycardia, collapse (limpness), loss of consciousness, drop in blood pressure

2. Classifications of clinical types in food allergy

There are many types from infancy to adulthood in food allergy. Table 2 summarizes the clinical types, age of onset, high frequency causative food, possibility of tolerance acquisition, possibility of anaphylactic shock and food-allergy mechanisms. The denotation of "infantile atopic dermatitis associated with food allergy" decided in above-mentioned course, is quite significant.

3. Symptoms

The symptoms triggered by food allergy are various but can be mainly classified into four categories; symptoms on skin, in the mucosa, those in the digestive system, those in the respiratory system, and generalized symptoms, as shown in Table 3. It was unexpectedly the first time for specialists from the concerned services to get together and to arrange and classify the symptoms.

4. Epidemiology

According to various researches on the food allergy prevalence rate, it is considered that prevalence of infants is around 5~10% and that in school children approximately 1~2%.¹⁾ No data exist on the prevalence of food allergy in adulthood in Japan. Across all generations the prevalence rate is therefore considered to be approximately 2% in Japan. The rate is reported to be 3-5% in France⁴⁾ and 3.5~4% in the USA.⁵⁾ One report shows that 6% of children three years old have medical histories of food allergy.⁶⁾

In the guideline, we presented the data from the nationwide food allergy monitoring investigation which a contributing investigator, deceased Prof. Y. Iikura and a current committee member Dr. Imai had made in 2000 and 2001, and showed causative allergens specific to ages.¹⁾ Within those two years, 3,882 cases of the doctor-diagnosed immediate type of food allergic response were accumulated by more than two thousands volunteer doctors' contribution. The investigation of monitoring adverse events by food allergy was carried out by the using postcards with return cards every 3 months for 2 years. Frequency of causative foods in

all ages were hen's eggs (38.3%), cow's milk products (15.9%), wheat (8.0%), shellfish (6.2%), fruits (6.0%), buckwheat (4.6%), fish (4.4%), peanut (2.8%). The ranking of hen's eggs, cow's milk products and wheat did not change from age 0 up to 3. As for the group of age 4 to 6, the ranking from the 3rd position downward was shellfish, fruits and peanut. From age 7 to adulthood, the first position of frequency of causative food was shellfish, and wheat, fruits and buckwheat were at higher positions. Causes were different between the types in which onset appears in infancy and in which it appears in adulthood. The most frequent among induced symptoms was skin symptom by 88.6%, then followed symptom in the respiratory system by 26.8%. Anaphylactic Shock came to 10.9%.

DIAGNOSIS

Although we surveyed a variety of examinations for food allergy such as measurement of antigen-specific IgE or skin prick test or histamine release test and its characteristics in the guideline, we stated that final diagnosis should be upon food challenge test. Food

Table 4. Methods and results of Food challenge test

[Medical check by doctor]											
Physical checkup											
Consulting patient's parents (regarding blood-test result and their request)											
After the explanation, let them sign the acceptance form.											
[Challenging foods]											
Powder from dried food (not for sale)											
[Schedule]											
	Food challenge										
Time (min.)	Start	15	30	45	60	90	2 h	3 h	4 h	6 h	24 h
Evaluation	●	●	●	●	●	●	●	●	●	●	●
Doses	1/20	1/10	1/5	3/10	Rest						
[When doctor confirms the symptom]											
Stop the challenge and provide a care to the symptom.											

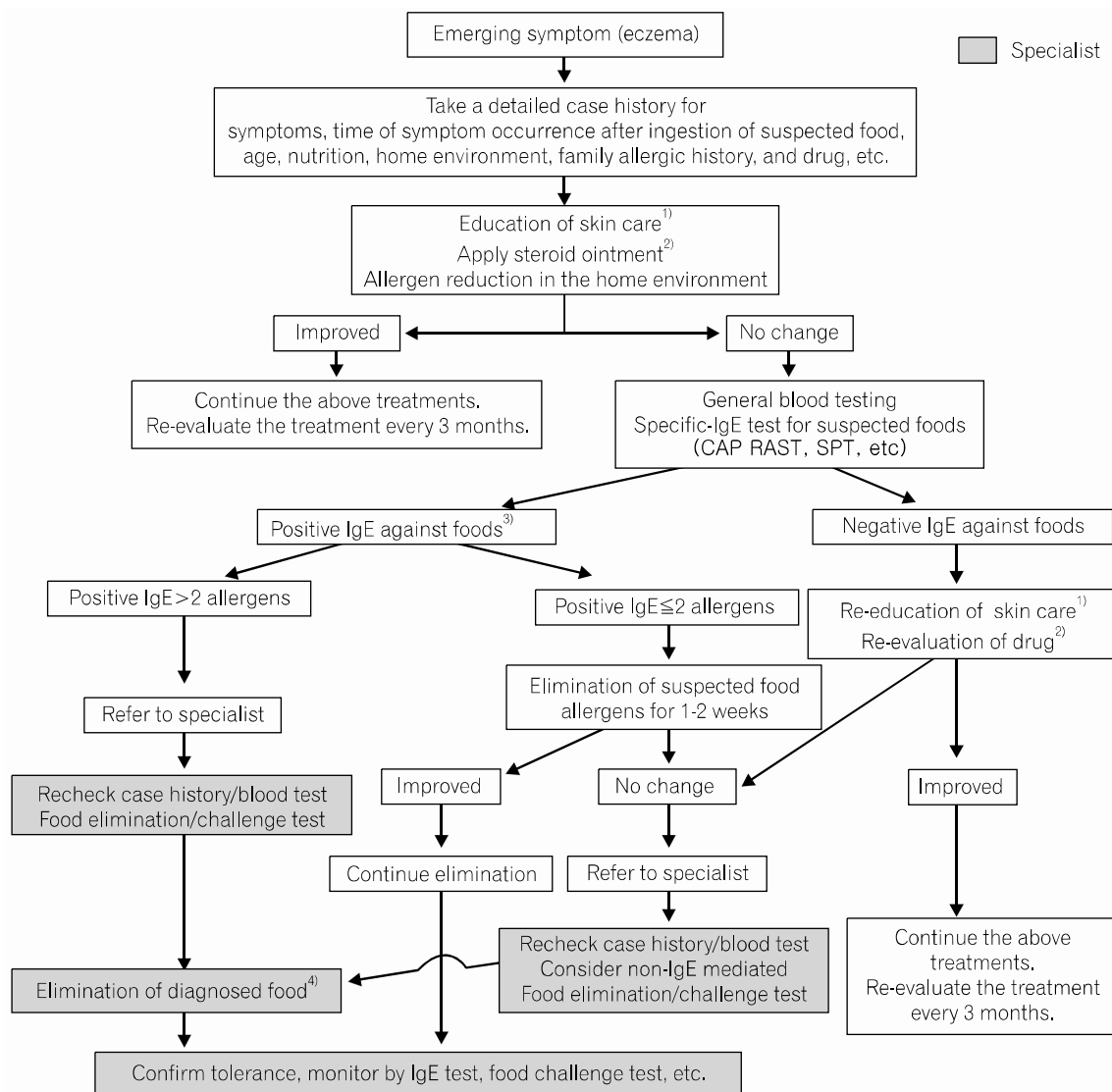


Result of blinded-food challenge tests

	Food-challenge test	IgE CAP RAST	Skin Prick Test
Hen's egg (whole)	229/379 (60%)	309/369 (84%)	189/213 (89%)
Hen's egg (yolk)	20/82 (24%)	66/81 (81%)	53/57 (93%)
Cow's milk	115/263 (44%)	194/259 (75%)	116/146 (79%)
Wheat	47/140 (34%)	117/140 (84%)	59/77 (77%)
Soybean	12/81 (15%)	62/78 (79%)	24/43 (56%)
Total	423/945 (45%)	748/927 (81%)	441/536 (82%)

challenge test has significance in two ways, of diagnosis of causative allergen and of judging acquisition of tolerance. Table 4 shows the results of food tolerance test on 945 cases which was done with a common protocol (blinded challenge, increasing the doses of food every 15 min) among “Food Provocation Network System in Japan” by the National Food Allergy Research Group supplying powdered-challenge foods (whole egg and egg yolk, cow’s milk, wheat, and soy) co-developed by Q.P. Corporation and

myself^{1,7)} The result indicates dissociation from positive rate of IgE CAPRAST with class 2 and up to be positive, and it proves the significance of food challenge test. Food challenge test should be carried out at a hospital with admission facilities under the direction of a well-trained doctor (specialist) with a lot of skill, and so promotion of alliance between general physician and specialists is desirable. In order to support it, it is indispensable for food challenge test to be acknowledged as medical care by



Note 1: Skin care
Cleaning with soap and moisturizing is essential for skin care.

Note 2: Drug treatment
Steroid ointment is the essential treatment for infantile atopic dermatitis.

Note 3: When providing the food sensitized via maternal milk to child, it is necessary to confirm by the food challenge test.

Note 4: Precautions for practicing the elimination diet
Monitor child's growth and development.
Always look for the possibility of ceasing the elimination diet.

Fig. 1. Procedure for diagnosis of food allergy (for “infantile atopic dermatitis associated with food allergy”).

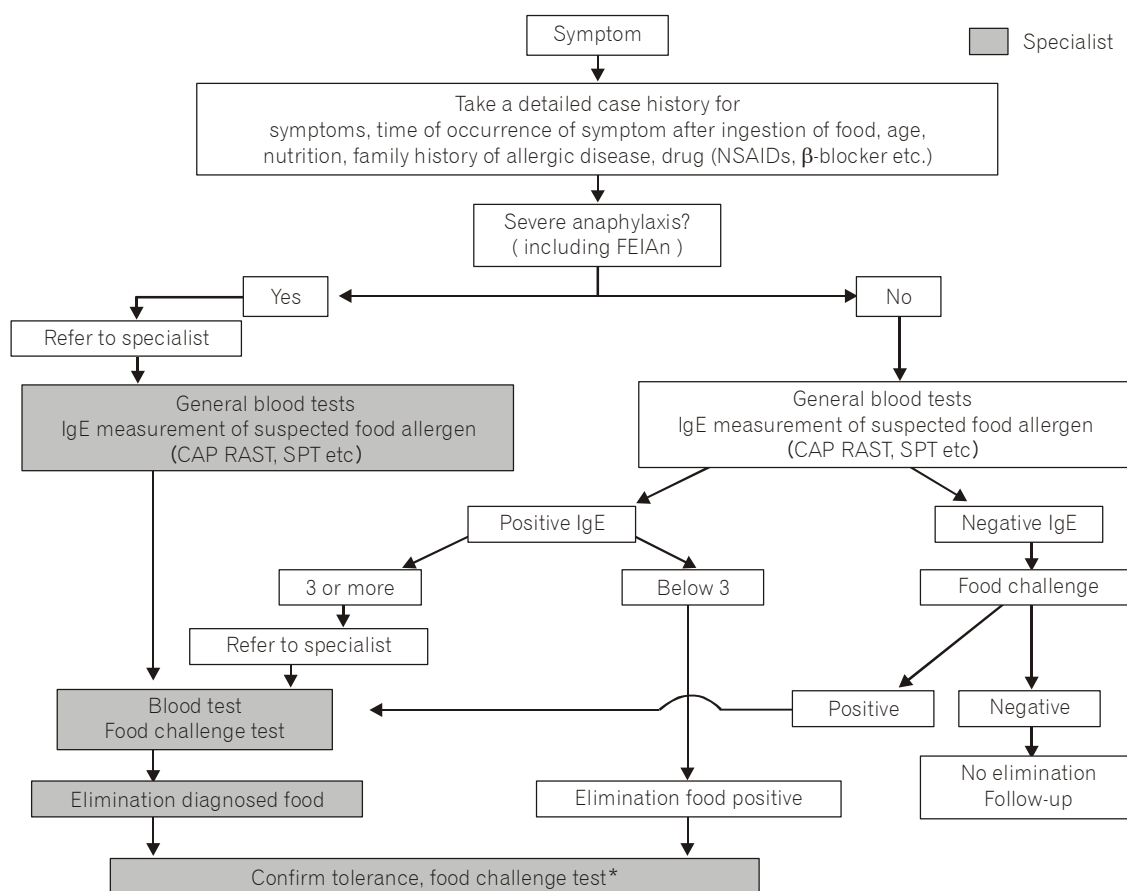


Fig. 2. Procedure for diagnosis of food allergy (for immediate type reaction). *Generally, patients who demonstrate immediate type reaction in later childhood are less likely to acquire tolerance.

health insurance system. In April 2006, Japanese government permit specialized allergists to perform food challenge tests as medical care covered by health insurance system, finally. We made out two types of flowcharts showing procedure for diagnosis of food allergy for infantile atopic dermatitis associated with food allergy (Fig. 1) and for immediate type reaction (Fig. 2), since diagnostic procedure is different in the two types of food allergy.

TREATMENT AND PREVENTION

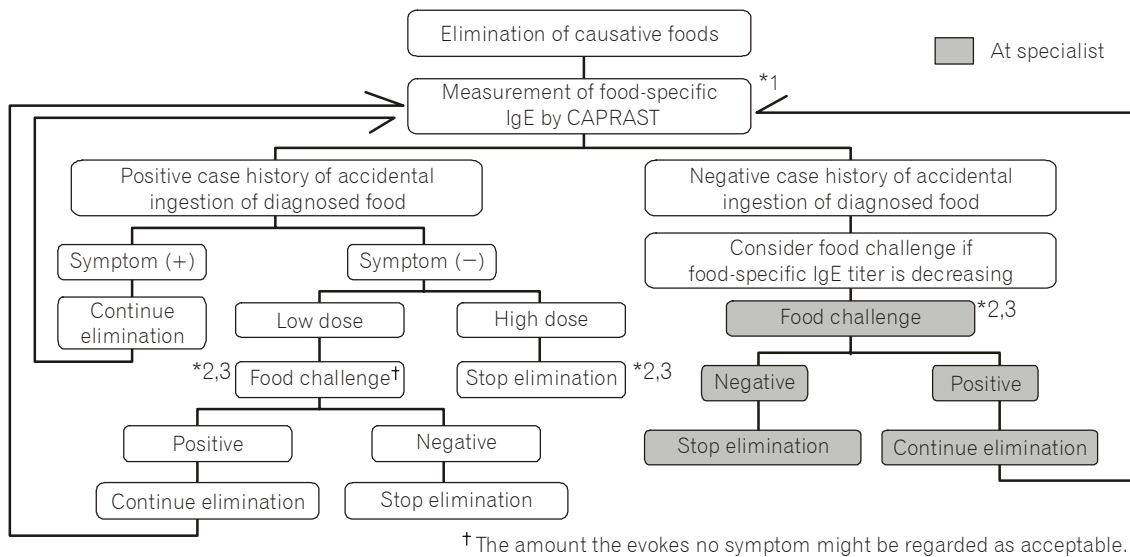
We clearly indicated that the fundamentals of treatment of food allergy are “minimal elimination of causative food (s)” based on correct diagnosis made by food challenge tests, and that medication is only subordinate.

According to the project committee’s consensus on primary prevention related to foods in the case of high risk infant, no particular prevention of food is to be done during pregnancy and lactation of mother.

Follow up after determination of causative food allergens is very important for treatment of food allergy patients, so we showed the follow-up flowchart in Fig. 3. Though judgment of tolerance acquisition should be fundamentally based on results of food challenge tests,⁷⁾ sometimes history of accidental intake is unexpectedly significant information in routine clinical situation. We also summarized information of contraindicated drugs for food allergy patients which is important in pharmacotherapy in the guideline.

CARE FOR FOOD-INDUCED ANAPHYLAXIS

With regard to care for anaphylaxis, Japan has come into a new stage with the approval of EPIPEN (auto-injector of epinephrine) to be used for food allergy in April 2005. As the word “anaphylaxis” is comprehensive and can be interpreted in various ways, we showed the grading of food-induced anaphylaxis according to clinical symptoms suggested by Sampson in Table 5.⁸⁾ For care for anaphylaxis, we presented flowcharts of procedure both pre-



《 Timing of examinations 》

	Below 3 yrs.	3–5 yrs.	Over 6 yrs.
*1: Food-specific IgE	Every 6 months	0.5–1 yr.	1 yr. or more
2: Food challenge test	0.5–1 yr.	1–2 yrs.	2–3 yrs.
*3: Methods of food challenge test	Open	Open, single-blind, double-blind	Open, single-blind, double-blind

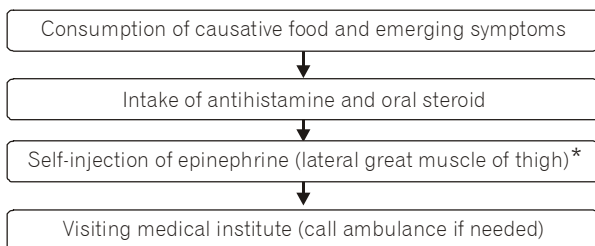
*Generally, the food challenge test should not be performed for the patient who has had anaphylaxis. However, in small infants, some become tolerant in regard to foods with which a child would have anaphylaxis.

Fig. 3. Follow up after determination of causative foods.

Table 5. Grading of food-induced anaphylaxis according to clinical symptoms

Grade	Skin	GI tract	Respiratory tract	Cardiovascular	Neurological
1	Localized pruritus, flushing, urticaria, angioedema	Oral pruritus, oral “tingling”, mild lip swelling	-	-	-
2	Generalized pruritus, flushing, urticaria, angioedema	Any of the above, nausea and/or emesis x’s 1	Nasal congestion and/or sneezing	-	Change in activity level
3	Any of the above	Any of the above plus Repetitive vomiting	Rhinorrhea, marked congestion, sensation of throat pruritus or tightness	Tachycardia (increase > 15 beats/min)	Change in activity level plus anxiety
4	Any of the above	Any of the above plus diarrhea	Any of the above, hoarseness, “barky” cough, difficulty swallowing, dyspnea, wheezing, cyanosis	Any of the above dysrhythmia and/or mild hypotension	“Light headedness” feeling of “pending doom”
5	Any of the above	Any of the above loss of bowel control	Asphyxia	Severe bradycardia, and/or hypotension or cardiac arrest	Loss of consciousness

(Sampson H. Pediatrics 2003;111:1601-8)

Care for food-allergy symptom outside medical institution (pre-hospital care)

*The doctor should inform the patient in advance as to how to deal with the symptoms and prescribe the necessary drugs, in preparation for the case when the causative food is consumed.

† For the patient with a history of anaphylaxis, give guidance based on the following "Flowchart for care of anaphylaxis symptom in medical institution."

Flowchart for care of anaphylaxis symptom in medical institution

(Be cautious about double-dosing the drug when pre-hospital care has been given.)

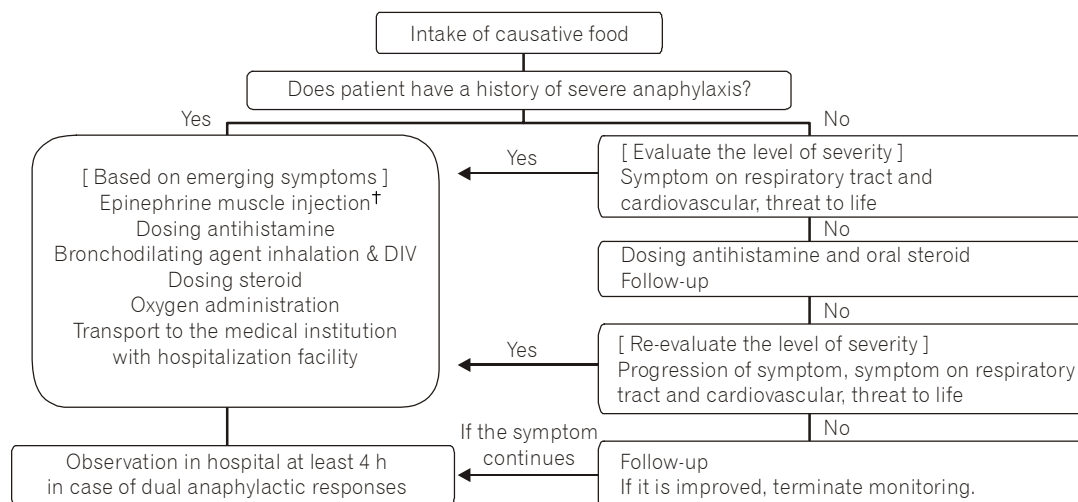


Fig. 4. Treatment of food-induced anaphylaxis in pre-hospital and hospital settings.

hospital and in medical institution (Fig. 4). In the flowchart of pre-hospital care, we explained the necessity of oral administration of anti-histamine and steroid drug, self-injection of epinephrine (EPIPEN), the timing of its use, and so on.

NUTRITION AND SOCIAL MANAGEMENT

In the guideline, the importance of careful observation of infants' growth and nutritional education by dietitians are clearly stated when doctors recommend elimination of multiple causative foods from infantile diets. Japanese food allergen labeling system (five food items; hen's egg, cow's milk, wheat, buckwheat and peanuts, mandated by ministerial ordinance and 20 food items recommended by notice) amended by food sanitary law in 2002 was also explained (Labeling for allergy Q&A <http://www.mhlw.go.jp/topics/0103/tp0329-2b.html>).

In most of kindergartens or elementary schools in Japan, they provide lunch for children. Management of food allergic children relevant to school lunch in kindergarten or school is not well

established. In the guideline, we proposed basic rules for the management of food allergic children (minimum complete elimination) and a sample of Instruction (certificate) for elimination diet (Fig. 5).

CONCLUDING REMARKS

The content and making process of "Food Allergy Management Guideline 2005" are introduced in this article. "Food Allergy Management Guideline 2005" can be downloaded as a PDF file from the following home page without charge: Clinical Research Center for Allergology and Rheumatology, National Hospital Organization, Sagamihara National Hospital: <http://www.hosp.go.jp/%7Esagami/rinken/crc/index.html> (English version will be available soon).

ACKNOWLEDGEMENT

I would like to express my appreciation to Dr. Jae-Won Oh for encouraging me to write this review article for the members

Name _____ (Male / Female)	
Date of Birth (Month/Date/Year) _____	
Diagnosis # 1 Food allergy	
# 2 _____	
# 3 _____	
1) Please eliminate the following foods completely. (Circle all that apply)	
1. Egg	4. Buckwheat
2. Milk	5. Peanut
3. Wheat	6. Others (_____)
(Remarks: Use of soy sauce Yes / No)	
2) Previous anaphylactic symptom (Circle that apply)	
Yes	No
If yes: Causative food (Allergen) _____	
Date (Month/Day/Year) _____	
3) How to deal with the symptom by taking the causative food (Circle all that apply)	
1. Medication (_____)	
2. Self-injection (EPIPEN® 0.3 mg/0.15 mg)	
3. Medical institution to be referred	
Name of medical institution _____	
Phone number: _____	
4) The content of this instruction needs to be revised 6 months/ 12 months later.	
Date (Month/Day/Year) _____	
Name of medical institution: _____	
Phone number: _____	
Doctor's name: _____	
*Please make a copy of this page and use.	

Fig. 5. Instruction (medical certificate) for elimination diet.

of Korean Academy of Asthma, Allergy and Clinical Immunology. I also appreciate immeasurable cooperation of the committee members shown in Table 1 and staff at Department of Pediatrics, Sagamihara National Hospital for the creation of "Food Allergy Management Guideline 2005". The establishment of "Food Allergy Management Guideline 2005" is fully supported by the Health and Labor Sciences Research Grants of the Research on Allergic disease and Immunology from the Ministry of Health,

Labor and Welfare.

Finally, I would like to dedicate this review article to deceased Prof. Yoji Iikura who introduced me to the field of Allergy, to Prof. Hugh A. Sampson who introduced me to the field of food allergy during my fellowship at Johns Hopkins University, and to my family who always supports my academic activity.

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