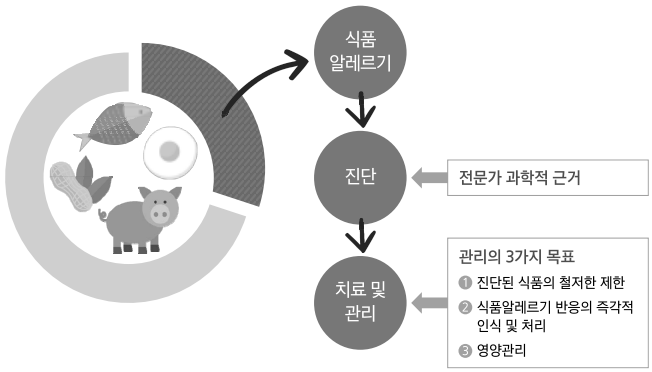
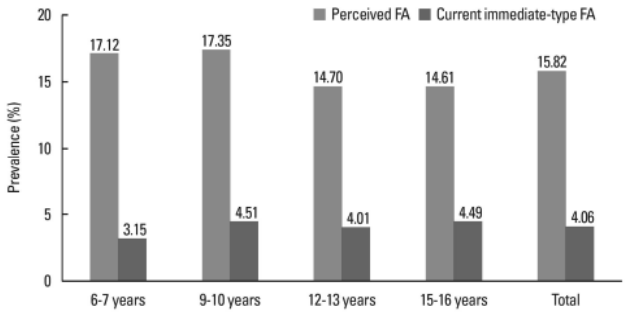
식품알레르기: 먹느냐 먹지 말아야 하느냐 그것이 문제

김지현
삼성서울병원 소아청소년과

식품 관리

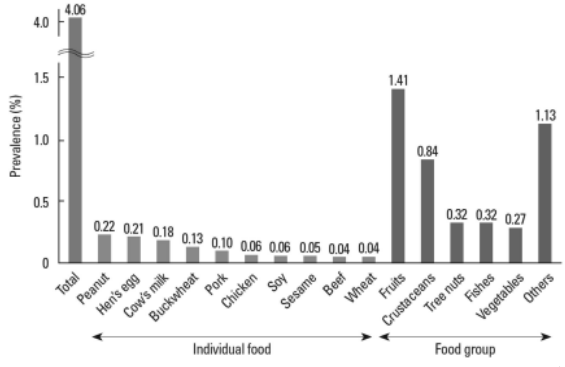


Prevalence of FA in Korean schoolchildren in 2015



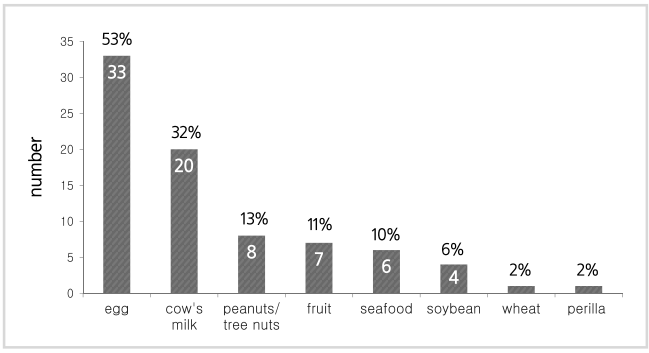
Allergy Asthma Immunol Res. 2017 ;9(5):410-416

Prevalence of current immediate-type FA in Korean schoolchildren in 2015



Allergy Asthma Immunol Res. 2017 ;9(5):410-416

Incidence and risk factors of immediate type FA in Korean infants in a birth cohort study *(Pediatr Allergy Immunol 2011;22:715-9)*



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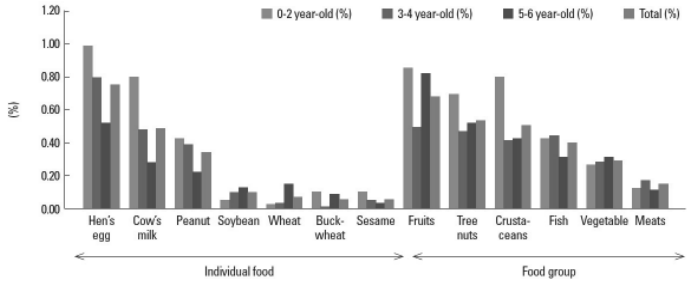
Prevalence of immediate type FA in early childhood



Allergy Asthma Immunol Res. 2014;6(2):131-136.

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A multicenter study on anaphylaxis caused by peanut, tree nuts, and seeds in children and adolescents

	Allergen	*n* (%)
Peanut		41 (32.5)
Tree nuts	Walnut	52 (41.3)
	Pine nut	9 (7.1)
	Cashew nut	6 (4.8)
	Almond	3 (2.4)
	Hazelnut	3 (2.4)
	Pecan	3 (2.4)
	Pistachio	1 (0.8)
	Macadamia nut	1 (0.8)
Seeds	Perilla	4 (3.2)
	Sunflower	2 (1.6)
	Sesame	1 (0.8)

Allergy 2017;72: 507-510.

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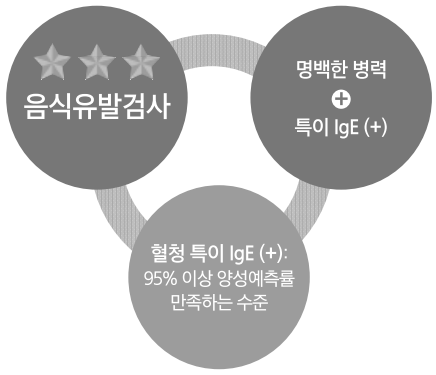
식품알레르기의 진단



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Diagnosis of anaphylaxis

1 Acute onset of an illness with involvement of the **skin, mucosal tissue**, or both *AND* ***AT LEAST ONE*** *OF THE FOLLOWING*
   a. Respiratory compromise
   b. Reduced BP or associated symptoms of end-organ dysfunction

2 **Two** or more of the following that occur rapidly after exposure to a *likely allergen* for that patient:
   a. Involvement of the skin-mucosal tissue
   b. Respiratory compromise
   c. Reduced BP or associated symptoms
   d. Persistent gastrointestinal symptoms

3 **Reduced BP** after exposure *to known allergen for that patient* (minutes to several hours):
   a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP
   b. Adults: systolic BP of less than 90 mmHg or greater than 30% decrease from that person's baseline

Sampson HA, et al, J Allergy Clin Immunol 2006;117:391-7

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Food-specific IgE levels predictive of clinical reactivity

Food	Serum IgE value (kU_A/L)	Positive predictive value
Milk		95
< 12 months old	≥ 5.0	
≥ 12 months old	≥ 15.0	
Egg white		98
< 24 months old	≥ 2.0	
≥ 24 months old	≥ 7.0	
Peanut	≥ 14.0	100
Fish	≥ 20.0	100
Tree nuts	≥ 15.0	95
Soybean	≥ 30.0	73
Wheat	≥ 26.0	74
Buckwheat	≥ 1.26	80

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Performance characteristics in Korean children by previously reported diagnostic decision points

Allergen	kU/L	OFC (+)	OFC (-)	sensitivity	specificity	PPV	NPV
Egg white (< 24 months old)	≥ 2	23	23	88.5%	68.5%	50.0%	94.3%
	< 2	3	50				
Egg white (≥ 24 months old)	≥ 7	19	10	73.1%	93.2%	65.5%	95.2%
	< 7	7	130				
Cow's milk (≥ 12 months old)	≥ 15	19	3	36.5%	98.2%	86.0%	83.7%
	< 15	33	170				

EW, egg white, CM, cow's milk; sIgE, specific immunoglobulin E; OFC, oral food challenge; PPV, positive predictive values; NPV, negative positive predictive values

Allergy Asthma Immunol Res, 2015;7:332-8
Allergy Asthma Immunol Res 2016;8:156-60

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Diagnostic Decision Point of Specific IgE Concentration is Different in Korean Children with Food Allergy

Allergen	Age	Specific IgE (kU/L)	
		NPV (90-99%)	PPV (90-100%)
Egg white	< 24 mo-old	3.45	28.1
	≥ 24 mo-old	1.8	22.9
Milk	≥ 12 mo-old	0.94	31.4
Peanut		0.7	10.3

Allergy Asthma Immunol Res, 2015;7(4):332-8
Allergy Asthma Immunol Res, 2016;8(2):156-60

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Clinical characteristics of food allergen components

Antigen	Component to food allergens	Results
Egg	Gal d 1 (ovomucoid)	OVM-sIgE was a good marker for reacting to heated egg. High levels of OVM-sIgE was associated with persistent egg allergy OVM was best to distinguish between allergy to raw only, and allergy to all forms of egg.
	Gal d 2 (ovalbumin)	OVA was the best test for the diagnosis of allergy to raw and cooked egg
Milk	Bos d 4 (alpha-lactoglobulin) Bos d 5 (beta-lactoglobulin)	Low levels of IgE to milk allergen components (casein, Bos d 4, Bos d 5) predicted outgrowth of milk allergy
	Bos d 8 (caseins)	High baseline IgE levels to milk components (casein, Bos d 4, Bos d 5) predict less successful milk oral immunotherapy
	Bos d 8 (caseins)	High levels of casein-sIgE was associated with persistent milk allergy Casein-sIgE predict clinical reactivity to baked milk Casein-sIgE were significantly reduced during low-dose-induction OIT
Wheat	Gliadin	high levels of IgE to gliadins was correlated with persistent wheat allergy and the development of asthma in children
	Omega-5 gliadin	Omega-5 gliadin was useful diagnostic marker in immediate type of wheat allergy High levels of omega-5 gliadin-sIgE was associated with severity of reaction during wheat challenge
	Omega-5 gliadin HMW-glutenin	Omega-5 gliadin and HMW-glutenin were causative antigens in WDEIA
	Lipid transfer protein (LTP)	Wheat lipid transfer protein was assosiated with Baker's asthma
	Alpha-amylase inhibitors	Alpha-amylase inhibitors and lipid transfer protein were associated with immediate type of wheat allergy

Allergol Int. 2016;65(4):378-87

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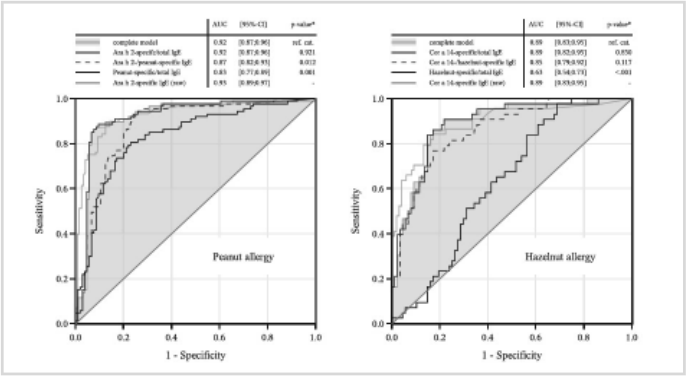
The component-specific to total IgE ratios do NOT improve peanut and hazelnut allergy diagnoses *J Allergy Clin Immunol 2016;137:1751-60*



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회피요법

주의 1
식품표시를 철저히 확인

주의 2
교차반응을 주의

주의 3
비의도적 섭취를 주의

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식품 등의 세부표시기준 (식약처 2015.3.13)

한국인에게 알레르기를 유발하는 것으로 알려져 있는 알레르기 유발물질은 함유된 양과 관계없이 원재료명을 표시하여야 하며, 표시대상과 표시방법은 다음과 같다.

(1) 표시대상: 난류(가금류에 한한다), 우유, 메밀, 땅콩, 대두, 밀, 고등어, 게, 새우, 돼지고기, 복숭아, 토마토, 아황산류, 호두, 잣, 키위, 닭고기, 조개, 굴, 전복, 홍합, 오징어, 쇠고기, 참깨를 함유한 원재료를 사용한 경우

(2) 표시방법: 원재료명 표시란 근처에 바탕색과 구분되도록 별도의 알레르기 표시란을 마련하여 알레르기 표시대상 원재료명을 표시하여야 한다.

우유, 이산화황 함유

삼성서울병원 아토피환경보건센터
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Types of Hypoallergenic Formulas

Types of formula	Example
"Nonallergenic" amino acid-based 치료 또는 예방 목적으로 가장 안전 완전히 소화 된 상태여서 아기의 소화 발달 자극하지 못함	Neocate, Neocate 1+, Ele-Care, and Nutri-Junior
Extensively hydrolyzed bovine casein 치료 또는 예방 목적으로 적절	매일 HA, Nutramigen, Pregestimil, and Alimentum
Extensively hydrolyzed bovine whey 치료 또는 예방 목적으로 적절	Alfa-Re, Profylac, Pepti-Junior, Nutrion Pepti, and Peptidi-Tutteli
Partially hydrolyzed bovine whey 예방 목적으로만 사용	아토케어, Good Start, Nan HA, Bebe HA, and Nidina HA
Extensively hydrolyzed soy 치료 또는 예방 목적으로 적절	Pregomin

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Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines: diagnosis and management of food allergy

Soy formulas should not be recommended before 6 months of age and at any age in the presence of gastrointestinal symptoms. From 6 to 12 months, it can be considered on a case-by-case basis

Currently, probiotic supplements cannot be recommended for the management of food allergy

Due to phytate or phyto-estrogen

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식재료 이용 수업 활동 시 주의사항

대상

- 극미량의 원인 식품에 접촉하여도 알레르기 증상을 일으키는 심각한 알레르기를 가진 아동

이유

- 식품을 먹지 않고 단지 만지거나 흡입하는 것 (냄새를 맡는 것) 만으로도 증상발생의 원인

예방

- 해당 아동을 미리 알고 있고 아동을 돌보게 되는 모두에게 알리는 것 중요 (특별활동 지도 교사 등)
- 발생 가능한 상황에 대하여 미리 조치함

삼성서울병원 아토피환경보건센터 Environmental Health Center for Atopic Diseases

약물요법

주의 1
두드러기,
혈관부종, 간지러움:
항히스타민제

주의 2
아나필락시스:
에피네프린

주의 3
아나필락시스:
2차 반응 나타날 수
있으므로 주의

Antihistamines for urticaria

J Clin Diagn Res. 2017:11(3): WC06-WC09.

Prehospital epinephrine injection

	Medicaid/managed Medicaid, n = 49	Other insurance or self-pay, n = 134
Severity		
Mild	23†	68‡
Moderate	22	52
Severe	3	11
Disposition		
Home	41	116
Floor	6	11
PICU	2	6
First epinephrine administration		
Before the PED	7	49§
In the PED	30	56

*Number of cases with no identified/reported insurance = 30.
†One case could not be assigned a severity grading.
‡Two cases could not be assigned a severity grading.
§P = .006 when comparing the location of epinephrine administration between Medicaid/managed Medicaid versus other insurance plus self-pay.

J Allergy Clin Immunol 2012:129:162-8

에피네프린 자가주사약의 부작용에 대한 우려?

Pediatrics, 2007;119:638-46.

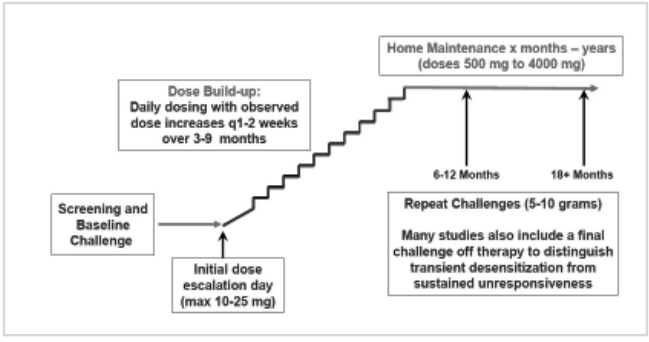
CLINICAL REPORT

Self-injectable Epinephrine for First-Aid Management of Anaphylaxis

Scott H. Sicherer, MD, F. Estelle R. Simons, MD, and the Section on Allergy and Immunology

Individuals and caregivers are often reluctant to use self-injectable epinephrine in anaphylaxis despite instruction to do so. This probably occurs for a variety of reasons, including failure to recognize anaphylaxis; spontaneous recovery from a previous episode; incorrectly thinking the episode is mild; reliance on oral H_1 antihistamines or asthma-relief inhalers such as albuterol; fear of needles and injections; epinephrine autoinjector not being available; and concern about adverse effects of epinephrine.[9] In contrast to transient pallor, tremor, anxiety, and palpitations, which are common and anticipated pharmacologic effects of epinephrine, serious adverse effects are generally not a concern for otherwise healthy children, although they have been reported when epinephrine was given in overdose, especially when it was administered intravenously in an overdose, given at an inappropriately high concentration, or infused too rapidly.[11,22,40]

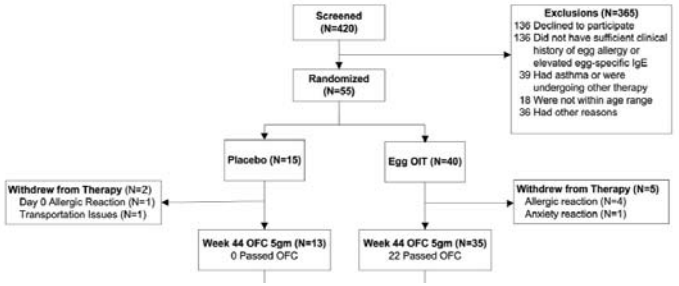
Schematic representation of the typical approach to oral immunotherapy (OIT)



J Allergy Clin Immunol 2016;137:937-82

Long-term treatment with egg OIT enhances sustained unresponsiveness that persists after cessation of therapy

J Allergy Clin Immunol 2016;137:1117-27.



Clinical outcomes with long-term OIT

Time from eOIT initiation	Desensitization	SU
Year 2*	30/40 (75%)	11/40 (27.5%)
Year 3	31/40 (77.5%)	18/40 (45.0%)
Year 4	31/40 (77.5%)	20/40 (50.0%)†

- SU: sustained unresponsiveness

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

POSITION PAPER

EAACI Food Allergy and Anaphylaxis Guidelines: diagnosis and management of food allergy

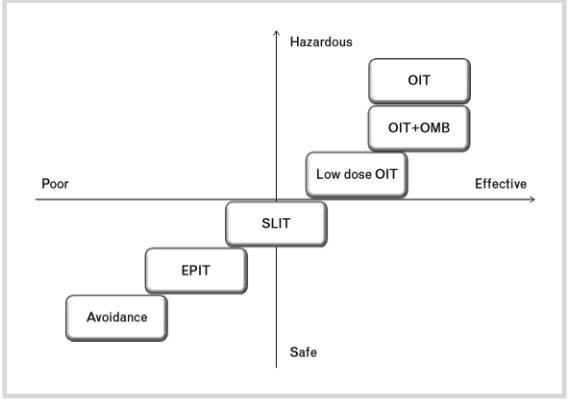
(B3) Specific immunotherapy

Food allergen-specific immunotherapy for primary food allergy is a promising immunomodulatory treatment approach (I), but it is associated with risk of adverse reactions, including anaphylaxis (I); it is therefore not currently recommended for routine clinical use

For patients with respiratory or other allergy symptoms to inhalant allergens that may also cause cross-reactive food allergy, specific immunotherapy is only recommended for the treatment of the respiratory symptoms, not for cross-reactive food allergy

(B4) Anti-IgE

The use of anti-IgE alone or in combination with specific immunotherapy is currently not recommended for the treatment of food allergy although it represents a promising treatment modality



(Ebisawa M. Curr Opin Allergy Clin Immunol 2016;16:396-403)

POSITION PAPER

WILEY Allergy

EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy

우유

Recommendations[a]	Evidence level	Grade of recommendation	Strength of recommendation	Other considerations
OIT is recommended as a treatment option to increase threshold of reaction while on treatment in children with persistent cow's milk allergy, from around 4-5 years of age.	I	A	Strong recommendation based on convincing evidence from SR and meta-analysis[18] including RCTs at low[7,9] or unclear risk of bias [44]	Risk of adverse reactions needs to be considered. Age recommendation is based on expert opinion
A recommendation cannot currently be made for OIT as a treatment option in children with persistent cow's milk allergy with the goal of post-discontinuation effectiveness	I	B	Weak as only one small RCT at high risk of bias[40]	Further studies needed

OIT should only be undertaken in highly specialized clinical centers with expertise and facilities

POSITION PAPER

WILEY Allergy

EAACI Guidelines on allergen immunotherapy: IgE-mediated food allergy

계란

Recommendations[a]	Evidence level	Grade of recommendation	Strength of recommendation	Other considerations
OIT can be recommended as a treatment option to increase the threshold of reaction while on OIT in children with persistent hen's egg allergy, from around 4 - 5 years of age	I	B	Moderate recommendation based on evidence for effect from SR and meta-analysis[18] including low risk of bias RCTs.[8,42] Studies are all small with some heterogeneity in results	Risk of adverse reactions needs to be considered. Age recommendation is based on expert opinion. Additional large studies required
A recommendation cannot currently be made for OIT as a treatment option to achieve post-discontinuation effectiveness in children with persistent hen's egg allergy	I	B	Strong recommendation based on only one RCT with low risk of bias[43]	After 4 years of OIT 50% of subjects achieved sustained unresponsiveness 4-6 weeks after stopping OIT.[43] Further studies needed

OIT should only be undertaken in highly specialized clinical centers with expertise and facilities

Avoidance of allergenic foods?

Effects of early nutritional interventions on the development of atopic disease in infants and children: The role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas

(Pediatrics 2008;121:183-91)

- There is no current convincing evidence that delaying their introduction beyond 4 to 6 months of age has a significant protective effect on the development of atopic disease. This includes delaying the introduction of foods that are considered to be highly allergic, such as fish, eggs, and foods containing peanut protein.

삼성서울병원 아토피환경보건센터
Environmental Health Center for Atopic Diseases

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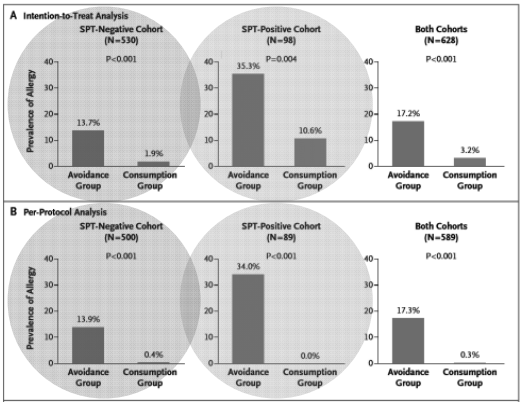
LEAP (Learning Early about Peanut Allergy) study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 26, 2015 VOL. 372 NO. 9

Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D., Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D., Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A., Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D., Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D., Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team*



(New Engl J Med 2015;372:803-13)

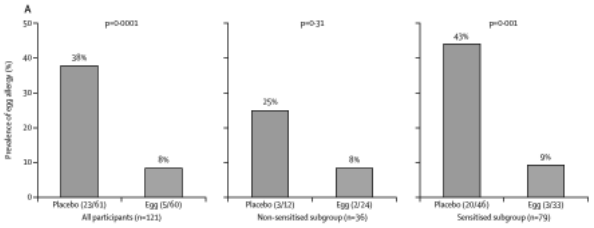
Randomized trials of peanut consumption in infants at risk for peanut allergy

(New Engl J Med 2015;372:803-13)

- In conclusion, the early introduction of peanuts significantly decreased the frequency of the development of peanut allergy among children at high risk for this allergy and modulated immune responses to peanuts

Two-step egg introduction for prevention of egg allergy in high-risk infants with eczema (PETIT): a randomised, double-blind, placebo-controlled trial

Osamu Natsume*, Shigenori Kabashima*, Junko Nakazato, Kiwako Yamamoto-Hanada, Masami Narita, Mai Kondo, Mayako Saito, Ai Kishino, Tetsuya Takimoto, Eisuke Inoue, Julian Tang, Hiroshi Kido, Gary W K Wang, Kenji Matsumoto, Hirohisa Saito, Yukihiro Ohya, for the PETIT Study Team†



(Lancet 2016 Epub ahead of print)

REVIEW ARTICLE

WILEY

Early introduction of allergenic foods for the prevention of food allergy from an Asian perspective—An Asia Pacific Association of Pediatric Allergy, Respirology & Immunology (APAPARI) consensus statement

TABLE 1 Infant feeding guidelines in Asia

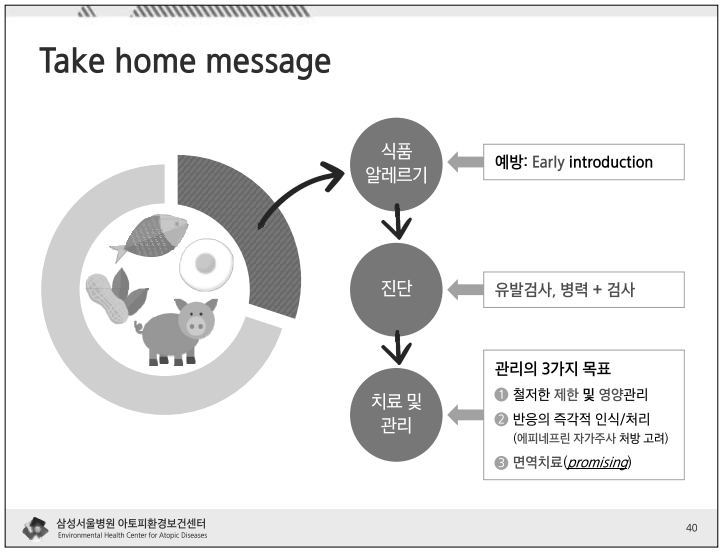
Country	Year	Recommendations for exclusive breastfeeding	Recommended Age for introduction of complementary foods	Recommendations on delaying solid introduction
India	2016	First 6 mo of life	After completion of 6 mo	Not mentioned
Japan	2017	Not specifically mentioned	5-6 mo of age	Delay not recommended
Korea	2008	Up to 6 mo of age	Depending on infant development	Not mentioned
Malaysia	2013	Up to 6 mo of age	6 mo	Not mentioned
Philippines	2017	At least 3-6 mo	Cooked egg: 4-6 mo Wheat: less than 6 mo Fish: 6-9 mo Peanut: 4-11 mo	Delay not recommended
Singapore	2010	At least 4-6 mo	4-6 mo	Delay not recommended

(Pediatr Allergy Immunol. 2018;29:18-27)

Recommendations for infant feeding and introduction of allergenic foods in infants in Asia

(Pediatr Allergy Immunol. 2018;29:18-27)

Recommendation 1—Healthy infants	
No changes to current feeding guidelines	
Introduce complementary foods at 6 mo of age Breastfeeding to continue alongside complementary food introduction up to 2 yr if possible, according to cultural practice	
Recommendation 2—At-risk infants (Healthy infants with a family history of atopy)	
No delay in introduction of allergenic foods - To be introduced in a sensible manner once weaning has commenced	
Recommendation 3—High-risk infants with Severe Eczema[a]	
Access to Allergy expertise readily available	*Limited access to Allergy expertise*
Allergy testing (skin prick tests and/or sIgE) to egg[b,c] (+ peanut in countries with high peanut allergy prevalence)[d]	
Supervised oral challenges in sensitized infants, followed by introduction of the allergenic food into the infant's regular diet if challenge negative[b]	Supervised oral food challenges to egg[b,c] (+ peanut in countries with high peanut allergy prevalence)[d] - To be performed in the office of a doctor trained in recognition and management of allergic reactions
Introduction of all allergenic foods should not be delayed	
Aggressive control of eczema	


Take home message
식품 알레르기
예방: Early introduction
진단
유발검사, 병력 + 검사
치료 및 관리
관리의 3가지 목표
❶ 철저한 제한 및 영양관리
❷ 반응의 즉각적 인식/처리
(에피네프린 자가주사 처방 고려)
❸ 면역치료(promising)
삼성서울병원 아토피환경보건센터
Environmental Health Center for Atopic Diseases
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