出國報告（出國類別：考察）

國際過敏免疫相關疾病之研討與進展
-食物過敏之診斷及治療

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摘要

參與歐洲過敏免疫年會後發現，台灣對於過敏疾病得診斷與治療非常的保守。以診斷而言，局限於抽血檢驗專一性過敏原，為目前最為廣泛的檢測方式，但實際上還有其他如皮膚測試、雙盲測試都是有效的輔助診斷，但台灣只有專案申請才能在特殊病歷上使用皮膚測試之過敏原檢測；而需要住院觀察的雙盲測試，也因健保規範和劾刪的疑慮，讓過敏醫師不願意收治病人住院檢查。而治療的部分，歐美已經廣泛使用的舌下減敏治療、口服減敏治療，也因為法規的限制，讓台灣民眾只能接受副作用較高的皮下減敏治療。因為健保和法規的限制，實在是讓人為台灣醫療感到憂心。

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Table 2 Food-induced allergic disorders (classified based on the underlying immunopathology)

Immunopathology	Disorder	Clinical features	Typical age group	Prognosis
IgE mediated	Pollen food allergy syndrome	Pruritus, mild edema confined to oral cavity	Onset after pollen allergy established (adult > young child)	May be persistent and may vary by season
	Urticaria/angioedema	Triggered by ingestion or direct contact	Children > adults	Depends on food
	Rhinoconjunctivitis/asthma	Accompanies food-induced allergic reaction but rarely isolated symptoms May be triggered by the inhalation of aerosolized food protein	Infant/child > adult, except for occupational disease	Depends on food
	Gastrointestinal symptoms	Symptoms such as nausea, emesis, abdominal pain, and diarrhea triggered by food ingestion	Any age	Depends on food
	Anaphylaxis	Rapid progressive, multisystem reaction	Any age	Depends on food
	Food-dependent, exercise-induced anaphylaxis	Food triggers anaphylaxis only if ingestion is followed temporally by exercise	Onset in late childhood/adulthood	Presumed persistent
Mixed IgE and cell mediated	Atopic eczema/dermatitis	Associated with food in 30–40% of children with moderate/severe eczema	Infant > child > adult	Usually resolves
	Eosinophilic gastrointestinal disorders	Symptoms vary depending on the site of the intestinal tract involved and degree of eosinophilic inflammation	Any age	Likely persistent
Cell mediated	Dietary protein-induced proctitis/proctocolitis	Mucus-laden, bloody stools in infants	Infancy	Usually resolves
	Food protein-induced enterocolitis syndrome	Chronic exposure: emesis, diarrhea, poor growth, lethargy Re-exposure after restriction: emesis, diarrhea, hypotension a couple of hour after ingestion	Infancy	Usually resolves

Modified from Sicherer and Sampson (86) with permission.

Key questions addressed in the supporting systematic reviews: diagnosis and management

1. **What is the epidemiology (i.e., frequency, risk factors, and outcomes) of food allergy in Europe and how does this vary by time, place, and person?**
2. What is the diagnostic accuracy of tests aimed at supporting the clinical diagnosis of food allergy?
3. What is the effectiveness of pharmacological and nonpharmacological interventions for the management of acute, non-life-threatening food-allergic reactions?
4. What is the effectiveness of pharmacological and nonpharmacological interventions for the longer-term management of food allergy?

Prevalence

Table 3 Summary of the pooled prevalence of food allergy (FA) in Europe, by age and region: studies published January 1, 2000–September 30, 2012*

	Self-reported food allergy		Sensitization to at least one food allergen (point prevalence)		Symptoms + sensitization to at least one food allergen (point prevalence)		Convincing clinical history or positive food challenge† (point prevalence)	Positive open food challenge or DBPCFC† (point prevalence)
	Life time prevalence	Point prevalence	Positive specific IgE	Positive skin prick test	Symptoms + positive specific IgE	Symptoms + positive skin prick		
All	17.3 (17.0–17.6)	5.9 (5.7–6.1)	10.7 (9.4–10.6)	3.6 (2.7–3.3)	2.7 (1.7–3.7)	1.5 (1.3–1.7)	2.6 (2.1–3.1)	0.9 (0.8–1.1)
Age			6X					
Children (0–17 years)	17.4 (16.9–18.0)	6.9 (6.6–7.2)	12.2 (11.4–13.1)	3.0 (2.7–3.3)	3.6 (2.8–4.4)	1.5 (1.3–1.7)	2.6 (2.1–3.1)	1.0 (0.8–1.2)
Adults (≥18 years)	17.2 (16.0–17.6)	5.1 (4.8–5.3)	4.1 (3.2–5.1)	–‡	2.2 (0.8–3.7)	–‡	–‡	0.9 (0.8–1.0)
Region§								
Western Europe	23.8 (22.9–24.7)	3.3 (3.1–3.5)	11.7 (9.8–13.6)	1.8 (1.5–2.1)	2.6 (1.3–3.8)	1.4 (1.1–1.7)	–‡	3.1 (2.6–3.7)
Eastern Europe	41.6 (39.5–43.7)	3.3 (1.2–5.4)	–‡	–‡	–‡	–‡	–‡	–‡
Southern Europe¶	8.6 (8.2–9.0)	3.5 (2.5–4.5)	–‡	4.2 (2.2–6.3)	–‡	1.8 (1.3–2.3)	–‡	0.2 (0.1–0.3)
Northern Europe	30.3 (28.7–31.9)	14.5 (13.9–15.2)	9.8 (9.0–10.5)	5.4 (4.6–6.1)	3.0 (2.1–3.9)	1.6 (0.9–2.3)	2.6 (2.1–3.1)	1.1 (0.9–1.3)
Europe**	19.2 (18.6–19.8)	5.0 (4.6–5.5)	–‡	–‡	–‡	–‡	–‡	–‡

Diagnosis

- Patient's clinical history and examination
- Diagnostic tests for food allergy
  - In vivo SPT and sIgE for food allergens are the first-line tests to assess IgE sensitization.
  - Elimination diet for diagnostic purposes and oral food challenges are still gold standard for both IgE- and non-IgE-mediated food allergy.

Skin Test

- Possible under-representation of minor allergens or instability of the allergenic proteins → fresh foods
- ***Intra-dermal skin testing*** is not recommended
  (low specificity, high potential for irritant reactions, risk for systemic reactions)
- Sensitivity(70-100%) and specificity(40-70%) → similar to sIgE
- (+) control: histamine 10mg/ml; (-) control: N/S

  Cut off diameter >= 3mm after 15 min
- High-quality performance: peanut, egg, milk, hazelnut, fish, and shrimp
- Less-quality performance: soy and wheat.
  - For other plant-derived (carrot, celery, kiwi, lupine, maize, and melon) or animal-derived foods (chicken and pork), only single studies were included in the recent systematic analysis.
- ***Atopy Patch Tests*** are not recommended for routine diagnosis of food allergy

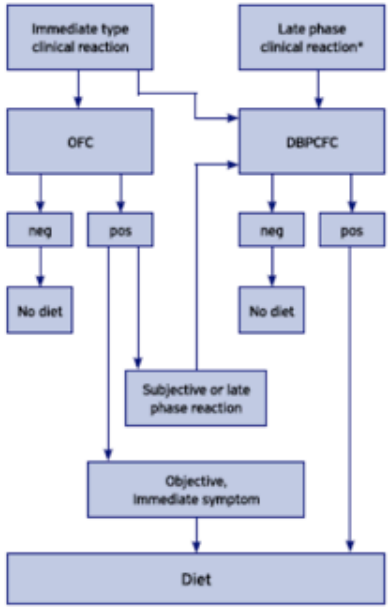
Elimination Diet

- Base on clinical history (specific allergen), sIgE, SPT
- Duration of avoidance: usually 2–4 weeks for IgE-mediated symptoms and longer for non-IgE ones [e.g., up to 6 weeks for eosinophilic esophagitis (EoE)].
- Follow by oral food challenges

Oral Food Challenge

Table 4 Indications for oral challenge tests

Indication	Rationale
Demonstrate allergy	Uncertain diagnostic outcome despite the use of detailed clinical history and IgE sensitization testing
	Suspected food-allergic reaction for which the cause is uncertain despite allergy testing (e.g., composite meal eaten)
	Determine threshold dose of causative allergen
Demonstrate tolerance	When allergy tests suggest tolerance but food has never been eaten and patients and/or parents too cautious to introduce at home
	Nonclinically relevant cross-reactivity suspected, for example a patient with a low positive IgE result to hazelnut but high positive birch pollen sensitization
	When the diet is restricted due to a suspicion that one or more foods are resulting in delayed allergic symptoms (e.g., eczema)
	Allergy suspected to have been outgrown
Monitor therapy for food allergy	To monitor response to immunomodulatory treatment in research setting



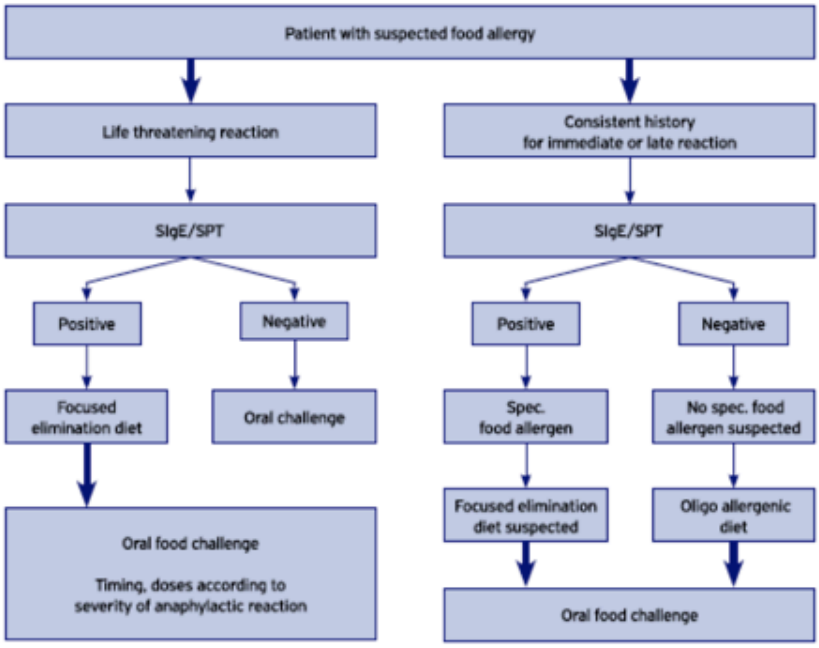
* Atopic dermatitis, GI upset

Table 5 Variables associated with oral food challenges

Variable	
Design	May be open (cumulative or incremental) or blinded (single- or double-blinded). Design selected according to the indication and purpose for which the challenge is being performed
Form of challenge food	The challenge food should closely replicate the usual edible form of the food or form of the food implicated in allergic reaction
	Food processing can significantly influence allergenicity of the food (e.g., baked *vs* raw egg)
	For oral food challenges performed to diagnose the pollen food syndrome, fresh fruit and vegetables should be used, as the responsible proteins are commonly heat labile
Choice of food matrix	Strictly avoid use of allergenic ingredients for individual patient
	Minimize the number of ingredients used
	Provide adequate allergen protein in a manageable portion size
	For placebo foods, sensory qualities should closely replicate those of active challenge food
Doses	
Number of doses	In most cases, half-logarithmic dose increments are indicated. If a negative outcome is anticipated, and there are no safety concerns, a single cumulative dose is appropriate
Initial dose	In clinical settings, 3 mg of food protein seems adequate for most common food allergens such as cow's milk, hen's egg, peanuts, and tree nuts. Lower doses are used for threshold studies in research setting or for patients at high risk of a severe reaction
Top dose	Equivalent to an 'age-appropriate' portion. 3 g of food protein seems adequate for the most common food allergens such as cow's milk, hen's egg, peanuts, and tree nuts
Time intervals between doses	15–30 min, but may be adjusted to the patient's history
Total challenge duration	Usually completed within 8 h (immediate symptoms) and 1–4 weeks (delayed symptoms)

Other Choices

- molecular or component-resolved diagnostic tests (CRD)
- Basophil activation tests (BATs)
  - High sensitivity and specificity than sIgE and SPT
  - cow's milk, egg, and peanut allergy
  - Limited to research purpose



Invalid Test

- Bioresonance 生物能共振
- kinesiology
- iridology
- hair analysis
- cytotoxic test
- IgG and IgG4 determination.

Unconventional tests including specific IgG testing

A number of expensive diagnostic alternative approaches are sometimes promoted to physicians and often used by complementary and alternative medicine practitioners in cases of suspected food allergy. Examples are bioresonance, kinesiology, iridology, hair analysis, cytotoxic test, and IgG and IgG4 determination. These tests are not currently validated and cannot be recommended in diagnosing food allergy (43–47). For example, IgG measurements cannot be correlated with any clinical symptoms or disease. Food-specific IgG4 levels indicate that the atopic individual has been repeatedly exposed to high doses of food components, which are recognized as foreign proteins by the immune system. Therefore, EAACI gave a clear recommendation not to use these tests

Key questions addressed in the supporting systematic reviews: diagnosis and management

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Acute management

- The patient at risk of severe reactions should be properly and timely identified (Expert opinion)
- **Antihistamines and mast cell stabilizers**
- children and adults with acute non-life-threatening symptoms from food allergy(C)
- Prophylactic treatment with antihistamines or mas cell stabilizers: not recommended

Long-term management strategies

- Elimination diet and dietary interventions
- Education: Patients, families, close relatives, and caregivers should be aware of risk situations and should be instructed in reading labels and how to avoid the relevant food allergens both in and outside the home
- Re-evaluated at regular intervals !!

Cow's Milk Allergy:

V Extensively hydrolyzed formula

V Amino acid-based formula

V soy-based formula: phytate and phyto-oestrogens content; cannot be recommended before 6 months of age

? Rice-base formula, Camel, donkey, or mare's milk

X Partial hydrolyzed formula, goat milk and sheep's milk

- Probiotics and prebiotics→ low evidence
- Pharmacological treatment: mast cell stabilizers→ low evidence
- Cofactor: physical exercise and NSAID, and others include alcohol, fever, and acute infection.
  - wheat-dependent exercise-induced anaphylaxis due to omega-5-gliadin sensitization
- Immunotherapy: SCIT. OIT. SLIT
- Anti-IgE (Omalizumab)

Challenges at regular intervals to assess development of tolerance

- **Repeated IgE testing** can be helpful to determine whether sensitization is decreasing (common in egg and milk allergy) and helpful to identify associated allergies [e.g., peanut, associated with tree nut, sesame].
- **OFCs** are the only tests that can predict with adequate certainty the achievement of tolerance.
- In cow's milk or hen's egg allergy, intervals for re-evaluation might be every 6–12 months.
- For peanut and tree nut allergy, OFC every 2 years in the absence of an accidental reaction would be more appropriate.

心得

期望台灣法令能鬆綁對過敏疾病診斷及治療的限制，讓臨床醫師能夠有更多方式能夠正確診斷及治療患者。也希望能夠加強宣導民眾，不要花上萬元的冤枉錢去做不實的檢測方法。

另外，在會場發現，歐洲會議強調減碳環保，減少紙張的浪費，因此在網路、電子資源方面的設備相當新穎而實用，例如利用 App 查詢課程表、還有線上學習的空間，讓學員可以利用空檔的時間補上錯過的課程。