Food Allergy: Diagnosis and Management

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Disclosure

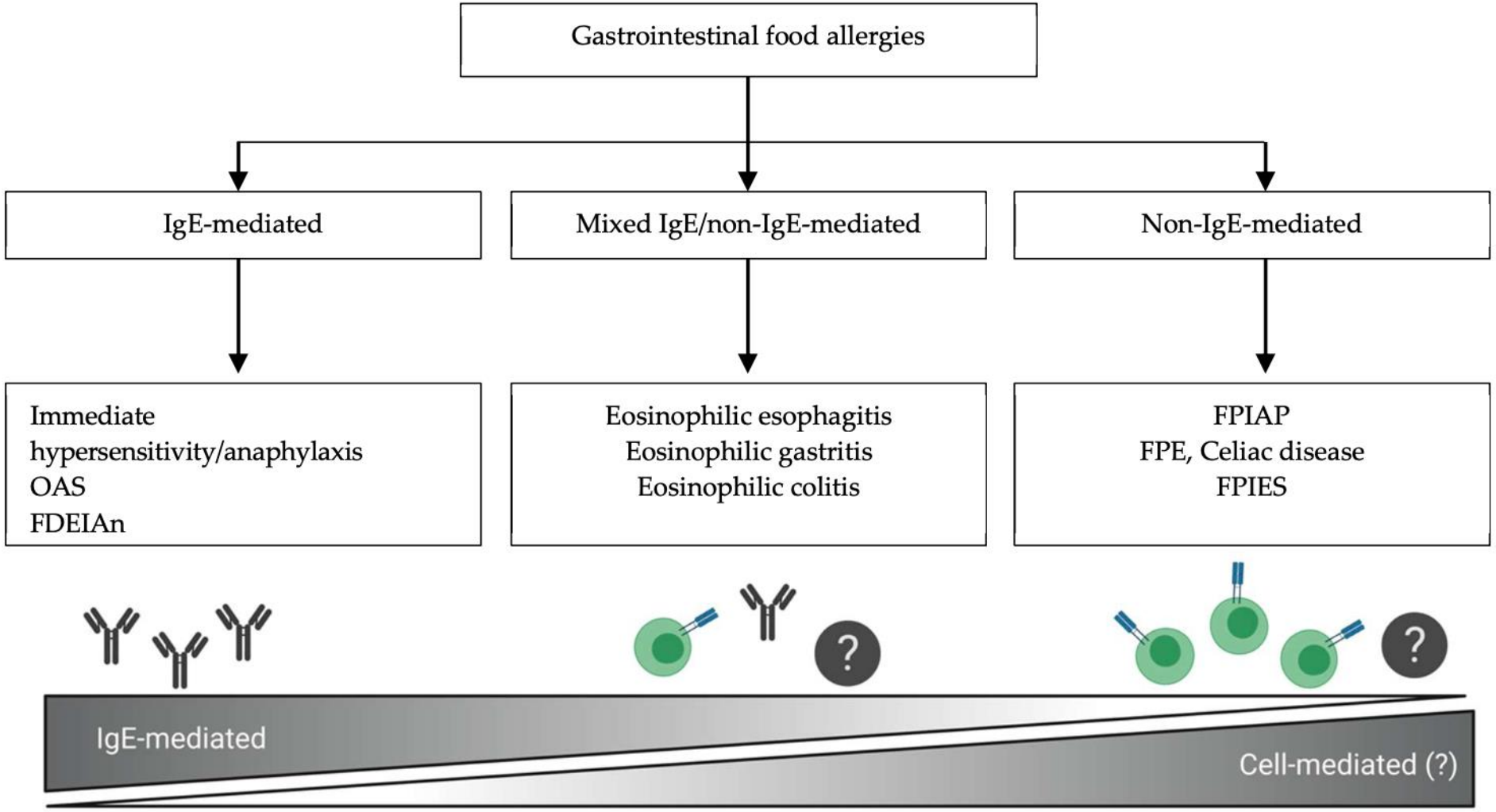
I have no actual or potential conflict of interest in relation to this presentation

Objectives

1. Give an overview of IgE-mediated gastrointestinal food allergies (FA)

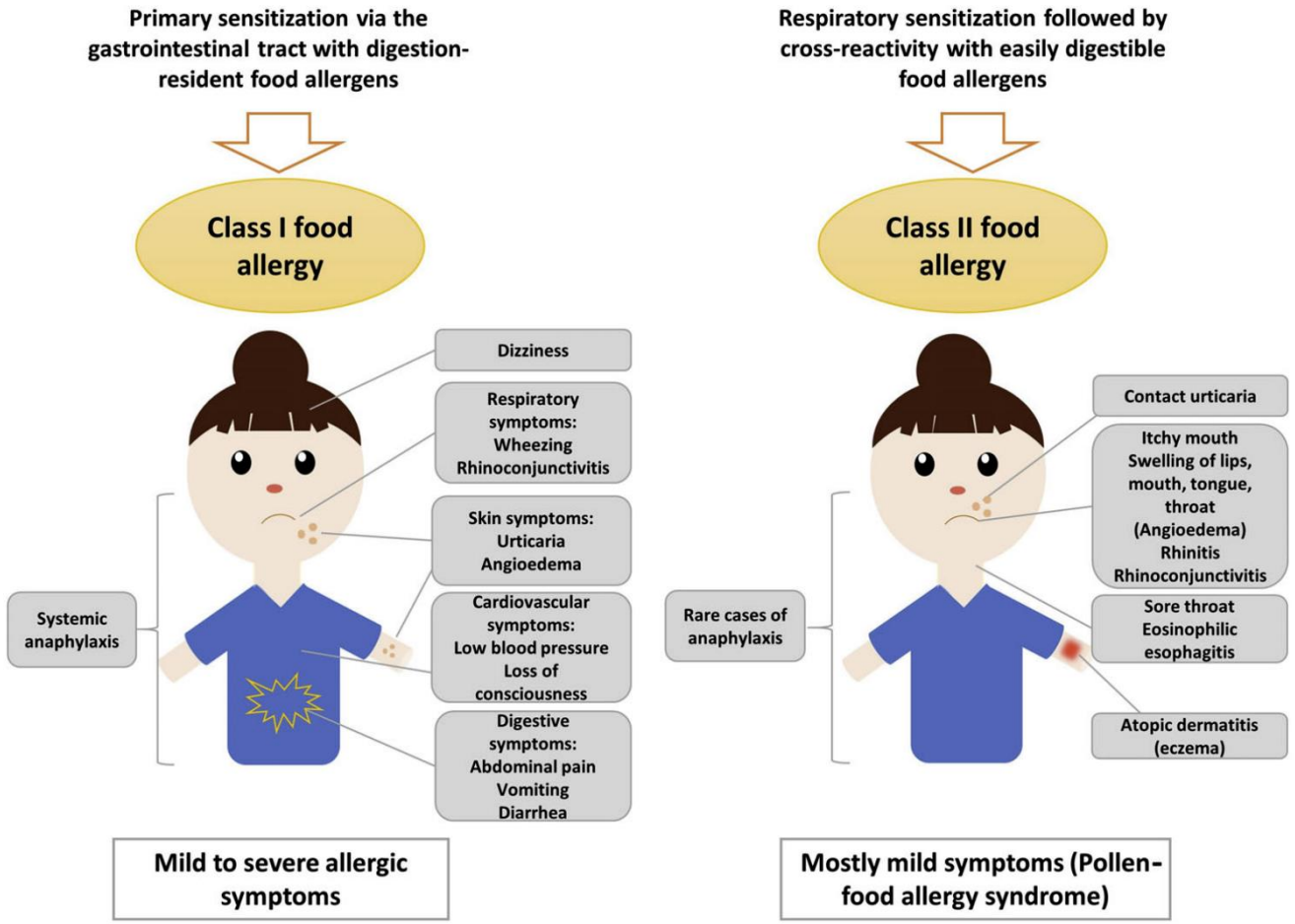
2. Discuss the diagnosis and management of IgE-mediated FA

Food allergic disorders



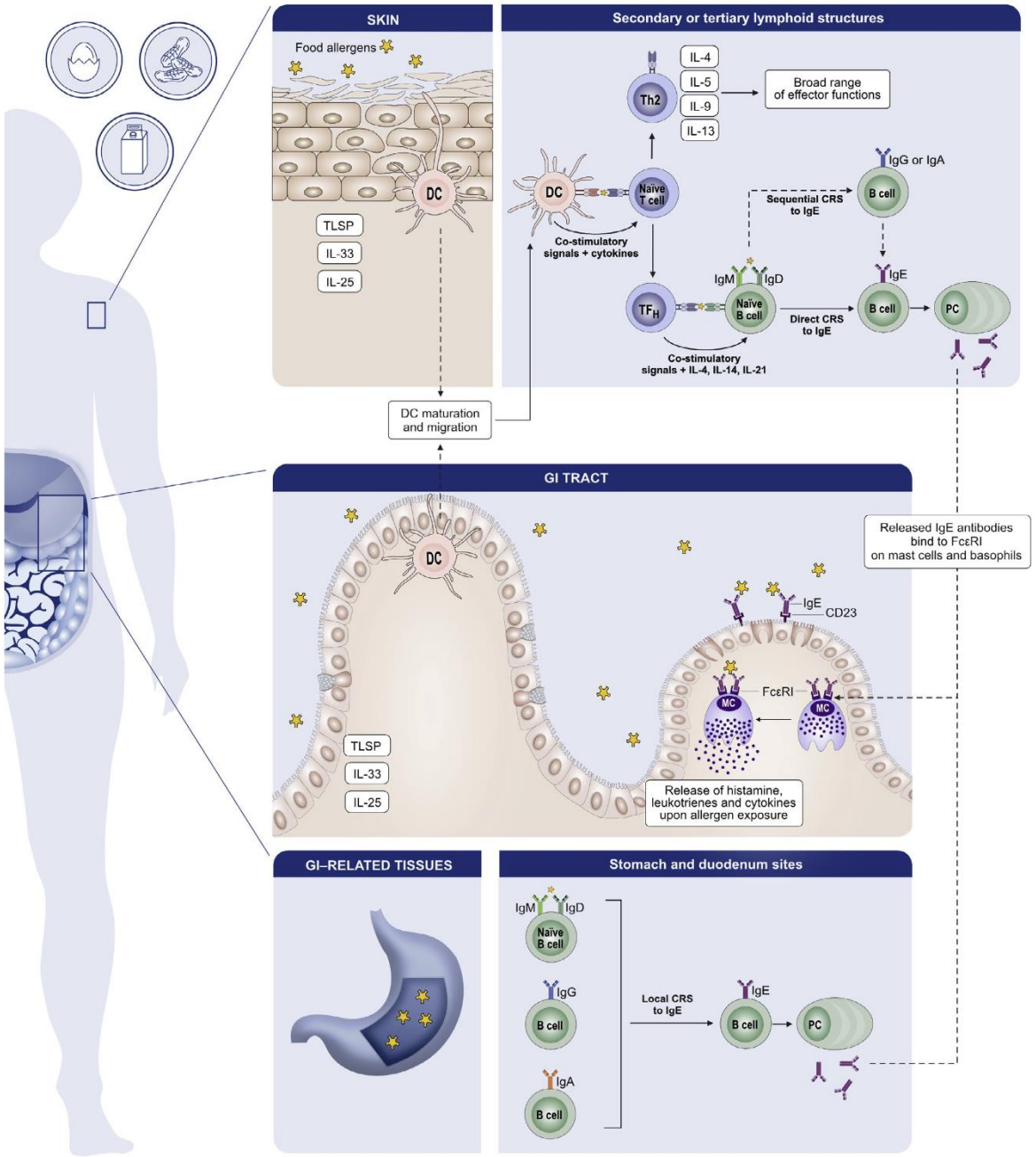
Nutrients 2020, *12*, 2086

Sensitization to class I and class II allergens is associated with different clinical symptoms



Front Immunol. 2021 Sep 23:12:742732.

Mechanisms of allergic sensitization



Allergy. 2021;76:1707–1717.

Key questions for an allergy-focused history

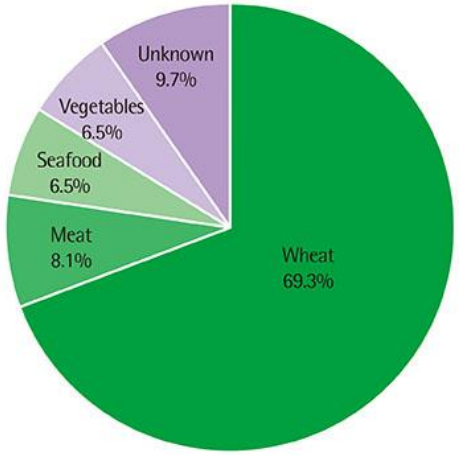
- Age at symptom onset
- Presenting symptoms—type and severity
- Speed of symptom onset and duration of symptoms
- Treatment for previous reactions
- Food(s) suspected
- Quantity of food
- Reproducibility of reactions
- Food processing
- Route of exposure
- Involvement of co-factors
- Setting of the reaction
- Potential for cross-reactivity
- Dietary history
- Previous/current food elimination
- Dietary adequacy
- History of concomitant atopic and other diseases
- Family history of atopic disease

Allergy. 2023;78:3057–3076.

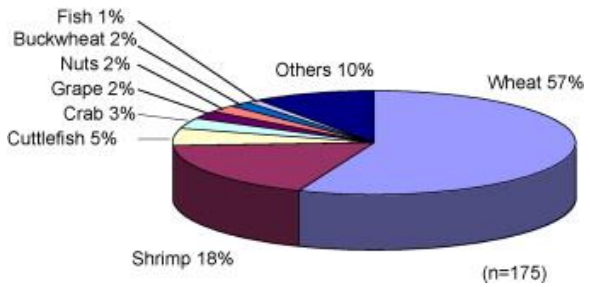
Typical IgE-mediated form of food allergy

- Infancy
- within minutes to 1–2 h
- Cutaneous: urticaria, angioedema, erythema, pruritus
- Gastrointestinal: vomiting, abdominal pain
- Respiratory: persistent cough, hoarse voice, wheeze, stridor, respiratory distress, nasal congestion
- Anaphylaxis
- Worsening of atopic dermatitis

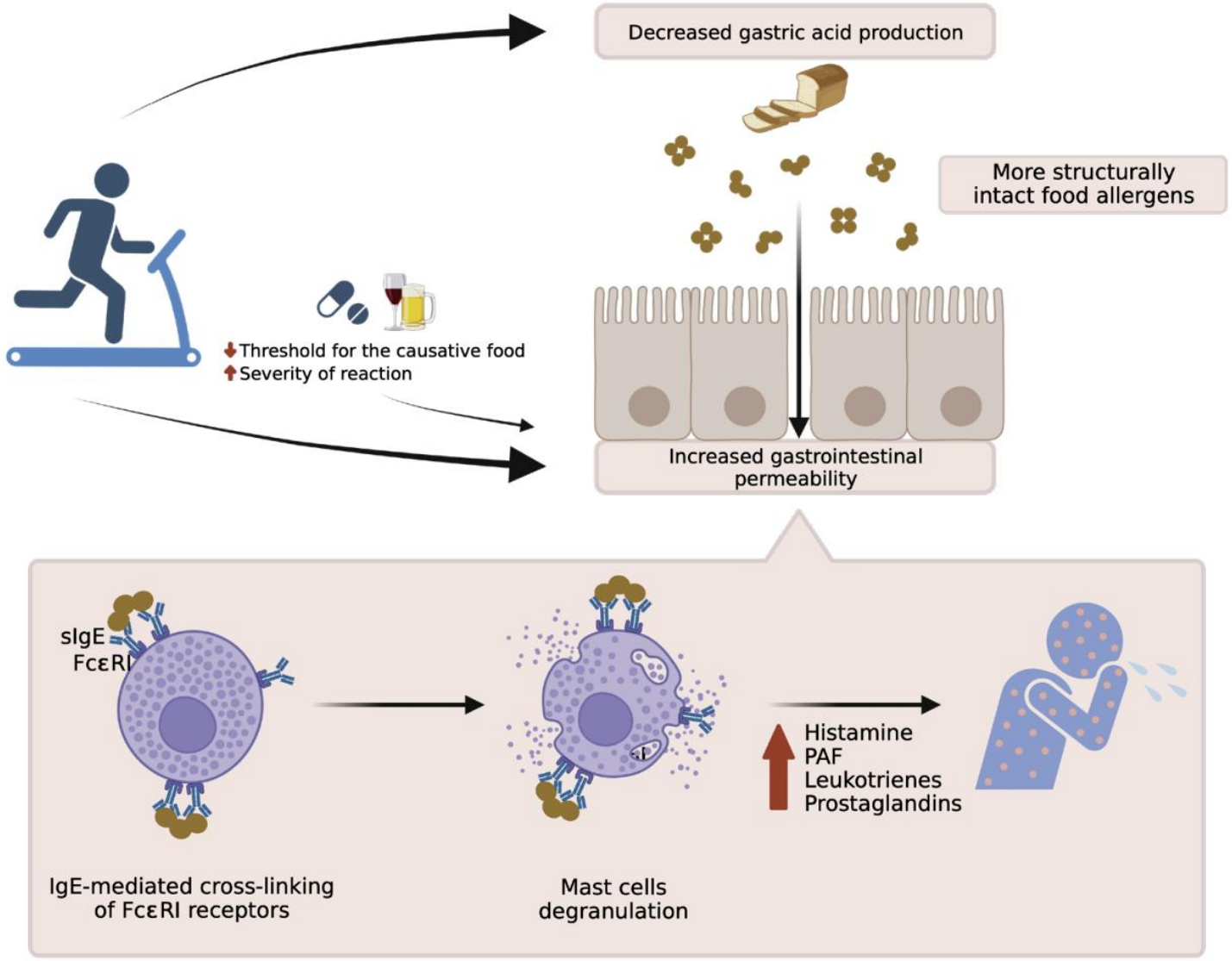
Food-dependent, exercise-induced anaphylaxis (FDEIA)



Korea

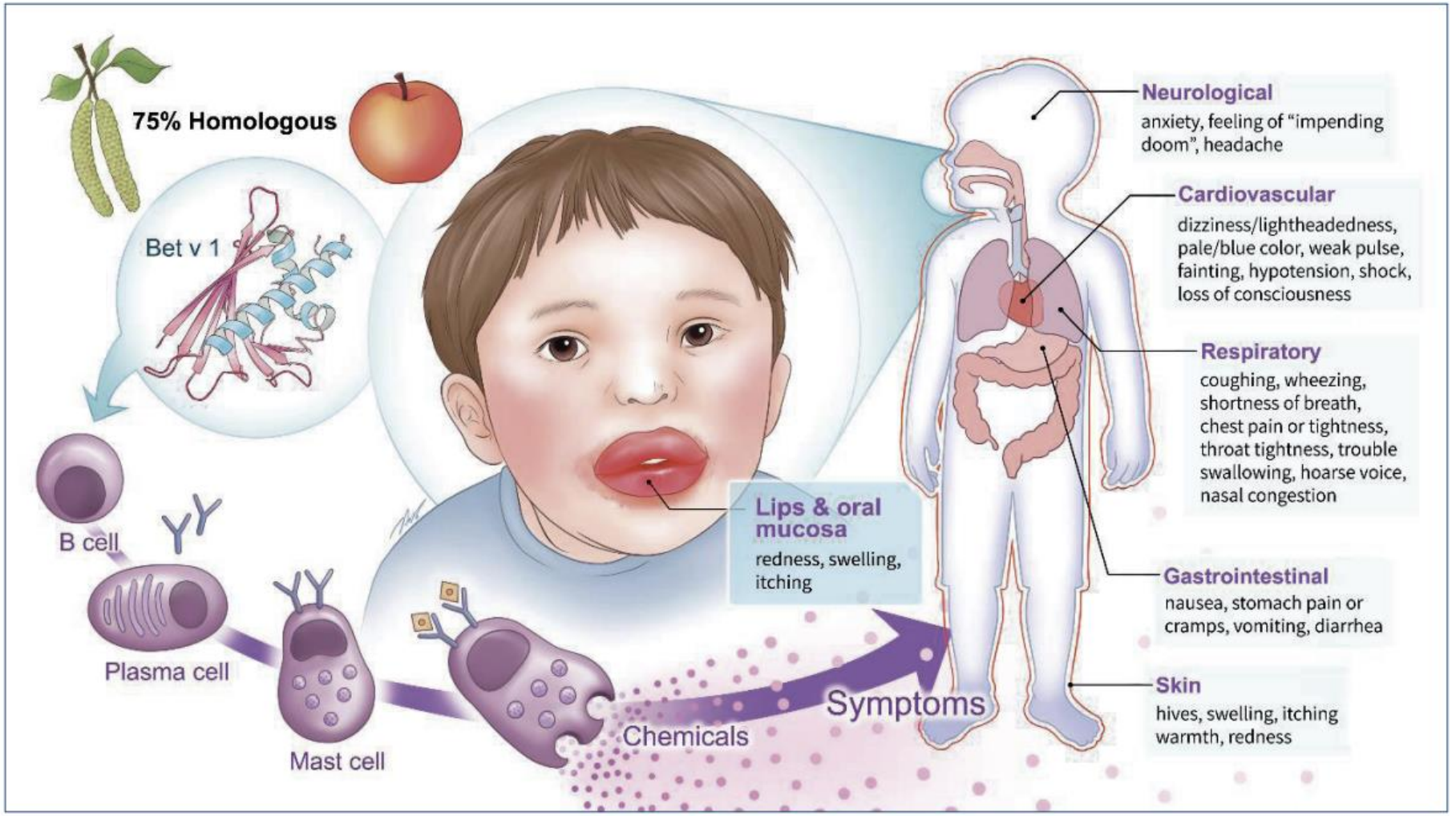


Japan



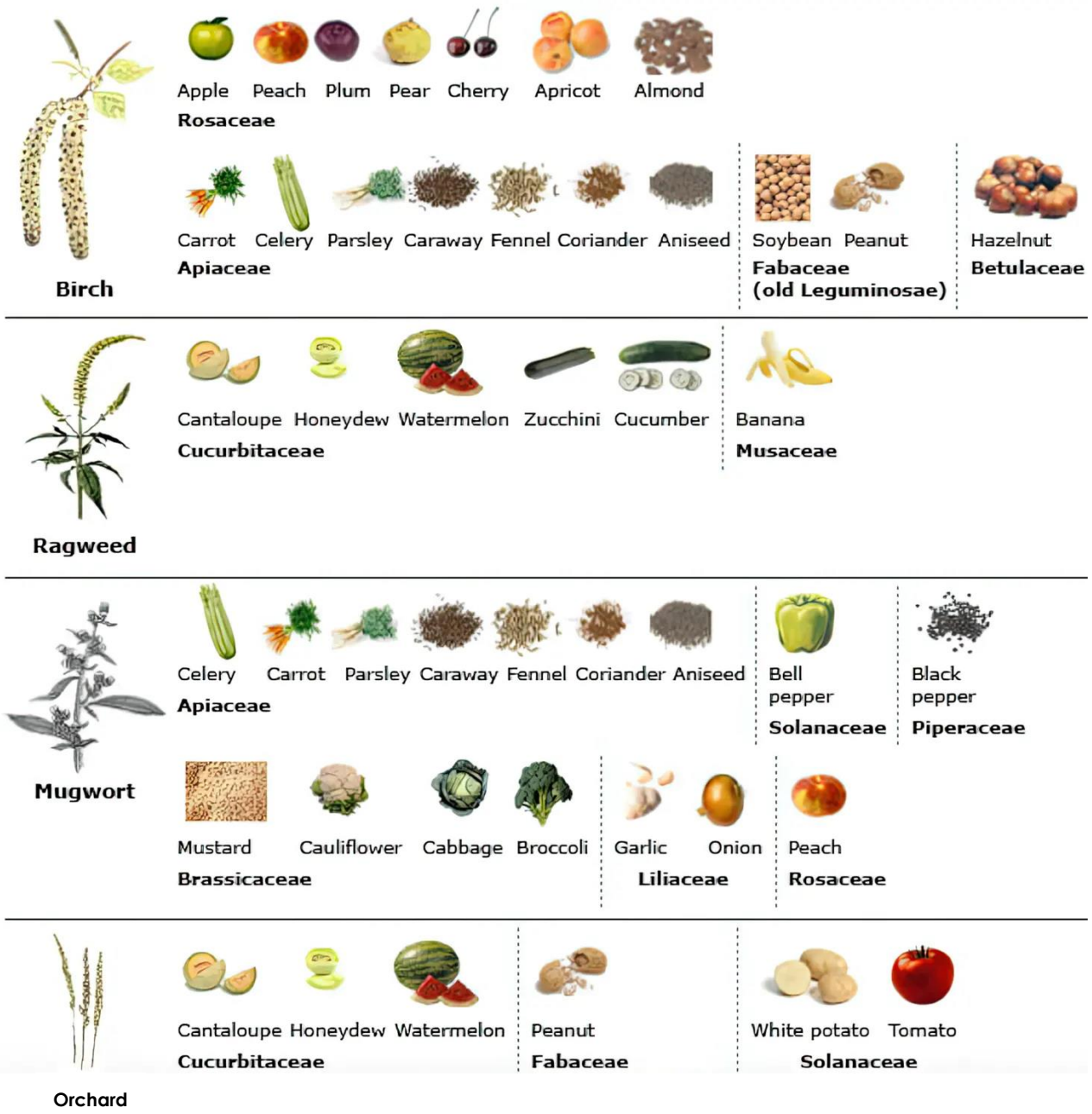
Foods 2023, 12, 3768

Pollen-food allergy syndrome in children



Clin Exp Pediatr. 2020 Dec; 63(12): 463-468.

Pollen food cross-reactivity

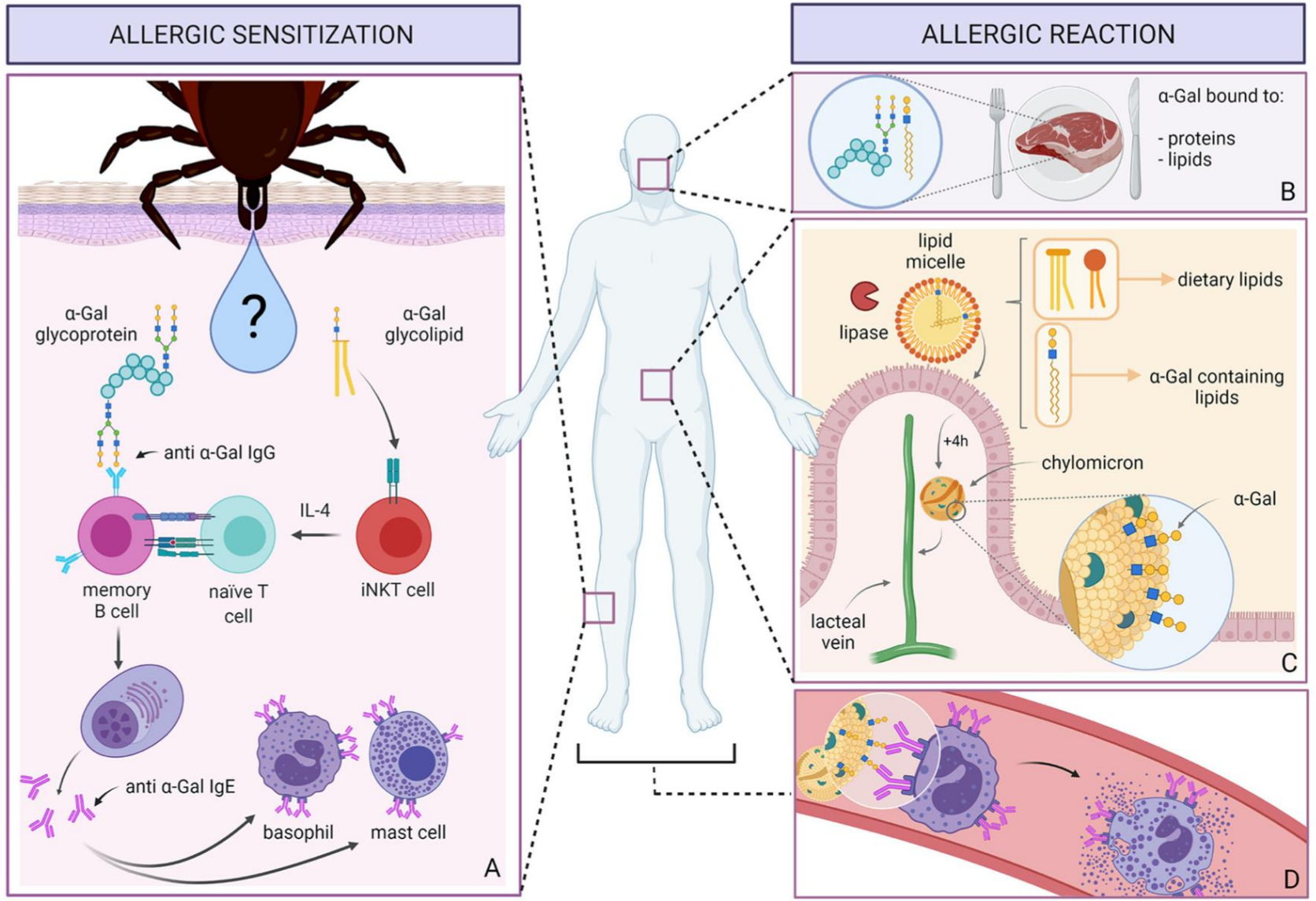


Allergic sensitization to α-Gal

Onset of symptoms: 2-6 hrs after meat ingestion

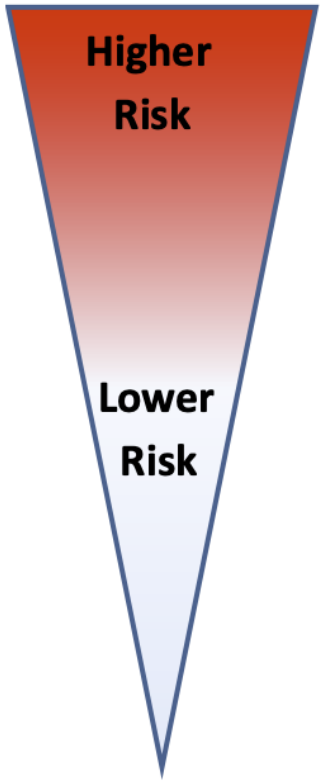
sIgE for a-Gal If : >2 IU/mL or more than 2% of the total IgE

SPT: is not helpful



Front Allergy. 2021 Dec 16;2:783279.

Risk of reactions in the α-Gal syndrome

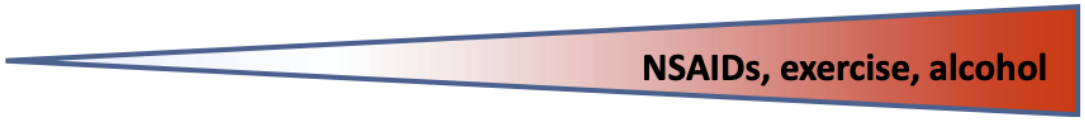


Food

- Beef, pork, and other meat, and also innards, of non-primate mammals
- Dairy, including milk and cheese
- Gelatin-containing foods

Medications/Biologic Therapies

- Cetuximab
- Gelatin plasma expanders
- Anti-venom (e.g. – CroFab)
- Bovine/porcine heart valves
- Gelatin-containing vaccines (e.g. – Zostavax, MMR)
- Heparin
- Pancreatic enzyme replacement (e.g. –pancrelipase & others)
- Gelcaps



Co-factors that may increase the risk or severity of reactions

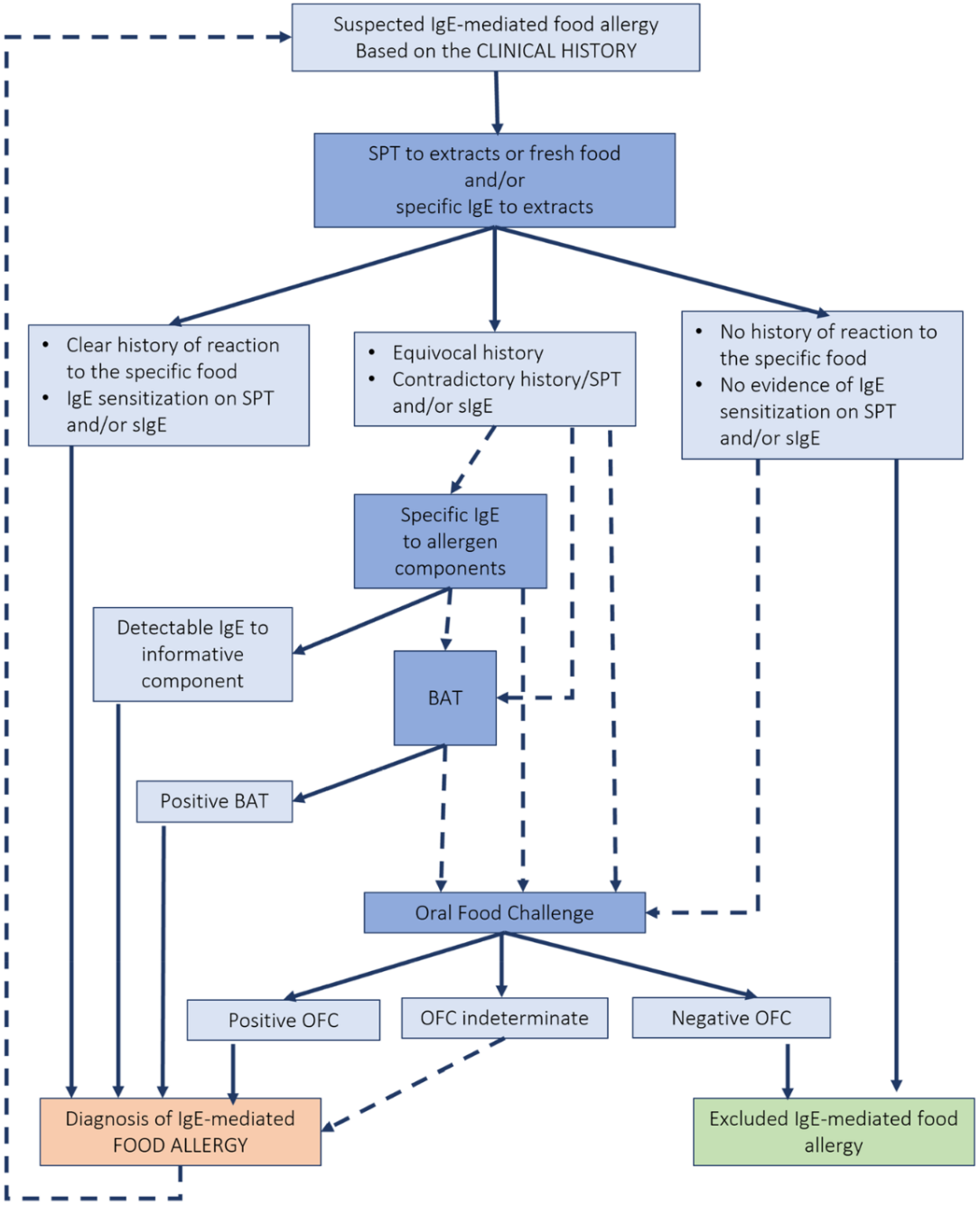
J Allergy Clin Immunol Pract 2020;8:15–23

Diagnosis of food allergy

- Clinical features
- Skin Prick Test (SPT)
- Specific IgE measurement
- Basophil activation test (BAT)
- Oral Food challenge (OFC)

IgE-mediated food allergy

EACCI guideline



Allergy. 2023;78:3057–3076.

Skin Prick Test

Food-specific sIgE highly predictive of clinical reactivity

Allergen	Diagnostic Decision Level kU_A/L[a]	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Egg white[185]	7	61	95	98	38
Infants ≤2 yr[186]	0.35	91	77	95	68
Ovomucoid for baked egg[56]	10.8	55	96	88	80
Cow's milk[185]	15	57	94	95	53
Infants ≤1 yr[187]	5	30	99	95	64
Casein for baked milk[188]	20.2	30	95	69	78
Peanut[185]	14	57	99	99	36
Fish[185]	20	25	100	99	89
Soybean[185]	30	44	94	73	82
Wheat[185]	26	61	92	74	87
Tree nuts[189]	15	Other values were not calculated and are not available.		95	

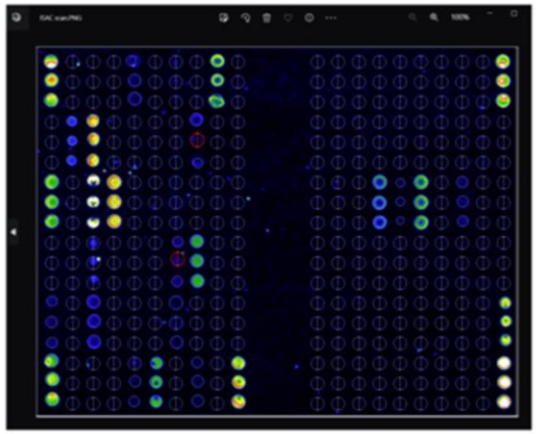
[a] kU_A/L = allergen-specific kilo units per liter.

Multiplex solid-phase immunoassays

Component resolved diagnosis (CRD)

A

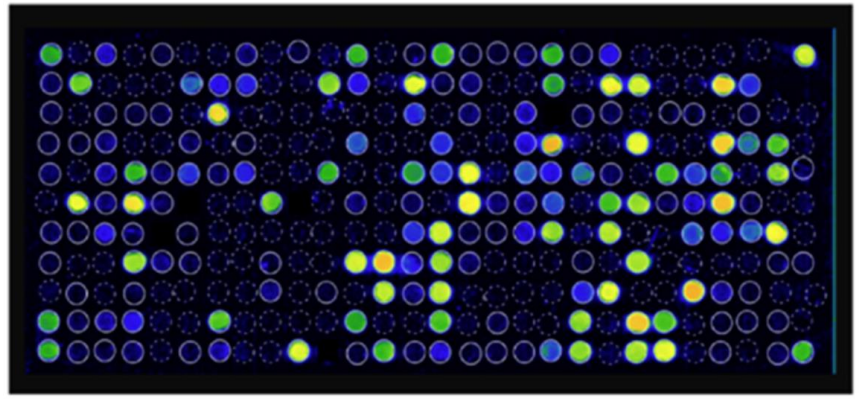
B



ISACE112i

A

B



ALEX2

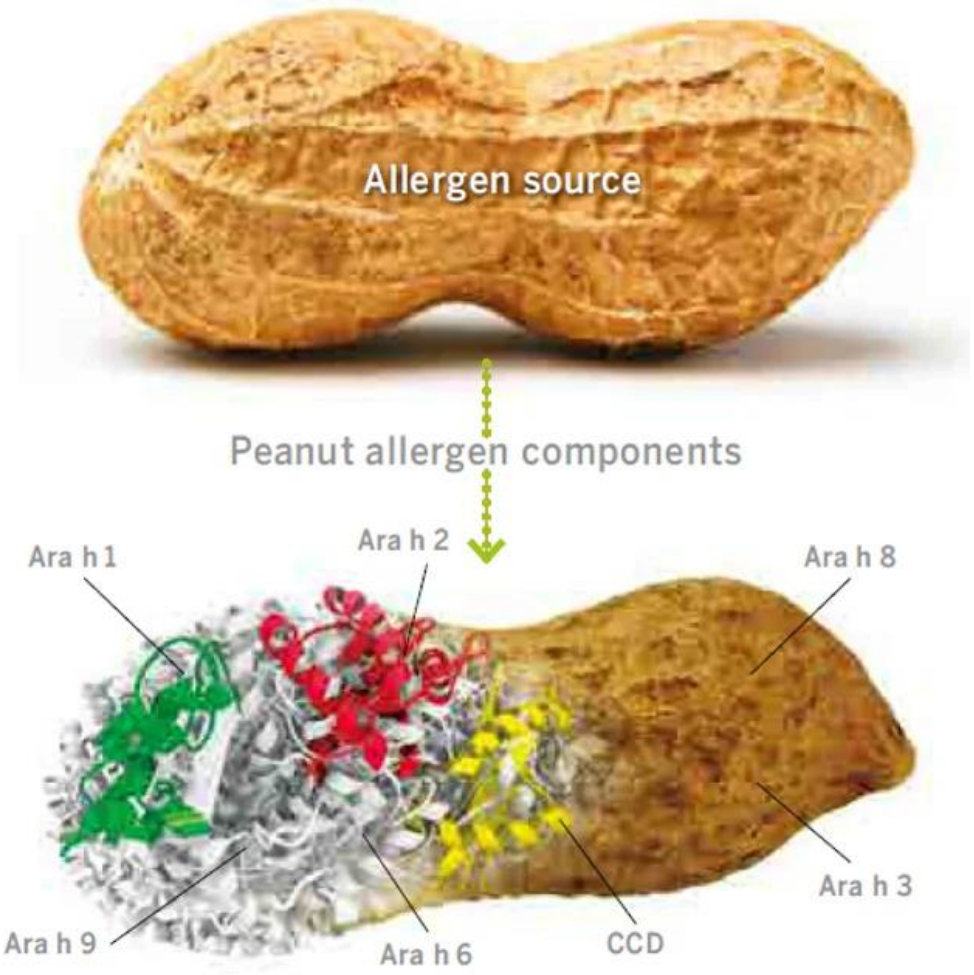
Peanut allergy

ALEX²
ALLERGEN LIST

macroarraydx.com

LEGUMES & NUTS

Component Extract	Allergen-code	Common name	Scientific name	Component	Biochemical designation
C	f513	Macadamia	Macadamia integrifolia	Mac i 2S Albumin	2S Albumin
E	f12	Pea	Pisum sativum		
C	f422	Peanut	Arachis hypogaea	Ara h 1	7/8S Globulin
C	f423	Peanut	Arachis hypogaea	Ara h 2	2S Albumin
C	f424	Peanut	Arachis hypogaea	Ara h 3	11S Globulin
C	f447	Peanut	Arachis hypogaea	Ara h 6	2S Albumin
C	f352	Peanut	Arachis hypogaea	Ara h 8	PR-10
C	f427	Peanut	Arachis hypogaea	Ara h 9	nsLTP
C	f803	Peanut	Arachis hypogaea	Ara h 15	Oleosin



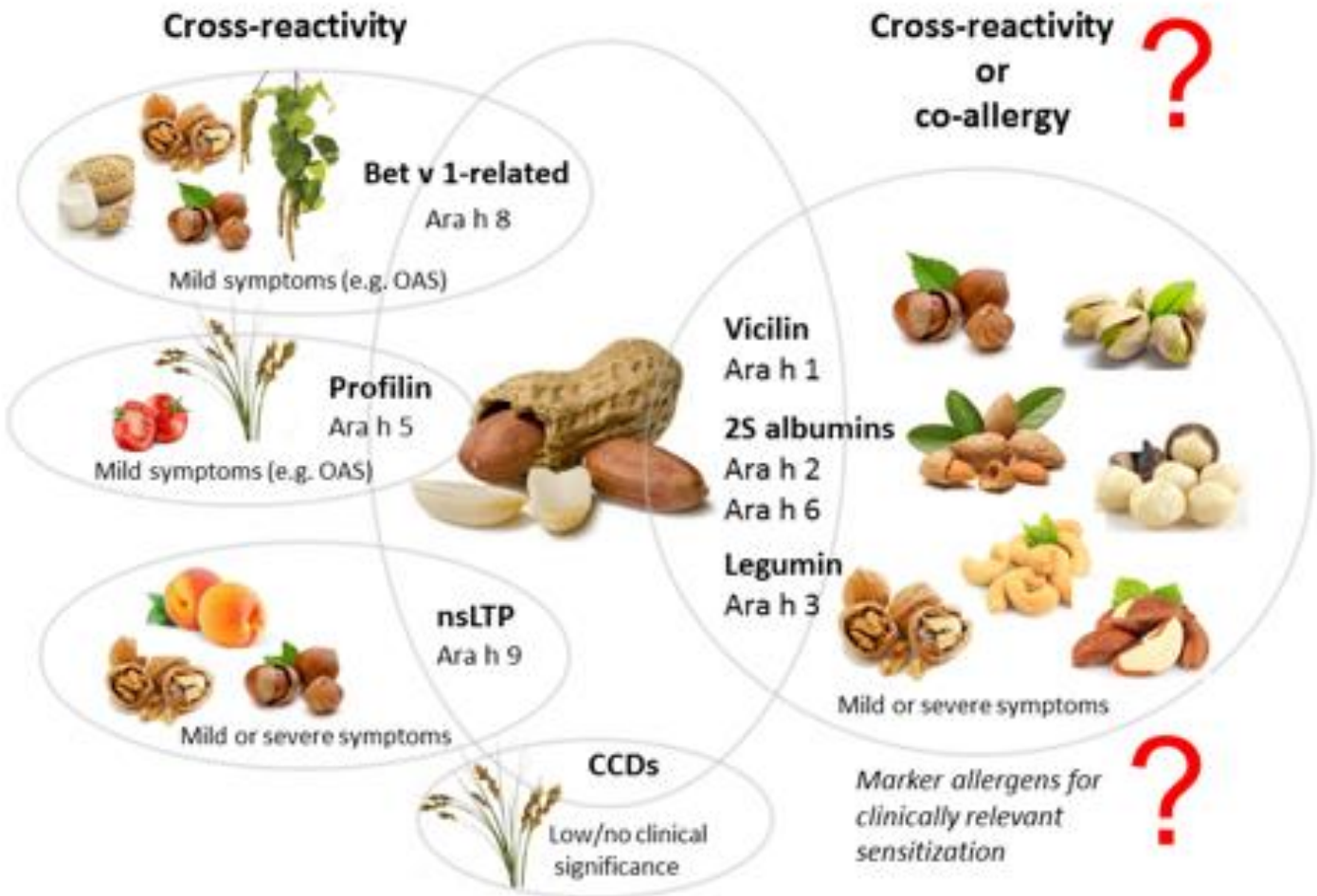
Peanut

Ara h 1, h 2, h 3
Severe systemic reactions.
Stable to heat and digestion.
Can cross-react with proteins in other seeds.

Ara h 8 (PR-10)
Local reactions.
Labile to heat and digestion.
Can cross-react with plant pollens.

Ara h 9, lipid-transfer protein (LTP)
Both systemic and local reactions.
Oral allergy syndrome (OAS).
Stable to heat and digestion.

Ara h 5 (Profilin)
Marker of grass pollen cross-reactivity.
Heat labile.
Oral allergy syndrome (OAS).

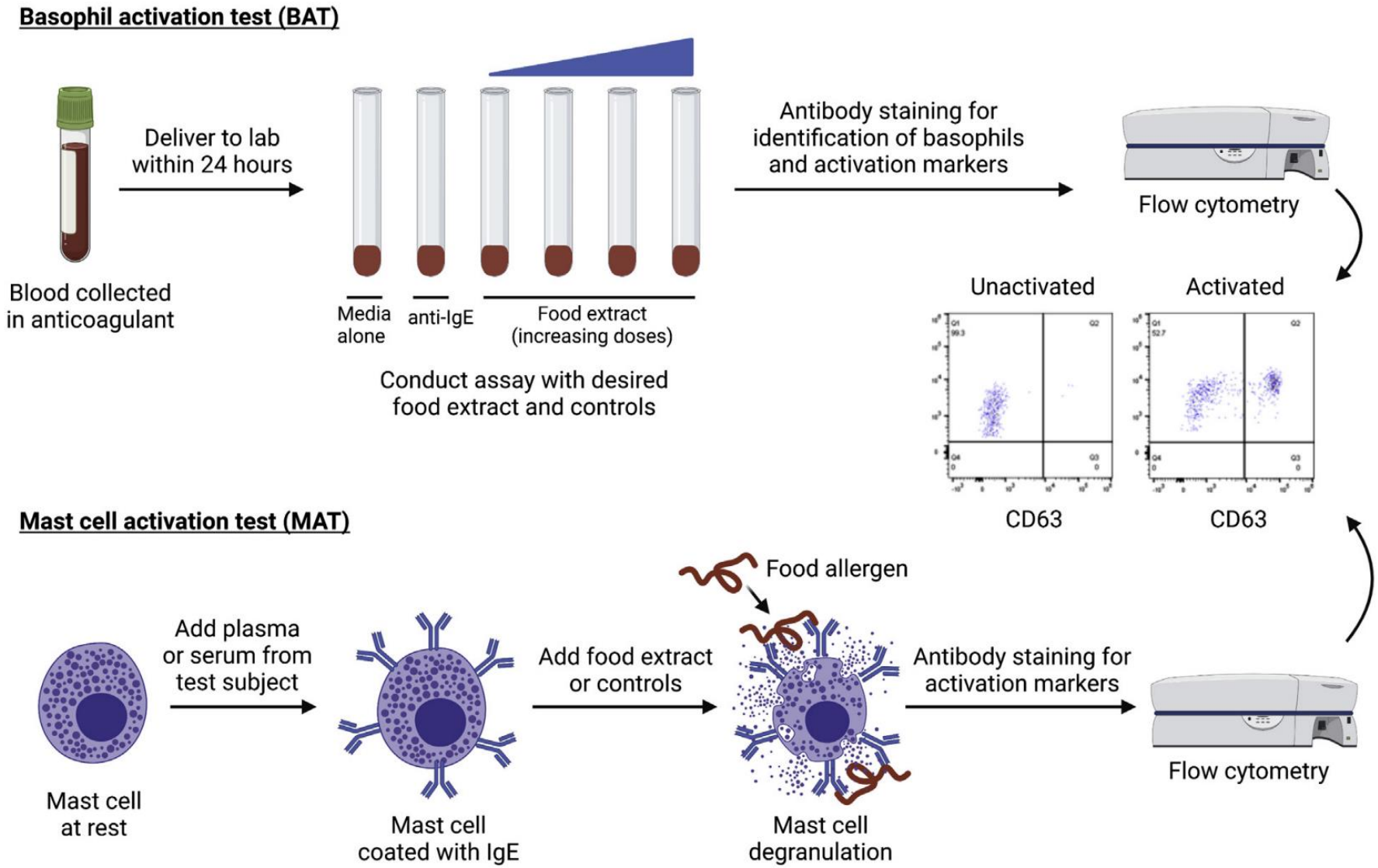


https://www.meduniwien.ac.at/ipa/med-biotech/mb/research.html

Common primary food allergies and their cross-reactivity

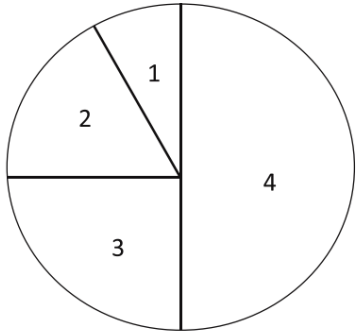
Primary Food Allergy	**Cross Reactive Food**	**Risk** (varies with region)
Crustacean Shellfish 	Other Crustaceans	~75%
	Mollusks/Bivalves (Clam, Mussel, Oyster, Squid) 	<50%
Mollusks/Bivalves 	Crustaceans (Crab, Shrimp, Lobster) 	>70%
Finned Bony Fish 	Other Finned Bony Fish	~50%
	Cartilaginous Fish (Dogfish, Ray, Shark) 	<5%
Peanut 	Tree Nuts (co-allergy)	~33%
	Lupine 	~20%
	Sesame (co-allergy)	10-15%
	Green Bean, Pea, Soy 	5-20%
Other Legumes		
If Soy 	Peanut	>75%
If Chick Pea 	Lentil, Pea 	>50%
Tree Nuts 	Other Tree Nuts	15-33%
	Sesame (co-allergy)	10-15%
If Walnut	Pecan 	~66-75%
If Pecan	Walnut 	>95%
If Cashew	Pistachio 	~66-83%
If Pistachio	Cashew 	>95%
If Peanut and Tree Nut	Sesame (co-allergy) 	50%
Milk (Cow) 	Milk (Sheep, Goat) 	>90%
	Milk (Camel, Mare) 	<5%
	Beef 	~10-20%
Wheat 	Barley, Rye 	<25%

J Allergy Clin Immunol Pract 2021;9:82–99



(J Allergy Clin Immunol Pract 2022;10:1–9)

Oral food challenge (OFC)

Four Dose Protocol	Six Dose Protocol
Divide the serving as outlined below. Dose 1 = 1/12th of the total serving Dose 2 = 1/6th of the total serving Dose 3 = 1/4 of the total serving Dose 4 = 1/2 of the total serving  	Dose 1 = 1% of total dose Dose 2 = 4% of total dose Dose 3 = 10% of total dose Dose 4 = 20% of total dose Dose 5 = 30% of total dose Dose 6 = 35% of total dose

BOX 2. An example of preparation for oral food challenge for IgE-mediated wheat allergy and calculation of doses consumed

1. Weigh* 10 g (2 teaspoons† = 10 mL) wheat flour.
2. Mix in 5 g (1 teaspoon = 5 mL) sugar.
3. Mix ingredients in applesauce for a total weight of 100‡ g (1/2 cup less 3 teaspoon or 115 mL).
4. Record timing, amount ingested, and any objective/subjective symptoms.

Cumulative dosing§:

Time (min)	% of total food	Amount of challenge food, g	Amount of wheat flour, g
00	0.1%	0.1	0.01
05	0.5%	0.5	0.05
20	1%	1	0.1
35	4%	4	0.4
50	10%	10	1
60	20%	20	2
70	20%	20	2
80	20%	20	2
90	24.4%	24.4	2.44
Total	100%	100 g	10 g

J Allergy Clin Immunol Pract 2020;8:75–90

Indications for an OFC

- Identify foods causing acute reactions for initial diagnosis of food allergy and for monitoring resolution of food allergy
- Determine whether food allergens associated with chronic conditions such as atopic dermatitis or allergic eosinophilic esophagitis will cause immediate reactions
- Expand the diet in persons with multiple dietary restrictions, usually because of subjective complaints such as headaches or hyperactive behavior
- Assess the status of tolerance to cross-reactive foods
- Assess the effect of food processing on food tolerability, eg, fruits and vegetables that may be tolerated in cooked form in the pollen-food allergy syndrome

J Allergy Clin Immunol 2009;123:S365-83.

Handheld Devices Promising for Detecting Food Allergens

Management checklist of food allergy (4As)

Avoidance

- Avoid offending and cross-reactive foods
- Read food labels carefully
- Be aware of food allergens in meals
- Be aware of cofactor(s)

Adrenaline

- Self-carry self-injectable adrenaline
- Know how and when to use adrenaline
- Check proficiency of adrenaline use at every clinic visit

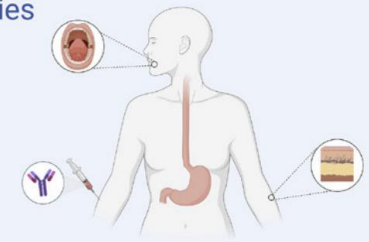
4As Management Checklist for **Food allergy**

Action plan

- Self-carry an anaphylaxis card or other food allergy identification document
- Self-carry a written action plan
- Health care service providers should inform patients and emergency contact persons

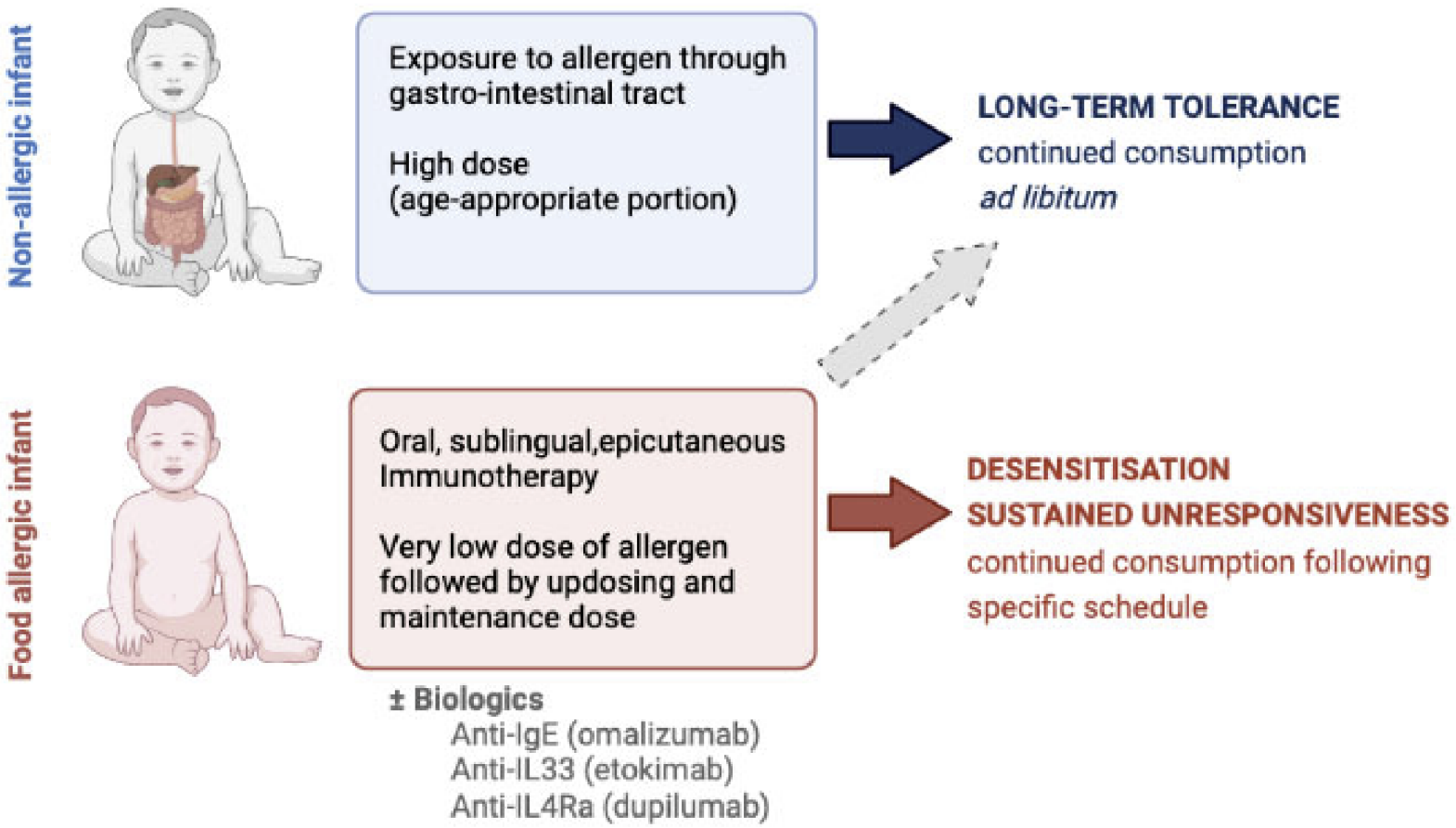
Advanced treatments

- Implement multidisciplinary approaches to care involving allergists, nutritionist, patients, and and their families
- Consider Immunotherapy and/or biologic therapies



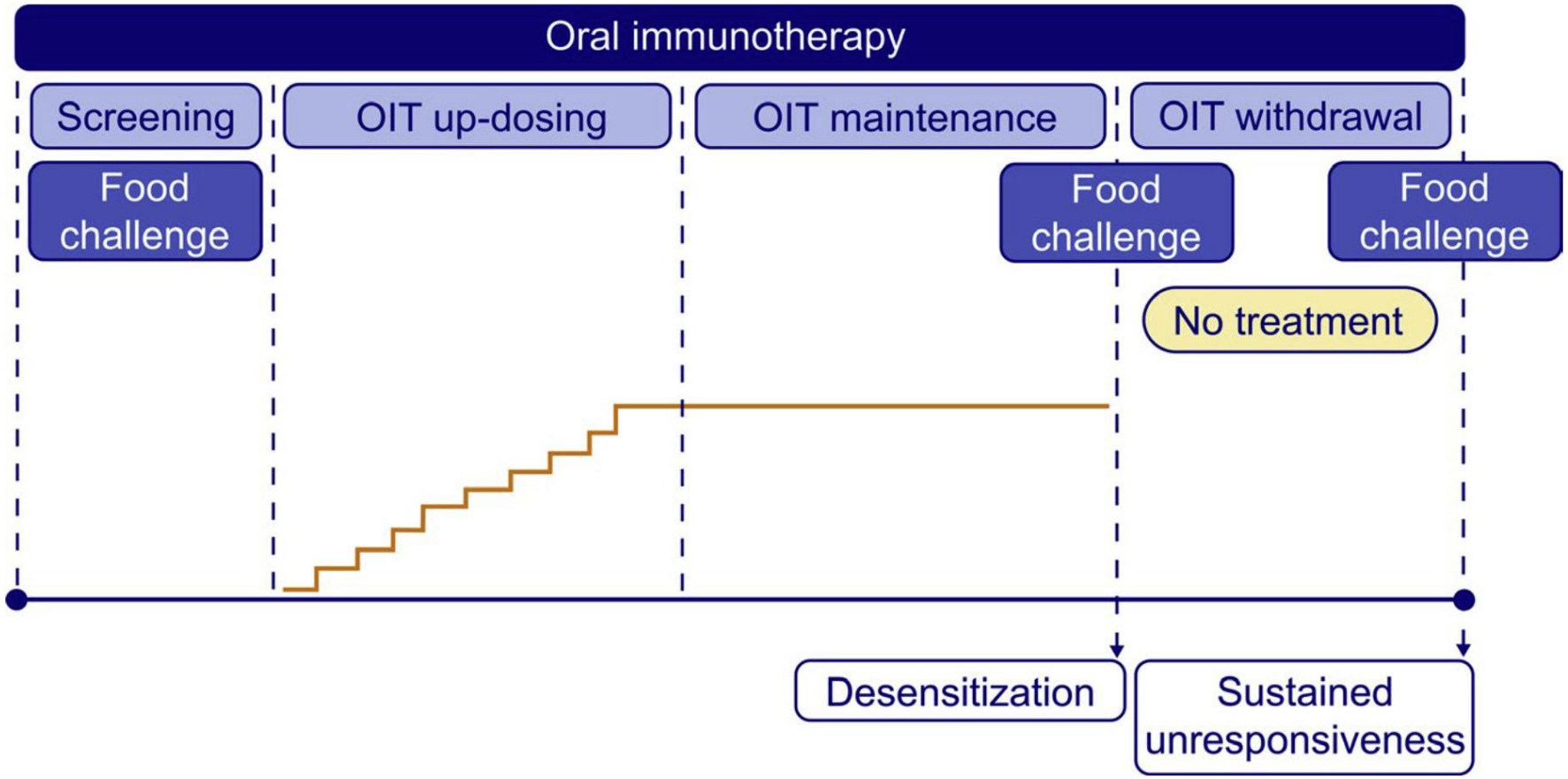
Asian Pac J Allergy Immunol. 2022 Dec;40(4):308-320.

Oral tolerance induction



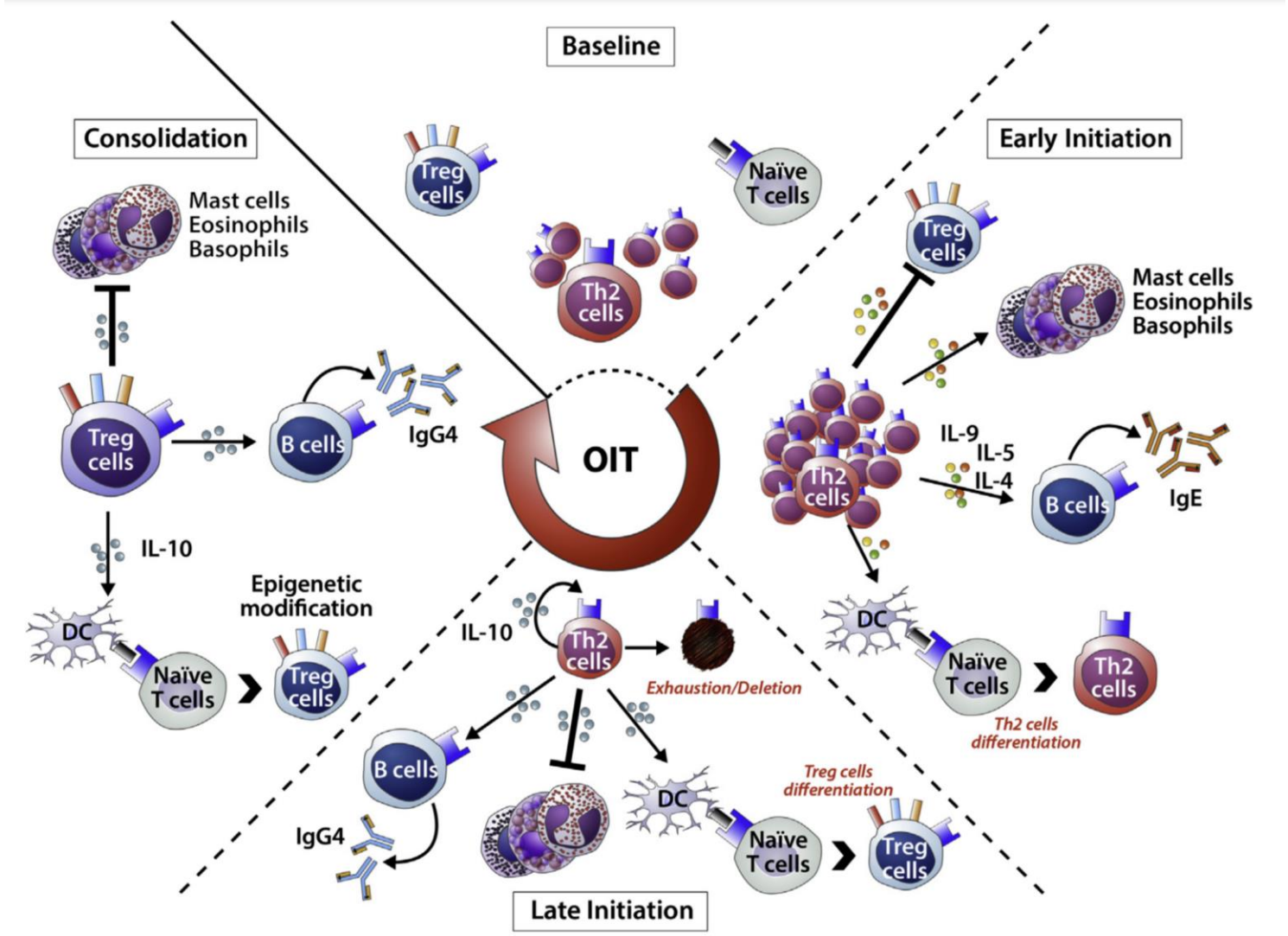
Foods 2022, 11, 3386. h

Oral Immunotherapy (OIT)



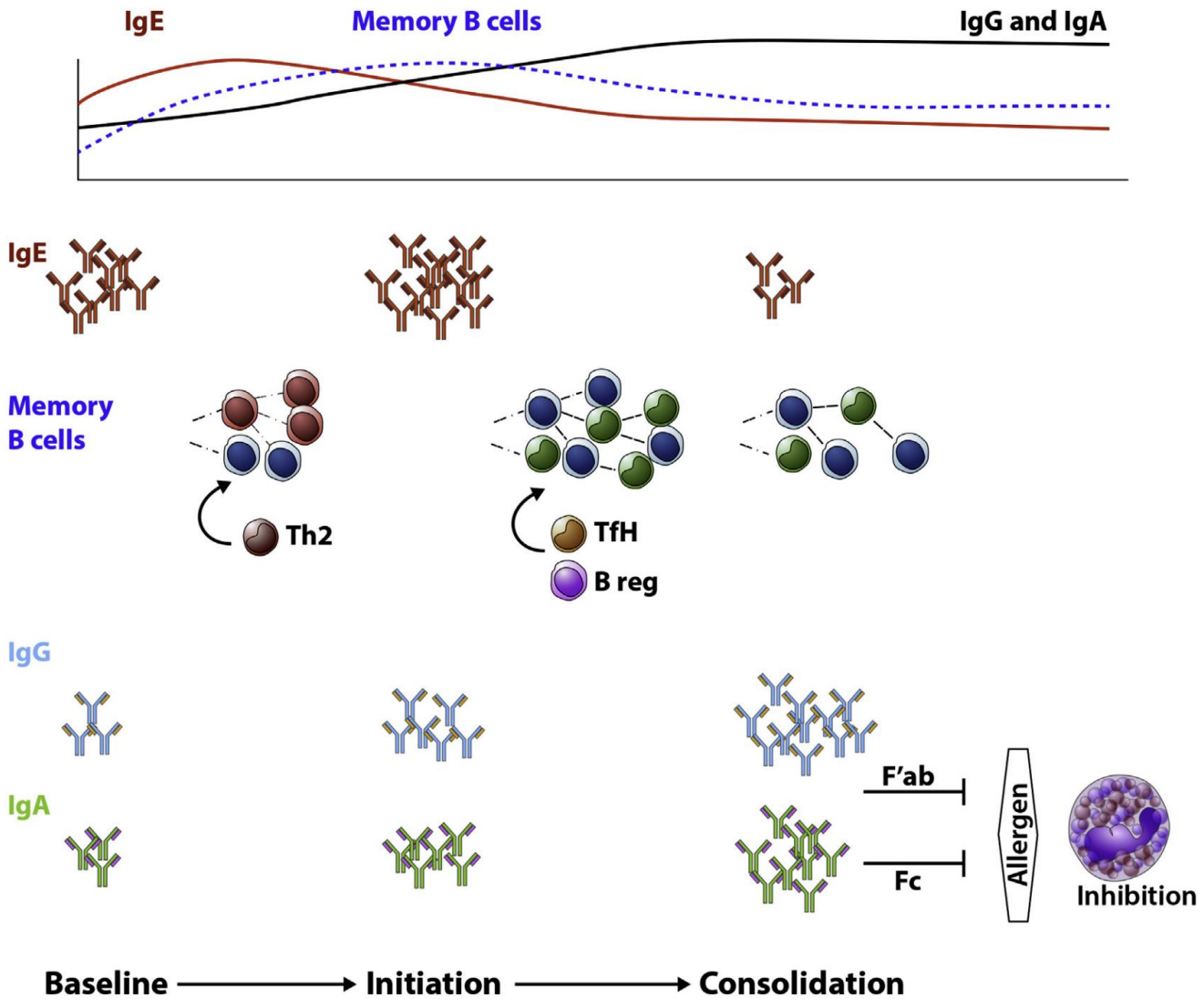
Allergy. 2020;75:1316–1326

Sequential immune mechanisms of OIT



J AllergyClin Immunol 2018;141:491–8.

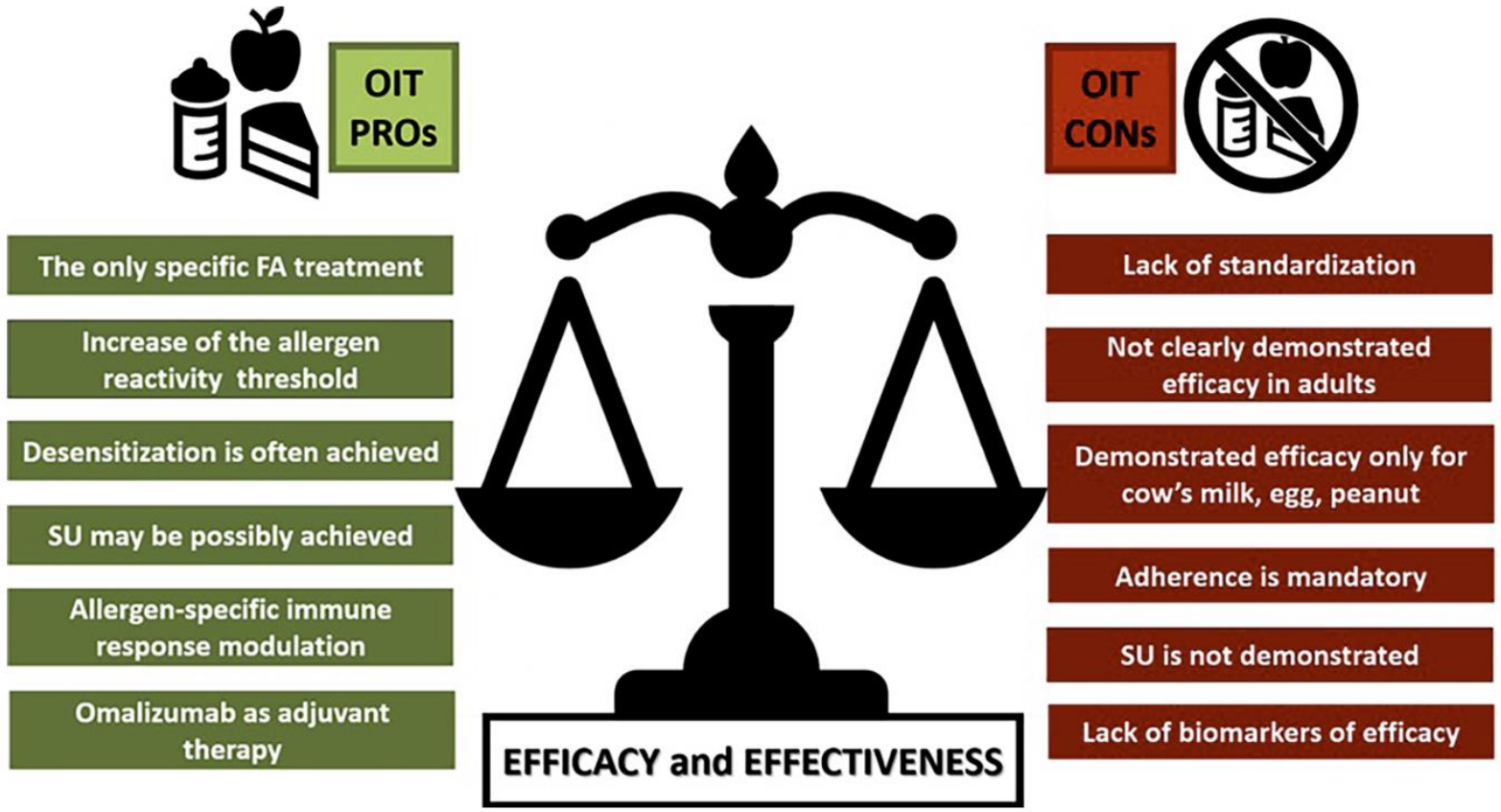
Humoral mechanisms of OIT



J Allergy Clin Immunol 2018;141:491–8.

Oral Immunotherapy (OIT)

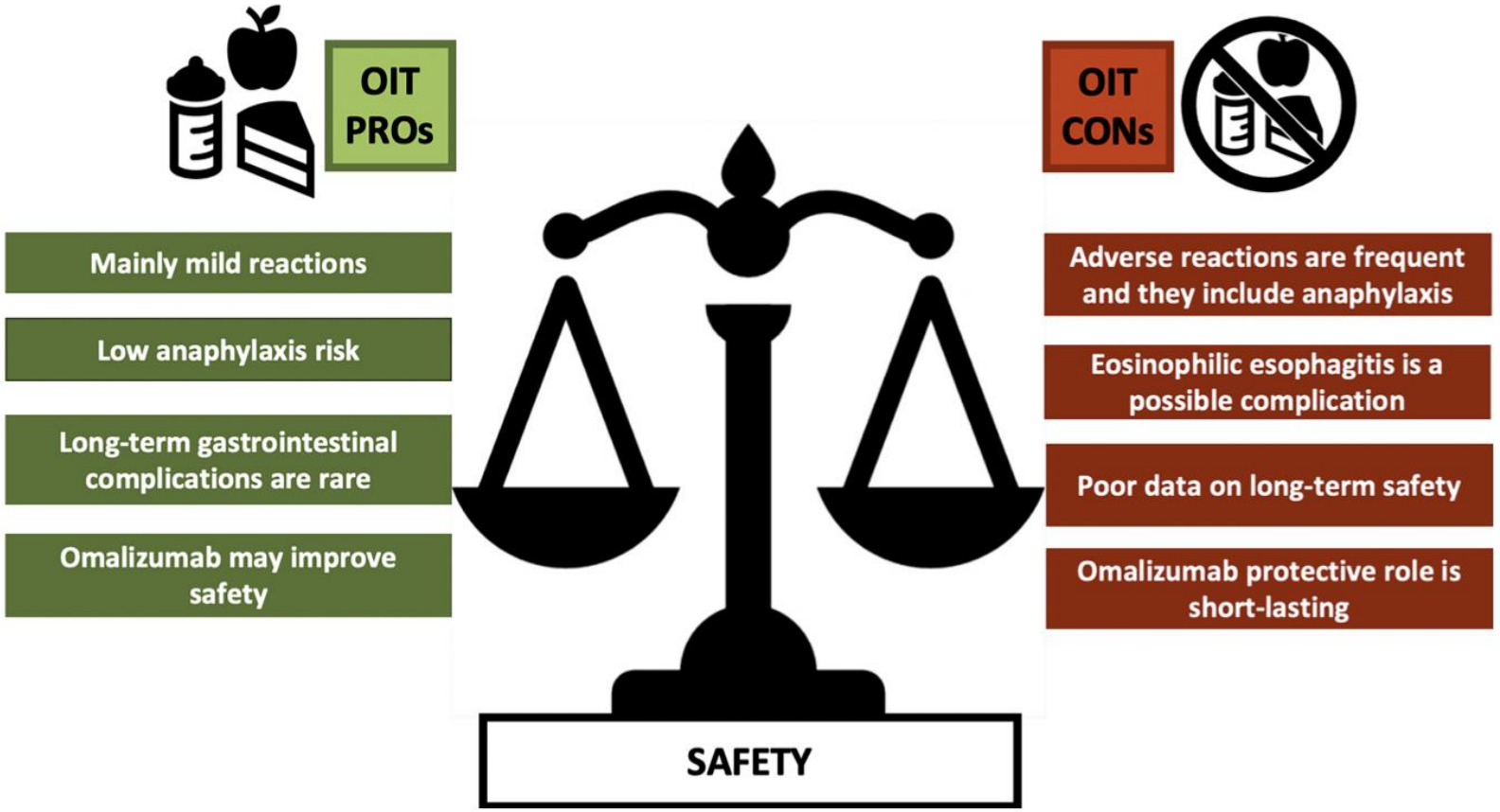
Efficacy and Effectiveness



Front. Immunol. 12:636612.

Oral Immunotherapy (OIT)

Safety

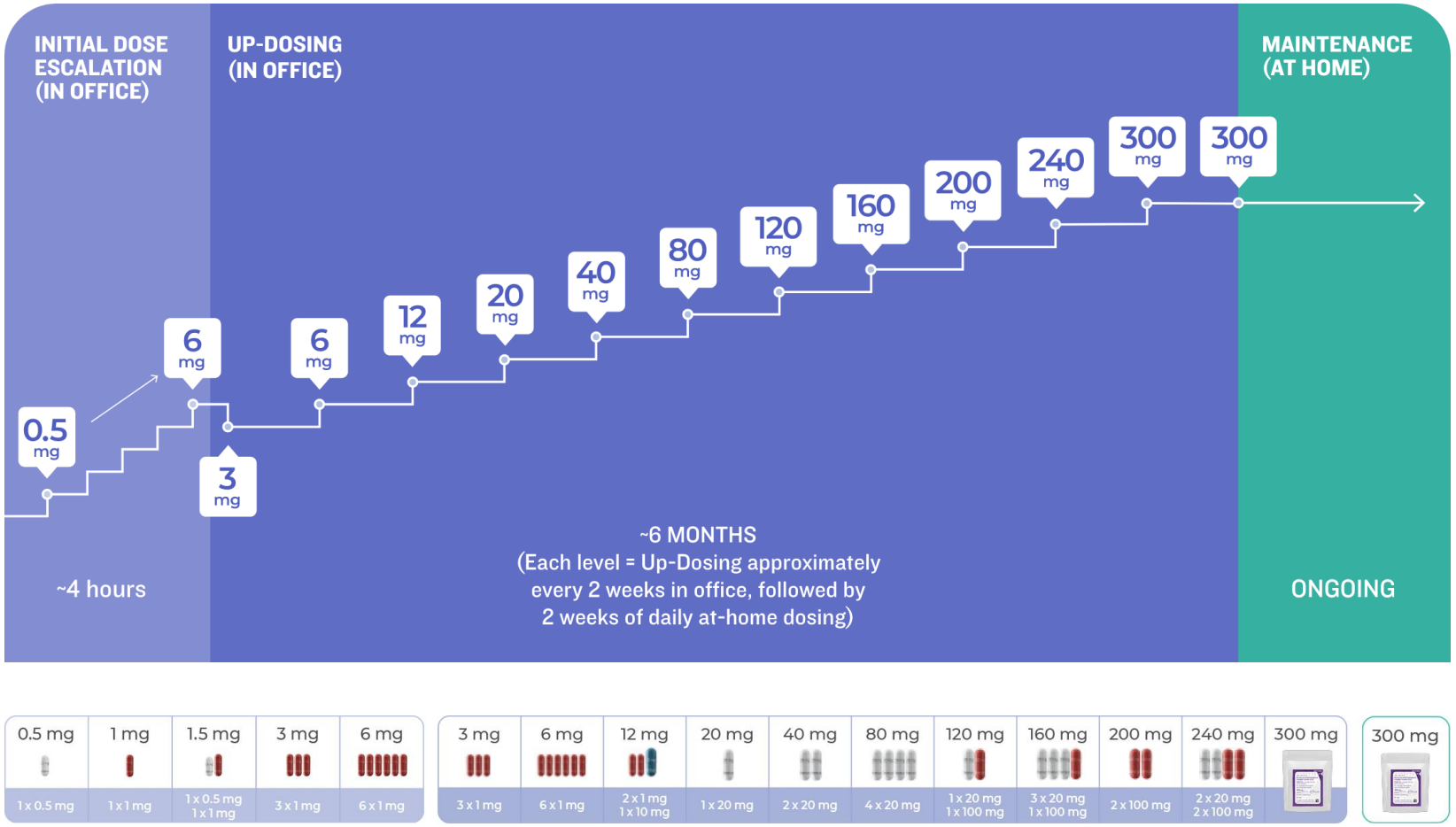


Front. Immunol. 12:636612.

Palforzia®
Peanut (*Arachis hypogaea*)
Allergen Powder-dnfp

aimmune™ THERAPEUTICS
A Nestlé Health Science Company

- an OIT product
- FDA approval: Jan 31 2020
- Patients 4–17 years of age

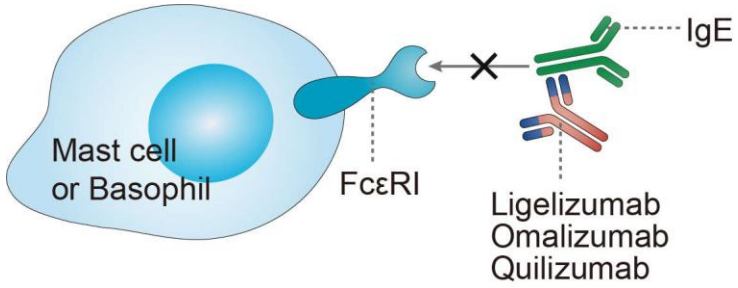


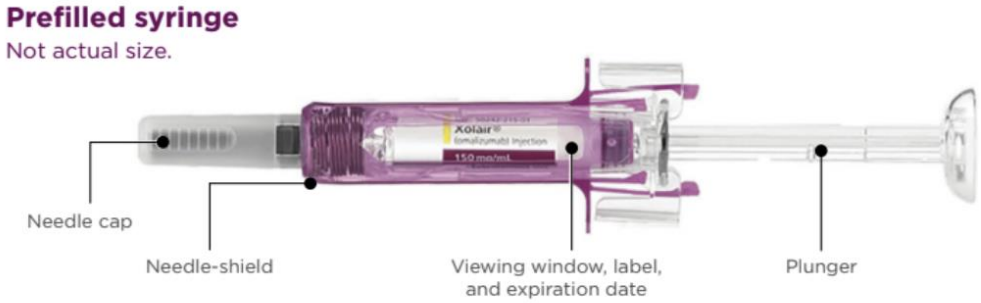
Epicutaneous Immunotherapy (EPIT)

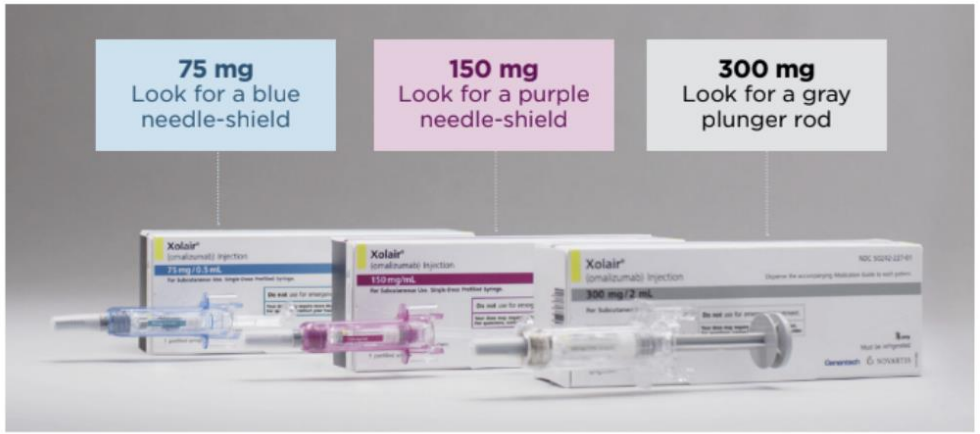
The Role of Biologics in the Treatment of Food Allergy

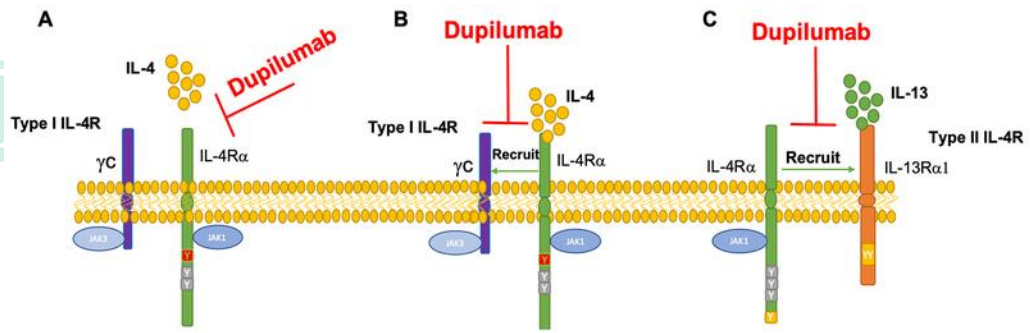
Xolair® Omalizumab
FOR SUBCUTANEOUS USE 75 mg ▪ 150 mg ▪ 300 mg

- **XOLAIR is the only FDA-approved treatment to reduce allergic reactions, including severe reactions such as** anaphylaxis**, following accidental exposure to one or more foods**
- **16 Feb 2024**
- **Patients >= 1 years old**









DUPIXENT® (dupilumab) Injection

200mg · 300mg

- FDA approved for EOE
- May 2022: > 12 years
- Jan 2024: >= 1 years

WEIGHT-BASED DOSING AND OPTION TO ADMINISTER AT HOME OR IN OFFICE[1]

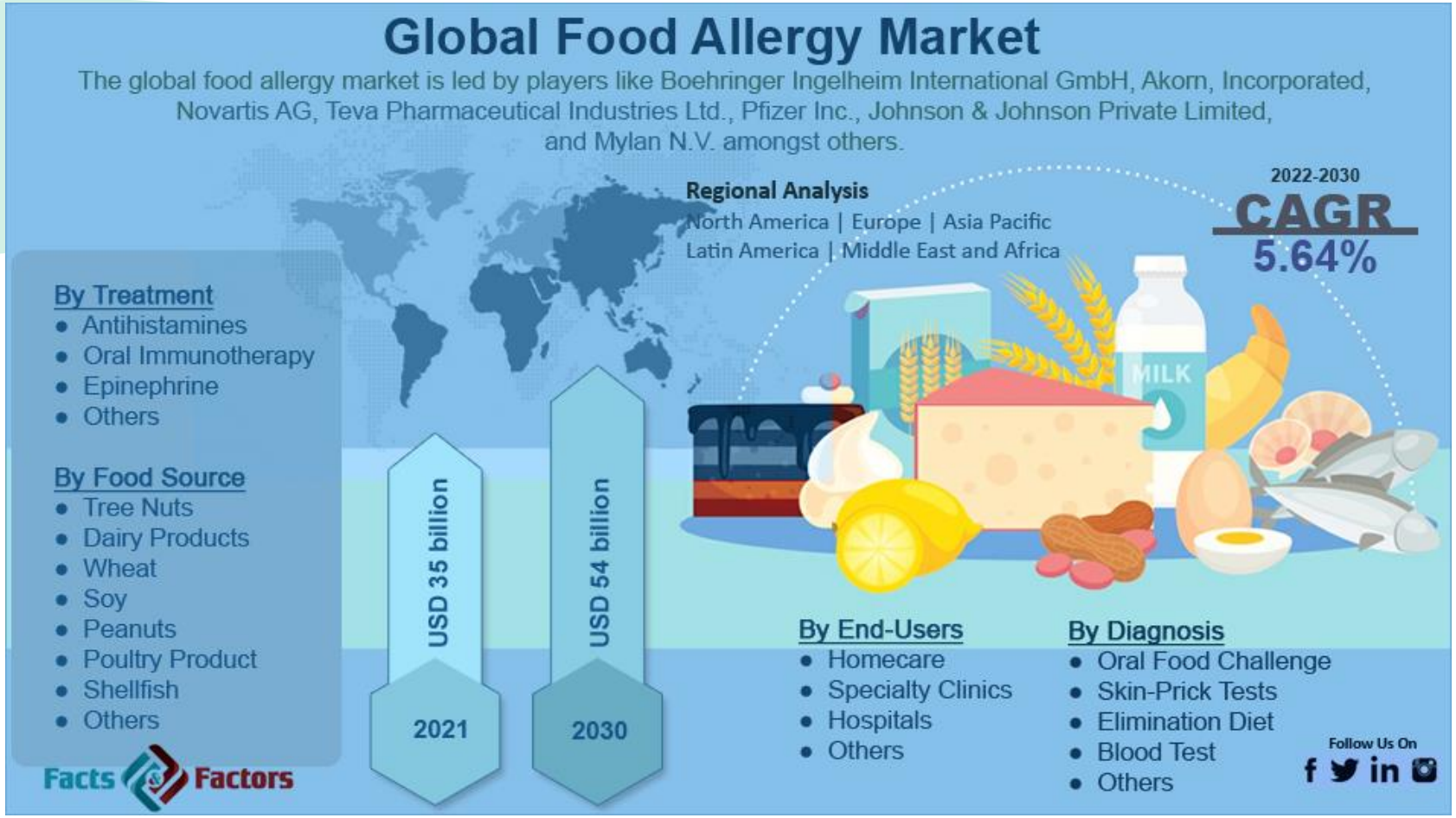
Weight-tiered dosage regimen[1]

1+ YEAR OF AGE

No loading dose

15 to <30 kg	Every 2 weeks	200 mg[a] 1 pre-filled pen or syringe
30 to <40 kg	Every 2 weeks	300 mg[b] 1 pre-filled pen or syringe
≥40 kg[c]	Every week	300 mg[b] 1 pre-filled pen or syringe

[a] 200 mg=1.14 mL solution.[1]
[b] 300 mg=2 mL solution.[1]
[c] The recommended dosage of 300 mg QW for pediatric subjects 1 to 11 years of age weighing ≥40 kg is based on modeled pharmacokinetic data to provide comparable exposures to the 300 mg QW dosage in adult and pediatric subjects 12 years of age and older weighing ≥40 kg with EoE.[1]



Key Companies in the Food Allergy Treatment Market

aimmune THERAPEUTICS · NOVARTIS · InnoUp · COUR · dbv technologies · VEDANTA BIOSCIENCES · Genentech A Member of the Roche Group · Rho · REGENERON · camallergy · alladapt IMMUNOTHERAPEUTICS