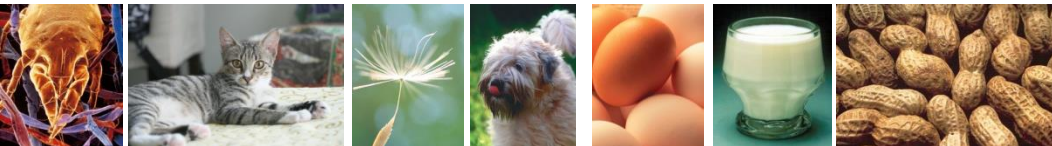




Mysteries of IgE blood tests in Allergy Diagnostics

Anthea Yeung
Sales & Marketing Manager
9 December 2019



When was the term "Allergy" born?

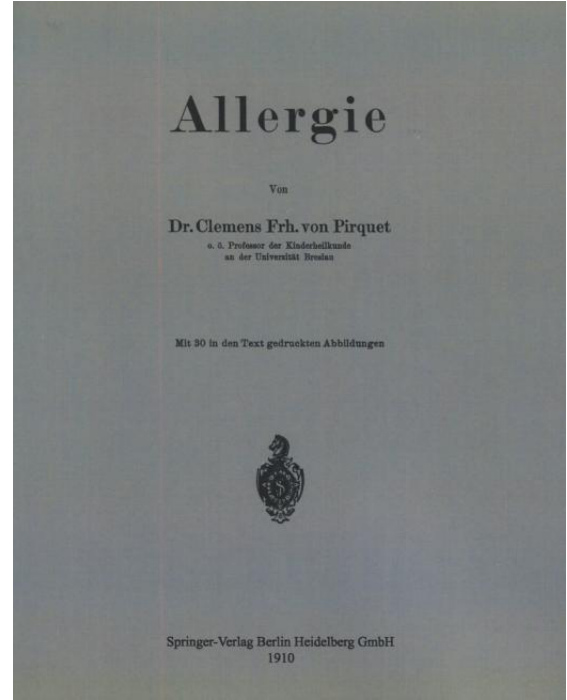
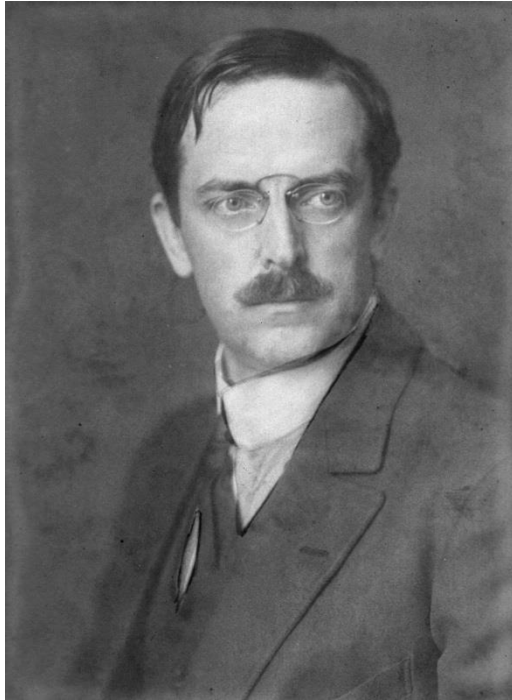
1706?

1806?

1906?



When was the term "Allergy" born?

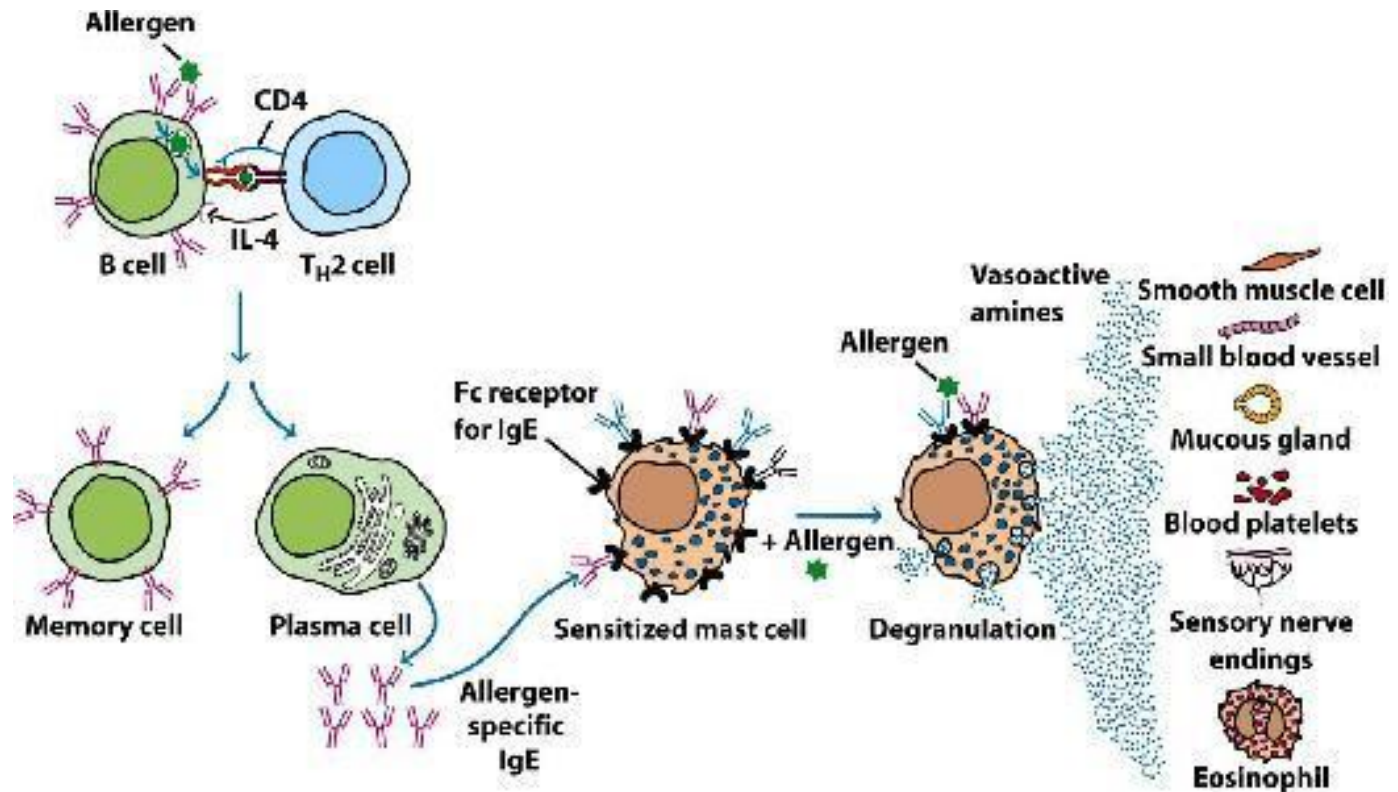


The word "allergy" first appeared on July 24, **1906** in the Munchener Medizinische Wochenschrift in an essay written by Clemens von Pirquet, a pediatrician from Vienna.



What is Allergy?

A chronic condition involving an abnormal reaction to an ordinarily harmless substance called an **allergen**. The immune system views the allergen as an invader and a chain reaction is initiated. White blood cells of the immune system produce **IgE antibodies**. These antibodies attach themselves to mast cells, causing a release of potent chemicals such as histamine, leukotrienes that cause symptoms.



Allergy Symptoms 過敏症狀



- itchy, swelling eyes 眼睛紅腫發癢
- nasal congestion 鼻塞
- runny nose 流鼻水
- sneezing, itching 打噴嚏，鼻癢
- eczema 濕疹
- swelling mucous membrane 黏膜腫脹
- diarrhea, abdominal pain 腹瀉，腹痛
- asthma 哮喘
- anaphylaxis 休克

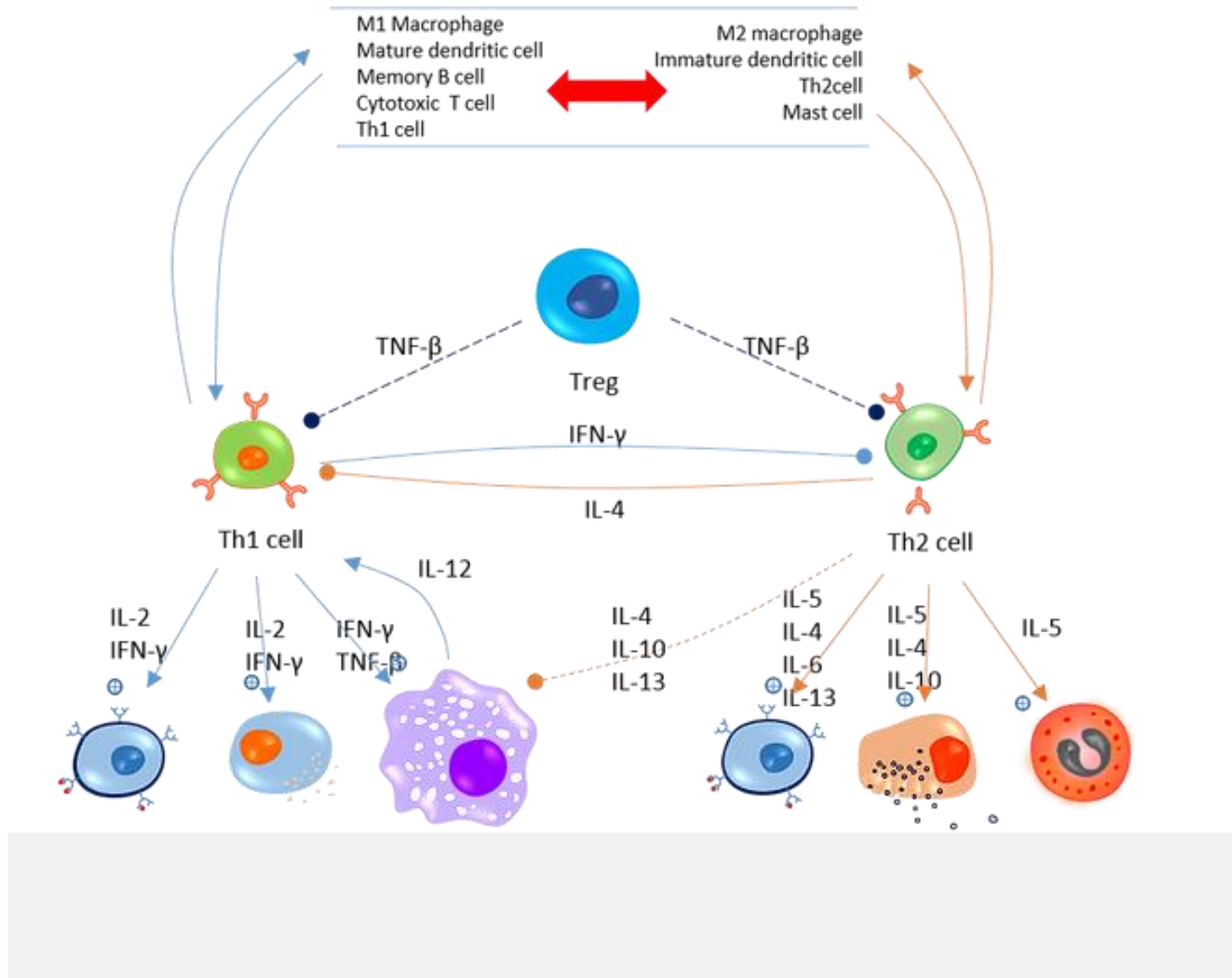


References:

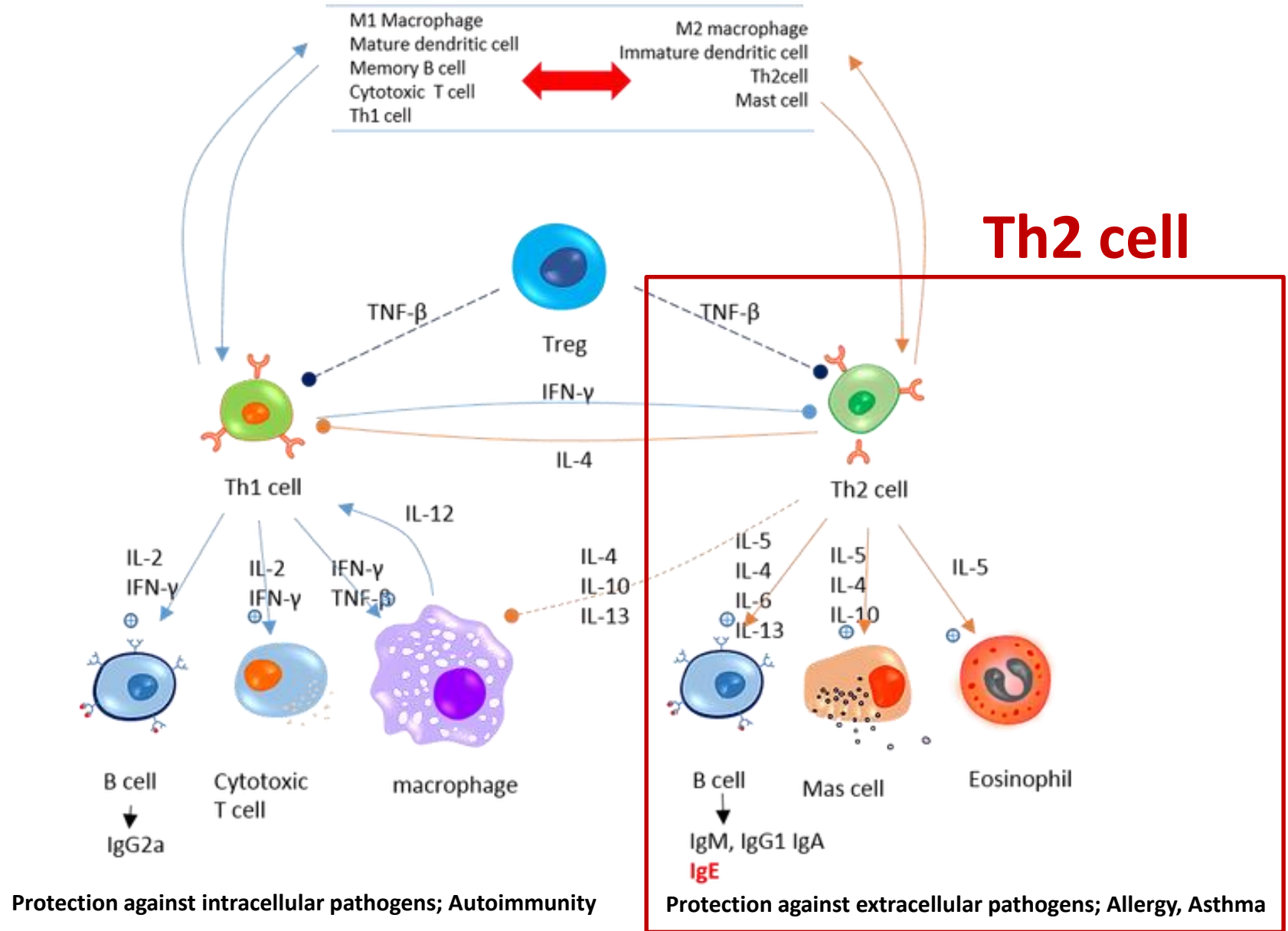
- American College of Allergy, Asthma & Immunology (ACAAI):

<http://acaai.org/allergies/symptoms>

Allergy – Th1 or Th2 directs allergic response?

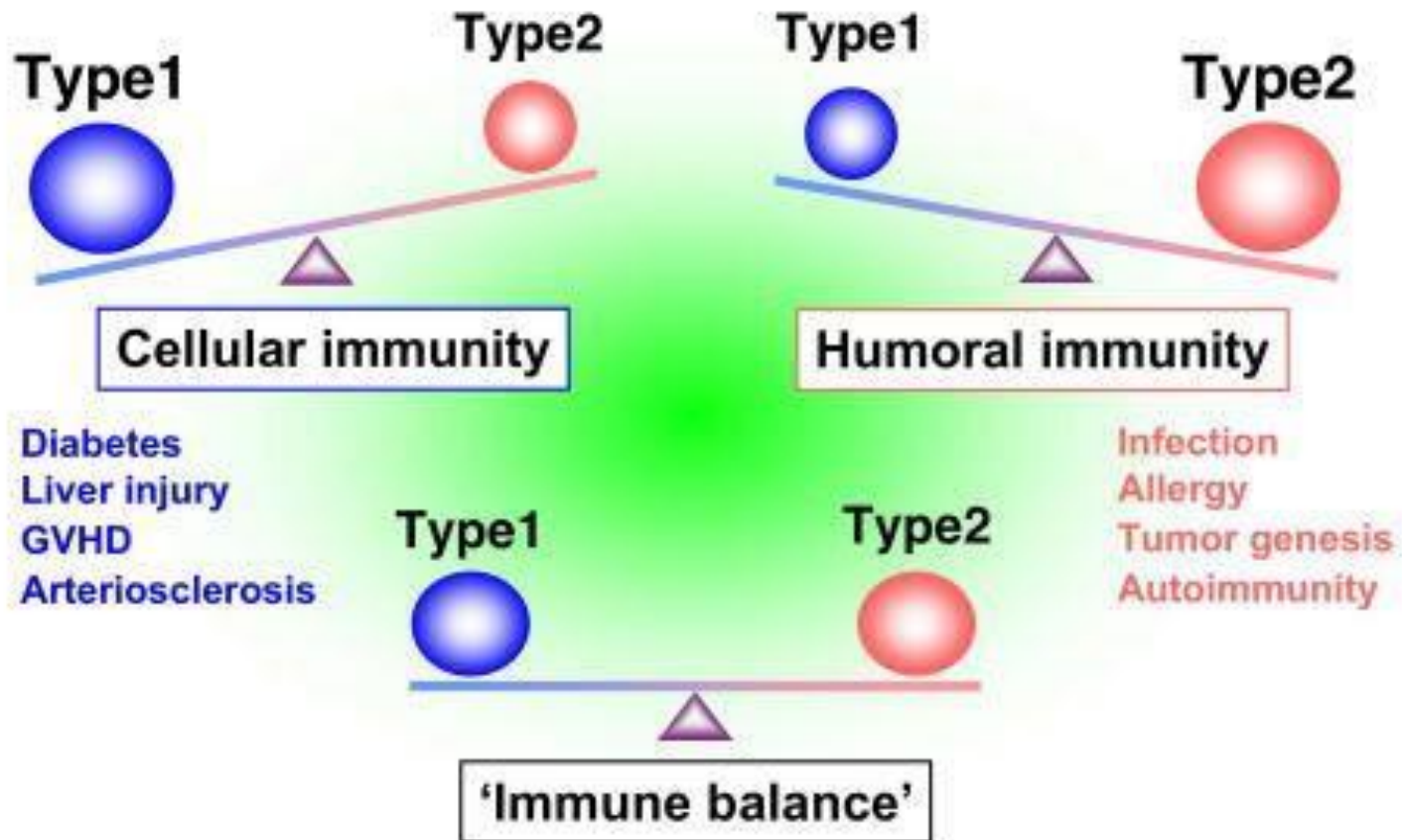


Allergy – Th1 or Th2 directs allergic response?



Allergy – Th1 or Th2 directs allergic response?

Regulation of 'Immune balance' is critical for our health



Allergy – Know our IgE

Immunoglobulin	Concentration in normal human blood
IgA	?
IgD	?
IgE	?
IgG	?
IgM	?

Allergy – Know our IgE

Immunoglobulin	Concentration in normal human blood
IgG	8 g/l*
IgA	3.5 g/l
IgM	1.5 g/l
IgD	0.03 g/l
IgE	0.00003 g/l (0.3 µg/l)**

*equals 11-18% of the total proteins in the blood

**1 kU/L = 2.4 ng/mL = 2.4 µg/l

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3206235/>

Allergy – Know our IgE

Immunoglobulin	Concentration in normal human blood	Half Life
IgG	8 g/l*	?
IgE	0.00003 g/l (0.3µg/l)**	?

*equals 11-18% of the total proteins in the blood

**1 kU/L = 2.4 ng/mL = 2.4 µg/l

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3206235/>

Allergy – Know our IgE

Immunoglobulin	Concentration in normal human blood	Half Life
IgG	8 g/l	20 days
IgE	0.00003 g/l (0.3µg/l)	2 days

*equals 11-18% of the total proteins in the blood

**1 kU/L = 2.4 ng/mL = 2.4 µg/l

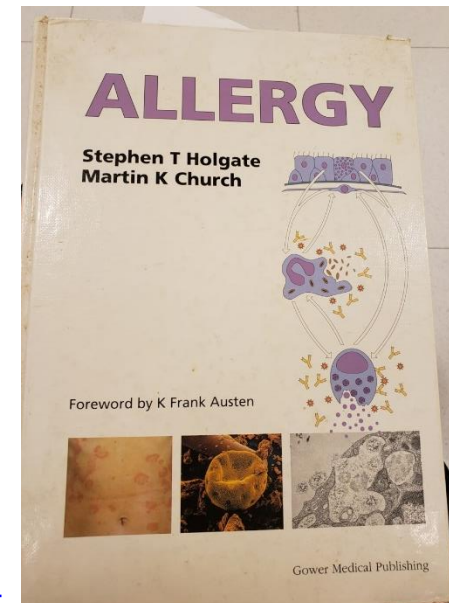
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3206235/>

Textbook: “Allergy”

by Stephen T Holgate, Martin K Church.

Gower Medical Publishing

<https://www.abebooks.co.uk/servlet/BookDetailsPL?bi=9011097402>



What is Allergen?

Aeroallergens: dust mite, cockroach, cat/dog dander, mold, pollens etc.

Food allergens: milk, egg white, wheat, tree nuts, peanuts, fish etc.

Drug allergens: Ampicilloyl, Amoxicilloyl, Penicilloyl G, Penicilloyl V etc.

References:

-European Academy of Allergology and Clinical Immunology (EAACI):





<http://www.eaaci.org/patients/allergic-and-immunologic-diseases-and-causes/what-is-an-allergy.html>

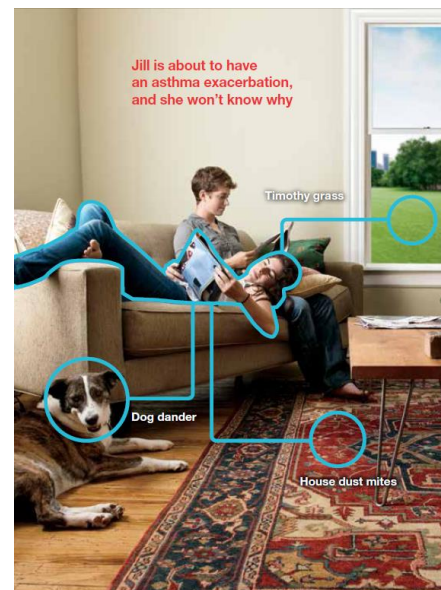
-World Allergy Organization (WAO): http://www.worldallergy.org/public/allergic_diseases_center/overview.php

-American Academy of Allergy, Asthma & Immunology (AAAAI): <https://www.aaaai.org/conditions-and-treatments/conditions-dictionary/allergy>



Common Allergens 常見致敏原

過敏疾病	症狀	懷疑致敏原 (南中國常見)
 濕疹、蕁麻疹	濕疹：皮膚發癢並出現紅疹，嬰兒常見於面頰，兒童則在手肘及膝蓋 蕁麻疹：皮膚發癢及呈紅色或蒼白色風團(風癩)	食物：牛奶、蛋白、黃豆、花生、核果、小麥、海鮮 環境：塵蟎、動物皮屑、葡萄球菌
 過敏性腸胃炎	慢性肚瀉 嘔吐 腹痛 拒絕進食	嬰兒：牛奶、蛋白、黃豆、花生 其他年齡人士：牛奶、蛋白、黃豆、花生、核果、小麥、海鮮、魚
 鼻敏感	鼻塞 經常打噴嚏、流鼻涕 眼和鼻發癢、咳嗽 疲乏、聽力下降	季節性：花粉、霉菌 持續性：塵蟎、動物皮屑、霉菌、蟑螂
 哮喘	呼吸急速 呼氣困難、咳嗽 支氣管痙攣	食物(幼兒)：牛奶、蛋白、黃豆、穀類、海鮮 食物(其他年齡人士)：花生、核果 環境：塵蟎、動物皮屑、霉菌、蟑螂、花粉



What is the prevalence of sensitizations?

J.Li et al. A multicenter study assessing the prevalence of sensitizations in patients with asthma and/or rhinitis in China. *Allergy* 2009; 64: 1083-1092

6304 patients, standardized questionnaire, skin prick tests with 13 common aeroallergens, Feb 2006 – Mar 2007, 17 cities with 24 participating centres.

Allergens	Overall prevalence
Cat dander	Pollen - <i>Artemisia vulgaris</i> 北艾, 多年生草本
Dog dander	Pollen - <i>Ambrosia artemisifolia</i> 豚草
Cockroach – <i>Blatella germanica</i>	Mixed mould I
Cockroach - American	Mixed mould IV
Mite – <i>Dermatophadoides farinae</i>	Mixed grass pollen
Mite – <i>Dermatophadoides pteronyssinus</i>	Mixed tree pollen
Mite – <i>Blomia tropicalis</i>	



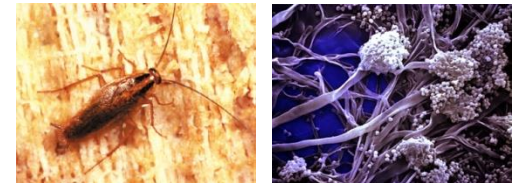
What is the prevalence of sensitizations?

Allergens	Overall prevalence
Mite – <i>Dermatophadoides farinae</i>	59.0%
Mite – <i>Dermatophadoides pteronyssinus</i>	57.6%
Mite – <i>Blomia tropicalis</i>	40.7%
Cockroach - American	16.1%
Dog dander	14.0%
Cockroach – <i>Blatella germanica</i>	11.5%
Pollen - <i>Artemisia vulgaris</i> 北艾	11.3%
Cat dander	10.3%
Pollen - <i>Ambrosia artemisifolia</i> 豚草	6.5%
Mixed mould I	6.3%
Mixed mould IV	4.4%
Mixed grass pollen	3.5%
Mixed tree pollen	2.2%



Common Allergens in Hong Kong

- Environment allergens
 - **House dust mite** - *D.pteronyssinus*, *D. farinae*
 - **Cockroach**
 - Dog dander
 - Cat dander
 - Molds
- Food allergens
 - **Egg white**
 - **Cow's milk**
 - Shrimp



Reference:

CK Wong et al. *Molecules* 2016, 21, 471

Ho, M.H., et al. *Asian Pac J Allergy Immunol*, 2012. 30(4): p. 275-84

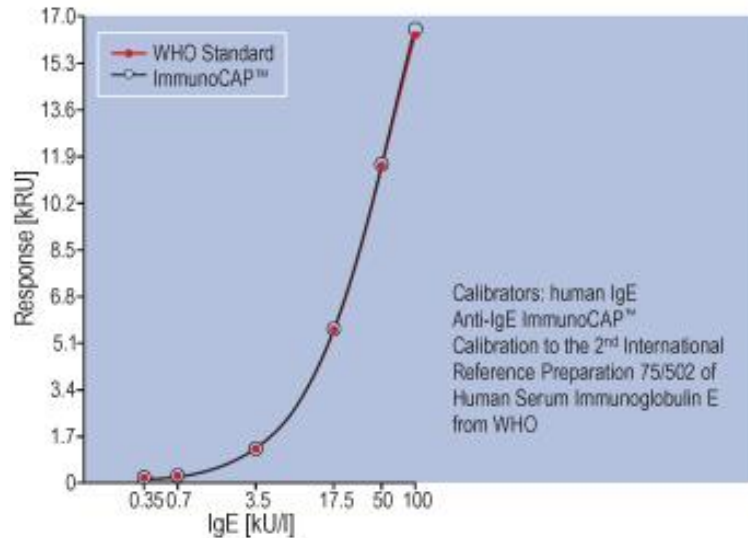
Hon, et al. *Pediatr Allergy Immunol*. 2011; 22: 50-53

Sun, et al. *Allergy* 2009; 64; 1083-1092

Leung TF, et al. *Pediatr Allergy Immunol*. 2009 Jun;20(4):339-46. Epub 2008 Sep 17

Leung TF, et al. *Journal of Asthma*. Vol. 39, No. 6, pp. 523–529, 2002.

ImmunoCAP sIgE Test - History



- 1968 - WHO deemed the existence of a new immunoglobulin class - IgE
- Radioimmunoassay - test for IgE in serum
- 1974 - Pharmacia > Radioallergosorbent test / Phadebas RAST - measure isotopically labeled sIgE to specific allergen
- 1989 - Pharmacia launched CAP system - WHO standard 6-point calibration
- 1995 - Pharmacia launched UniCAP 100 - fully automated

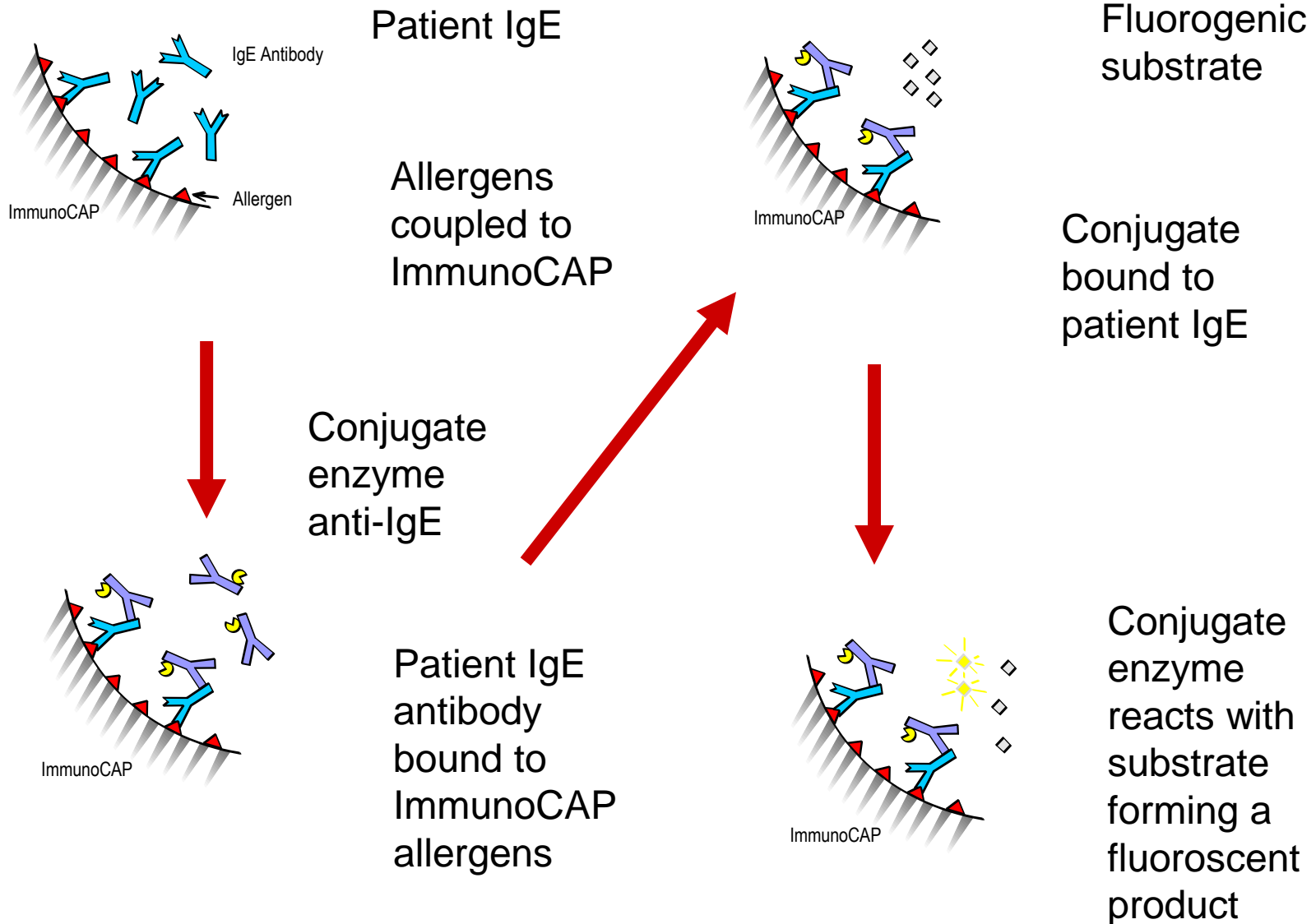
Phadia® 250



ImmunoCAP®
Is it allergy?

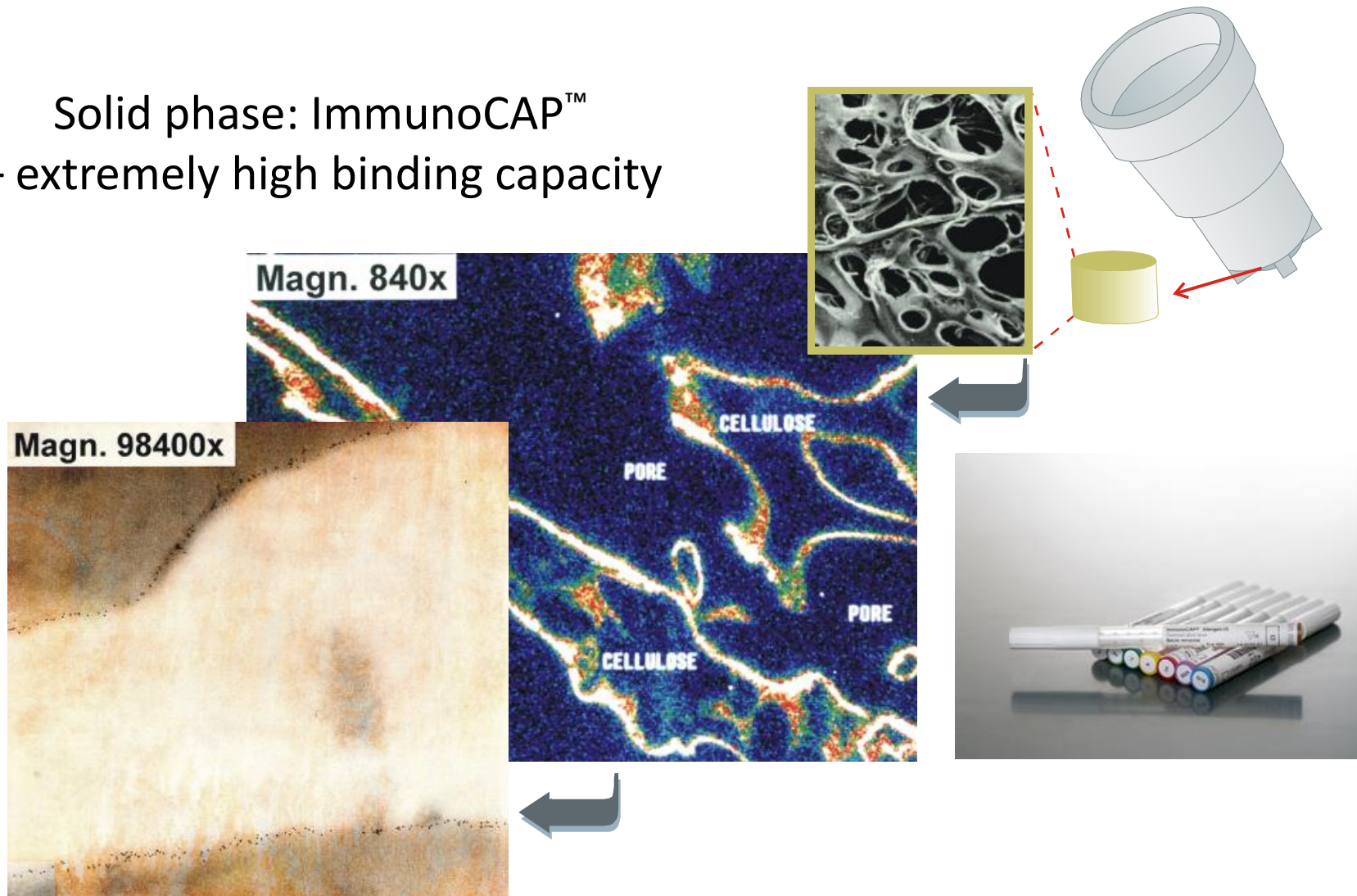
EliA™

ImmunoCAP sIgE Test - Principle



ImmunoCAP sIgE Test - Principle

Solid phase: ImmunoCAP™
– extremely high binding capacity



ImmunoCAP sIgE Test - Performance

The conventional way to present clinical validity

Sensitivity 89%
Specificity 91%

Dr's conclusion	UniCAP® Specific IgE		
	Positive	Negative	Total
Positive	1121	144	1265
Negative	360	3545	3905
Total	1481	3689	5170

The clinical performance of UniCAP Specific IgE was documented in clinical trials in six countries, Italy, Spain, Germany, The Netherlands, Sweden and Great Britain, on 894 patients with suspected allergy.

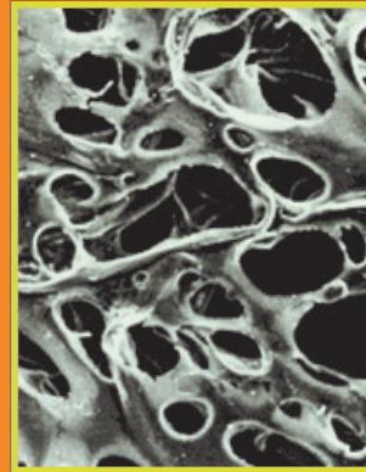
Clinical sensitivity and specificity were calculated as agreement between the test result and a specialist diagnosis based on the established diagnostic routines of the clinic.

Why ImmunoCAP...

- Recognized as **Gold Standard** for *in vitro* IgE testing
- Published in over **4,000 medical journals**
- FDA cleared, CE-IVD marked
- Production is ISO 13485 & GMP certified
- **Standardized to WHO IgE reference 75/502**
- Precise and accurate results: proven in extensive researches and external quality assessment programs (CAP, UKNeqas etc.)
- Being used in over 3,000 laboratories worldwide
- **Dedicated to allergy testing:** The broadest allergen coverage, including allergen components. Detailed information of every ImmunoCAP allergen can be found in our professional website:

thermoscientific.com/phadia

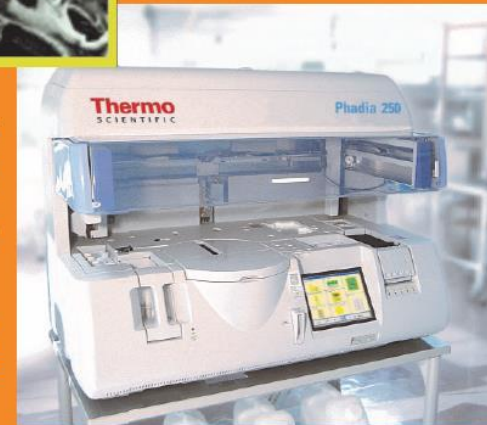
Sophisticated ImmunoCAP technology



Excessive allergen components are covalently bound to the high capacity, 3-dimensional cellulose polymer to give reliable results.

**Fully
Automated
Analyzer**

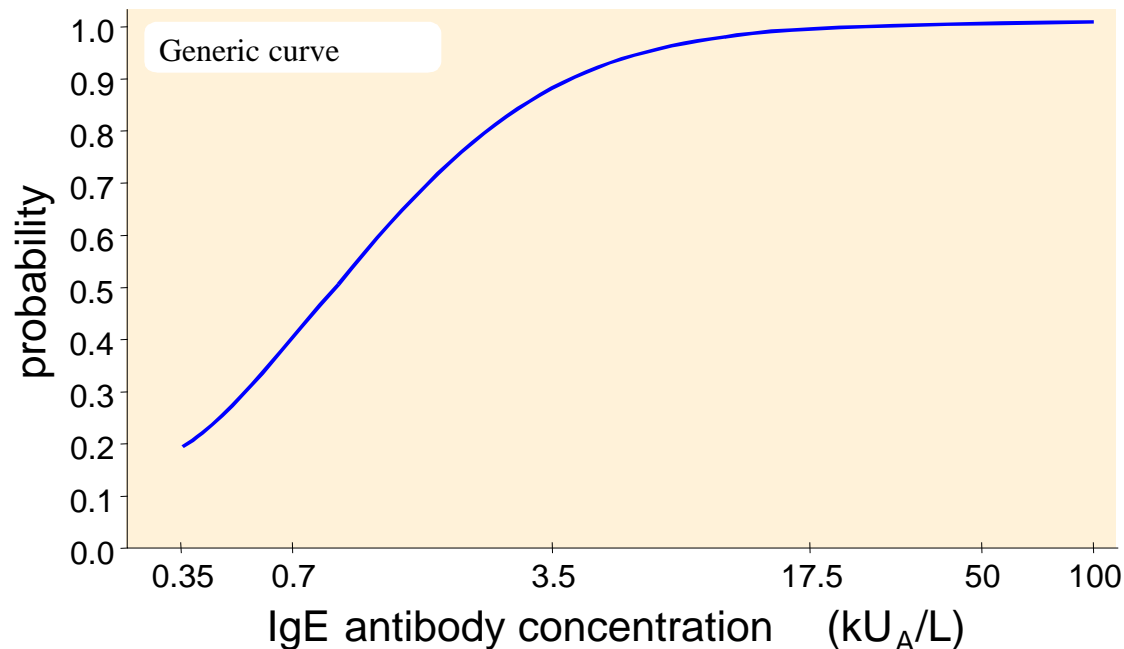
Standardized,
Precise



ImmunoCAP sIgE Test – result interpretation

Probability curve

Introducing the actual measured concentration of specific IgE in kU_A/L instead of simply positive results and still expressing the Dr's conclusion as negative or positive, we get a probability curve.



ImmunoCAP sIgE Test – result interpretation

Old

Quantitative Results (kU _A /l)	Level of Allergen Specific Antibody	Semi-Quantitative Results (Specific IgE Class)
< 0.35	Absent or undetectable	0
0.35 to < 0.7	Low	1
0.7 to < 3.5	Moderate	2
3.5 to < 17.5	High	3
17.5 to < 50	Very high	4
50 to < 100	Very high	5
100 and larger	Very high	6

Traditionally RAST TESTS have been reported as CLASS 0 to CLASS 6.
Class 0 indicates no allergy. Class 5 or 6 indicates high allergy

ImmunoCAP sIgE Test – result interpretation

**Increased concentration of serum IgE
= Increased likelihood of clinical symptoms**
(based on a reference material of >5.000 test results)

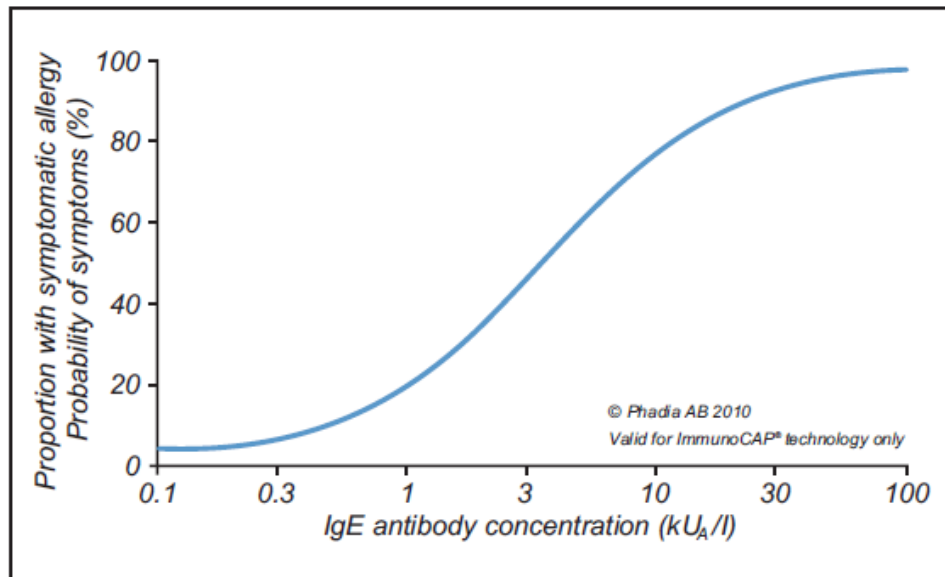
REFERENCE

Normal values:

ImmunoCAP Allergen <0.1 kU_A/l

ImmunoCAP Allergen mix/Phadiatop <0.35 kU_A/l

Result (kU _A /l)	IgE ab level	Symptom relation
<0.1	Undetectable	Unlikely
0.1 - 0.5	Very low	Uncommon
0.5 - 2	Low	Low
2 - 15	Moderate	Common
15 - 50	High	High
> 50	Very high	Very high

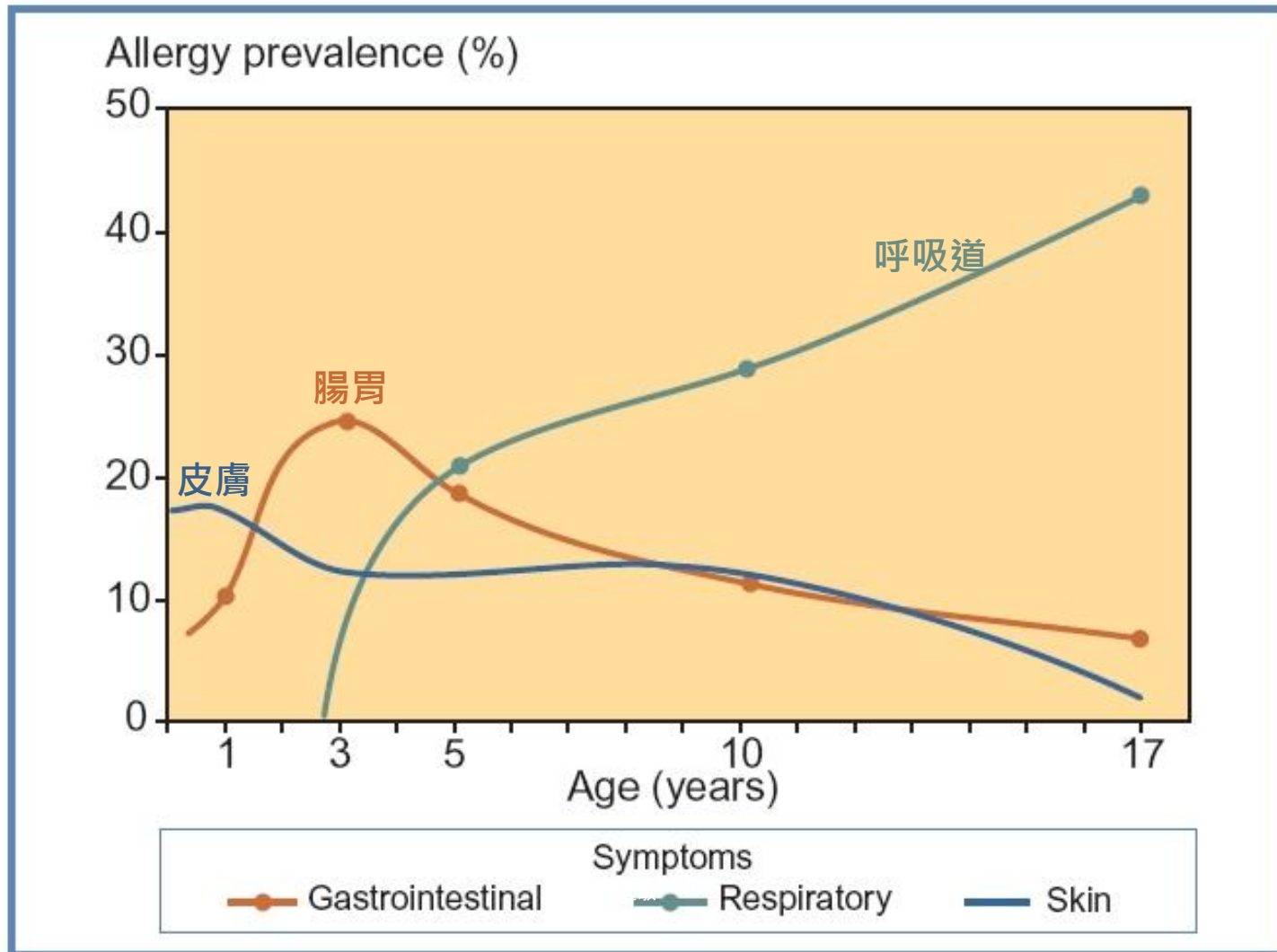


A general model for interpretation of IgE antibody levels in relation to clinical symptoms.

The slope of this curve may vary and shift more to the left or to the right due to different factors that should be considered for a final allergy diagnosis such as:

- Age
- Degree of atopy
- Allergen load
- Type of sensitizing allergens
- Previous symptoms
- Other triggering factors

Allergy March 過敏進行曲



Reference: Data from Saarinen. UM et al. Lancet 1995;346:1065-9.

Why Negative?

Thermo
SCIENTIFIC

Laboratory Report

ImmunoCAP Specific IgE 0 - 100

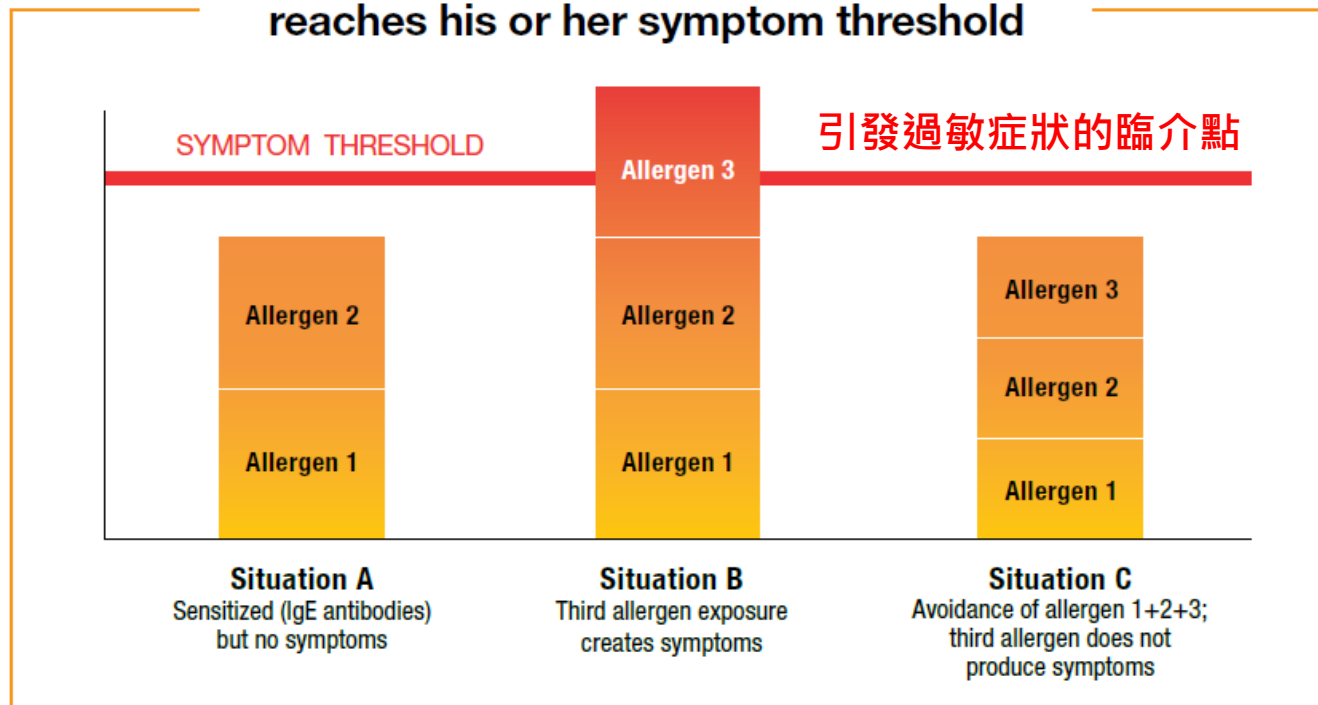
Identity	Test	Conc	Cut-off
Trump	f1 egg white	0.06	Negative
Trump	f2 cow milk	0.08	Negative
Trump	f13 peanut	0.02	Negative
Trump	f23 crab	0.05	Negative
Trump	f24 shrimp	0.08	Negative
Trump	China	>100	Positive



Why Negative? Symptom Threshold

致敏原超過臨介劑量便可能引發過敏症狀

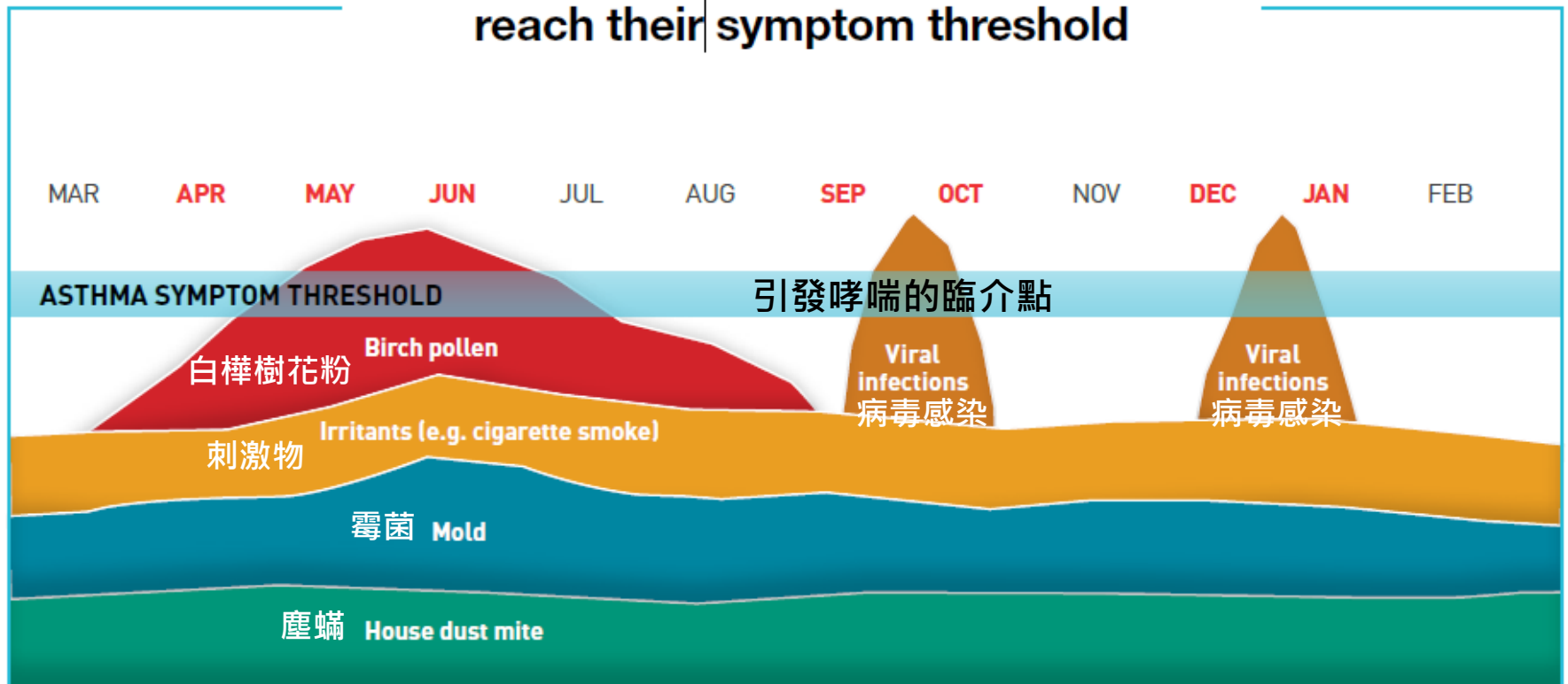
Symptoms appear when the patient reaches his or her symptom threshold



<https://www.thermofisher.com/diagnostic-education/patient/wo/en/understanding-allergies/symptom-threshold.html>

Why Negative? Symptom Threshold

Symptoms appear when asthma patients reach their symptom threshold



Why Negative? Histamine – Containing food

Fish

3	H	A		anchovies 鰵魚/鳳尾魚	
0	H!	A		fish (freshly caught or frozen)	Extremely depending on freshness and species
3	H!	A		fish (in the shop in the cooling rack or on ice)	Extremely depending on freshness and species
0	H!			trout (freshwater): brown trout, brook trout, rainbow trout	Perishable. Rapid histamine formation.
3	H	A		tuna	

Sea food

2	H!		L	bivalves (mussels, oysters, clams, scallops, ...)	
2	H!		L	crab	
2	H!		L	crab	
2	H!		L	crawfish	
2	H!		L	crayfish	
2	H!		L	langouste	
2	H!		L	lobster	
2	H!		L	oysters	
2	H!		L	prawn	
2	H!		L	rock lobsters	
2	H!		L	seafood, sea food	
2	H!		L	shellfish	(e.g. mussels, oysters, crab, lobster, shrimp)
2	H!		L	shrimp	
2	H!		L	spiny lobsters	

Histamine	
0	Well tolerated, no symptoms expected at usual intake
1	Moderately compatible, minor symptoms, occasional consumption of small quantities is often tolerated
2	Incompatible, significant symptoms at usual intake
3	Very poorly tolerated, severe symptoms
-	No general statement possible
?	Insufficient or contradictory information

Why Negative? Histamine Toxicity

Fish e.g. tuna, mackerel, mahi mahi, **anchovy**, herring, bluefish, amberjack, markin that contain naturally high levels of the chemical histidine

Inadequate refrigeration
Spoiled fish



Histamine-producing bacteria
e.g. *Photobacterium phosphoreum*
e.g. *Raoultella planticola*

Histamine Toxicity

Patients have unusually low levels of enzyme diamine oxidase



Any sIgE blood test for *Bombax ceiba* 木棉



Any sIgE blood test for *Bombax ceiba* 木棉

Parasites

Tree Pollens

Weed Pollens

Venoms

Special Allergen Service

Laboratory Excellence

AUTOIMMUNITY TESTING PRODUCTS

Laboratory Excellence

Connective Tissue Diseases

Rheumatoid Arthritis

Antiphospholipid Syndrome

Vasculitis and anti-GBM associated Diseases

Celiac Disease/Other Gastrointestinal Diseases

Thyroid Diseases

Miscellaneous

PHADIA LABORATORY SYSTEMS

Phadia 100

Phadia 250

Phadia 1000

Phadia 2500

Phadia 5000

SOFTWARE & SERVICES

ImmunoCAP ISAC Xplain

Phadia IDM

Phadia LabCommunity

Phadia MIA

Quality Club

Sycamore

Allergens

Code	Name	Latin name
t19	Acacia	<i>Acacia longifolia</i>
t5	American beech	<i>Fagus grandifolia</i>
t73	Australian pine	<i>Casuarina equisetifolia</i>
t37	Bald cypress	<i>Taxodium distichum</i>
t56	Bayberry	<i>Myrica cerifera</i>
t1	Box-elder	<i>Acer negundo</i>
t212	Cedar	<i>Libocedrus decurrens</i>
t45	Cedar elm	<i>Ulmus crassifolia</i>
t206	Chestnut	<i>Castanea sativa</i>
t3	Common silver birch	<i>Betula verrucosa</i>
t14	Cottonwood	<i>Populus deltoides</i>
t222	Cypress	<i>Cupressus arizonica</i>
t214	Date	<i>Phoenix canariensis</i>
t207	Douglas fir	<i>Pseudotsuga taxifolia</i>
t205	Elder	<i>Sambucus nigra</i>
t8	Elm	<i>Ulmus americana</i>
t18	Eucalyptus, Gum-tree	<i>Eucalyptus spp</i>
t25	European ash	<i>Fraxinus excelsior</i>
t2	Grey alder	<i>Alnus incana</i>
t44	Hackberry	<i>Celtis occidentalis</i>
t4	Hazel	<i>Corylus avellana</i>
t209	Horn beam	<i>Carpinus betulus</i>
t203	Horse chestnut	<i>Aesculus hippocastanum</i>
t23	Italian/Mediterranean/Funeral cypress	<i>Cupressus sempervirens</i>
t17	Japanese cedar	<i>Cupressus japonica</i>
t24	Japanese cypress	<i>Chamaecyparis obtusa</i>
t208	Linden	<i>Tilia cordata</i>
t11	Maple leaf sycamore, London plane	<i>Platanus acerifolia</i>

Any sIgE blood test for *Bombax ceiba* 木棉

ALLERGY TESTING PRODUCTS

- ImmunoCAP Lab Tests
- ImmunoCAP Rapid Point-of-Care
- ImmunoCAP ISAC Multiplexing
- ImmunoCAP Molecular Allergology
- ImmunoCAP Allergen Information
 - Allergen Components
 - Drugs
 - Epidermals and Animal Proteins

Common silver birch

Allergens Common silver birch

Code: t3

Latin name: *Betula verrucosa*

Source material: Pollen

Family: Betulaceae

Common names: Common Silver Birch, Common Birch, Birch, Birch tree

Synonym: *B. pendula*



References

Further Reading

rBet v 1 t215

rBet v 2 t216

rBet v 4 t220

Allergens

Birch pollen contains at least 29 antigens (5). Allergens of molecular weights of 29.5, 17, 12.5, and 13 kDa had been isolated (6-7).

The following allergens have been characterised:

- Bet v 1, a 17 kDa protein, a ribonuclease and a PR-10 protein (8-17).
- Bet v 2, a 15 kDa, a profilin (11,15-25).
- Bet v 3, a 24 kDa calcium-binding protein (19,26).
- Bet v 4, a 9 kDa calcium-binding protein (20,27-29).
- Bet v 5, a 35 kDa isoflavone reductase-related protein (30-32).
- Bet v 6, a 30-35 kDa protein, PCBER (Phenylcoumaran benzylic ether reductase) (33).
- Bet v 7, a 18 kDa protein, a cyclophilin (34).
- Bet v 11 (39).

The following recombinant allergens have been expressed:

- rBet v 1 (35).
- rBet v 2 (25,36-38).

Any sIgE blood test for *Bombax ceiba* 木棉

Australia/New Zealand Weed Risk Assessment adapted for Florida.

Data used for analysis published in: Gordon, D.R., D.A. Onderdonk, A.M. Fox, R.K. Stocker, and C. Gantz. 2008. Predicting Invasive Plants in Florida using the Australian Weed Risk Assessment. *Invasive Plant Science and Management* 1: 178-195.



Our mission is to enable our customers to make the world healthier, cleaner and safer

Desktop Calendar 坐檯曆

<i>Bombax ceiba</i> (red silk-cotton tree)			
Question number	Question	Answer	Score
1.01	Is the species highly domesticated?	n	0
1.02	Has the species become naturalised where grown?		
1.03	Does the species have weedy races?		
2.01	Species suited to Florida's USDA climate zones (0-low; 1-intermediate; 2-high)	2	
2.02	Quality of climate match data (0-low; 1-intermediate; 2-high)	2	
2.03	Broad climate suitability (environmental versatility)		
2.04	Native or naturalized in habitats with periodic inundation		
2.05	Does the species have a history of repeated introductions outside its natural range?	y	
3.01	Naturalized beyond native range	n	-2
3.02	Garden/amenity/disturbance weed	n	0
3.03	Weed of agriculture	n	0
3.04	Environmental weed	n	0
3.05	Congeneric weed	n	0
4.01	Produces spines, thorns or burrs	y	1
4.02	Allelopathic	y	1
4.03	Parasitic	n	0
4.04	Unpalatable to grazing animals		
4.05	Toxic to animals	n	0
4.06	Host for recognised pests and pathogens		
4.07	Causes allergies or is otherwise toxic to humans	n	0
4.08	Creates a fire hazard in natural ecosystems	n	0
4.09	Is a shade tolerant plant at some stage of its life cycle	n	0
4.1	Grows on infertile soils (oligotrophic, limerock, or excessively draining soils)		
4.11	Climbing or smothering growth habit	n	0
4.12	Forms dense thickets	n	0
5.01	Aquatic	n	0
5.02	Grass	n	0
5.03	Nitrogen fixing woody plant	n	0

4.07 Causes allergies or is otherwise toxic to humans
Answer: NO

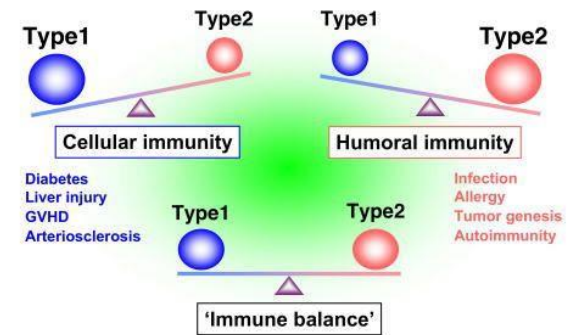
Immunotherapy

To desensitize the specific allergens

To provide lasting relief

- Sublingual immunotherapy (SLIT)
- Subcutaneous immunotherapy (SCIT)

Regulation of 'Immune balance' is critical for our health



<https://acaai.org/allergies/allergy-treatment/allergy-immunotherapy>

<https://www.aaaai.org/conditions-and-treatments/library/allergy-library/immunotherapy-can-provide-lasting-relief>

<https://www.medpagetoday.com/allergyimmunology/allergy/63516>

<https://www.odactra.com/what-are-house-dust-mite-allergies>

Helpful link

- Allergy in Hong Kong, Allergy Alliance, Sep 2014
 - http://www.allergy.org.hk/final_review.pdf
- Hong Kong Institute of Allergy
 - <http://www.allergy.org.hk/>
- Allergy Clinical and Experimental Allergy
 - www.ingenta.com/journals/browse/bsc/cea
- Annals of Allergy, Asthma and Immunology
 - <http://allergy.edoc.com>
- World Allergy Organization
 - www.worldallergy.org
- European Academy of Allergology and Clinical Immunology
 - www.eaaci.net
- American Academy of Allergy, Asthma and Immunology
 - www.aaaai.org
- American College of Allergy, Asthma & Immunology
 - www.acaai.org
- ImmunoCAP Allergy tests
 - thermoscientific.com/phadia
 - <http://www.phadia.com/zh-TW/> [中文]

Thank you!

