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Allergy

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Paediatric Update Course – Royal London

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Allergy testing

- Investigation… but not as we know it

Allergy testing

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Scratch/Prick Testing

- In vitro
- Hista[illegible]m cross-li[illegible]ound on mast c[illegible]

Serological Testing

- In vivo
- Free serum, unbound IgE molecules collected and measured in assay

Test scenario

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- ***Advice & Guidance request from locum GP***
  - *"Please interpret these allergy test results so we can advise the family"*

Total IgE		200	
sIgE	Fish mix	positive	
sIgE	Cow's milk	< 0.35	
sIgE	Egg white	2.3	(Grade 2)
sIgE	Wheat	< 0.35	
sIgE	Peanut	5.2	(Grade 3)
sIgE	Cat	33.3	(Grade 4)

Test scenario

- ***Advice & Guidan[illegible]equest fr[illegible]locum GP***
  - *"Please inte[illegible]s so we can advise the fam[illegible]*

Total IgE			
sIgE			
sIgE			
sIgE			(Grade 2)
sIgE			
sIgE	Peanut	5.2	(Grade 3)
sIgE	Cat	33.3	(Grade 4)

Test scenario – *history*

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- 5 year old boy
- Seen by ENT for hayfever and sent for allergy tests

- Previous suspected reaction to a meal
  - Generalised urticaria, wheeze
    - *Prawn cocktail crisps*
    - *Peanut butter on toast*
    - *Glass of milk (1st exposure to peanut)*

- Mother then says niece has a food allergy to egg and that her daughter has lactose intolerance

- He eats egg and fish regularly

Test scenario

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Total IgE		200	
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sIgE	Cat	33.3	(Grade 4)

Specific IgE *(sIgE)*

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sIgE

sIgE

sIgE

sIgE

sIgE

IgE mediated reaction

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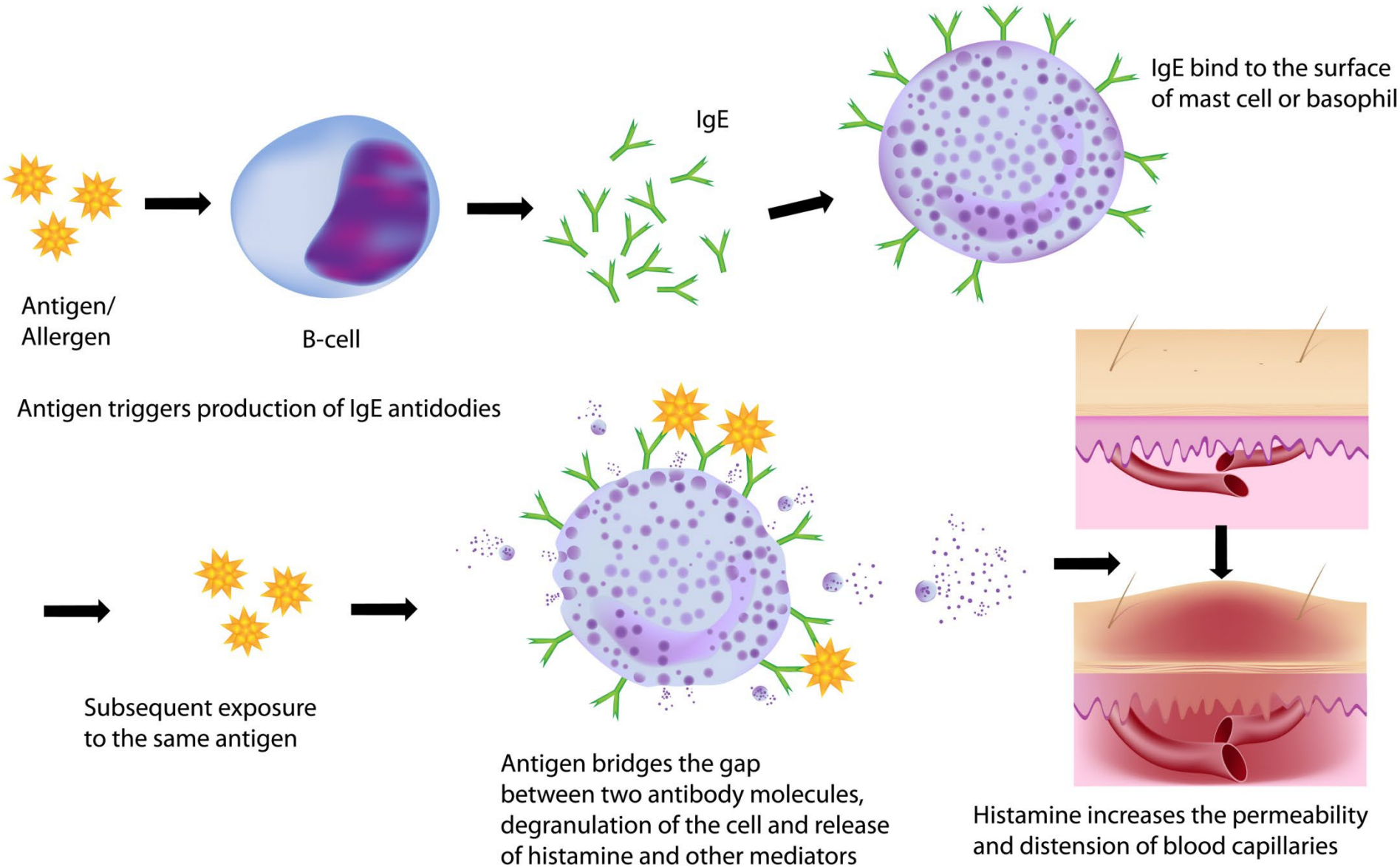

IgE – what is tested

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- Bloods tests
  - *Total IgE*
  - *RAST (radio-allergo-sorbe*
  - *Specific IgE testing*

IgE – what is tested

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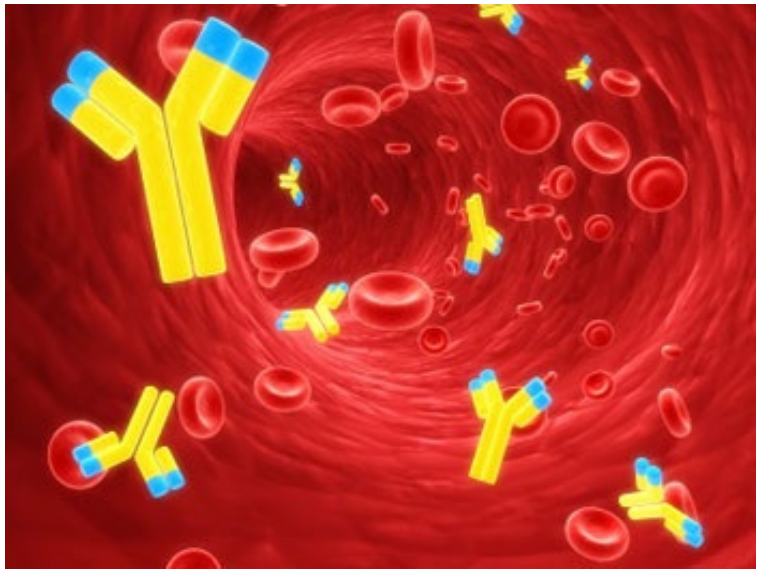

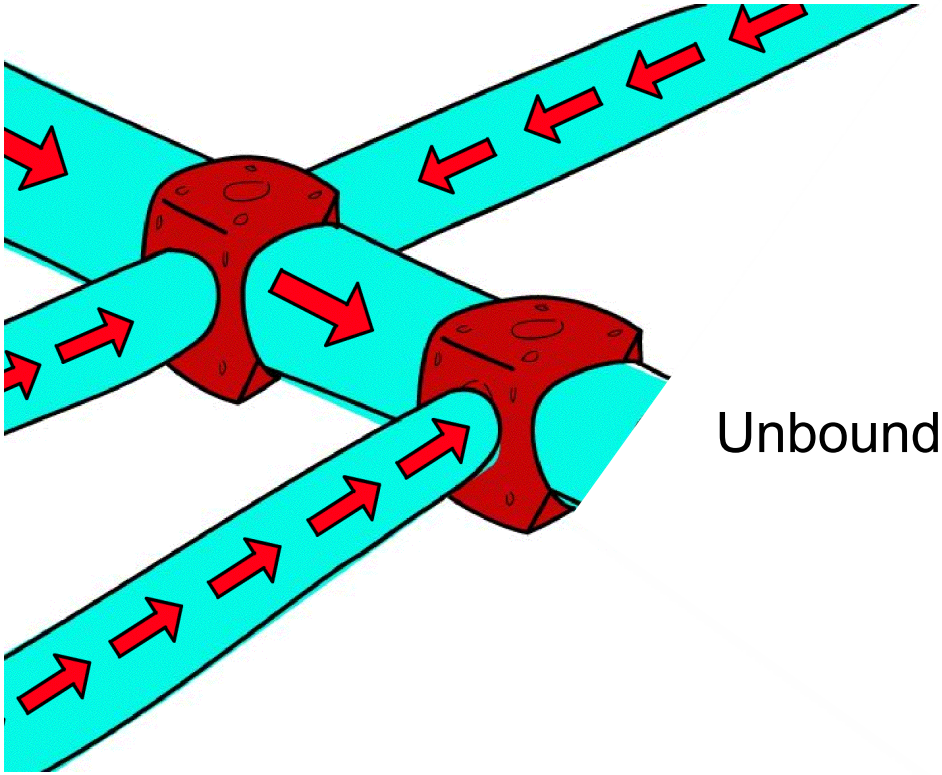

Unbound IgE in serum

IgE – what is tested

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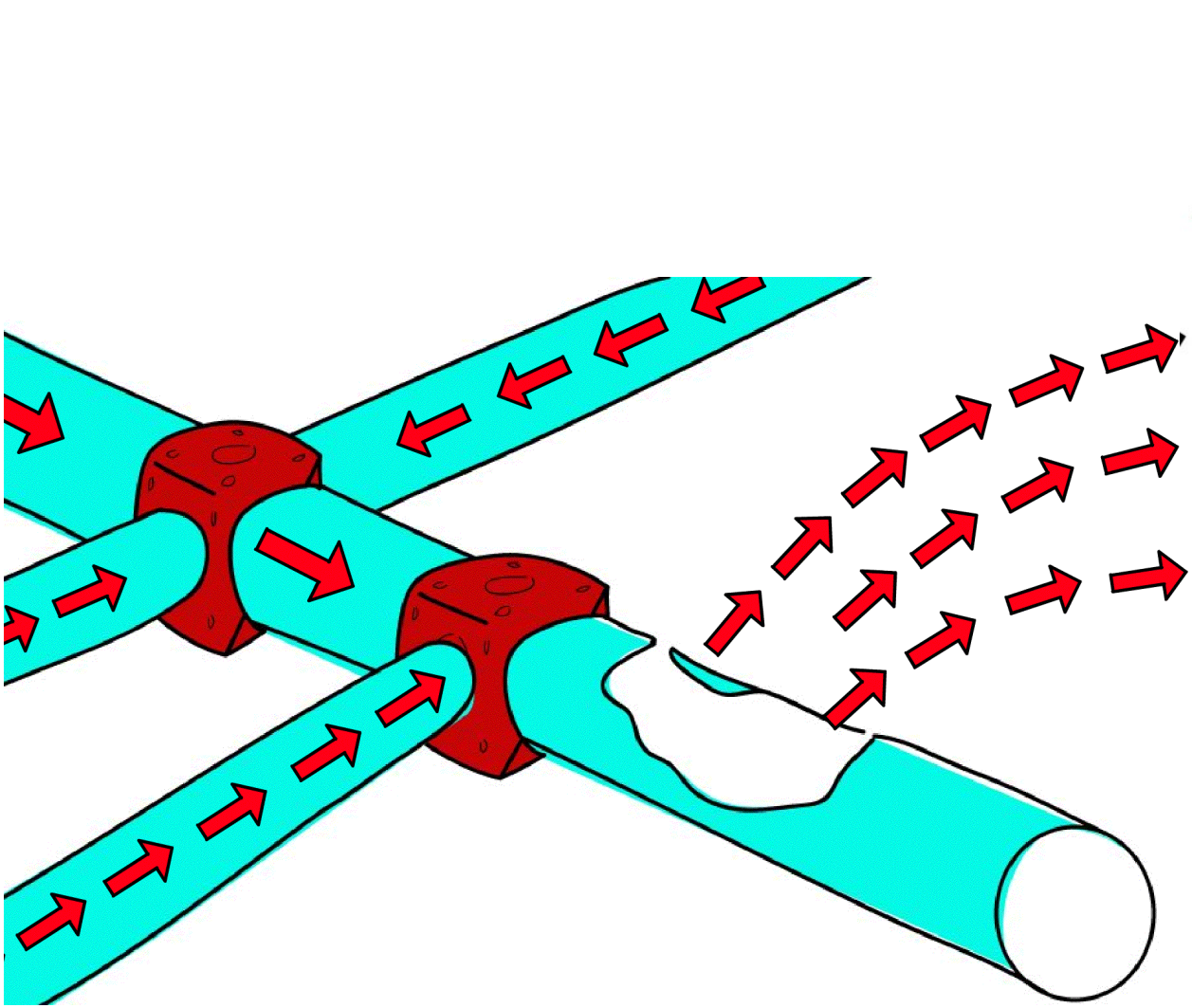

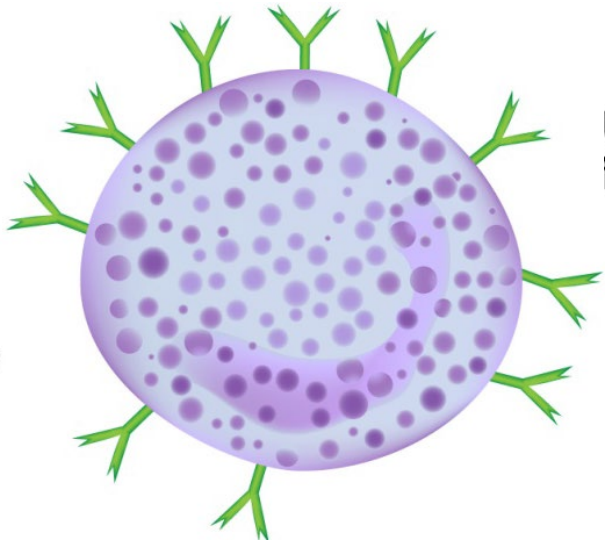

IgE in tissues bound to mast cells

Specific IgE testing *(sIgE)*

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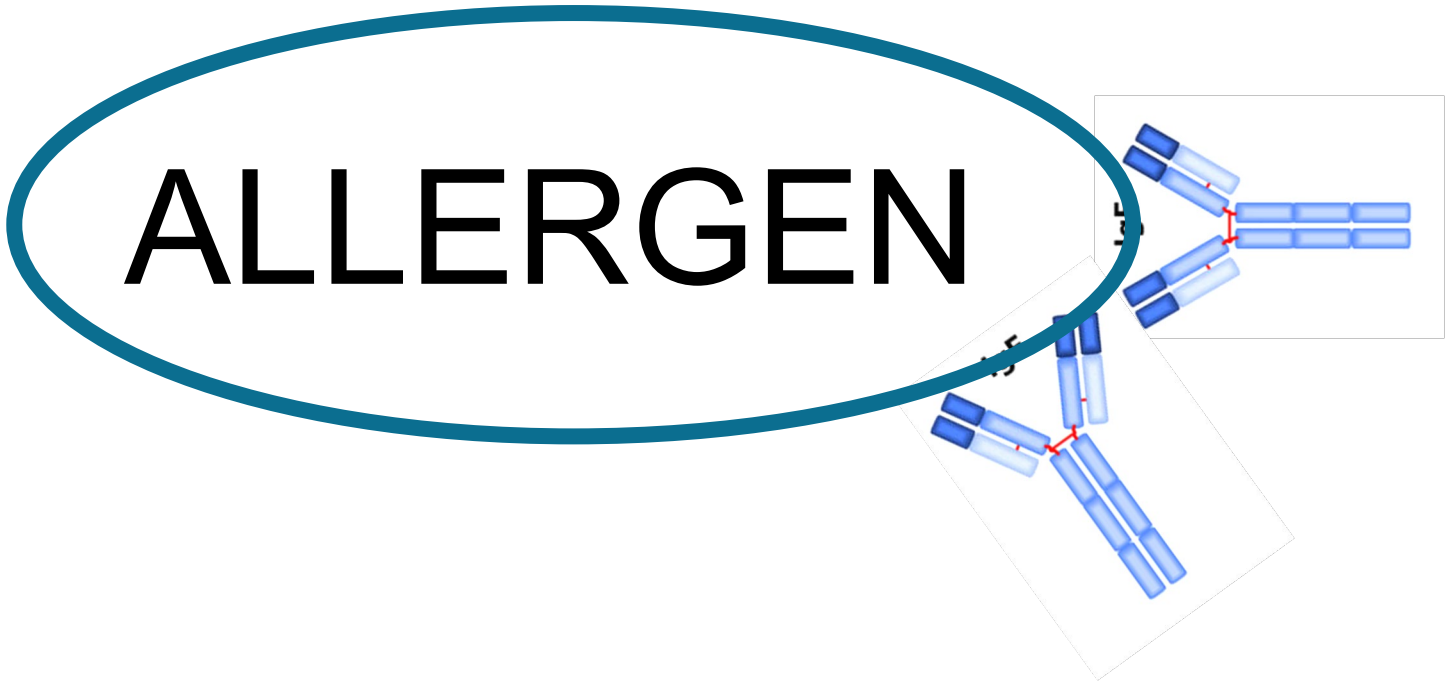

Historically a specific IgE of > 0.35 kunits/L is considered

POSITIVE

Specific IgE testing *(sIgE)*

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- The result gives an indication of .....

How likely is the patient to react to that food

≠ severity

≠ how little food will cause a reaction (e.g. traces)

≠ cannot compare between patients

≠ cannot compare different foods in the same patient

Test scenario

- So “Grade” has no clinical relevance
- Cannot compare one food with another

sIgE Egg white	2.3
sIgE Peanut	5.2

Without history allergy testing is a guessing game

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Specific IgE testing

- Finding specific IgE (sIgE) > 0.35 & no history available

  = SENSITISATION

  ≠ Allergy

- ↑ sIgE + clear history of reaction to that food

  = ALLERGY

Specific IgE testing

- Detection of ↑ sIgE and no acute reaction when that food is eaten

  = TOLERANT

Specific IgE testing

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Specific IgE testing

- Detection of ↑ sIgE and no acute reaction when that food is eaten

  = TOLERANT

- *Long term* unnecessary removal of food that is sensitised but tolerated risks the patient losing tolerance and developing an acute allergy

Unnecessary exclusion

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Test scenario

- Eats egg regularly = tolerant
- Peanut 1st exposure = he is allergic

sIgE Cow's milk	< 0.35
sIgE Egg white	2.3
sIgE Wheat	< 0.35
sIgE Peanut	5.2
sIgE Cat	33.3

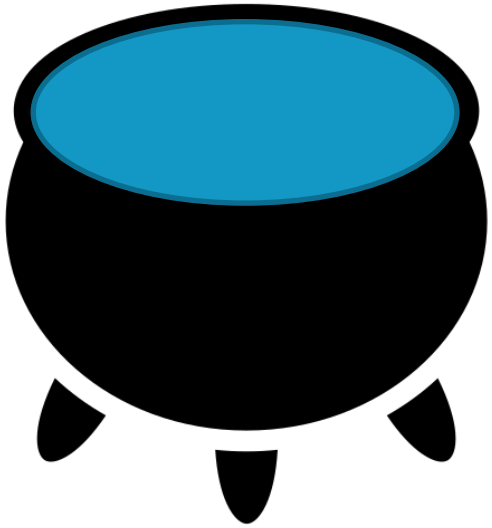
Test scenario

- ***"What about the fish?"***

sIgE	Fish mix	positive

IgE *mixes*

- “Easier to order”
- “Tests for everything”



IgE *mixes*

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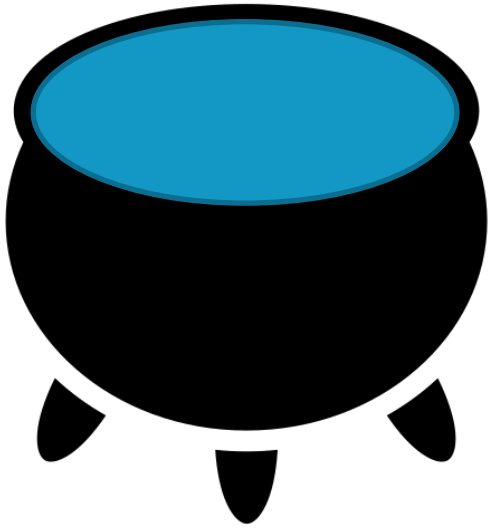

Nut mix

(1) Almond
(2) Peanut
(3) Coconut
(4) Hazelnut
(5) Walnut
(6) Cashew

IgE *mixes*

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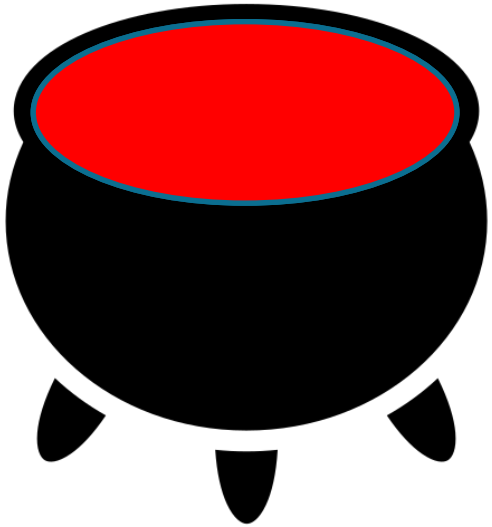
PATIENT 1:



Nut mix

Almond

Peanut

Coconut

Hazelnut

Walnut

Cashew

IgE *mixes*

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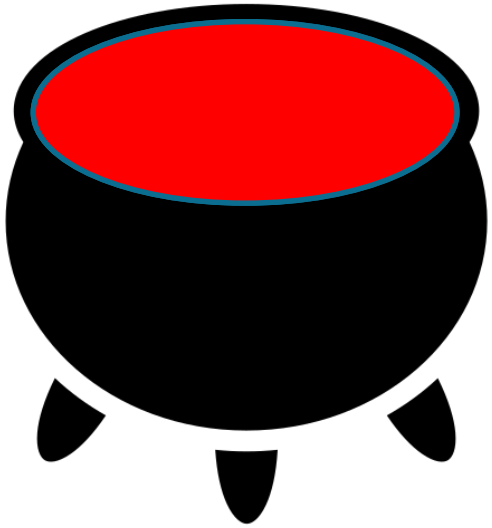
PATIENT 1:

Your result:

Nut mix - *POSITIVE*



IgE *mixes*

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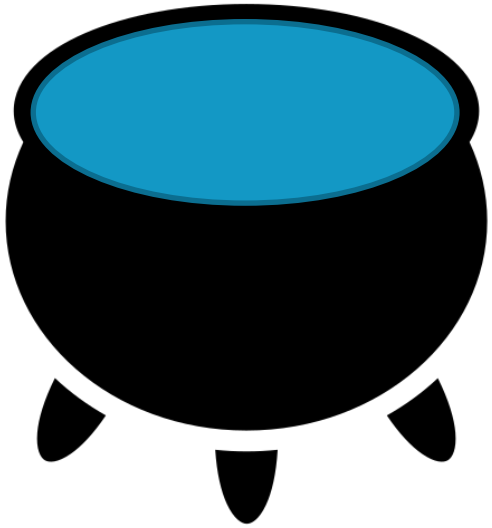
PATIENT 2:



Nut mix

Almond

Peanut

Coconut

Hazelnut

Walnut

Cashew

IgE *mixes*

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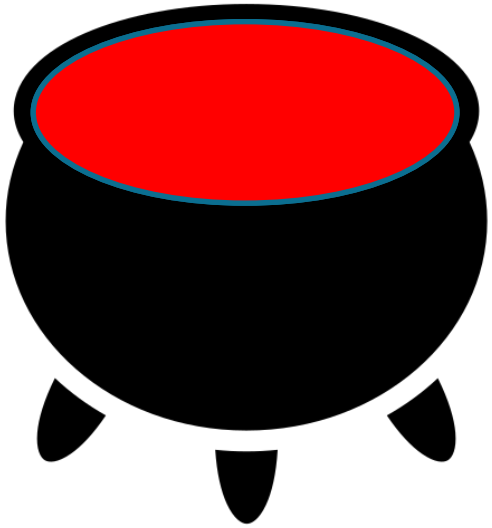
PATIENT 2:

Your result:

Nut mix - *POSITIVE*



IgE *mixes*

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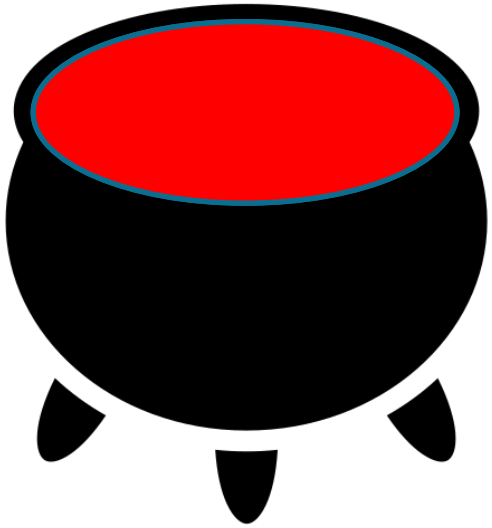
A positive mix result
does NOT mean
the patient is allergic to ALL the foods
contained within the mix



Test scenario

- ***"What does this mean?"***

Total IgE	200

Total IgE

- Not a screening test for allergy

- High levels (> 500, e.g. eczema) can cause false positive specific IgE results

Zidarn M, Silar M, Vegnuti M, Korosec P, Kosnik M. The specificity of tests for anti-beta-lactam IgE antibodies declines progressively with increase of total serum IgE. *Wien Klin Wochenschr*. 2009;121(9-10):353-356

Yousef E, Haque AS. A pilot study to assess relationship between total IgE and 95% predictive decision points of food specific IgE concentration. *Eur Ann Allergy Clin Immunol*. 2016;48(6):233-236

Grabenhenrich L, Lange L, Härtl M, et al. The component-specific to total IgE ratios do not improve peanut and hazelnut allergy diagnoses. *J Allergy Clin Immunol*. 2016;137(6):1751-1760.e8

Total IgE

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Total IgE < 500

Total IgE > 500

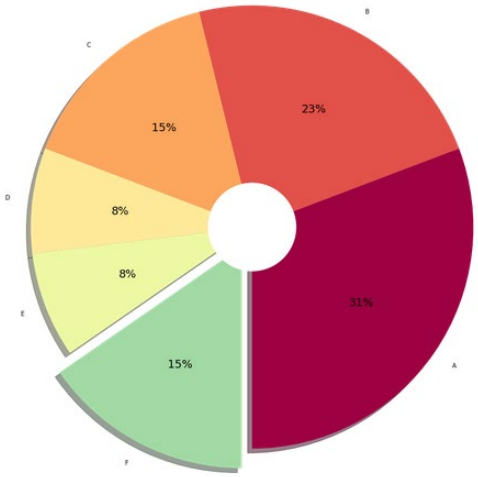
- *high risk of being given a fake*
- *only gets risker the higher the number*

Total IgE

- Does not add up to all the specific IgE present

- Very low levels (< 5) can result in fals

Sinclar & Peters *Clin Pathol 2004;57:956–959*



Test scenario

- Unlikely to be false positive sIgE due to high IgE

Total IgE	200

Age vs. sIgE

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Can sIgE tests be used in conjunction with a clinical history to make an accurate diagnosis of IgE-mediated food allergy in a 3-month-old child?

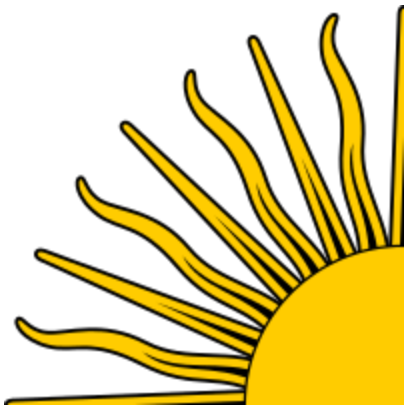
- In healthy children, total IgE levels start to increase in the first 6 weeks of life
- IgE continues to increase progressively up to 10-15 years of age
- At any age, a negative test cannot rule out food allergy in the presence of a suggestive history

My suggestion

- Consider specific IgE as either positive or negative

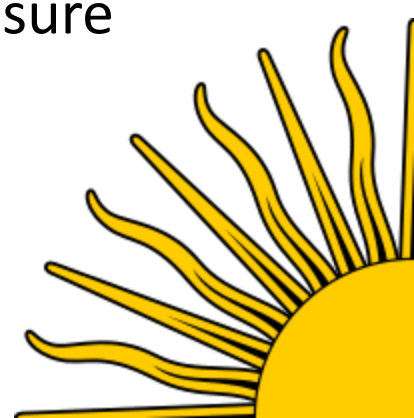
For example:

○ sIgE Peanut	10.1	=>	Positive
○ sIgE Cow's milk	0.4	=>	Positive
○ sIgE Wheat	0.02	=>	Negative



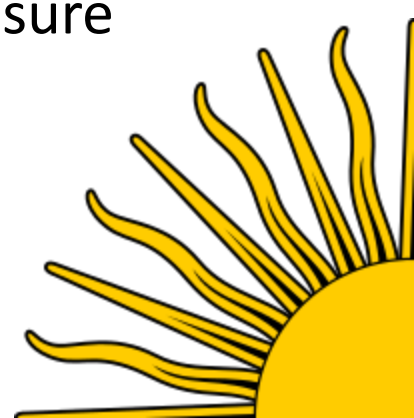
My suggestion

- Investigating an ACUTE reaction with a **+ ve test**
  - If the history is convincing for that food
    - **AVOID it**
  - If patient still eats the food with NO ACUTE REACTION
    - **Keep in the diet**
  - If patient has never eaten the food before or unsure
    - **AVOID it until see an allergist**



My suggestion

- Investigating an ACUTE reaction with a **- ve test**
  - If the history is convincing for that food
    - **AVOID it**
  - If patient still eats the food with NO ACUTE REACTION
    - **Keep in the diet**
  - If patient has never eaten the food before or unsure
    - **No need to avoid**



Generic reference ranges for sIgE

Range (kU/L)	*RAST grade*	*Description*	*Interpretation*
< 0.1		Undetectable	Consider other causes apart from IgE mediated allergy
0.1 – 0.35		Detectable, low	In rare cases patients with antibody levels in this range may experience clinical symptoms. *Correlate with clinical findings*
0.36 – 0.69	1	Low	Increased sIgE to an allergen only indicates sensitisation A diagnosis of IgE-mediated allergy requires evidence of both sensitisation and clinical reactivity.
0.7 – 3.45	2	Moderate	
3.46 – 17.4	3	High	
17.5 – 49.0	4	Very high	
50 - 99	5		
> 100	6		

ALL SPECIFIC IgE TEST RESULTS SHOULD ALWAYS BE CORRELATED WITH CLINICAL HISTORY

Don’t forget very high or very low total IgE will affect diagnostic accuracy

Generic reference ranges for sIgE

Range (kU/L)	*Description*	*Interpretation*
< 0.1	**Negative**	Consider other causes apart from IgE mediated allergy
0.1 – 0.35		In rare cases patients with antibody levels in this range may experience clinical symptoms. *Correlate with clinical findings*
0.36 – 0.69	**Positive**	Increased sIgE to an allergen only indicates sensitisation A diagnosis of IgE-mediated allergy requires evidence of both sensitisation and clinical reactivity.
0.7 – 3.45		
3.46 – 17.4		
17.5 – 49.0		
50 - 99		
> 100		

ALL SPECIFIC IgE TEST RESULTS SHOULD ALWAYS BE CORRELATED WITH CLINICAL HISTORY

Don’t forget very high or very low total IgE will affect diagnostic accuracy

Non-IgE reactions

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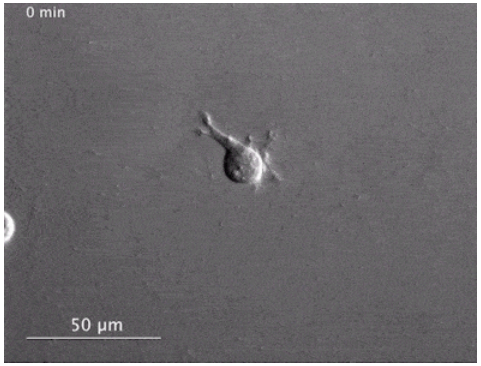

- Cell-mediated reaction (type IV hypersensitivity)
- Skin prick & sIgE testing **will not detect** this kind of allergy
- Only validated test - elimination diet + re-introduction

Non-IgE mediated allergy

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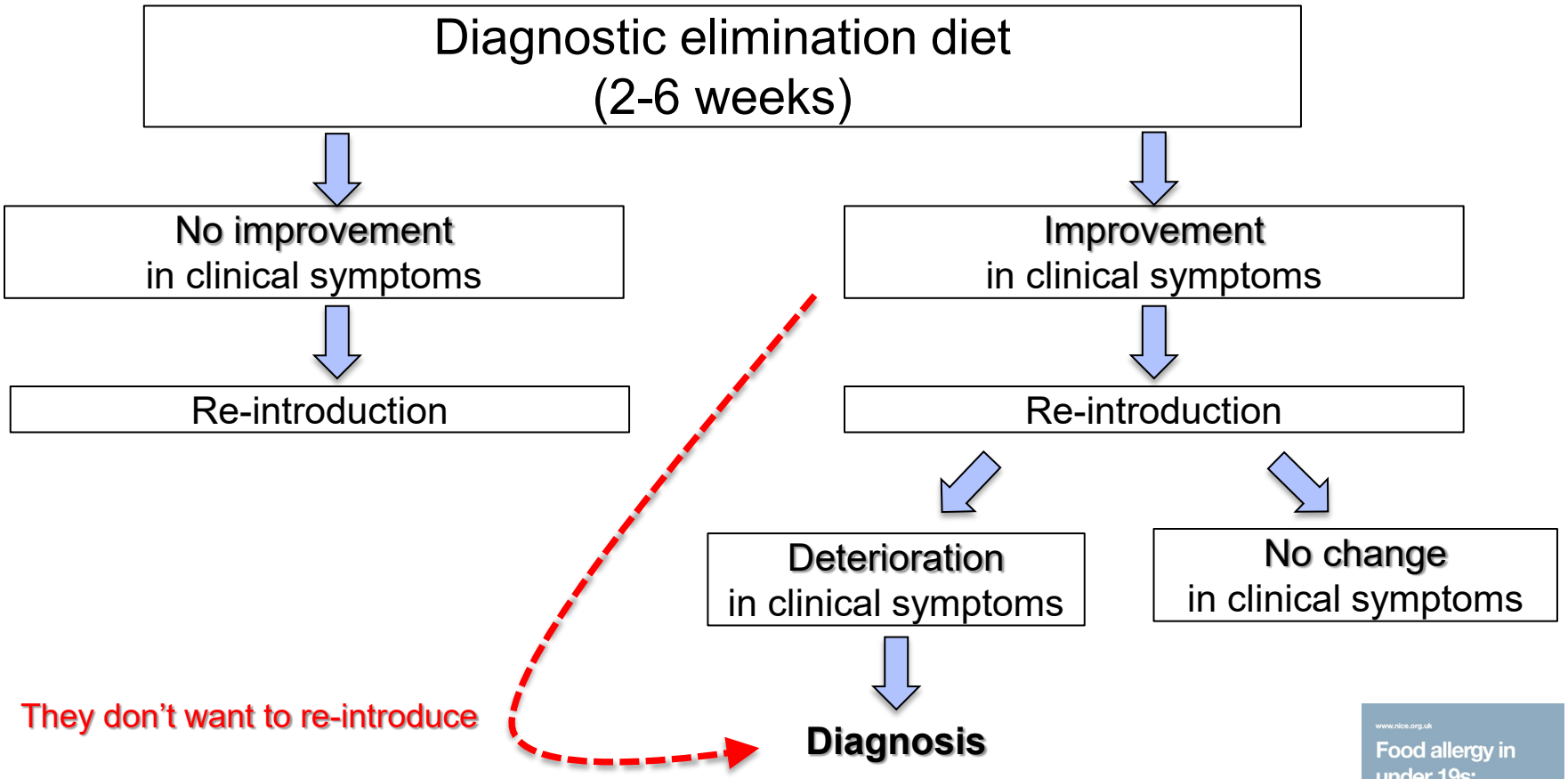
- only ONE diagnostic test



Seek advice from a dietitian with appropriate competencies, about nutritional adequacies, timings of elimination and reintroduction, and follow-up

www.nice.org.uk
Food allergy in under 19s: assessment and diagnosis | Guidance and guidelines | NICE

Alternative testing

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- Not validated and not used in NHS

IgG Food Antibody Results

Dairy		Vegetables		Fish/Shellfish		Nuts and Grains	
Casein	0	Alfalfa	VL	Clam	0	Almond	VL
Cheddar cheese	VL	Asparagus	0	Cod	0	Buckwheat	0
Cottage cheese	VL	Avocado	3+	Crab	VL	Corn	3+
Cow's milk	VL	Beets	VL	Lobster	1+	Corn gluten	1+
Goat's milk	VL	Broccoli	VL	Oyster	0	Gluten	0
Lactalbumin	0	Cabbage	3+	Red snapper	0	Kidney bean	0
Yogurt	VL	Carrot	3+	Salmon	0	Lentil	0
Fruits		Celery	3+	Sardine	0	Lima bean	0
Apple	0	Cucumber	0	Shrimp	0	Oat	1+
Apricot	0	Garlic	1+	Sole	0	Peanut	0
Banana	0	Green Pepper	VL	Trout	0	Pecan	3+
Blueberry	VL	Lettuce	VL	Tuna	0	Pinto bean	0
Cranberry	0	Mushroom	1+	**Poultry/Meats**		Rice	VL
Grape	1+	Olive	VL	Beef	0	Rye	0
Grapefruit	1+	Onion	VL	Chicken	0	Sesame	1+
Lemon	0	Pea	VL	Egg white	0	Soy	0
Orange	0	Potato, sweet	VL	Egg yolk	VL	Sunflower seed	0
Papaya	0	Potato, white	VL	Lamb	0	Walnut	VL
Peach	VL	Spinach	1+	Pork	0	Wheat	1+
Pear	0	String bean	1+	Turkey	0	**Miscellaneous**	
Pineapple	0	Tomato	VL			Yeast	1+
Plum	VL	Zucchini	VL			Cane sugar	1+
Raspberry	VL					Chocolate	VL
Strawberry	VL					Coffee	VL
						Honey	0

Total IgE

	Inside	Outside	Reference Range
Total IgE *		298.0	<=87.0 IU/mL

0 None Detected VL Very Low 1+ Low 2+ Moderate 3+ High

Summary

- Allergy tests are of extremely limited value without an allergy focused history

- Total IgE is not a screening tool for allergies

- IgE allergy tests do not relate to:
  - severity
  - amount that will cause a reaction
  - non-IgE mediated allergies