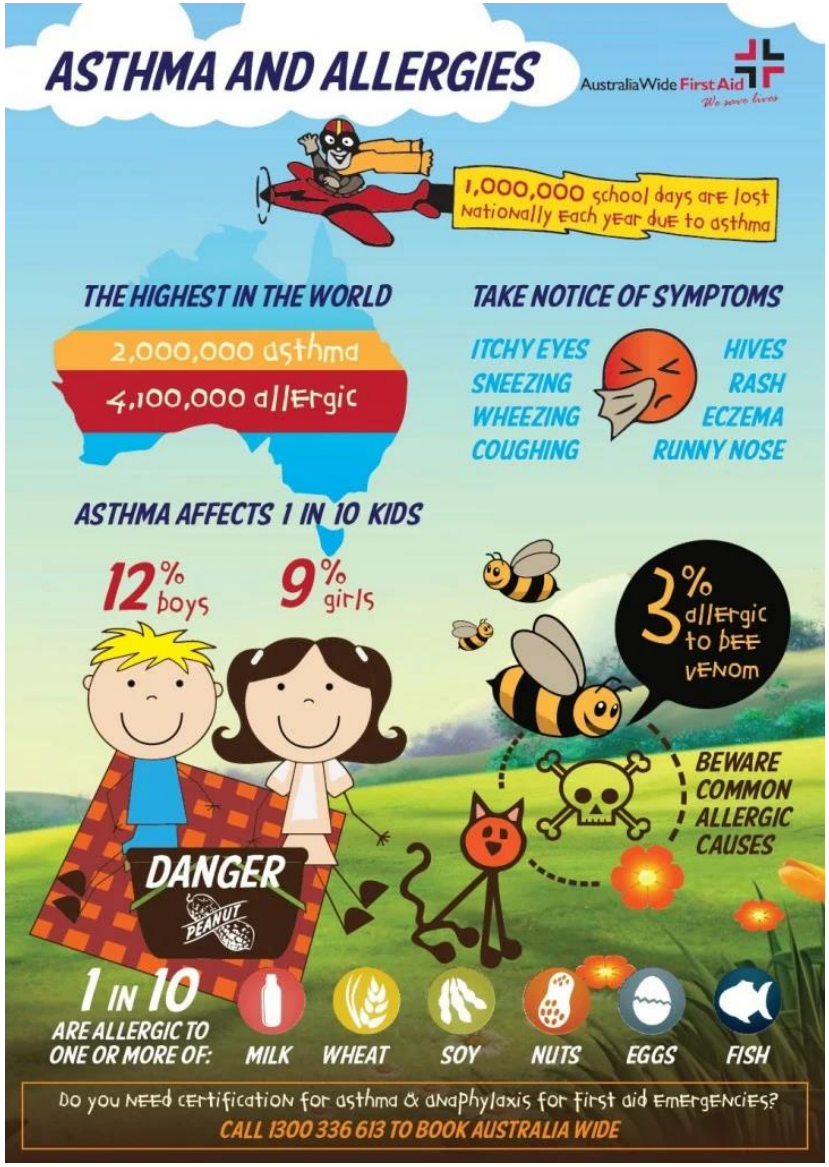


Asthma, Allergy and Anaphylaxis

Dr Paddy Dennison

Consultant Respiratory/GIM

University Hospital Southampton NHS
NHS Foundation Trust

What to cover

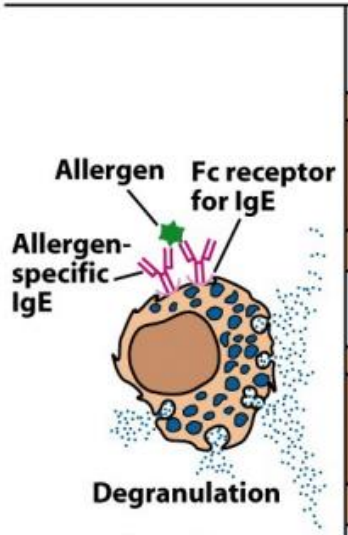
- Definitions (briefly)
- What tests are we doing in the asthma patient?
- Why is it important to know about allergy in your asthma patient?
- Anaphylaxis top tips
- Not going to cover immunotherapy too much
- COI: I am not an allergologist/allergist..

Definitions

- Why
  - Need to be clear what is
    - Allergy
    - Sensitivity (sulphites, salicylates)
    - Intolerance/Adverse effect of drug
    - Other e.g. symptoms of bronchial hyperreactivity, psychological issues..
  - Often hard to untangle, but may have profound impact, especially if related to treatments e.g. inhaler/steroid/antibiotic ‘allergies’

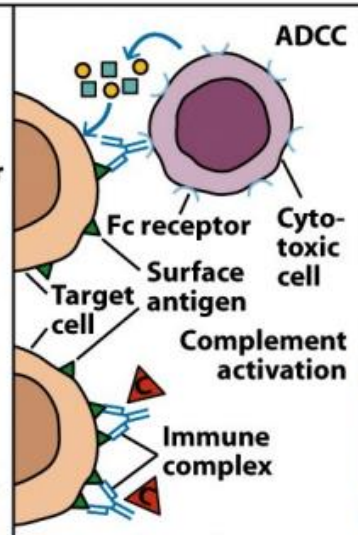
Definitions

- ‘Atopy’ – Genetic predisposition to develop allergic reactions/develop allergen specific IgE.
- ‘Sensitisation’ – above plus exposure leading to generation of specific IgE molecules against a sensitising agent.
- ‘Allergy’ – clinical manifestation of above wherein exposure to sensitising agent leads to symptoms

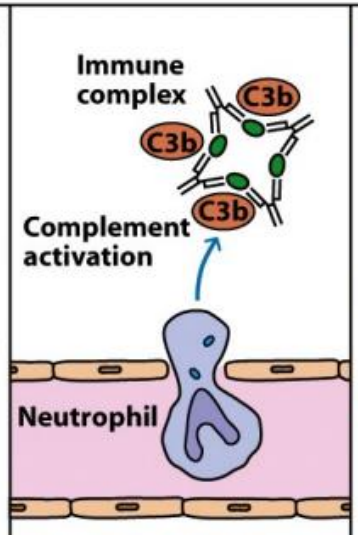


Type I

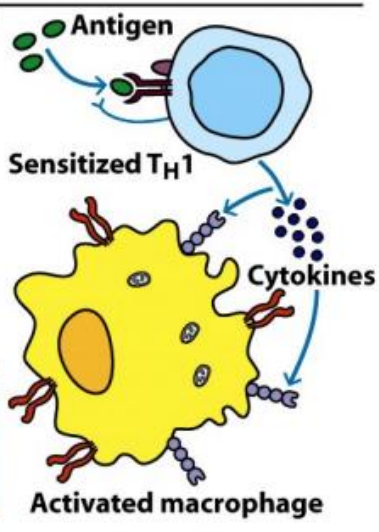
IgE-Mediated Hypersensitivity	IgG- or IgM-Mediated Cytotoxic Hypersensitivity	Immune Complex–Mediated Hypersensitivity	Cell-Mediated Hypersensitivity
Ag induces cross-linking of IgE bound to mast cells and basophils with release of vasoactive mediators.	Ab directed against cell surface antigens meditates cell destruction via complement activation or ADCC.	Ag-Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils.	Sensitized T_H1 cells shown above release cytokines that activate macrophages or T_C cells that mediate direct cellular damage. T_H2 cells and CTLs mediate similar responses.
Typical manifestations include systemic anaphylaxis and localized anaphylaxis such as hay fever, asthma, hives, food allergies, and eczema.	Typical manifestations include blood transfusion reactions, erythroblastosis fetalis, and autoimmune hemolytic anemia.	Typical manifestations include localized Arthus reaction and generalized reactions such as serum sickness, necrotizing vasculitis, glomerulonephritis, rheumatoid arthritis, and systemic lupus erythematosus.	Typical manifestations include contact dermatitis, tubercular lesions, and graft rejection.



Type II



Type III



Type IV

Figure 15-1
Kuby IMMUNOLOGY, Sixth Edition

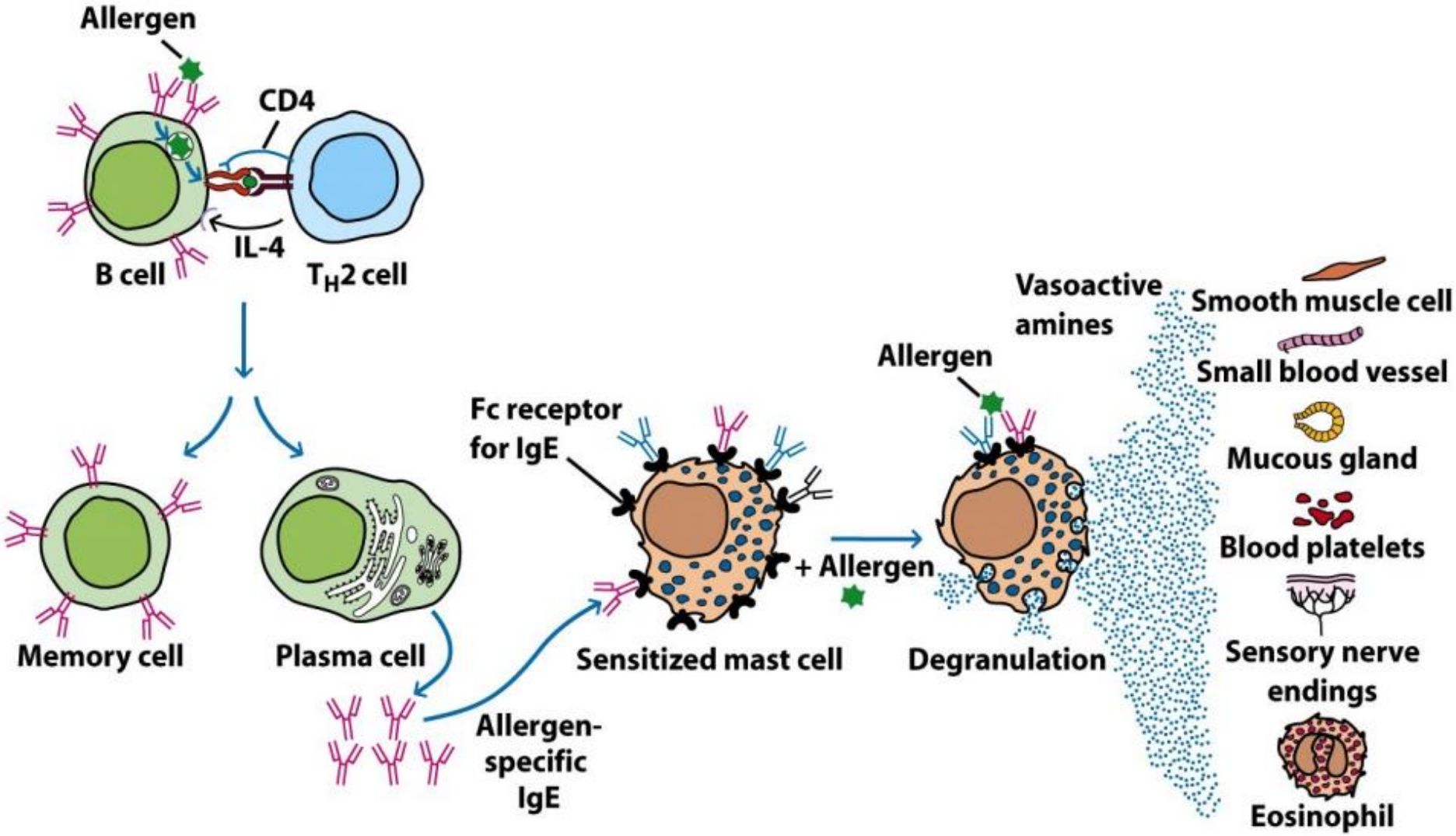


Figure 15-2
Kuby IMMUNOLOGY, Sixth Edition

TABLE 15-1 Common allergens associated with type I hypersensitivity

Proteins
- Foreign serum
- Vaccines

Plant pollens
- Rye grass
- Ragweed
- Timothy grass
- Birch trees

Drugs
- Penicillin
- Sulfonamides
- Local anesthetics
- Salicylates

Foods
- Nuts
- Seafood
- Eggs
- Peas, beans
- Milk

Insect products
- Bee venom
- Wasp venom
- Ant venom
- Cockroach calyx
- Dust mites

Mold spores

Animal hair and dander

Latex

Table 15-1
Kuby IMMUNOLOGY, Sixth Edition

History, history, history

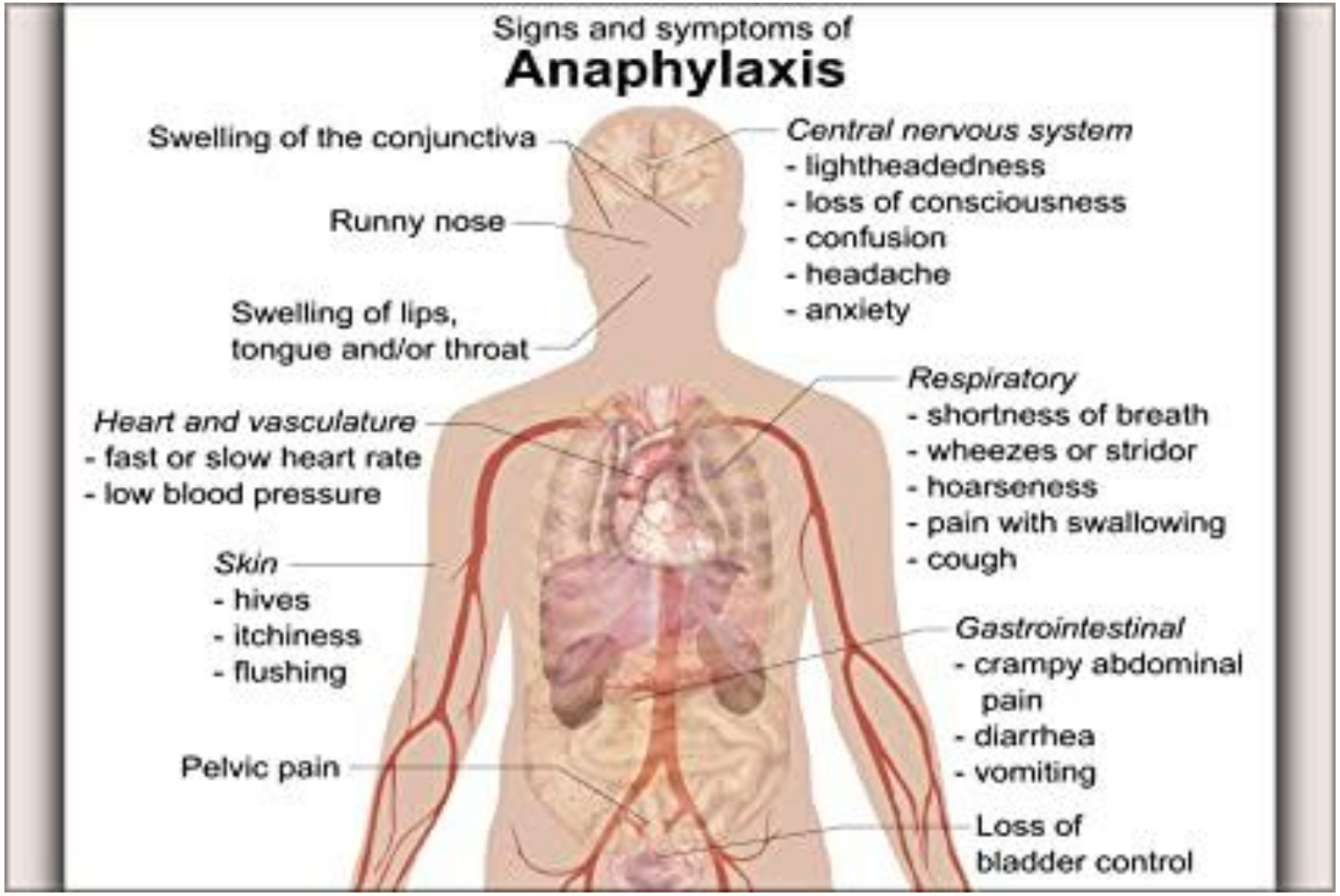
- What triggers your asthma/symptoms?
- (If unusual how/when does it do this)
- What reaction do you get? (upper airway vs lower airway vs systemic)
- Focus on airborne allergens for asthma
- Food charts for asthma/anaphylaxis
- Curveball: Food dependent exercise induced anaphylaxis

Asthma vs anaphylaxis

- Asthma
  - respiratory specific reaction, which may have allergenic and non-allergenic triggers, environmental/airborne e.g. mould, pollen, pet dander, HDM, etc.
  - How common?
    - Asthma -1 in ~11
    - Atopic sensitization in asthma - varying % according to definition used and population e.g. 85% of childhood severe asthmatics, far less common in adult onset (34%)
    - 'Atopic march' (atopy→allergic rhinits→asthma)

Asthma vs anaphylaxis

- Anaphylaxis
  - 1 in 50(!)
  - broader clinical manifestation, multisystemic
  - Usually allergen ingestion, also insect stings, latex medication (including vaccines!).
  - Skin reactions common but absent in 10-20%
  - 9 most common allergens: peanut, tree nuts (almonds, Brazil nuts, cashews, hazelnuts, pecans, pistachios and walnuts), shellfish, fish, milk, eggs, soy sesame and wheat


Signs and symptoms of
Anaphylaxis
Swelling of the conjunctiva
Runny nose
Swelling of lips, tongue and/or throat
Heart and vasculature
- fast or slow heart rate
- low blood pressure
Skin
- hives
- itchiness
- flushing
Pelvic pain
Central nervous system
- lightheadedness
- loss of consciousness
- confusion
- headache
- anxiety
Respiratory
- shortness of breath
- wheezes or stridor
- hoarseness
- pain with swallowing
- cough
Gastrointestinal
- crampy abdominal pain
- diarrhea
- vomiting
Loss of bladder control


Average time to respiratory or cardiac arrest due to anaphylaxis:
Food allergy =
30 MINUTES
Venom allergy =
15 MINUTES
Medication allergy =
5 MINUTES
Source: Clinical & Experimental Allergy, Volume 30, Issue 8

Anaphylaxis top tips

- As clear a history as you can e.g. not just ‘rash’, objective tests e.g BP, PR, etc
- Medication dosage, brand, labels
- Tryptase levels during/within an hour, and baseline (after the event e.g. >4 hrs (as tends to disappear by then)
- Refer to allergy for all but most barndoor – access to allergy dieticians, reinforce advice, fancy treatments e.g. AIT

How to measure allergy in asthma?

- Total IgE
  - Increased in allergic diseases, atopic dermatitis tends to have highest levels (>AA>PAR>SAR)
  - No specific cutoff, nor can be used as exclude if low
  - Can be increased in non-allergic conditions
  - Used in advanced treatments i.e. omalizumab

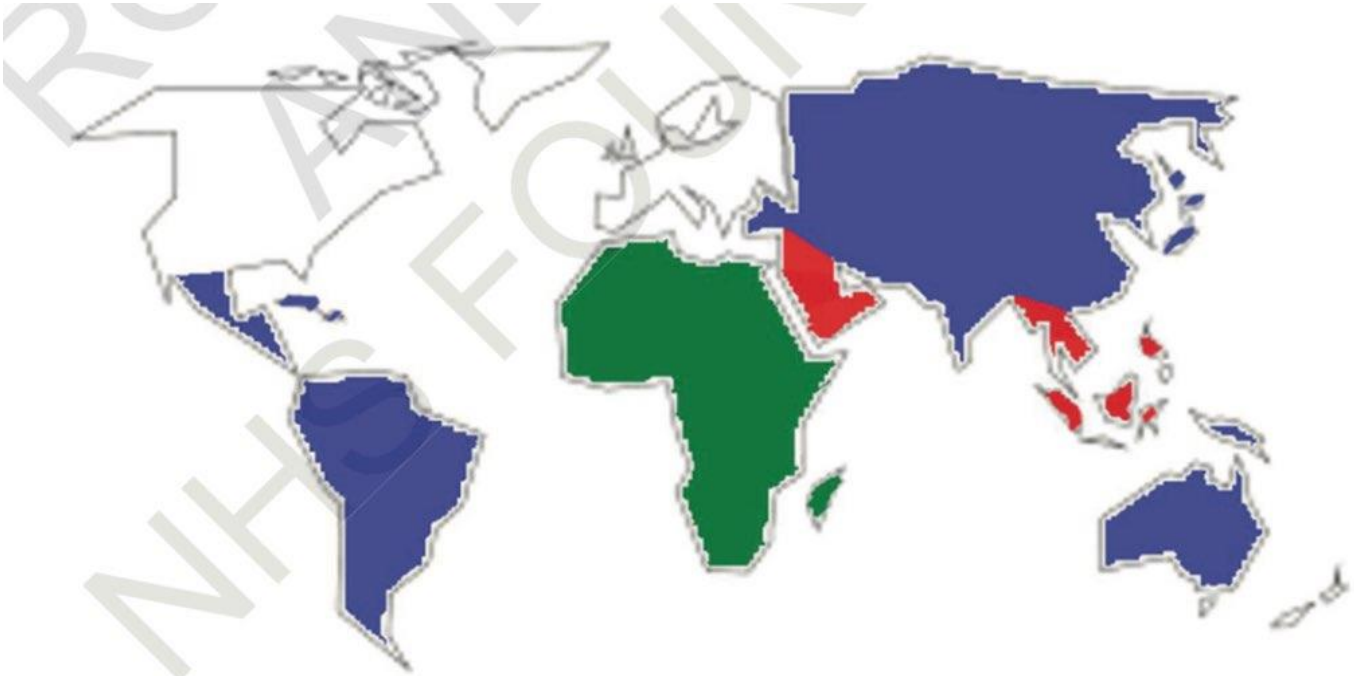
Conditions associated with elevated serum IgE*

Infectious diseases	Parasitic: ▪ *Ascariasis* ▪ *Schistosomiasis* ▪ *Strongyloidiasis*
	Human immunodeficiency virus (HIV) infection
	Mycobacterium tuberculosis
	Cytomegalovirus
	Epstein-Barr virus
	Leprosy
	Candidiasis
Atopic diseases	Allergic bronchopulmonary aspergillosis
	Allergic fungal rhinosinusitis
	Atopic dermatitis
	Allergic asthma
	Allergic rhinitis
Immunodeficiencies	Hyperimmunoglobulin E syndrome (multiple mutations)
	Wiskott-Aldrich syndrome
	Netherton disease
	Nezelof syndrome
	Immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome (IPEX)
	Omenn syndrome
	Atypical complete DiGeorge syndrome
Inflammatory diseases	Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
	Kawasaki disease
	Kimura disease
Neoplasms	Hodgkin lymphoma
	IgE myeloma
Others	Tobacco smokers
	Cystic fibrosis
	Nephrotic syndrome
	Bone marrow transplantation
	Graft versus host disease
	Bullous pemphigoid
Drug effect	Aztreonam, penicillin G

IgE: immunoglobulin E.
* Allergic disease is the most common etiology of elevated IgE in industrialized countries, whereas parasitic infection is the most common cause in developing countries.

Graphic 83457 Version 13.0

Parasite testing as an aside..



Strongyloides Plus Toxocara Serology

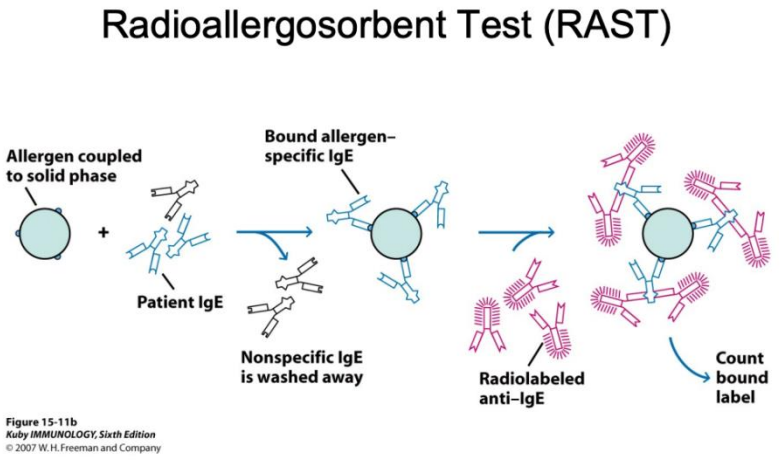
Strongyloides Plus Toxocara Plus Schistosoma Serology

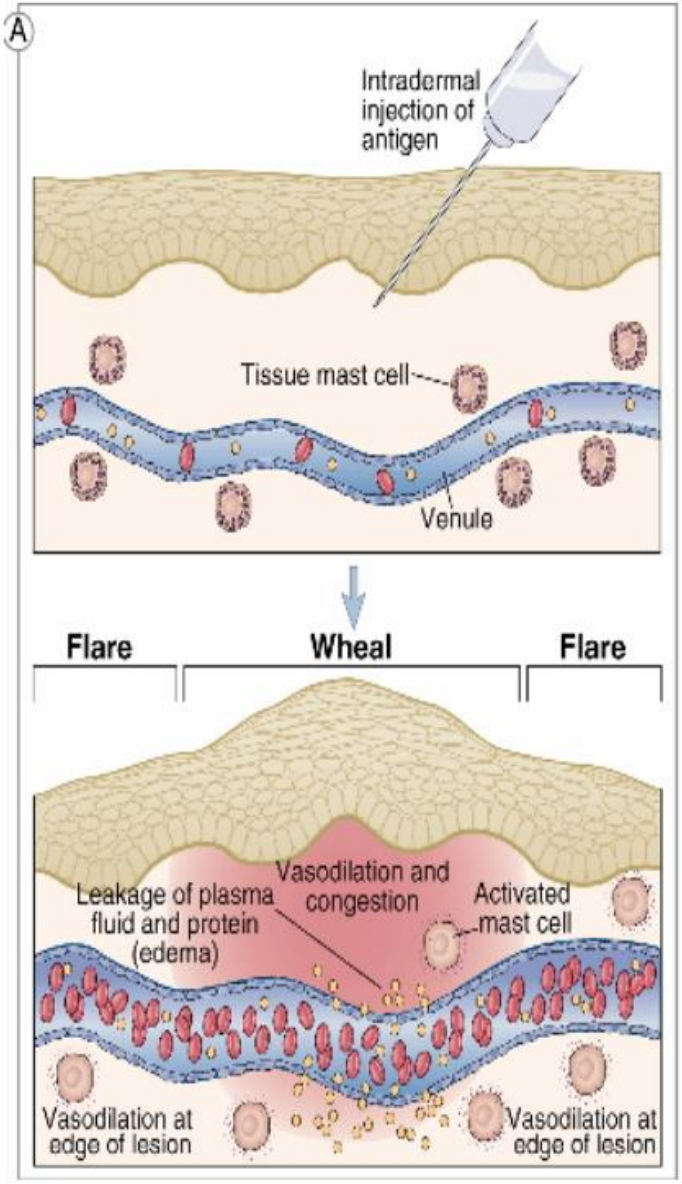
Strongyloides Plus Toxocara Plus Schistosoma Plus Filaria Serology

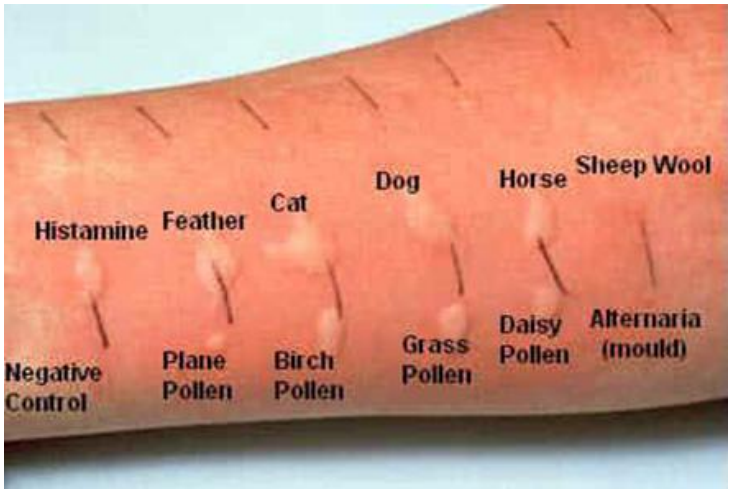
Additional Stool sample for Ova, Cysts and Parasites for any patients at High-Risk

How to measure?

- Specific IgE
  - Blood test (RAST) (radioallergosorbent test using radio-osotopes, actually now enzyme/fluorescnce)
  - Skin prick tests
- Pro's and cons of each
  - Sensitivity
  - Need for venepuncture
  - Immediate vs delayed result
  - Antihistamines, antidepressants causing negative control







Abbas, Lichtman & Pillai,19-8

Does size matter?

- Size of the wheal/'grade' of RAST
- Some correlation with lung function/AHR (Marinho et al Clin Transl Allergy, 2011)
- Possible correlation with sIgE levels and SAE requiring hospital admission (Murray et al, 2007, All Clin Immun Int J World Allergy Org 2007)

Results are expressed in terms of a grade or as a serum concentration of specific IgEGrade 0 = <0.35KUA/L (negative)

Grade 1 = 0.35-0.7KUA/L (weak positive)

Grade 2 = 0.7-3.5KUA/L (positive)

Grade 3 = 3.5-17.5KUA/L (positive)

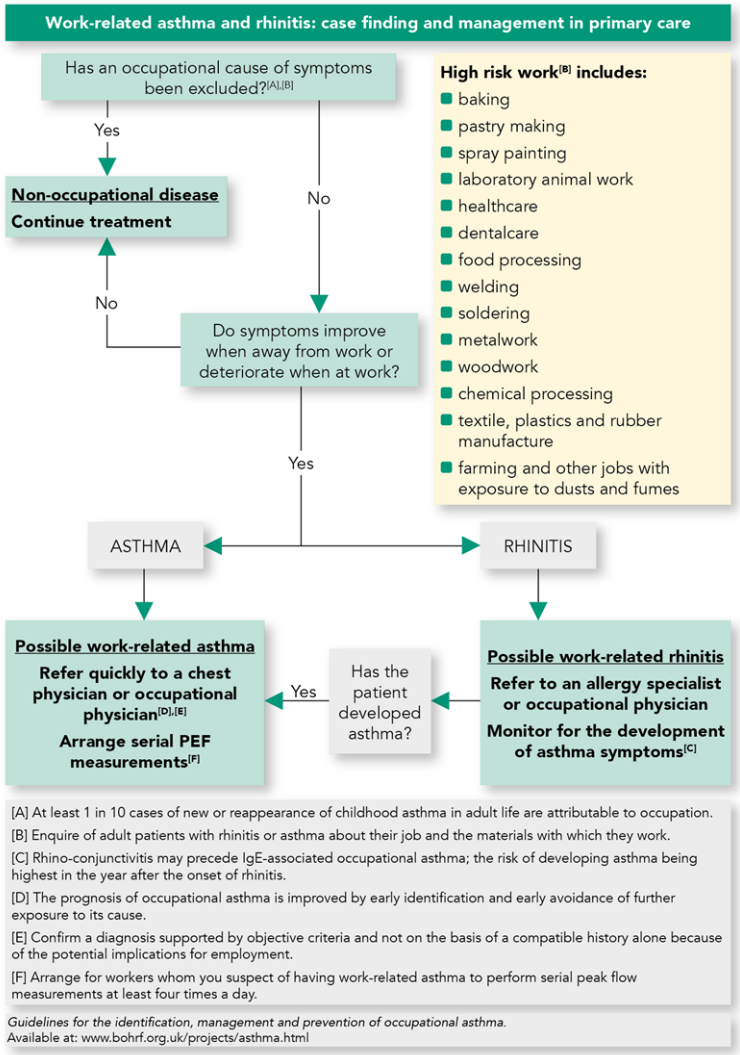
Grade 4 = 17.5-52.5KUA/L (strong positive)

Grade 5 = 52.5-100KUA/L (strong positive)

Grade 6 = >100KUA/L (strong positive)Note Units are arbitarily related to total IgE international reference concentration)

Occupational/workbase placed asthma (WBA)

- Clear History
- Baseline spirometry
- Workbase placed spirometry/serial peak flow – 'Oasys' software at www.occupationalasthma.com
- SPT if possible*
- Inhalational challenge/workbase-placed challenge



* BOHRF recommends only for HMW allergens (flour, latex, animal proteins, grain dust) not LMW allergens (isocyanates, metals, anhydrides, plicatic acid) as not IgE-mediated

Sulphite sensitivity

- Sensitivity, not allergy i.e. no SPT/blood test. Mechanism not known
- Anti-browning/microbial agent, widely used
- Suspect on history – dried fruits, potatoes, wine, some seafood.
- ?~ 4% of asthmatics (Bush et al, Am J Med 1986, Buckley et al JACI 1985), ? More in female
- May or may not be relevant to asthma control
- Dietary sheet/avoidance, involvement of allergy dietician
- No problems with sulphates, or Sulphur*.

	Common sources
Drinks	Cordials, fruit juices, beer, wine, soft drinks, instant tea.
Other liquids	Commercial preparations of lemon and lime juice, vinegar, grape juice.
Commercial foods	Dry potatoes, gravies, sauces, fruit toppings, maraschino cherries, pickled onions, Maple syrup, jams, jellies, biscuits, bread, pies, pizza dough.
Fruit	Dried apricots, and sometimes grapes will be transported with sachets of the sulfite containing preservative. Dried sultanas do not normally contain sulfites.
Salads	Restaurant may add sulfites to preserve their colour of salads and fruit salads.
Crustaceans	Sulfur powder may be added on top of crustaceans to stop them discolouring.
Meat	Sulfites are sometimes added illegally to mincemeat or sausage meat.
Other foods	Gelatin, coconut.

* No more problems than anyone else gets from inhaling/ingesting Sulphur i.e. irritant/toxic

Salicylate sensitivity/Intolerance

- AERD – 'Aspirin exacerbated respiratory disease'
  - More adult onset, association with nasal polyps, Samter's triad
- Not IgE-mediated allergy i.e. no SPT/blood test
- Abnormal biochemical response to the pharmacological effects of the drug(s)
- Acute reactions to NSAIDs typically begin 30 minutes to 3 hours after NSAID ingestion, peak at one to two hours after onset, and generally resolve by three hours from onset
- Mechanism not fully understood, dysregulation of Arachidonic Acid metabolism leading to leukotriene overproduction.
- Suspect on history – aspirin, NSAID sensitivity, dietary (spices, toothpaste/mouthwash, alcohol, other)
- 7% of asthma, 14% of severe asthma, 9-10% if CRS/NP, (Rajan et al JACI 2015)
- Dietary sheet/avoidance, involvement of allergy dietician

What are salicylates?

Salicylates occur naturally in many foods. If your child is sensitive to salicylates, the traffic light system is a good way to help you to manage their symptoms.

What are the symptoms of a salicylate reaction?

Some people are more sensitive to salicylates than others. Salicylate intolerance can cause:

- Rashes
- Swelling
- Diarrhoea

If these symptoms are causing your child discomfort, for example itching, ensure that their skin is cleaned if it has had contact with the foods and if necessary, antihistamine can be used to treat the symptoms. It is rare for a salicylate reaction to become serious.

Traffic light system

Salicylate concentration can be reduced by simply cooking and peeling certain fruits and vegetables.

We have divided foods using a traffic light system by the amount of salicylate they contain:

- **low (green)**
- **moderate (yellow)**
- **high (red)**

No foods should be completely avoided.
Meals should contain mostly food items from yellow and green groups. Unlike more serious food allergies, red group foods do not have to be strictly avoided.

Red group foods are not banned, but can be tolerated in small amounts as part of an otherwise low salicylate meal.

Most families find the right balance for their children without undue restriction.

Fruit	banana, lime, pear (peeled), golden delicious apple (peeled, green variety only), pawpaw, pomegranate, tamarillo, fresh figs, lemon, mango, passion fruit, persimmon, red delicious apple (peeled), rhubarb, papaya
Vegetables	bamboo shoot, cabbage - (green/white), celery, green split peas, lentils, swede, lettuce (iceberg), beans (dried, not borlotti), peas (dried), potatoes (if peeled), Brussel sprouts, borlotti beans, chives, garlic, yellow split peas, leek, mung bean sprouts, red cabbage, shallot, chickpeas fresh asparagus, beetroot, cauliflower, green beans, onion, marrow, potato (white with peel), pumpkin, sweetcorn, tomato, turnip, frozen spinach
Dairy	butter, cheese (not blue vein), milk, yoghurt - natural only but you can add your own fruit.
Grains	barley, buckwheat, millet, oats, rice, rye, wheat.
Seeds and nuts	poppy seeds cashew nuts hazelnuts, pecan, sunflower seeds
Sweeteners	maple syrup, white sugar golden syrup
Meat, Fish, Eggs	meat, fish, poultry and eggs - are generally salicylate free but do not eat any processed meat Liver, prawns, shellfish
Herbs and spices	malt vinegar, saffron, sea salt, soy sauce (if free of spices), fennel (dried), fresh parsley fresh coriander leaves
Oils and fats	sunflower oil, soya oil, canola oil ghee
Beverages	decaffeinated coffee, milk, Ovaltine, homemade pear juice, soya milk, rice milk, water dandelion coffee, pear juice
Other	carob powder, cocoa, tofu.
Fruit	kiwi fruit, loquat, custard apple lychee, pear (with peel)
Vegetables	aubergine - peeled, carrot, lettuces other than iceberg, tomato juice, mushrooms, tinned asparagus, beetroot, black olives, sweetcorn, dessicated coconut, new potatoes
Dairy	blue vein cheese
Seeds and nuts	peanut butter, walnuts pumpkin seeds
Sweeteners	molasses. raw sugar
Beverages	cola, rose hip tea
Fruit	avocado, apples, cantaloupe melon, cherries, grapefruit, mandarin, mulberry, nectarine, peach, watermelon, tangerine, apricots, blackberry, blackcurrant, blueberry, cranberry, dates, plum, grapes, guava, orange, pineapple, strawberry, sultana, currants, prunes, raisin, raspberry, red currant,

Why is it important to know about allergy in your asthma patient?

- Prevention - possibly, but not yet there
- Avoidance – on the whole, no
- Immunotherapy – yes but not in the UK
- Standard treatments – not really
- Advanced treatments - yes

Why is it important to know about allergy in your asthma patient?

- ? Prevention better than cure

- Hygiene hypothesis/modifying immune development in early life (either by inducing tolerance or preventing sensitisation)

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Coronavirus (COVID-19) resources

Mono and multifaceted allergen reducing interventions for the primary prevention of asthma in children at high risk of developing asthma

Published 2009

Multifaceted approaches reduce likelihood of developing asthma by half, NNT 17

BTS 2019: “However, the effect of these multifaceted interventions on wheeze reported by parents was inconsistent and there was no beneficial effect on night-time coughing or breathlessness. These interventions can be costly, demanding and inconvenient to families, and the cost effectiveness is not established. Healthcare professionals can discuss and support this intervention in families who are motivated to follow the demanding programme.”

Immunotherapy

- See Tak's talk
- Can learn from peanut allergy prevention?

Allergen avoidance

Allergen Avoidance in Allergic Asthma, Cipriani et al Front Pediatric 2017

Interventions to eliminate or reduce airborne allergens in the indoor environment.

House dust mite
Use bed-encasing for mattress and duvet/pillows (pore diameter <10 µm)
Wash bedding weekly in hot water and dry in a heated drier
Remove dust mite reservoirs (i.e., toys and stuffed animals, carpets)
Reduce indoor humidity (less than 50%)
Vacuum with a HEPA filter bag
Remind that chemicals to kill mites or denature proteins have a modest effect
Pets
Remove pet from bedrooms and everywhere the child spends a lot of time
Clean accurately upholstered furniture, walls, and carpet
Remove upholstered furniture and carpet if possible
Encase the mattress and pillows with bed encasing (pore diameter <6 µm)
Keep the pet clean with frequent washes
Use a HEPA air filter
Cockroach and pests
Inspect to detect hiding places debris (grease, kitchen) and identify food sources
Store food in sealed containers
Exterminate with pesticides or bait traps
Remove clutter and seal holes or cracks in the home
Indoor molds[a]
Reduce indoor humidity (less than 50%)
Remove contaminated carpets, wallpaper, and woodwork
Treat washable surfaces with detergent and water and then dry completely
Repair water leaks
Pollens
Keep windows closed
Bath to remove allergens from hair and body
Consider to use HEPA air filtration
Consider same principles for outdoor mold avoidance

HEPA, high-efficiency particulate air.

[a]*Level of evidence is largely based on experts opinion.*

Modified from Platts-Mills (30) and Baxi and Phipatanakul (8).

How effective is it/what to do?

- H
  - flake off,
  litate their

High-altitude treatment in severe asthma: Effective and needed in an era of precision medicine

J.H. Kappen*, J.C.C.M. in 't Veen, G.J. Braunstahl

  - High bedding, upho d curtains
  - Varia fail')
  - Coml st
    - En
    - Re iture/reservoirs
    - Reduce humidity
    - HEPA filter

Guidelines opinion on avoidance - HDM

- BTS/SIGN 2019:

A	Healthcare professionals should not recommend house dust mite aeroallergen avoidance for the primary prevention of asthma.
B	Physical and chemical methods of reducing house dust mite levels in the home (including acaricides, mattress covers, vacuum cleaning, heating, ventilation, freezing, washing, air filtration and ionisers) should not be routinely recommended by healthcare professionals for the management of asthma.

- GINA

Box 3-9 (continued) Non-pharmacological interventions – Summary

Intervention	Advice/recommendation	Evidence
Avoidance of indoor allergens	• Allergen avoidance is not recommended as a general strategy in asthma	A
	• For sensitized patients, there is limited evidence of clinical benefit for asthma in most circumstances with single-strategy indoor allergen avoidance	A
	• Remediation of dampness or mold in homes reduces asthma symptoms and medication use in adults	A
	• For patients sensitized to house dust mite and/or pets, there is limited evidence of clinical benefit for asthma with avoidance strategies (only in children)	B
	• Allergen avoidance strategies are often complicated and expensive, and there are no validated methods for identifying those who are likely to benefit	D

Box 3-10. Effectiveness of avoidance measures for indoor allergens

Measure	Evidence of effect on allergen levels	Evidence of clinical benefit
House dust mites		
Encase bedding in impermeable covers	Some (A)	Adults - none (A) Children - some (A)
Wash bedding on hot cycle (55–60°C)	Some (C)	None (D)
Replace carpets with hard flooring	Some (B)	None (D)
Acaricides and/or tannic acid	Weak (C)	None (D)
Minimize objects that accumulate dust	None (D)	None (D)
Vacuum cleaners with integral HEPA filter and double-thickness bags	Weak (C)	None (D)
Remove, hot wash, or freeze soft toys	None (D)	None
Pets		
Remove cat/dog from the home	Weak (C)	None (D)
Keep pet from the main living areas/bedrooms	Weak (C)	None (D)
HEPA-filter air cleaners	Some (B)	None (A)
Wash pet	Weak (C)	None (D)
Replace carpets with hard flooring	None (D)	None (D)
Vacuum cleaners with integral HEPA filter and double-thickness bags	None (D)	None (D)
Cockroaches		
Bait plus professional extermination of cockroaches	Minimal (D)	None (D)
Baits placed in households	Some (B)	Some (B)
Rodents		
Integrated pest management strategies	Some (B)	Some (B)
Fungi		
Remediation of dampness or mold in homes	A	A
Air filters, air conditioning	Some (B)	None (D)

This table is adapted from Custovic et al[330]

GINA Asthma Guidelines 2020

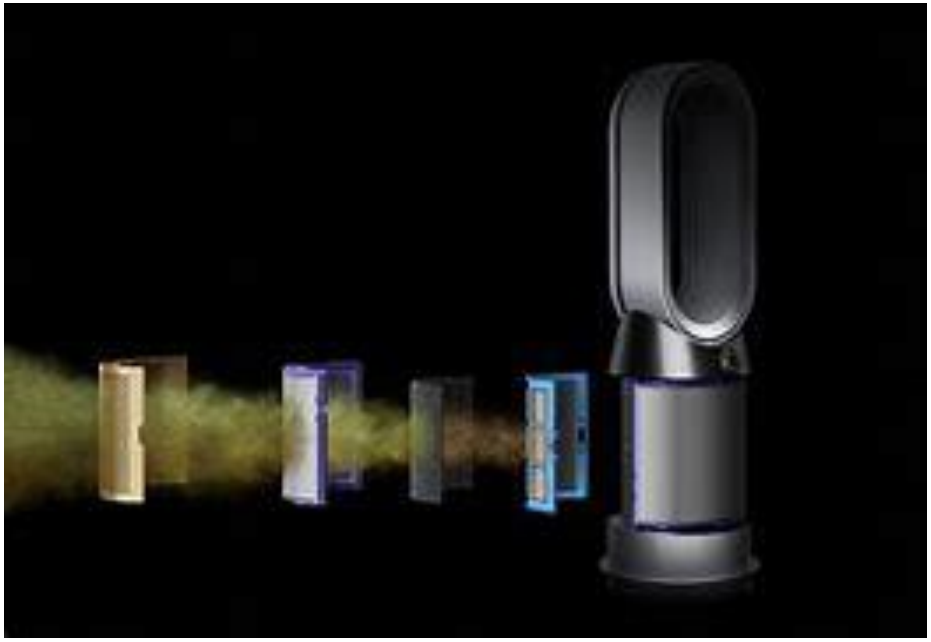
How else to avoid them?

- Laminar air flow hood device
- 2 large phase III studies
  - 4A Asthma
    - Reduced exacerbations but only in severe (GINA 4/5) and poorly controlled
  - LASER trial
    - Enrolled GINA 4/5
    - No significant effect on exacerbations
    - High placebo response

How else to avoid them

“Effect of nocturnal Temperature-controlled Laminar Airflow on the reduction of severe exacerbations in patients with severe allergic asthma: a meta-analysis” Chauhan et al, Eur Clin Resp J 2021

Results: The pooled dataset included 364patients. Patients with more symptoms at baseline (ACT<18 or ACQ7>3; N=179), had a significant mean 41% reduction in severe exacerbations (RR=0.59 (0.38-0.90); p=0.015) in favour of TLA. Higher ACQ7 cut-points of 3.5-4.5 resulted in significant reductions of 48-59%.More uncontrolled patients based on AQLQ total and symptom domains ≤3.0 at baseline also showed a significant reduction in severe exacerbations for TLA vs. placebo ((47% (p=0.037) and 53% (p=0.011), respectively). The meta-analysis also confirmed a significant difference in AQLQ-responders ((Minimal Clinically Important Difference)≥0.5; 74% vs. 43%, p=0.04).



How effective is it/what to do?

- Pets
  - "Environmental assessment and exposure control: a practice parameter--furry animals", Ann Allergy Asthma Immunol 2012
    - "The most important factor contributing to the amount of cat allergen in a house is the presence of a cat"
    - Cat allergen concentrations increase with numbers of cats in the house (but not strangely dog), but no other factors contributory i.e. length of cat hair, cat sex, time spent indoors
    - No safe genetically modified cat or dog (as more than one allergen possible)
    - Similar reservoirs to HDM i.e. upholstered furniture, carpets, etc
    - Change clothes when travelling from 'high cat allergen environment' to 'low cat allergen environment'
  - Avoidance is the best policy, where not possible, measures as per HDM (Encasing, vacuuming with HEPA filter, etc), difficult to know if washing weekly affects levels.
  - Few RCTs but small e.g. "Effect of pet removal on pet allergic asthma , Shirai et al, Chest 2005, 20 pts

Guidelines opinion on avoidance - pets

- BTS/SIGN 2019:

> Animal allergens, particularly from cats and dogs, are potent provokers of asthma symptoms. The reported effects of removal of pets from homes are paradoxical, with either no benefit for asthma[332, 333] or a potential for continued high exposure to induce a degree of tolerance.[334] In homes where there is no cat but still detectable cat allergen, there may be a benefit from introducing additional avoidance measures such as high-efficiency vacuum cleaners for patients allergic to cats, although there is insufficient evidence on which to base a recommendation.[331]

- GINA

Box 3-9 (continued) Non-pharmacological interventions – Summary

Intervention	Advice/recommendation	Evidence
Avoidance of indoor allergens	• Allergen avoidance is not recommended as a general strategy in asthma	A
	• For sensitized patients, there is limited evidence of clinical benefit for asthma in most circumstances with single-strategy indoor allergen avoidance	A
	• Remediation of dampness or mold in homes reduces asthma symptoms and medication use in adults	A
	• For patients sensitized to house dust mite and/or pets, there is limited evidence of clinical benefit for asthma with avoidance strategies (only in children)	B
	• Allergen avoidance strategies are often complicated and expensive, and there are no validated methods for identifying those who are likely to benefit	D

allerca
lifestyle pets

"Our kitty is happy and playful, and bonding with each of us. We definitely love her. She is sweet and affectionate and is fast becoming the princess of the house. I cannot believe that I can cuddle with her, even rub her fur on my face, and I have no symptoms whatsoever."

REENGINEERING LIFE

CRISPR Could Finally Make the First Truly Allergy-Free Cat

One company is working on a DNA-altering injection to give pets

How effective is it/what to do?

- Other indoor allergens (cockroach/mould)

- BTS/SIGN 2019

> Although fungal exposure has been strongly associated with hospitalisation and increased mortality in asthma, no controlled trials have addressed the efficacy of reducing fungal exposure in relation to control of asthma. Cockroach allergy is not a common problem in the UK and studies of attempts to avoid this allergen elsewhere have produced conflicting results.[331]

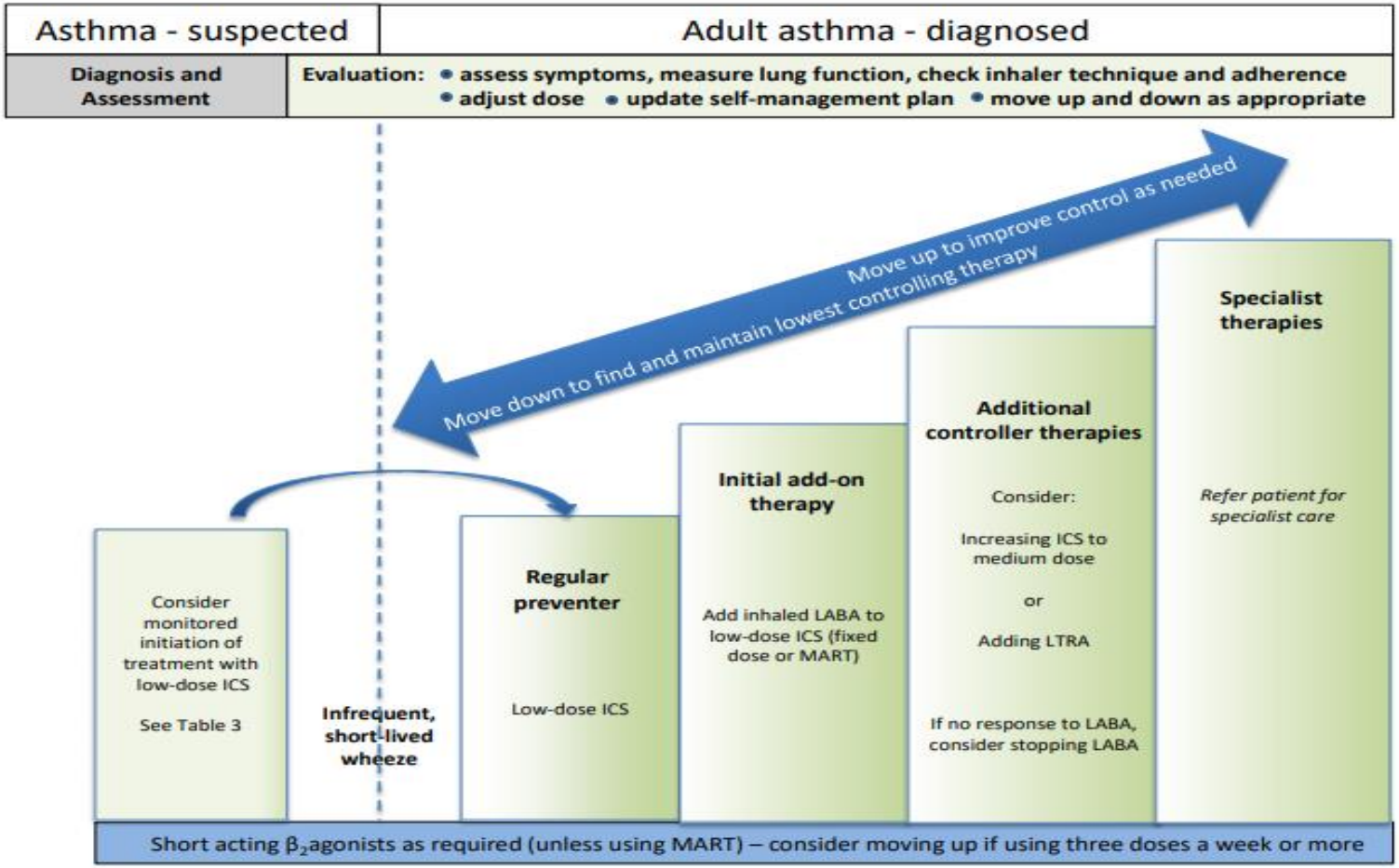
- GINA 2020

> *Cockroaches*: avoidance measures for cockroaches are only partially effective in removing residual allergens[331] and evidence of clinical benefit is lacking.
>
> *Fungi*: fungal exposure has been associated with asthma exacerbations. The number of fungal spores can best be reduced by removing or cleaning mold-laden objects.[332] Air conditioners and dehumidifiers may be used to reduce humidity to less than 50% and to filter large fungal spores. However, air conditioning and sealing of windows have also been associated with increases in fungal and house dust mite allergens.[333]

Allergen immunotherapy

- Sub-cutaneous Immunotherapy (SCIT) and sub-lingual immunotherapy (SLIT)
- UK/European/US differences
- See Tak's talk

Does it affect standard/lower down asthma treatment?



SIGN 158
British guideline on the management of asthma
A national clinical guideline

Southampton NHS
NHS Foundation Trust

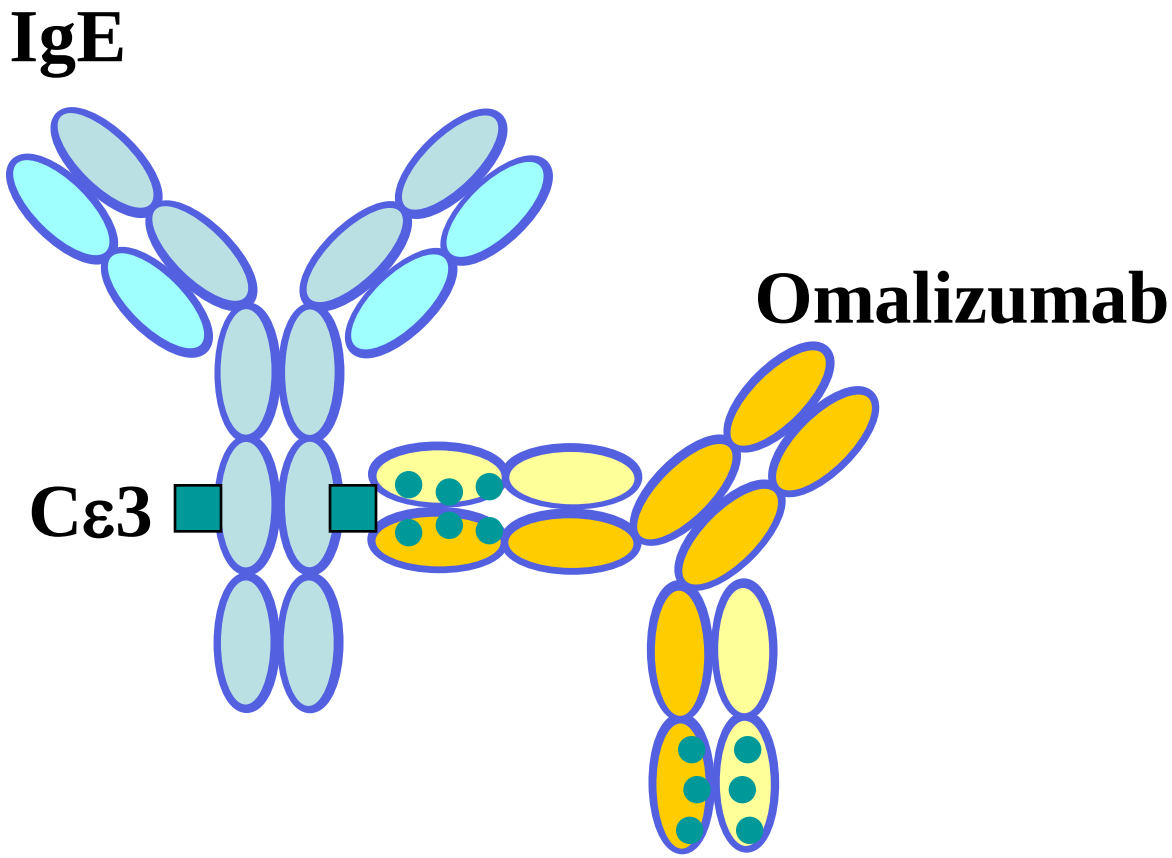
Does it affect standard/lower down asthma treatment?

- Montelukast more effective in Asthma and Allergic Rhinitis
- Antihistamines
  - Aubier et al, Allergy 2001
    - Cetirizine reduced nasal challenge-induced BHR
  - Baena-Cagnani et al, Int Arch Immunol 2003
    - Desloratidine as good as monteleukast in patients with AR and asthma, improved symptom scores, some effect on lung function

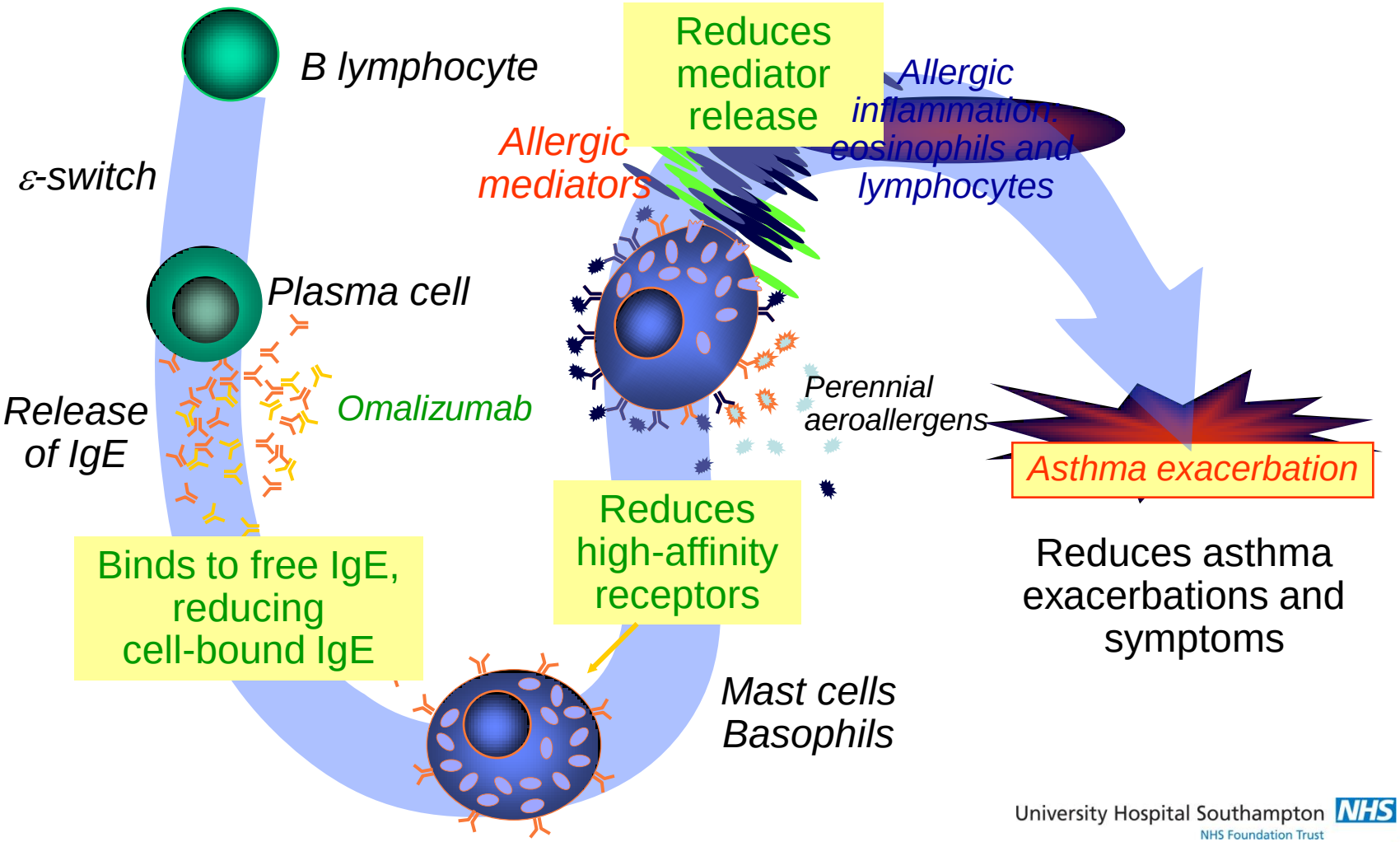
What about ‘(step 5)/specialist therapies’?

- Monoclonals, omalizumab
- Evidence for effectiveness other monoclonals in allergic asthma

Humanized monoclonal anti-IgE antibody: Omalizumab



Omalizumab mechanism of action in IgE-mediated asthma



Beyond step 5 - omalizumab

- Licensing criteria
  - >12 years old
  - Atopy (positive SPT/specific IgE to perennial aeroallergen)
  - IgE 30-1500 (and compatible weight)
  - Reduced lung function (FEV1 <80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high dose inhaled corticosteroids, plus a long-acting inhaled beta2-agonist.

NICE Guidelines TA278

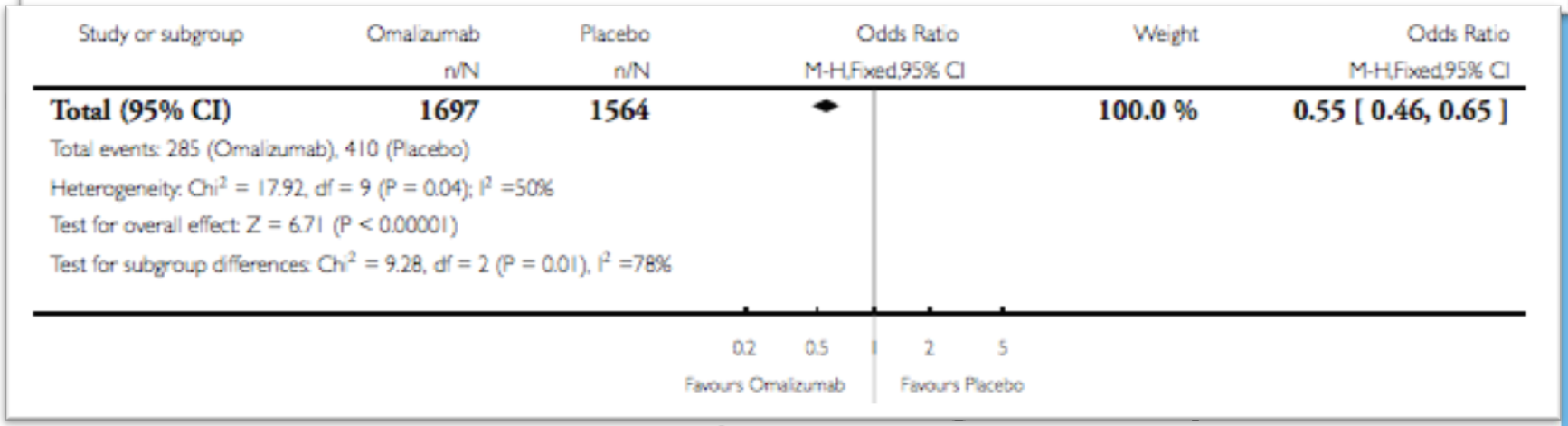
- Omalizumab is recommended as an option for treating severe persistent confirmed allergic IgE-mediated asthma as an add-on to optimised standard therapy in people aged 6 years and older

- Who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year)*

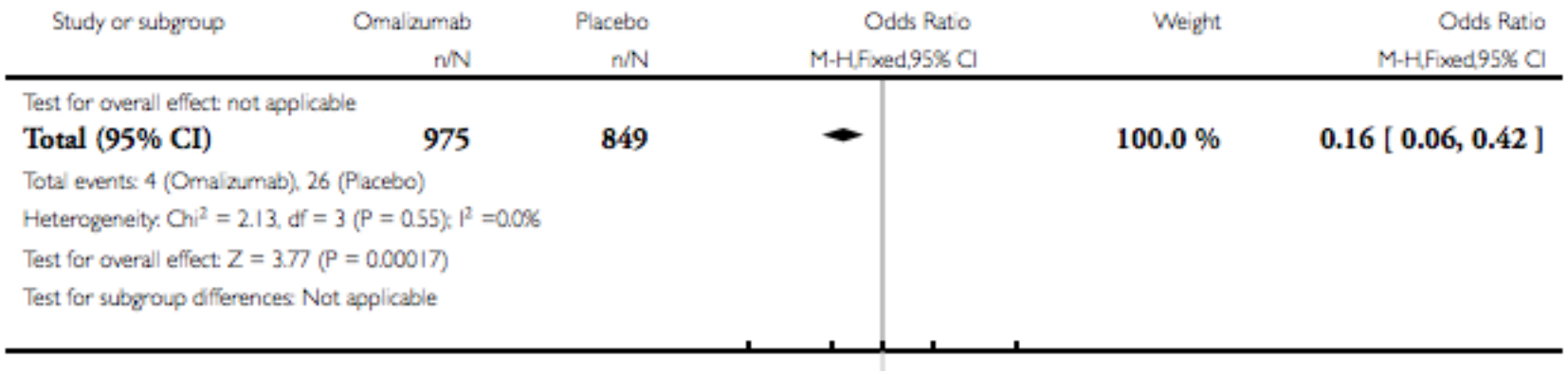
* Initially based on hospitalizations (NICE TA133)

Effects of omalizumab

Analysis 1.1. Comparison 1 Subcutaneous omalizumab + steroid versus placebo + steroid (stable steroid), Outcome 1 Number of participants with at least one exacerbation (ICS and OCS users).



Analysis 1.3. Comparison 1 Subcutaneous omalizumab + steroid versus placebo + steroid (stable steroid), Outcome 3 Hospitalisations.



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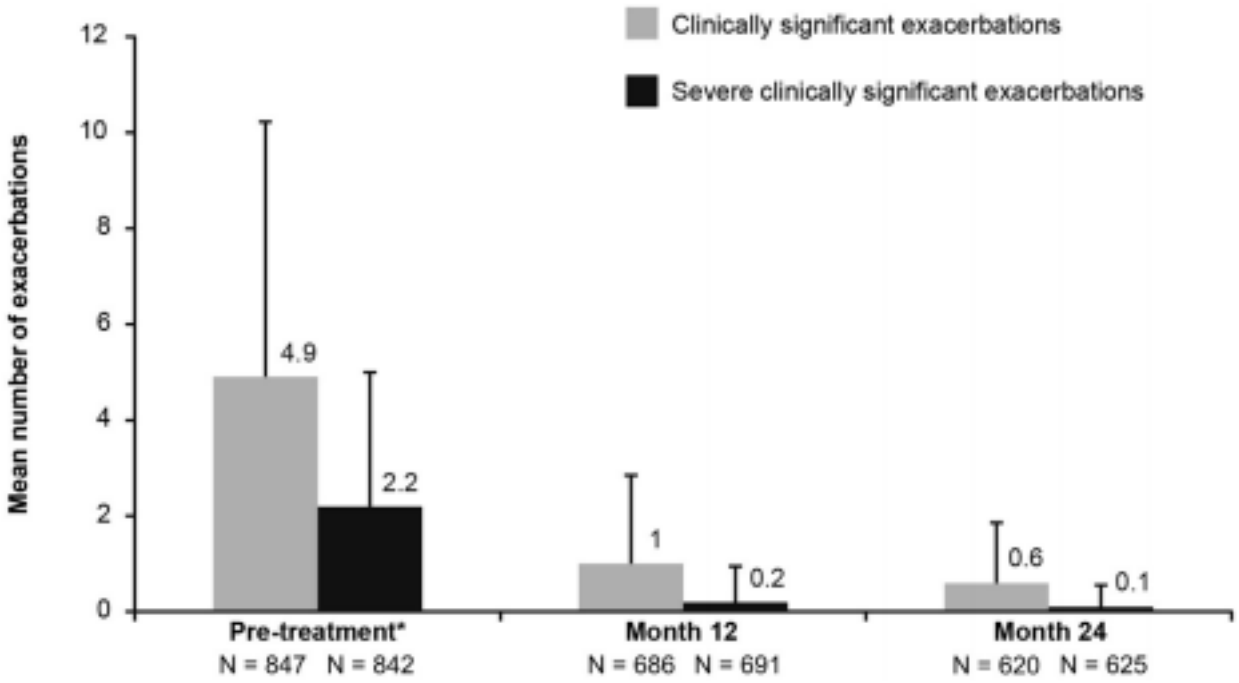
Effects of omalizumab



The eXpeRience registry: The 'real-world' effectiveness of omalizumab in allergic asthma

G.-J. Braunstahl [a,*], C.-W. Chen [b], R. Maykut [c], P. Georgiou [d], G. Peachey [d], J. Bruce [c]

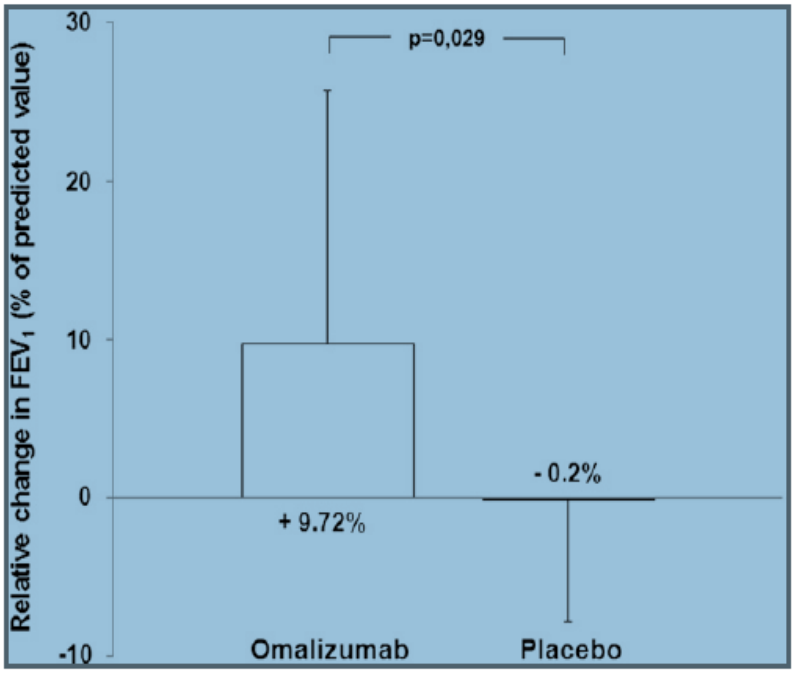
Effects of omalizumab

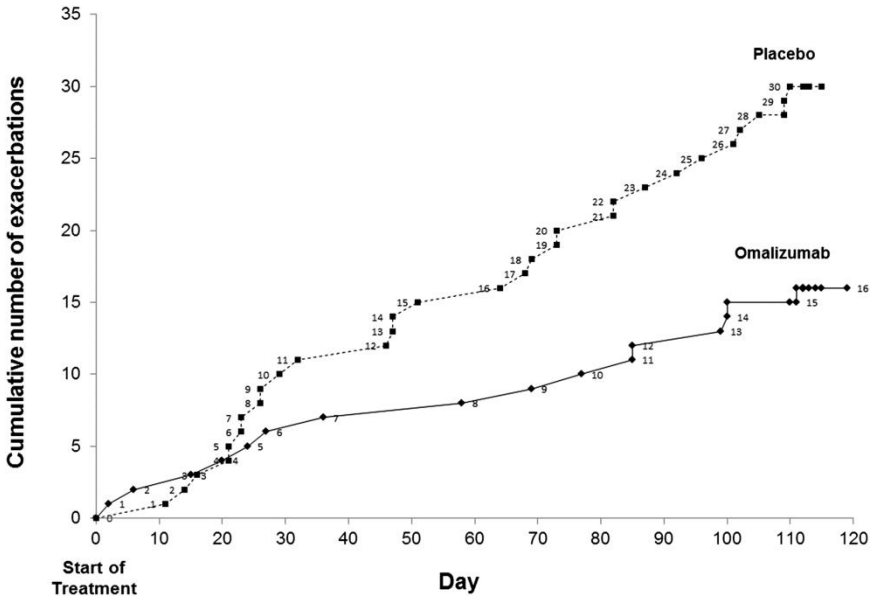
	Patients receiving continuous OCS at baseline (n=90)	Patients not receiving continuous OCS at baseline (n=46)
OCS use over 1 year pre-omalizumab, g	6.8±4.34	3.0±2.44
OCS reduction† (%)	36	26
Patients reducing/stopping OCS‡, n (%)	59 (65.6)	28 (60.9)
Responders#, n (%)	71 (78.9)	41 (89.1)
Change in exacerbations† (%)	-54.6***	-49.3***
Change in hospitalizations† (%)	-60.6***	-61.9***
Change in A&E visits† (%)	-68.1***	-73.6***
Change in % predicted FEV_1 at week 16†, (%)	+8.7±15.08**	+14.7±26.15

The APEX study: A retrospective review of responses of severe allergic asthma patients to omalizumab on continuous or non-continuous oral corticosteroids in UK clinical practice

Omalizumab in non-atopic asthma

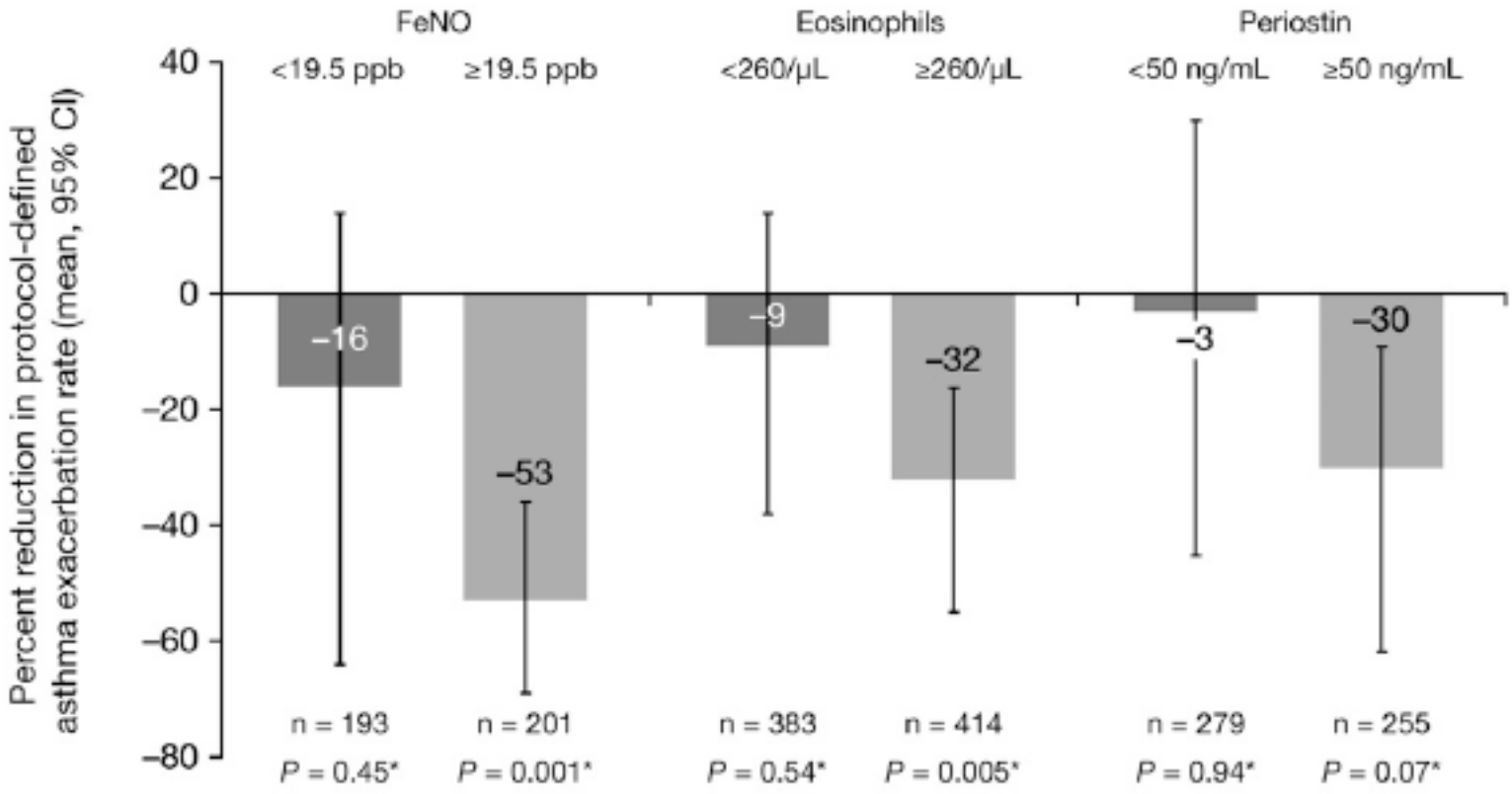
Garcia et al Chest 2013





"…Total serum IgE levels ranged from 30 to 700 IU/mL"

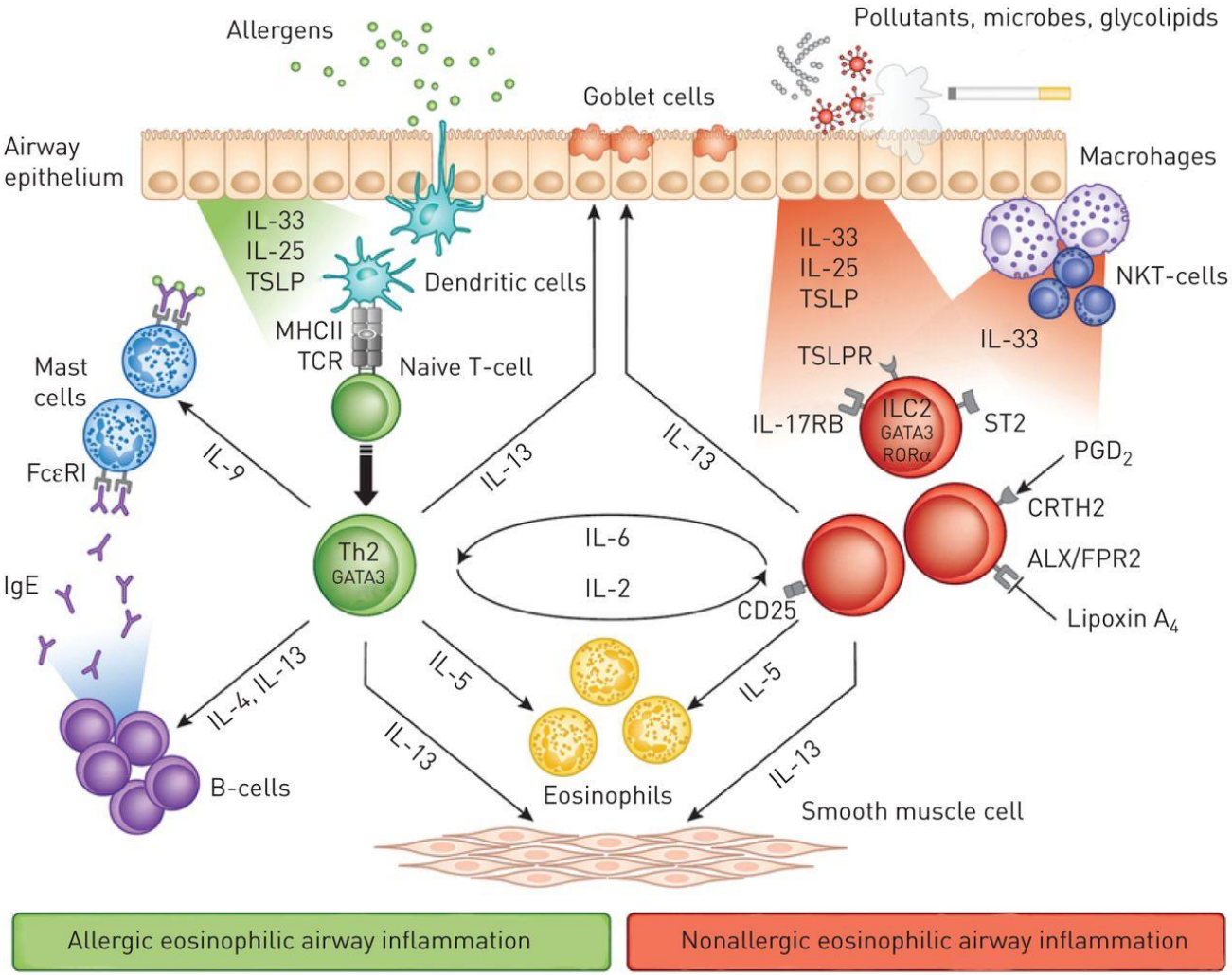
Predictive Biomarkers for Omalizumab efficacy



Exacerbation rates						
	Low FeNO at baseline	High FeNO at baseline	Low eosinophils at baseline	High eosinophils at baseline	Low periostin at baseline	High periostin at baseline
Omalizumab	0.60	0.50	0.65	0.70	0.73	0.66
Placebo	0.71	1.07	0.72	1.03	0.72	0.93

Hanania et al AJRCCM 20

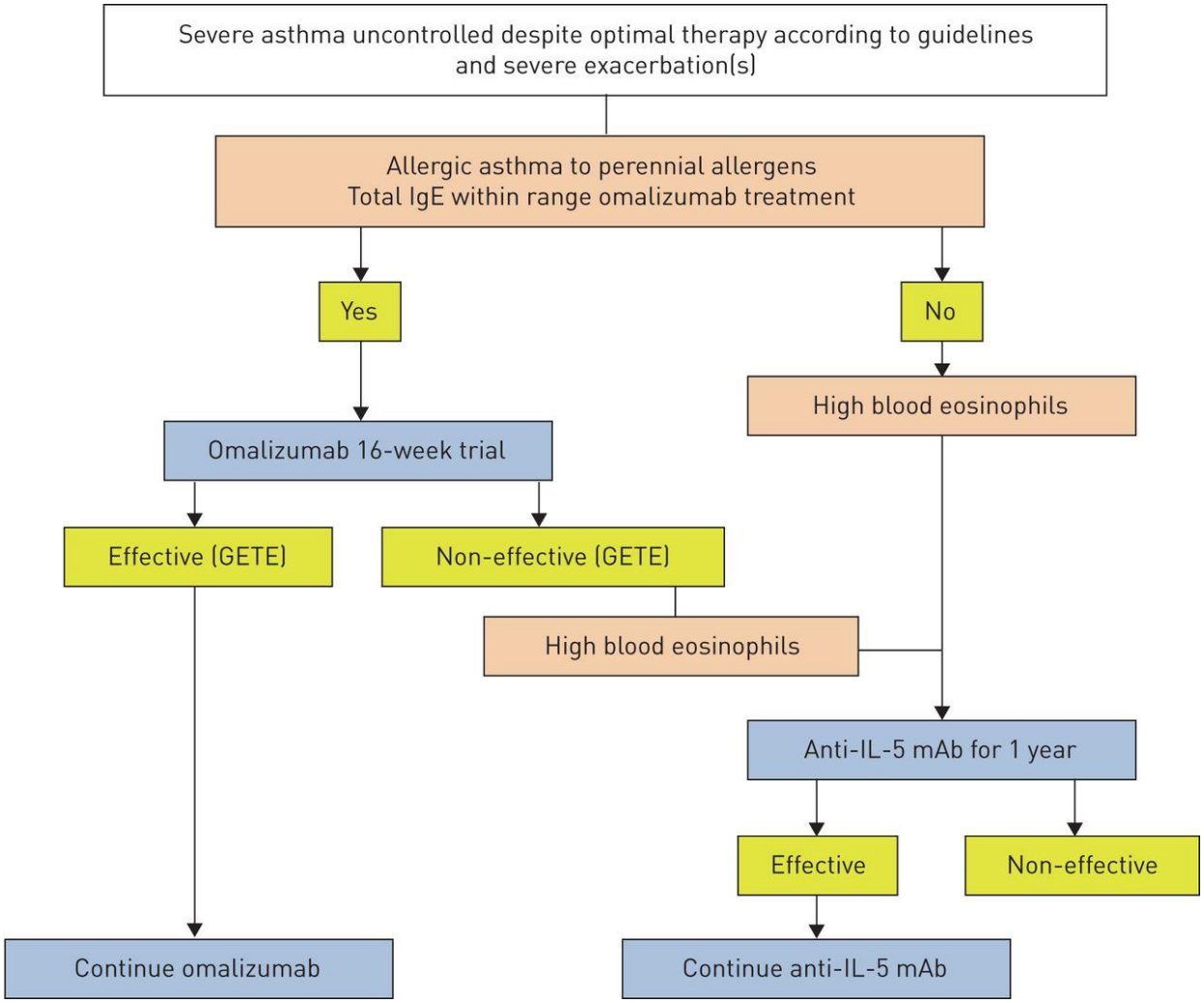
Two different pathways lead to eosinophilic airway inflammation in asthma.



Jantina C. de Groot et al. ERJ Open Res 2015;1:00024-2015

University Hospital Southampton NHS
NHS Foundation Trust

Care pathways for biologics in asthma.



Jean Bousquet et al. Eur Respir J 2017;50:1701782

University Hospital Southampton NHS
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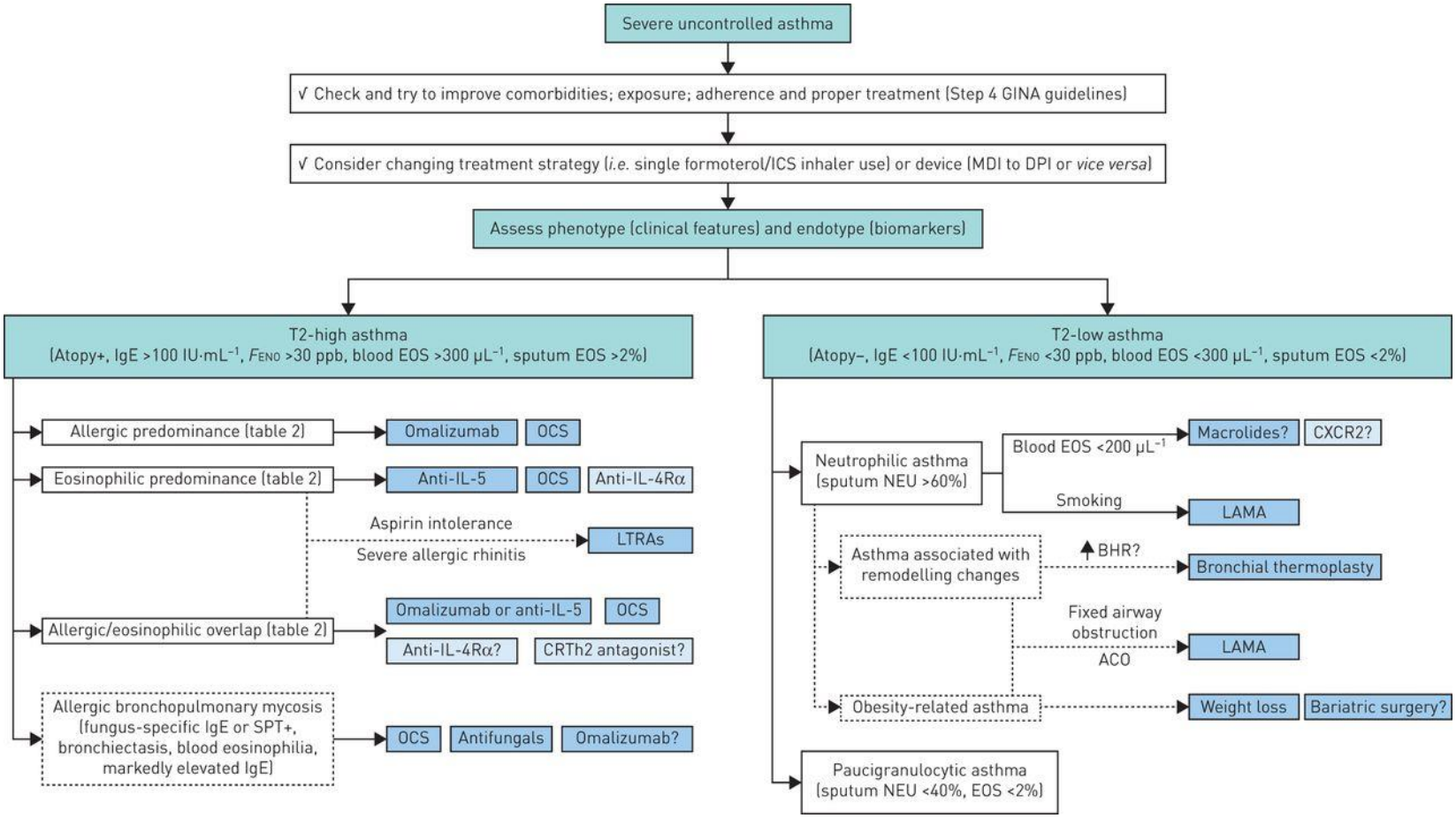
A stepwise therapeutic approach in severe uncontrolled asthmatic subjects.



Eleftherios Zervas et al. ERJ Open Res 2018;4:00125-2017

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TABLE 2

Clinical features and biomarkers that can be used to differentiate between allergic and eosinophilic T2-high severe asthma

	A: allergic-predominant asthma	B: eosinophilic-predominant asthma
1	Early onset	Late onset
2	SPT/RAST+ with clinically significant allergies#	SPT/RAST– or + with no clinically significant allergies
3	IgE >100 IU·mL^{-1}	IgE <100 IU·mL^{-1}
4	Allergic rhinitis	Nasal polyps
5	High F_{ENO} (30–50 ppb)	Very high F_{ENO} (>50 ppb)
6	Blood eosinophils <300 cells·µL^{-1}	Blood eosinophils >300 cells·µL^{-1}#

SPT: skin prick test; RAST: radioallergosorbent test; F_{ENO}: exhaled nitric oxide fraction. Check the number of relevant patient characteristics per column. If a patient has more features from column A or B it is more likely that he/she has allergic- or eosinophilic-predominant asthma, respectively. If the patient shares features from both columns, it is more likely that he/she suffers from eosinophilic/allergic overlap asthma. #: obligatory characteristics for allergic and/or eosinophilic asthma.

Benralizumab efficacy by atopy status and serum immunoglobulin E for patients with severe, uncontrolled asthma

Bradley E Chipps [1], Paul Newbold [2], Ian Hirsch [3], Frank Trudo [4], Mitchell Goldman [3]

The role of mepolizumab in atopic and nonatopic severe asthma with persistent eosinophilia

Original Article

Dupilumab Efficacy in Patients with Uncontrolled, Moderate-to-Severe Allergic Asthma

Just as effective, regardless of total IgE/atopic status

What have we covered

- Definitions and the importance of correct labels
- What tests are we doing in the asthma patient?
- Why is it important to know about allergy in your asthma patient?
  - A lot of the time it is not…
  - Advanced therapies (Omalizumab)
- Anaphylaxis


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HIVES
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RUNNY NOSE
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12% boys
9% girls
3% allergic to BEE VENOM
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DANGER
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