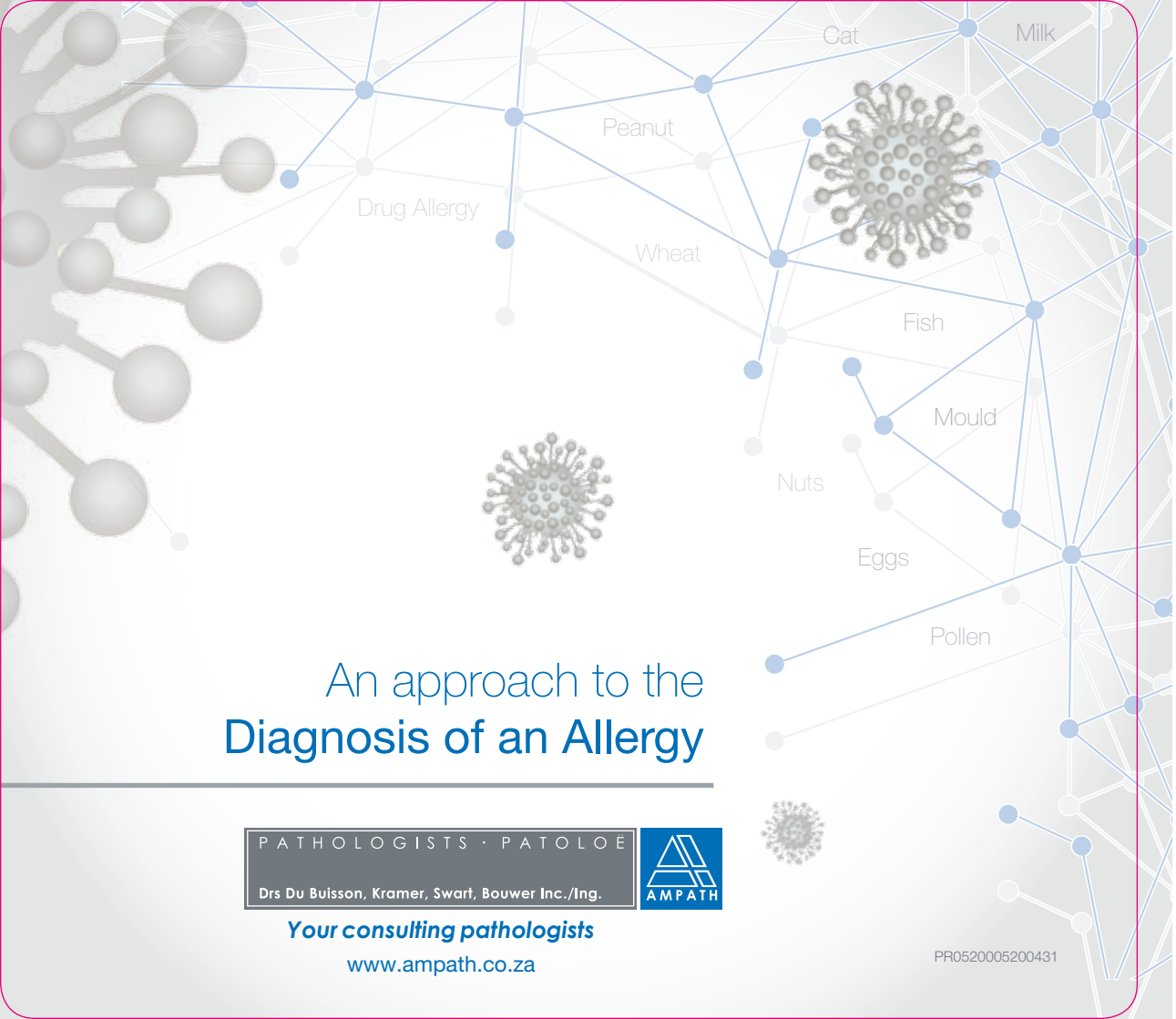

An approach to the Diagnosis of an Allergy

PATHOLOGISTS · PATOLOË

Drs Du Buisson, Kramer, Swart, Bouwer Inc./Ing.

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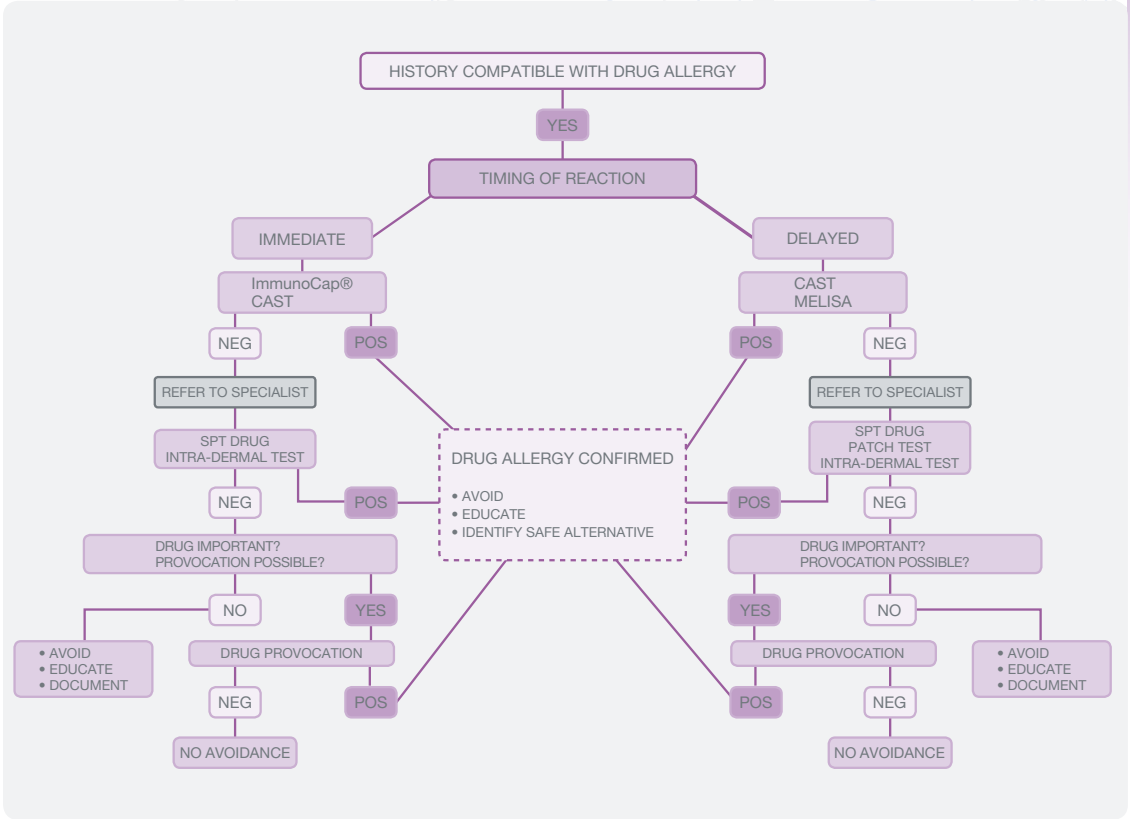
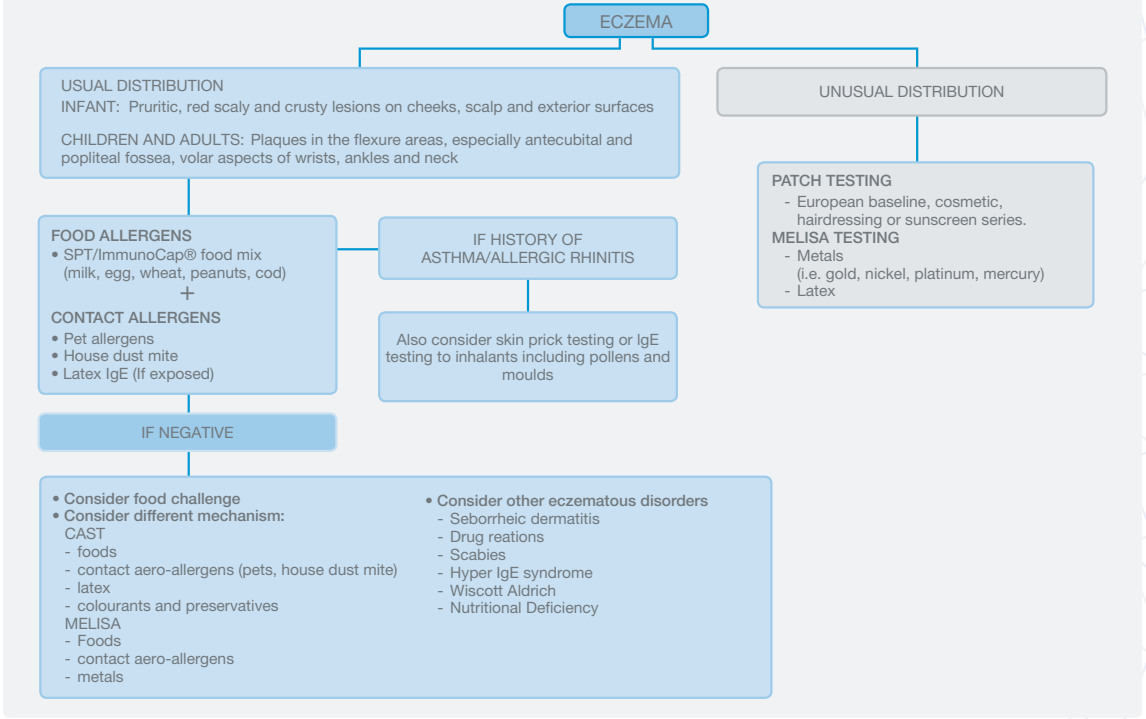
AN APPROACH TO DRUG ALLERGY DIAGNOSIS - MADE EASY WITH A FLOW DIAGRAM



CLINICAL PEARLS

- When testing for penicillin allergy, patients should be tested to the penicillin ring, major and minor determinants and relevant side-chains.
- A beta lactam ring is also found in cephalosporins (2-5% penicillin cross-reactivity), carbapenems (1% penicillin cross-reactivity) and monobactams (no cross-reactivity)
- Quinolones frequently cause drug allergy and cross-reacts with other quinolones.
- Macrolides don't often cause allergies and cross-reactivity between macrolides is uncommon.
- NSAID allergy is common. Aspirin, diclofenac and ibuprofen are the best indicators of NSAID allergy. Please distinguish between Aspirin allergy and Aspirin exacerbated respiratory disease, where cox-inhibition leads to greatly induced leukotrine production. This is not a true allergy and patients may present with nasal polyps and asthma.
- Local anaesthetic allergy is common, but patients may tolerate 1/more alternate local anaesthetics.
- Radiocontrast medium allergy is caused by an immunological reaction to quaternary iodine components. This does not cross-react with iodated table salt or seafood.

AN APPROACH TO ECZEMA AND DERMATITIS

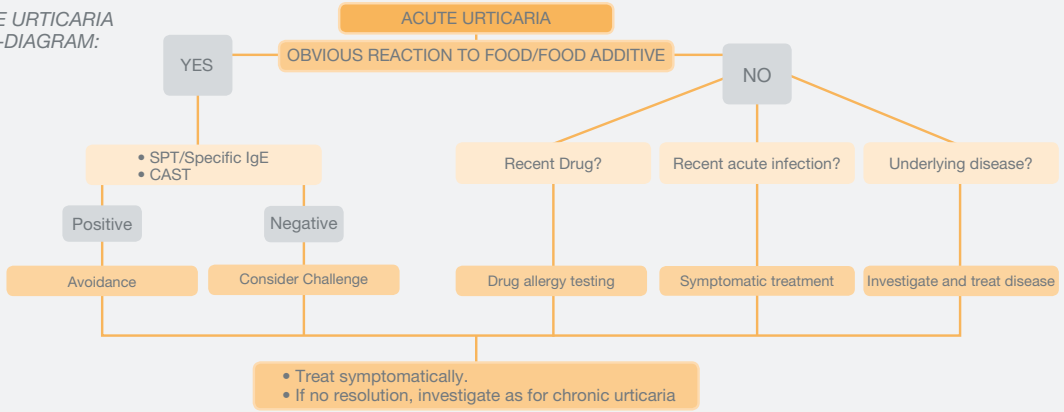


CLINICAL PEARLS

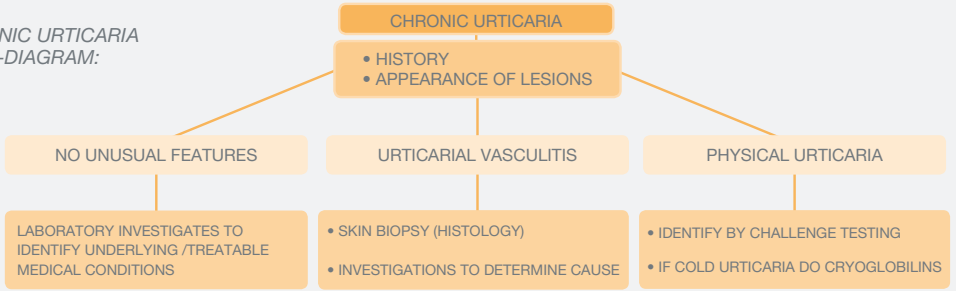
- Patients with eczema have an intrinsic/impaired skin barrier defect, but allergen exposure causes flares in atopic patients.
- Common allergens are food allergens or contact inhalant allergens like dust mite or animal danders.
- Patients with very high IgE levels, as is commonly seen in atopic eczema, can lead to multiple positive allergy tests (cross-reactivity and non-specific binding). An ISAC test is not influenced by non-specific binding and can identify cross-reactivity, therefore is recommended in these patients.
- Patients with an unusual distribution of their rash should be investigated for contact dermatitits (patch testing).

THE FOLLOWING FLOW-DIAGRAMS ASSISTS WITH AN APPROACH TO ACUTE AND CHRONIC URTICARIA:

ACUTE URTICARIA FLOW-DIAGRAM:



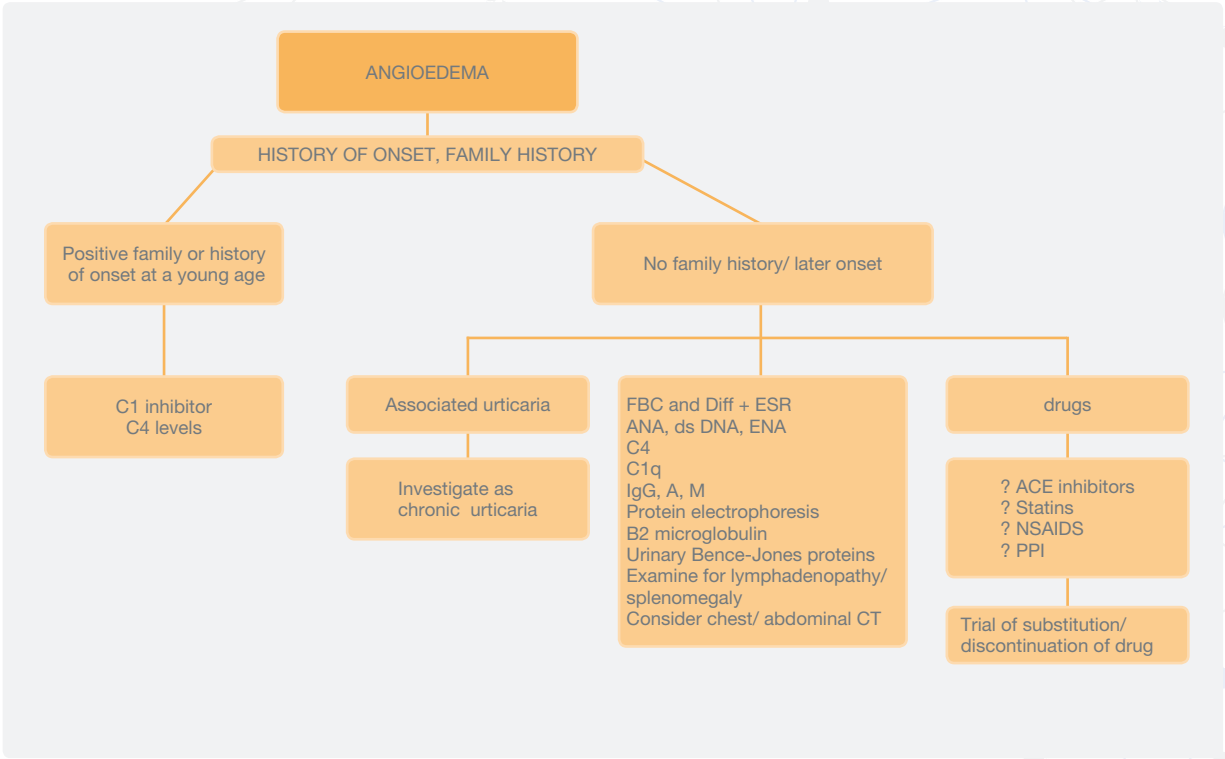
CHRONIC URTICARIA FLOW-DIAGRAM:



AN APPROACH TO URTICARIA

CLINICAL PEARLS

- Urticaria may be triggered by multiple factors in genetically susceptible individuals, e.g. infections, autoimmunity, malignancies, hypersensitivity and physical or psychological factors.
- Allergy is rarely (5-10%) the cause of chronic urticaria.
- The most common allergens implicated are drugs, foods, colourants and preservatives.
- Urticaria is itchy, not painful. It may be associated with angioedema.
- Suspicious features of urticarial vasculitis is painful or non-itchy lesions that last > 24 hours on the same spot and heal with bruising or scarring.
- Physical urticarias include dermatographism, delayed pressure urticaria, cholinergic urticaria, aquagenic urticaria and vibrational urticaria and should be diagnosed from clinical history.

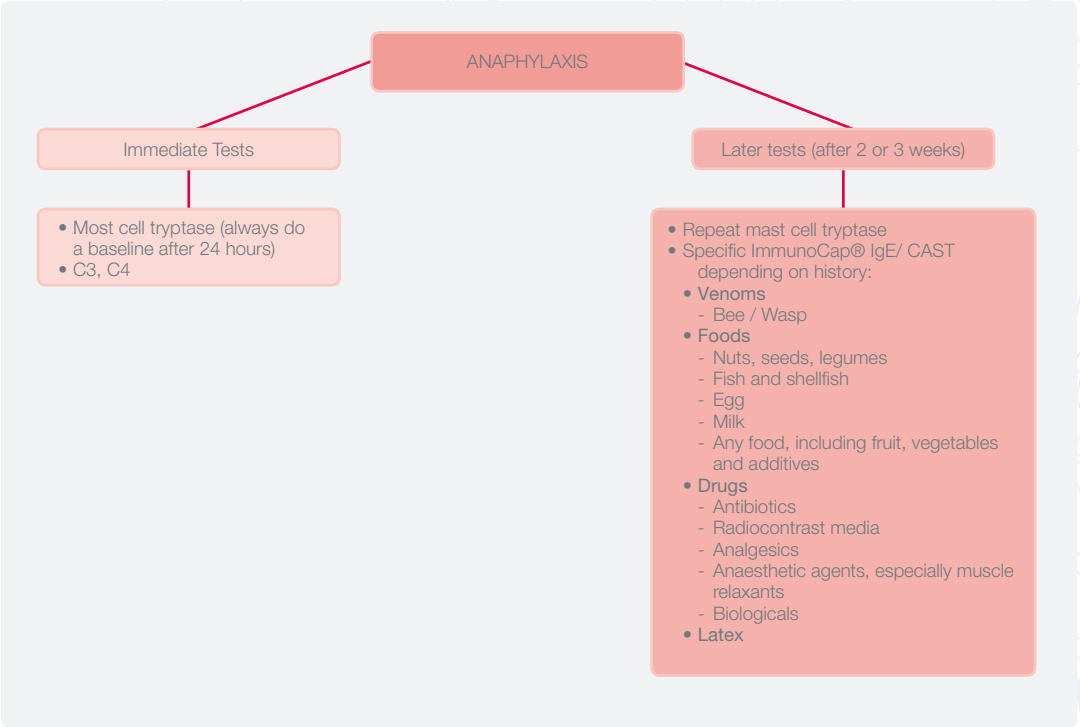


AN APPROACH TO ANGIOEDEMA

CLINICAL PEARLS

- Angioedema is not itchy, but “tingly”, burning or painful.
- If urticaria/ itch is prominent, investigate and manage as for urticaria.
- Hereditary angioedema (HAE) usually presents early or with a positive family history.
- Angioedema with urticaria is not HAE.
- The most common cause of angioedema in adults is ACE inhibitors or NSAIDS.
- Angioedema (without urticaria) is not an allergy and patients should be investigated for an underlying disease, . e.g. autoimmunity or malignancy.

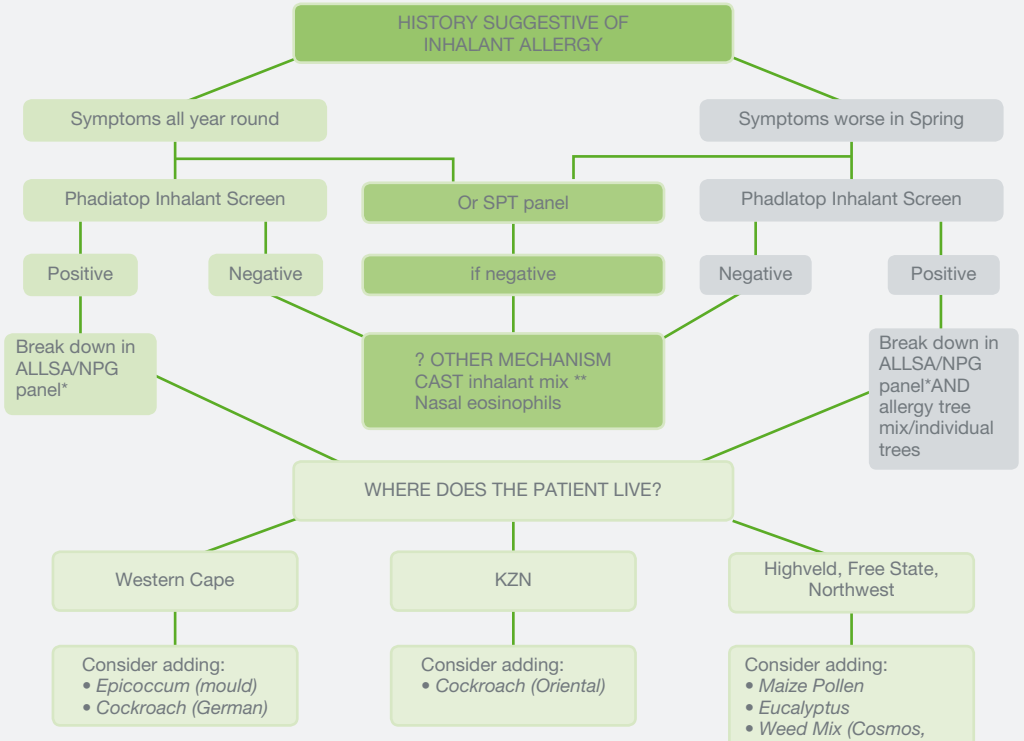
AN APPROACH TO THE DIAGNOSIS OF ANAPHYLAXIS



AN APPROACH TO THE DIAGNOSIS OF ANAPHYLAXIS

CLINICAL PEARLS

- Mast cell tryptase is very important to diagnose anaphylaxis and is positive in anaphylactic (IgE mediated) and anaphylactoid (non-IgE mediated) reactions.
- Always do a baseline tryptase level at least 24 hours later.
- Do not investigate for the anaphylaxis trigger within 2-3 weeks of the reaction as basophils in CAST tests may have increased background activation and IgE may be negative due to increased consumption.
- Consider co-factor dependant anaphylaxis e.g. wheat induced – exercise – induced anaphylaxis (LTP/ Ω – 5 – gliadin), NSAID or alcohol co-factor anaphylaxis.



* ALLSA/NPG panel: Bermuda grass, Rye grass, Alternaria (mould), Cladosporium (mould), Aspergillus (mould), D.pteronyssinus (mite), B.tropicalis (mite), cat, dog

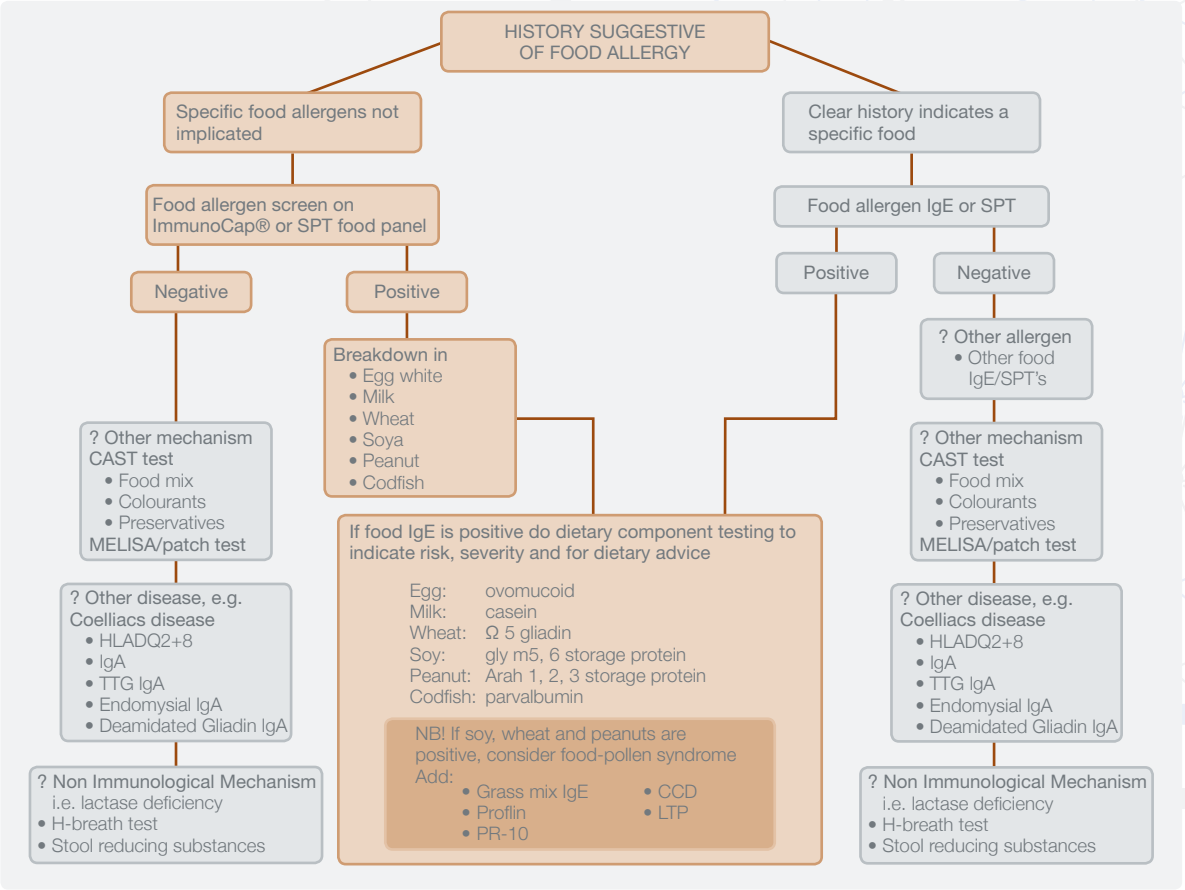
** Request specific allergen breakdown if CAST inhalant mix is positive and phadiatop is negative.

AN APPROACH TO INHALANT ALLERGY

CLINICAL PEARLS

- The majority of inhalant allergies are IgE mediated, therefore IgE mediated testing, e.g. Phadiatop/ skin prick tests are recommended as first line tests.
- In patients with a history highly suggestive of inhalant allergies and negative IgE allergy tests, consider.
  a) Another mechanism
     - Do CAST inhalant screen.
     - Do nasal mucus smear for eosinophils.
  b) Another allergen
     - ?Tree pollen, animal, weed, occupational allergen.
- The most allergenic tree pollens in South Africa are plane tree, oak, olive, cypress, eucalyptus, pine, acacia, willow, poplar, mulberry ash and elder.
- Screening tests (Phadiatop) for inhalant allergies should always be broken down if positive, so individual allergens can be identified for avoidance or immunotherapy.
- Patients are often sensitized to cross-reactive components that occur in pollens and foods of plant origin. Test for these components, nl. LTP, PR-10, Profilin and CCD in patients sensitized to pollens and foods of plant origin.

THE FOLLOWING DIAGNOSTIC TOOLS ARE KEY IN THE ASSESSMENT OF A POSSIBLE FOOD ALLERGY:



CLINICAL PEARLS

- It is important to distinguish between immediate (<2 hours) hypersensitivity reactions, which are usually IgE / basophil mediated and delayed reactions, which may include other immune mechanisms. Testing should be requested accordingly.
- Screening with a food mix (IgE or CAST) should always be broken down if positive.
- Consider allergy to food additives like colourants and preservatives in addition to the specific food allergens.
- In patients with symptoms suggestive of wheat hypersensitivity and negative allergy tests, please consider testing for Coeliac disease.
- Oral allergy syndrome (OAS) is usually caused by pollen-food cross-reactivity. Test for pollen allergy and cross-reactive pollen components: IgE to LTP, PR-10, profilin and CCD.
- Relevant components should be requested if food-specific IgE is positive to advise on risk, avoidance and prognosis.
- ISAC testing should be considered in patients with multiple food and inhalant allergies.

FOOD ALLERGEN COMPONENTS: EGG, MILK, FISH, SHELLFISH

THE MOST IMPORTANT ALLERGEN COMPONENTS:

EGG WHITE				EGG YOLK
Ovomucoid Gal d 1	Ovalbumin Gal d 2	Conalbumin Gal d 3	Lysozyme Gal d 4	Egg serum albumin Gal d 5
• Highly allergenic • Heat stable • Severe and persistent allergy	• Heat labile • May tolerate well-cooked egg			• Occurs in egg yolk, chicken meat and feathers

MILK				
Casein Bos d 8	α lactalbumin Bos d 4	β lactoglobin Bos d 5	Bovine serum albumin Bos d 6	Lactoferrin Bos d lactoferrin
• Heat stable • Most important allergen • Severe and persistent allergy • Cross-reacts between mammals (eg: goats milk)	• Main whey proteins • Heat labile • Patients react more severely to fresh milk. May tolerate boiled/ baked milk, long-life milk, hard cheese and yoghurt.		• Occurs in milk and beef/red meat. • Heat labile, may tolerate well cooked milk and dairy. • Cross-reaction with other mammals.	• Heat labile. • May be used as a preservative in beef and nasal sprays.

FISH		SHELLFISH
Cod pavalbumin Cyp c 1	Carp parvalbumin Gad c 1	Tropomyosin Pen a 1
• Heat stable • Broad cross-reactivity, marker for general fish sensitization. • Parvalbumin content of different fish species may vary, e.g. lower levels in tuna.		• Heat stable muscle protein. • Found in crustaceans, molluscs, insects and mites with clinical cross-reactivity.

FOOD ALLERGEN COMPONENTS: POLLEN, PEANUT, SOYA, WHEAT

POLLEN CROSS REACTIVE			
Profilin	*PR-10*	*LTP*	*CCD*
• Heat labile • OAS	• Heat labile • OAS • Mild to severe symptoms	• Heat stable • OAS • Severe clinical symptoms or anaphylaxis	• Usually no clinical symptoms

PEANUT						
Storage Proteins				*Profilin*	*PR-10*	*LTP*	*CCD*
Ara h 1	*Ara h 2*	*Ara h 3*	*Ara h 6*	*Ara h 5*	*Ara h 8*	*Ara h 9*	*CCD*
• Stable to heat and digestion • Risk of anaphylaxis • Cross-reactive with other nuts and seeds							

SOYA					
Storage Proteins		*Profilin*	*Gly m 4*	*LTP*	*CCD*
Gly m 5	*Gly m 6*		*PR-10*		
• Associated with severe reactions • Heat stable			• May have severe reactions		

WHEAT					
Ω 5 Gliadin *Tri a 19*	*αBωW* *Gliadins*	*Profilin*	*PR-10*	*Tri a 14* *LTP*	*CCD*
• Risk marker for systemic reactions • Wheat allergy persistence • Wheat dependent exercise induced anaphylaxis	• Marker of severe reactions • Marker of wheat allergy persistence.			*Wheat dependent exercise induced anaphylaxis.*	

FOOD ALLERGEN COMPONENTS: POLLEN, PEANUT, SOYA, WHEAT