MADX
MACRO ARRAY DIAGNOSTICS

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WHY MOLECULES IN ALLERGY DIAGNOSTICS?

PROBLEMS WITH EXTRACTS

Due to variations in allergen concentration and composition, different allergen extracts may yield different IgE levels for the same serum sample in specific IgE testing. If the patient is exclusively sensitised to an allergen of a source that is not contained in the extract, a false negative result is obtained. Contamination of extracts with allergens from other sources can cause false positive results.

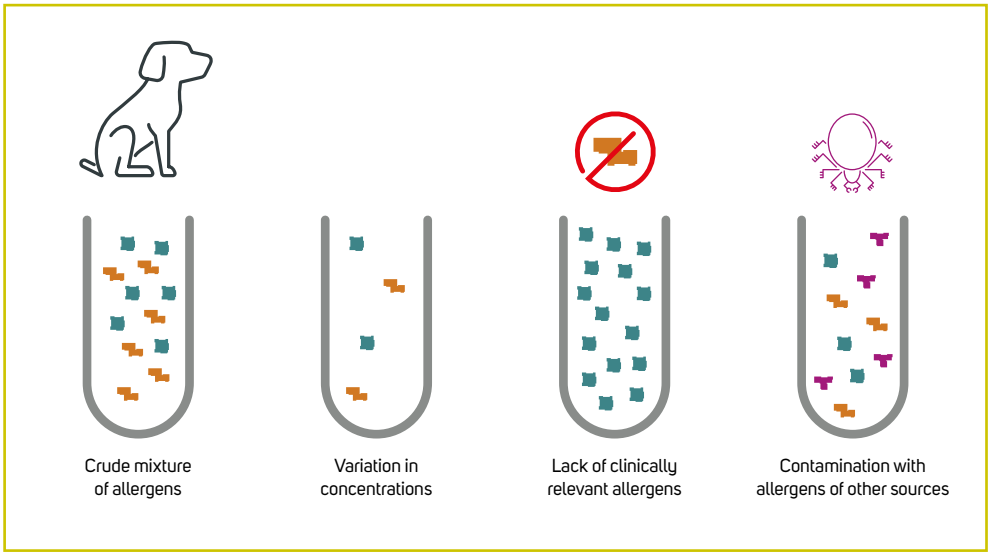

Figure 5: Problems with extracts.

HIGHER SPECIFICITY

Individual, specific molecules from an allergen enable precise diagnostics. Allergen extracts are a mixture of different molecules. It can be unclear which specific molecule triggers the allergic reaction.

ACCURACY OF DIAGNOSIS

Traditional allergy tests using extracts cannot tell if a person is truly allergic to multiple sources (co-sensitisation) or just reacting to similar proteins found in different sources (cross-sensitisation).

This is one of the reasons why molecular allergy diagnostics was developed. It uses individual molecular allergens instead of crude mixtures, making it easier to identify exactly what someone is allergic to and leading to more accurate results and better treatment options.

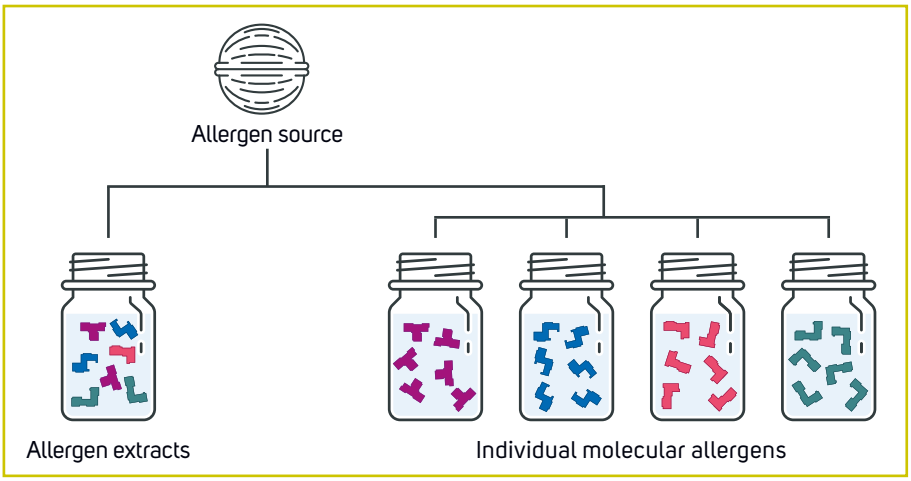

Figure 1: Allergen extracts and individual molecular allergens.

Selection of AIT based on extract-based diagnostics

Clinical history	Extract-based diganostics	AIT indication
Strong rhinitis during early and late spring	SPT: Birch extract (+) SPT: Grass extract (+)	Birch (+) Grass (+)

Molecular allergy diagnostics (MAD) (co- or cross-sensitisation)

Bet v 1 - allergen marker for birch pollen sensitisation

Phl p 1, 2, 5, 6 - allergen markers for grass pollen sensitisation

Added value of MAD for AIT selection

	Molecular allergy test	Diagnostics: co- and cross-sensitisation	AIT indication
Scenario 1	Bet v 1 (+) Phl p 1 (+)	co-sensitisation to birch and grass	Birch (+) Grass (+)
Scenario 2	Bet v 1 (+) Phl p 1, 2, 5, 6 (-)	cross-sensitisation	Birch (+) Grass (-)
Scenario 3	Bet v 1 (+) Bet v 4 (+) Phl p 1 (+) Phl p 7 (+)	genuine sensitisation (co-) to birch and grass with reactivity to panallergens	Birch (+) Grass (+)

Figure 2: Comparison of molecular and extract-based allergy diagnosis for prescription of allergen-specific immunotherapy (AIT).

ACCURACY OF RISK MANAGEMENT

Using molecular allergens instead of extracts offers a key advantage: it allows doctors to distinguish between allergies that carry a high risk of severe reactions and those that are mostly harmless, even from the same source.

This is because molecular allergens provide more precise information, helping to identify exactly which parts of the allergen are triggering the reaction. With this clarity, doctors can offer safer treatment options.

Unstable Proteins ⟶ Stable Proteins

	Profilin	PR-10	nsLTP	Storage protein
Cross-reactivity	high	high	low to moderate	low to moderate
Stability concerning heat, digestion	unstable	unstable	stable	stable
Clinical relevance	low: inhalative symptoms, OAS	low: inhalative symptoms, OAS (Bet v1 homologues partially heat resistant – systemic reactions)	high: OAS to anaphylaxis	high: frequent systemic reactions

Figure 3: Examples of protein families classified based on their cross-reactivity, stability, and clinical manifestations.

ACCURACY OF THERAPY RECOMMENDATIONS

If a patient shows clinical and IgE reactivity to two allergen sources "A" and "B", it is possible to differentiate if he/she is truly sensitised to "A" and cross-sensitised to "B" or vice versa, or if he/she is truly sensitised to both, in terms of co-sensitisation.

The first two cases could be an indication for immunotherapy only to A or to B but not to both, while in the latter case, immunotherapy to both allergen sources might be indicated.

With this approach, accuracy of allergy diagnosis and therapy recommendations can be immediately improved. Genuine sensitisations can be identified which is of extreme importance for AIT prescription, since unnecessary AIT treatment may result in new IgE sensitisation.

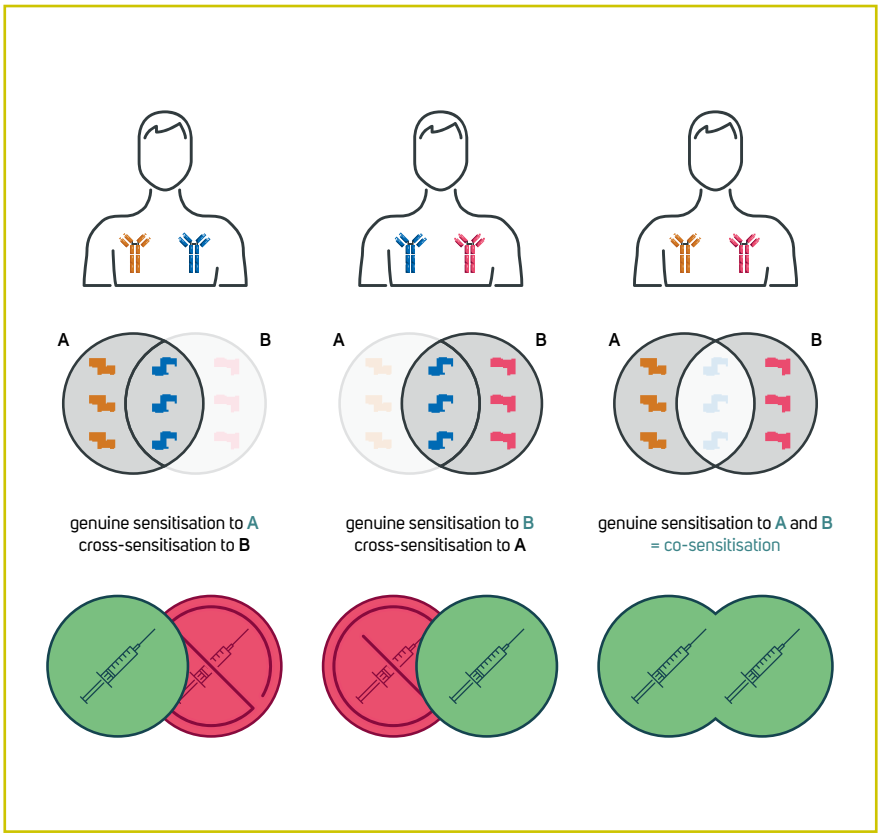

Figure 4: Differentiation between co- and cross-sensitisation by molecular allergy diagnosis and the implication for AIT indication.

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