Allergic rhinitis – clinical immunology perspective

Metro North Health

Queensland Government

- Allergic rhinitis
  - Prevalence
  - Pathophysiology
  - Diagnostics
  - Common allergens
  - Medical therapy
  - Atopic comorbidities
  - Non allergic rhinitis

  - Immunotherapy

- Important to note:

  - Adult focused talk
  - Not exhaustive discussion

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About ASCIA Allergic rhinitis e-training for health professionals

ASCIA Allergic rhinitis e-training for health professionals has been developed by ASCIA to provide accessible, consistent and evidence-based training for medical practitioners and other health professionals in Australia and New Zealand at no charge. ASCIA Allergic rhinitis e-training for health professionals has been updated in March 2022

ASCIA gratefully acknowledges all of the generous supporters of ASCIA education resources, as listed on the ASCIA website https://www.allergy.org.au/about-ascia/sponsors

Learning outcomes:

- Recognise the clinical features of allergic rhinitis and possible co-existent conditions.
- Understand the uses and limitations of allergy testing.
- Identify pharmacotherapy options available and when to consider allergen immunotherapy.
- Know when to refer to a specialist.

This course is suitable for medical practitioners (including GPs, paediatricians and physicians), pharmacists, nurse practitioners, nurses, dietitians and other healthcare professionals

https://etraininghp.ascia.org.au/

What is allergic rhinitis / conjunctivitis

- Inflammatory disorder of nasal mucosa
- Caused by allergic reaction to pollen, dust mite, animal based allergen or others
- High QoL impact

Symptoms suggestive for AR (when related to allergen exposure)[3]	Symptoms LESS suggestive for AR[3]
2 or more of the following symptoms for > 1 hour on most days: • Runny nose • Sneezing, especially paroxysmal • Nasal obstruction • Nasal itch • Ocular symptoms like itch, redness or tearing	• Unilateral symptoms • Discoloured secretions • Facial or nasal pain • Recurrent epistaxis • Smell disorder (anosmia) • Posterior rhinorrhoea (post nasal drip) with thickened mucus • Isolated rhinorrhoea

Hellings, P. W., Scadding, G., Bachert, C., Bjermer, L., Canonica, G. W., Cardell, L. O., Carney, A. S., Constantinidis, J., Deneyer, L., Diamant, Z., Durham, S., Gevaert, P., Harvey, R., Hopkins, C., Kjeldsen, A., Klimek, L., Lund, V. J., Price, D., Rimmer, J., … Fokkens, W. J. (2020). EUFOREA treatment algorithm for allergic rhinitis. *Rhinology Journal*, *58*(6), 618–622. https://doi.org/10.4193/Rhin20.376

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  - Seasonal – outdoor allergens. Predictable, reproducible
  - Perennial – indoor allergens.

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TABLE 1.1

Pattern and severity of allergic rhinitis

Pattern	
Intermittent	**Persistent**
<4 days/week or <4 weeks	>4 days/week and >4 weeks
Severity	
Mild	**Moderate to severe, ≥1 of:**
• Normal sleep	• Abnormal sleep
• Normal daily activities, sport or leisure	• Impaired daily activities, sport or leisure
• Normal work and school performance	• Abnormal work and school performance
• No troublesome symptoms	• Troublesome symptoms

Adapted from Bousquet et al. 2001.[2]

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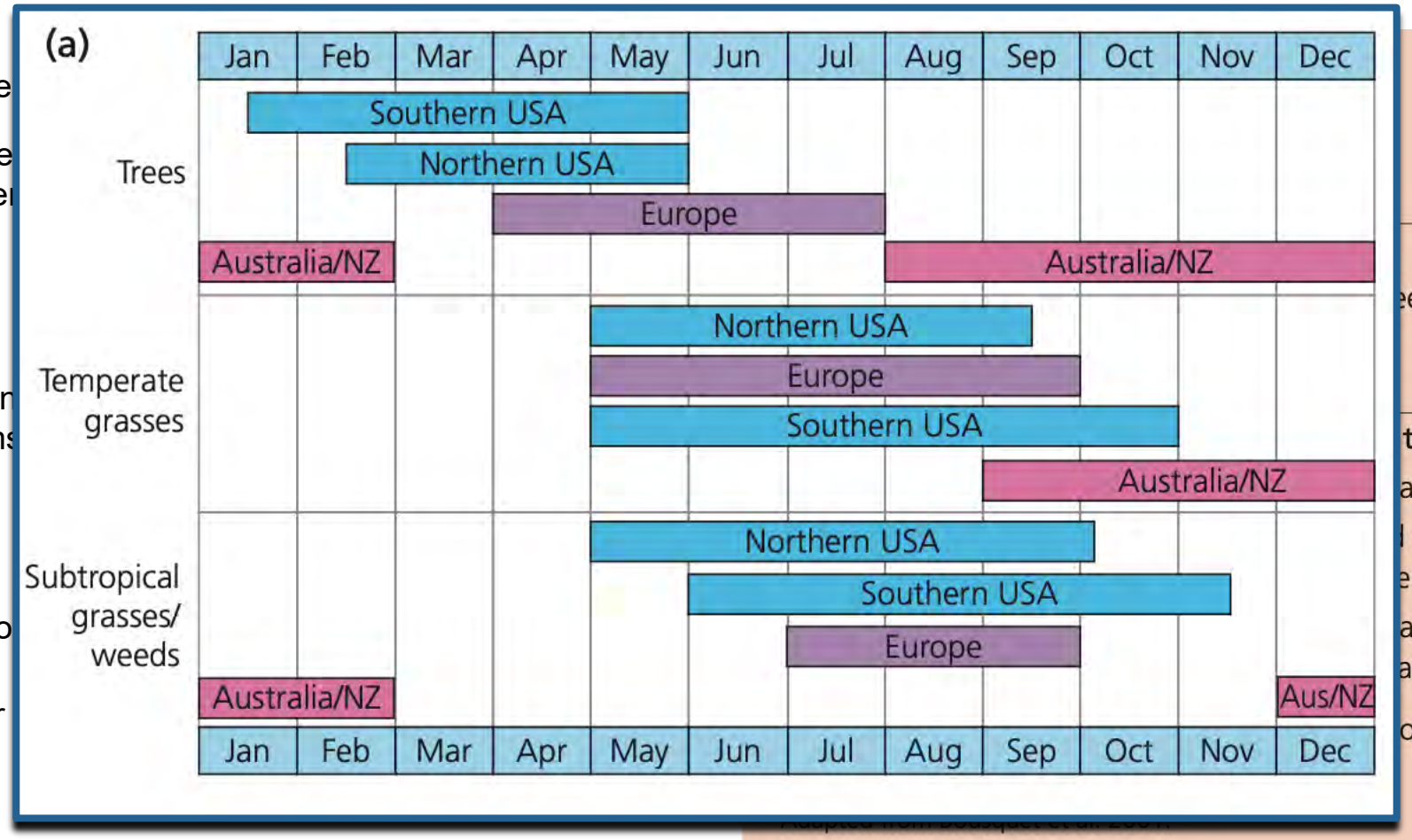

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What is allergic rhinitis

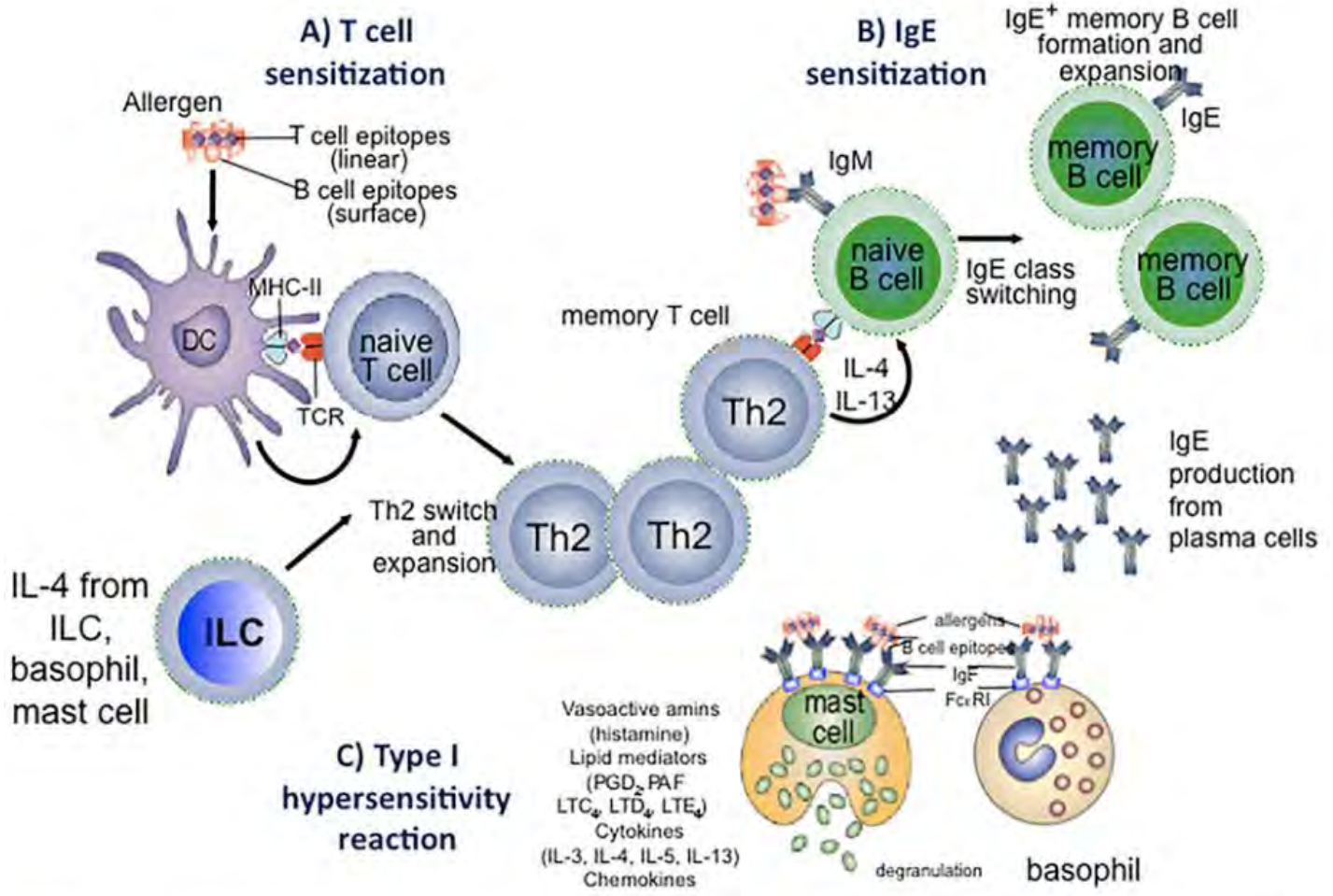

Figure 1 Sensitization and type I hypersensitivity reaction. A) T cell sensitisation, clonal expansion and memory Th2 cell development after allergen presentation to T cells, B) IgE sensitization after Th2 cell naïve B cell interaction, C) Type I hypersensitivity reaction after cross-linking of the FcεRI bound IgE molecules by allergens on mast cells.

Akdis, C.A., Agache, I. & Hellings P. **Global Atlas of Allergic Rhinitis and Chronic Rhinosinusitis. 2015. EEACI**

What is allergic rhinitis

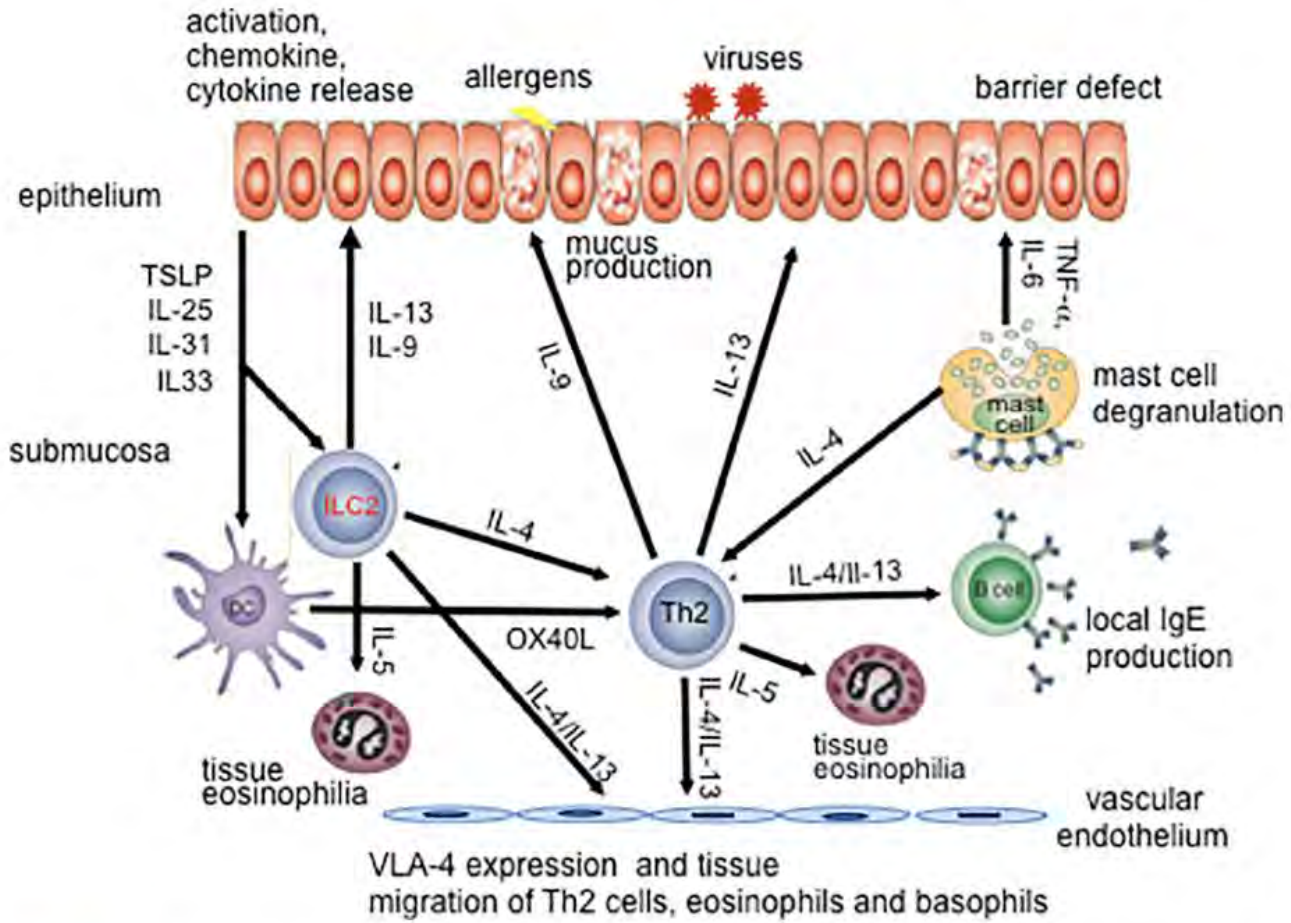

Figure 1 Type 2 inflammation and cytokine network in the AR nose. AR inflammation develops as a combination of innate and adaptive immune response and involvement of resident tissue cells. Epithelial activation and cytokine release (TSLP, IL-25, IL-31, IL-33) leads to type 2 innate lymphoid cells (ILC2) activation. IL-4 from mast cells and ILC2s augments the Th2 response. TSLP-induced OX-40-ligand from DC induces a Th2 response. IL-4 and IL-13 lead to B cell activation and local IgE production. IL-5 from Th2 cells and ILC2 promotes tissue eosinophilia. IL-4 and IL-13 activate the endothelium for tissue migration of eosinophils, basophils and Th2 cells. Multiple Th2 (IL-9, IL-13) and pro-inflammatory cytokines (TNF-α, IL-6) released from ILC2, Th2 and mast cells activate the epithelium.

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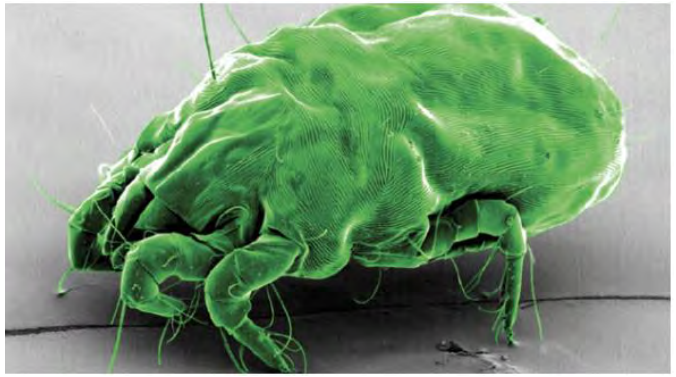
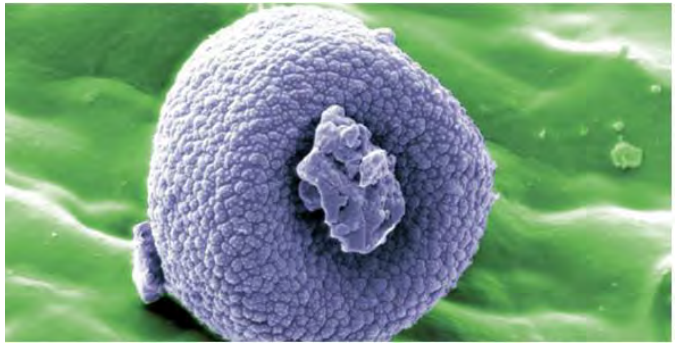
Allergens of interest

- House dust mite
  - 4 subtypes, with *D. farina* and *D. pteronyssinus* most common.
  - *B. tropicalis* important for tropical regions
  - Persistent allergen (in QLD) = persistent symnptoms



- Grass allergy
  - In QLD – largely subtropical grasses
  - Considered seasonal, but may be worsening/exacerbation rather than off/on



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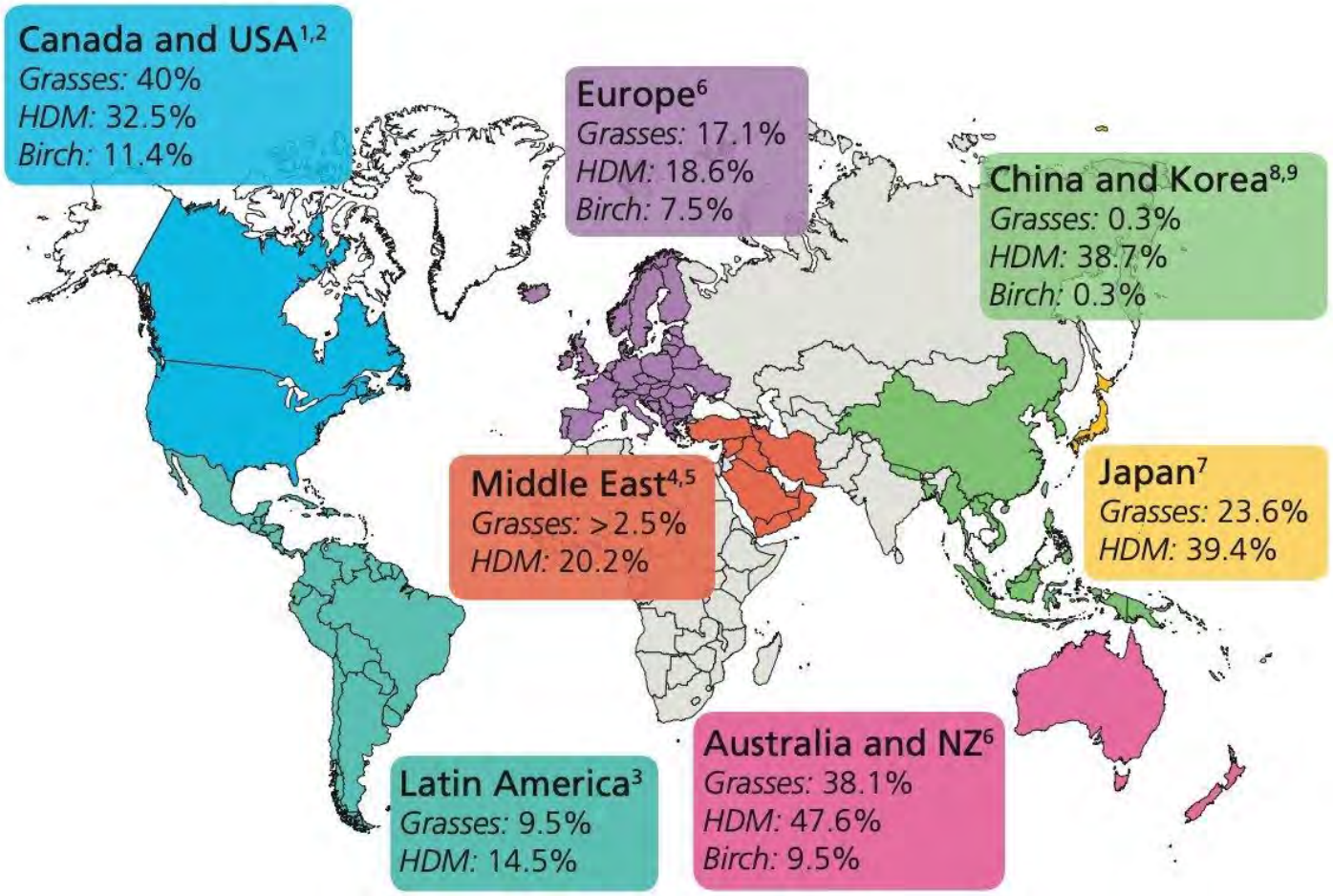

Figure 2.1 Worldwide prevalence of common aeroallergen sensitizations. Adapted from data from multiple sources.[1–9]

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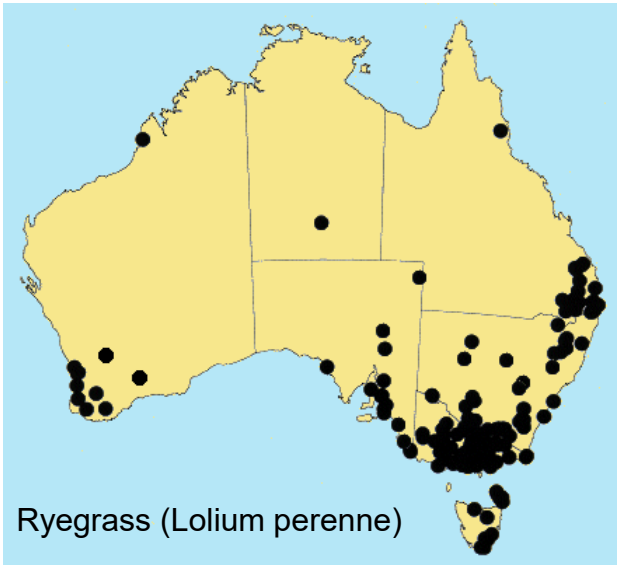
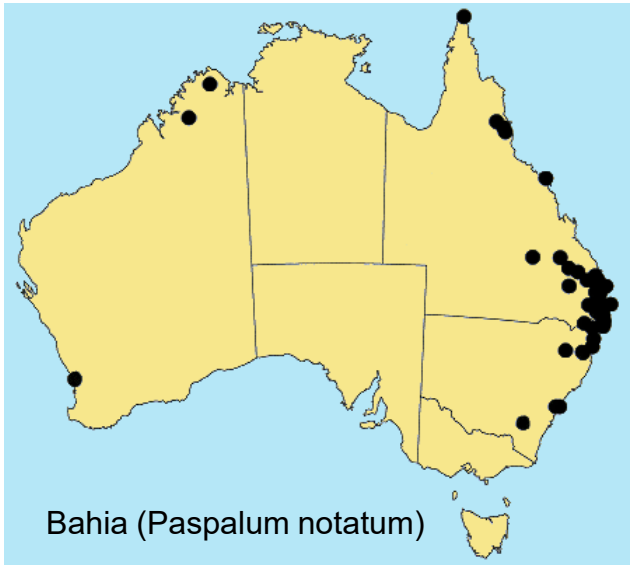
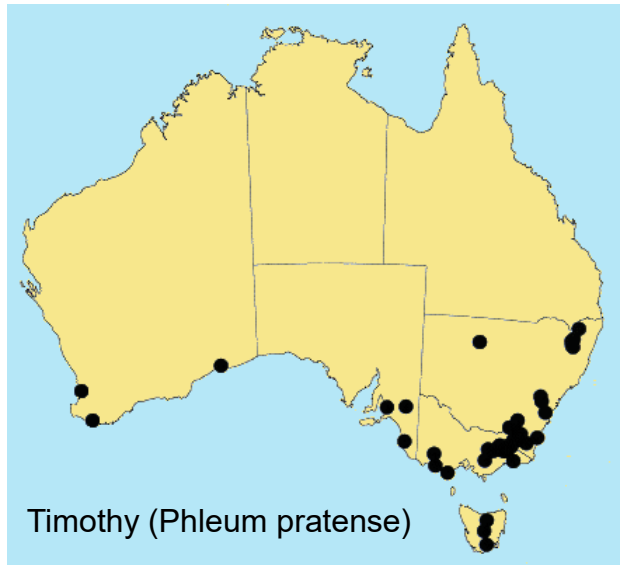
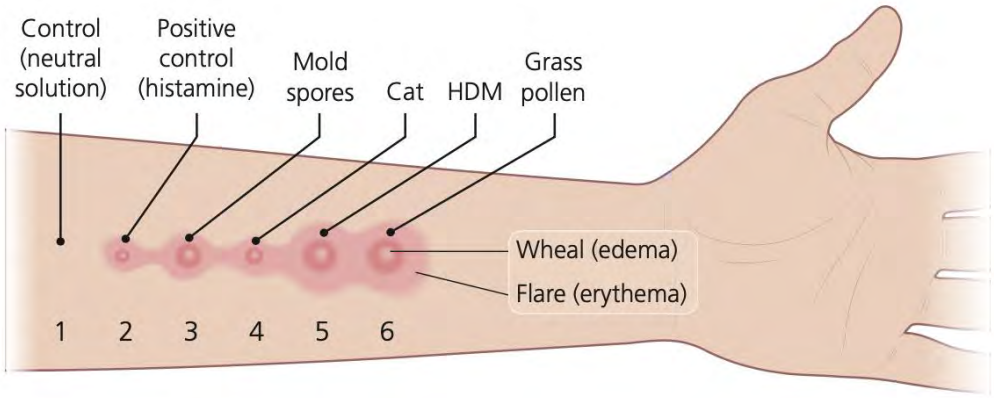
Grass maps from AusGrass







Sensitisation



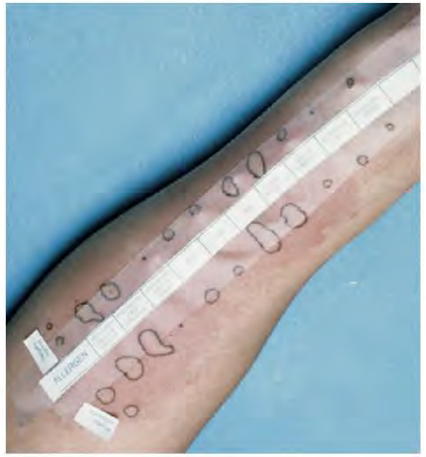
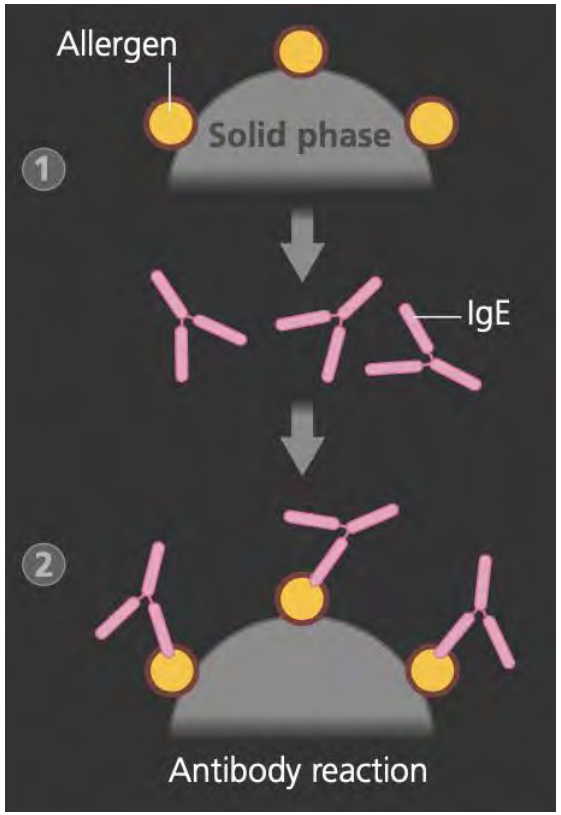
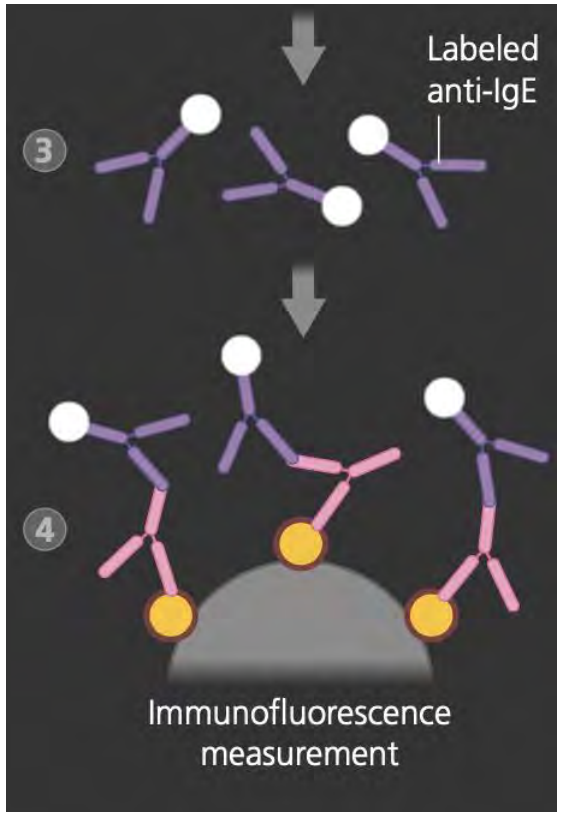


Figure 3.2 Skin prick testing.
A positive test gives a wheal-and-flare reaction. The bigger the reaction, the more severe the allergy. Patients often respond to several allergens.





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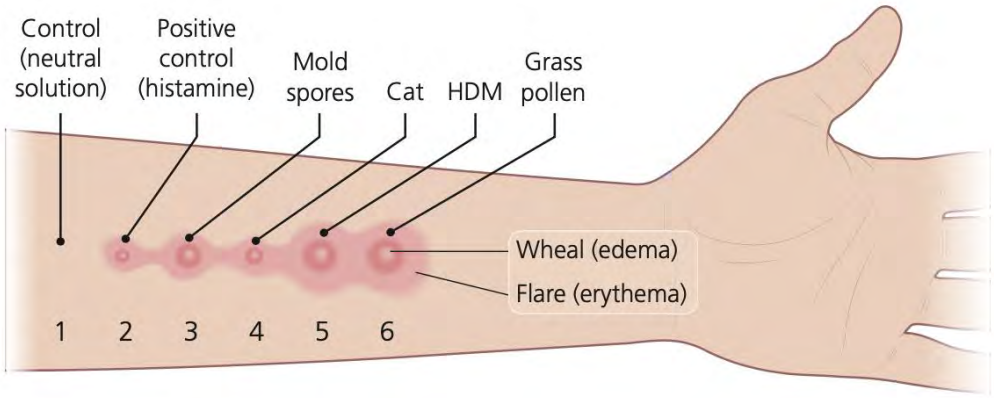

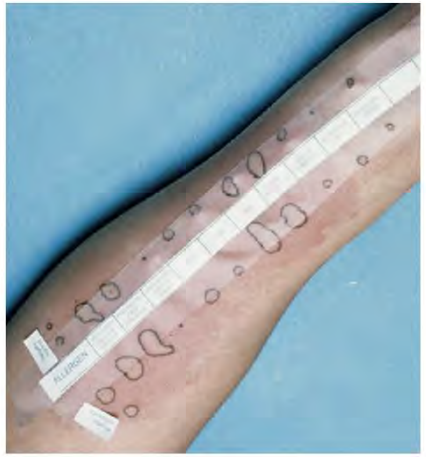

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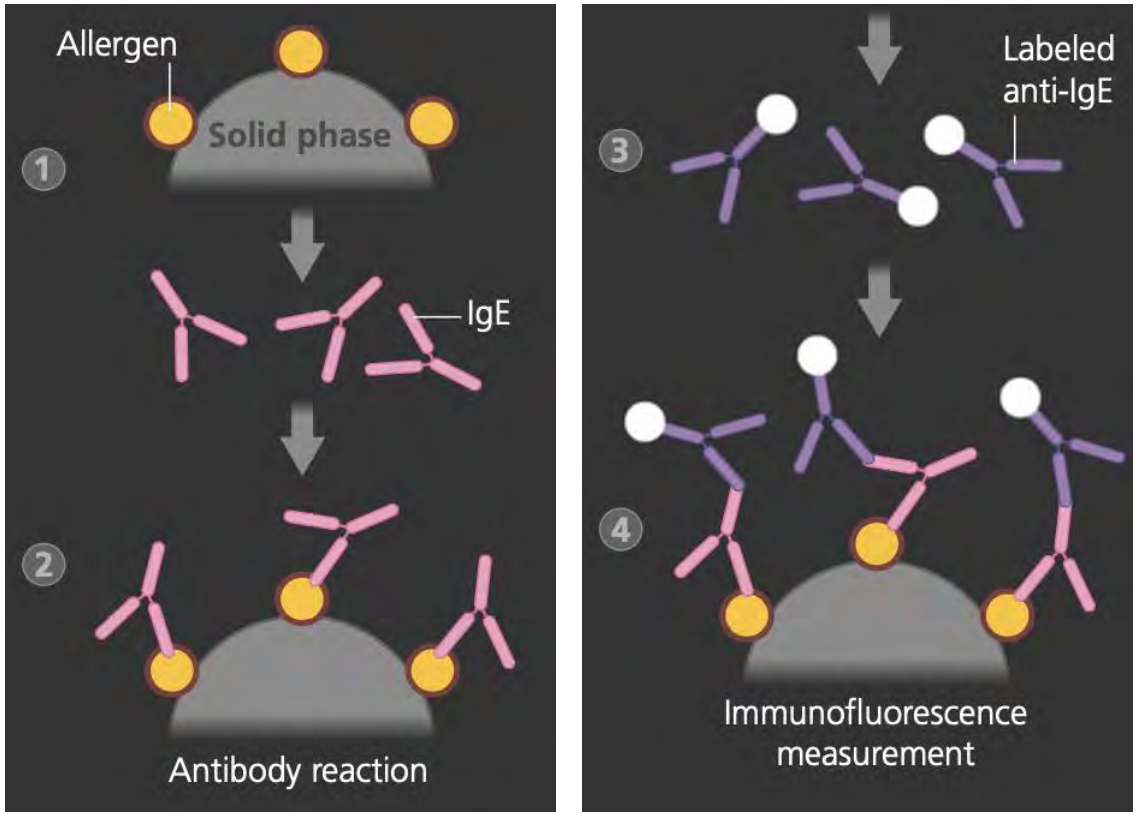

My opinion

Most relevant AR related RAST/specific IgE in SE Queensland = “HDM mix”, “grass mix” (Bahia, Bermuda, Johnson and Rye) and “animal mix”

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Diagnostics

- Combination of sensitisation and appropriate clinical symptoms

- Can have “sensitisation” without clinical disease
  - Eg smokers may have elevated IgE for unknown reasons.
  - Eg elevated IgE may be associated with normal phenotype

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When to suspect comorbid asthma?[3]

Questions to your patient

- ☐ Have you had an episode or recurrent episodes of wheezing?
- ☐ Do you have troublesome cough, especially at night/ during awakening/excercise?
- ☐ Do you cough or wheeze after exercise?
- ☐ Do you experience extended common cold/laryngitis/ bronchitis?
- ☐ Does your chest feel tight or do you feel impaired breathing out?

If **YES** to any of these question: your patient might be asthmatic.

- Comorbid asthma can be significant (to be discussed later regarding treatment options)

- Asthma treatments have own unique pathways (beyond scope of today’s talk)

- However, poor control of AR can be associated with poor control of asthma

Hellings, P. W., Scadding, G., Bachert, C., Bjermer, L., Canonica, G. W., Cardell, L. O., Carney, A. S., Constantinidis, J., Deneyer, L., Diamant, Z., Durham, S., Gevaert, P., Harvey, R., Hopkins, C., Kjeldsen, A., Klimek, L., Lund, V. J., Price, D., Rimmer, J., … Fokkens, W. J. (2020). EUFOREA treatment algorithm for allergic rhinitis. *Rhinology Journal*, *58*(6), 618–622. https://doi.org/10.4193/Rhin20.376

Case study #1

- 19yo M second year university student, grew up in Victoria and moved to Brisbane aged 13
- Lifelong perennial nasal symptoms – worse since moving to QLD
- Background mild asthma, eczema in childhood. Uses salbutamol MDI rarely
- Lives with family. Has a cat at home
- What is likely explanation? Treatment? Investigations?

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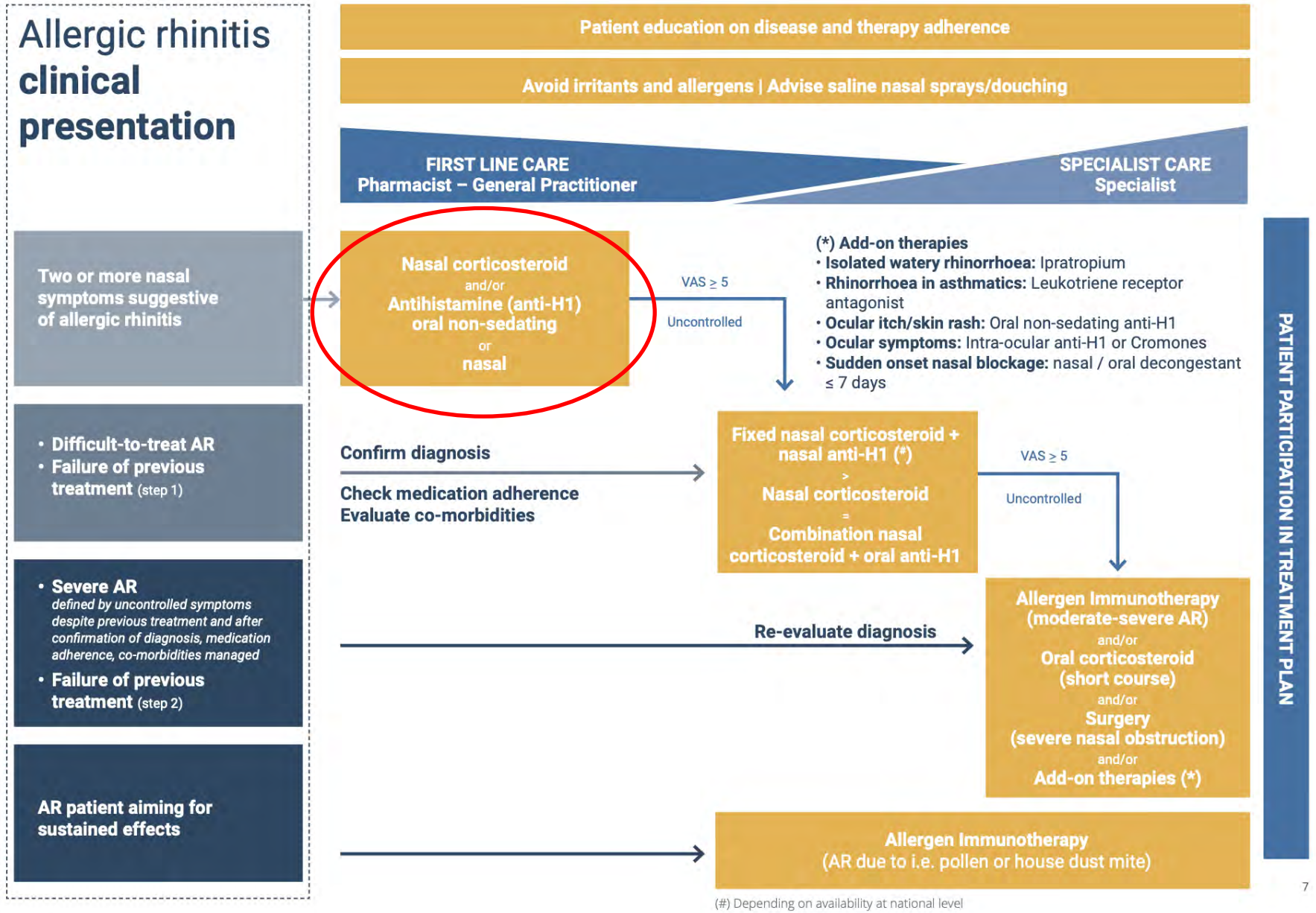
- Pattern:
  - Suspicious for house dust mite
  - ?contribution from cat?
- Testing:
  - Diagnostics of bloods or skin testing (depends on availability)
  - With RAST – useful to highlight what you want to test
  - “RAST – HDM, grass mix, cat”
- Treatment:
  - See over



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INFORMATION PAPER

Intranasal Spray Technique

nasal spray | allergic rhinitis

Download PDF

This information paper provides an overview of current evidence for optimal technique when administering intranasal sprays, which are used in the long-term management of allergic rhinitis.

https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/information-paper/intranasal-spray-technique

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Information
FOR PATIENTS, CONSUMERS AND CARERS

Allergen Minimisation

Allergies are very common in Australia and New Zealand, affecting around 20% of people at some time in their lives. Allergy is also one of the major factors associated with the cause and persistence of conditions such as allergic rhinitis, eczema and asthma. Identifying the allergen/s causing the symptoms is an essential part of treating allergic diseases.

In some cases the offending allergen may be obvious. However, in other cases your doctor will need to consider your medical history together with the results of allergy tests (skin prick tests or allergen specific IgE blood tests), which may require referral to a clinical immunology/allergy specialist.

Once the allergens are correctly identified, the following practical advice on avoiding or minimising your exposure to known allergens may help.

House dust mites are common allergens in Australia and New Zealand

House dust mites are the most common allergen source in humid areas such as coastal cities and towns. Levels of dust mite allergies are lower in drier inland areas. There is no easy way of removing house dust mites. Regardless of what advertisements may say, there is no vacuum cleaner, dust mite spray or dry cleaning that will completely eliminate dust mites.

Depending on the severity of symptoms, and in the case of childhood asthma, eczema, chronic or recurrent sinusitis, and middle ear infections with dust mite as a provoking trigger, the following advice may help.

House dust mite minimisation

The first room to tackle is the bedroom and in particular the bedding, where we spend the greatest number of consecutive hours. A combination of the following four measures is recommended:

- **Wash sheets, pillow cases and other bedding weekly in hot water (>60°C).** This will kill dust mites and wash away the allergen they produce. If you cannot wash in hot water, use a commercial product containing tea tree or eucalyptus oils, formulated to kill dust mites in cold water. If washing normally, hot tumble drying of washed items for ten minutes after they are dry, will kill dust mites. Dry cleaning is not as effective as it will kill house dust mites but won't remove the allergen they produce.
- **Cover mattress, pillow and quilt with dust mite resistant covers.** Some health funds may provide a rebate for the purchase of these items. The covers must be washed every two months. If covers are not available, wash blankets and non-encased washable doonas every three months in hot water.
- **Remove sheepskins or woolen underlays from the bed and bedroom.**
- **Remove all soft toys from the bed and bedroom.** Replace them with wooden or plastic toys which can be washed. If keeping soft toys, wash them in eucalyptus oil weekly or place in the freezer overnight). Freezing soft toys overnight kills mites but does not remove the allergen.

The following advice can apply to bedrooms as well as other rooms in the house:

- **If possible, consider replacing carpets with hard floors** such as wood, tiles, linoleum, concrete, where practical and affordable. Carpets can contain large amounts of house dust mite and animal allergens which cannot be completely removed by vacuuming.
- **Damp dust or use electrostatic cloths** to clean hard surfaces (including hard floors) weekly.
- **Vacuum carpets weekly**, note that vacuuming increases the amount of house dust mite allergen in the air for up to 20 minutes. Where possible, ask someone else to do the vacuuming and wait 20 minutes before re-entering the room. High efficiency particulate air (HEPA) filter vacuum cleaners may remove more

allergen than other vacuum cleaners, however, they still temporarily increase the amount of dust mite allergen in the air.

- **Reduce humidity** - Where possible, have a dry and well ventilated house, and adequate floor and wall insulation. Avoid using evaporative coolers (water cooled air conditioners) and unflued gas heaters, as these both release water into the air and can increase indoor dust mite and mould levels.
- **Windows** - Venetian blinds or flat blinds are easier to clean than heavy curtains. Other options include washable curtains or external shutters.
- **Consider house dust mite avoidance measures** when building a new home.
- **Consider leather or vinyl lounges instead of cloth.**

Pet dander minimisation

Exposure to pets (such as cats, dogs, guinea pigs, horses, rabbits, mice, rats), at home or work can trigger allergic reactions in some people. Cats and dogs are a major source of allergens in the home environment. The allergens come from the sweat glands in all cats and salivary glands in all dogs. Although the amount of allergen released can vary between breeds, there are no hypoallergenic animals or breeds.

As allergens are stuck to the hair and skin of pets, the allergens become airborne when the pet sheds their hair. The allergens can remain airborne for some time. Cat allergen is especially difficult to remove from homes. It can remain in the house for months after the cat has been removed. Cat allergen can also be found in places where cats have never lived. For example, it can be carried around on clothing to schools and offices.

The most effective method of allergen avoidance for people who are allergic to pets is removal of the pets from the home. For example, if there is no doubt that cat or other animal allergen is a major cause of symptoms then the best advice is for the animal to be removed from the home. It can be an emotional decision, but removing the pet should be considered.

If pets cause only minor problems, keeping pets out of bedrooms and living areas may be a compromise. Even then, it may take months after pet removal before allergen levels are reduced. The effectiveness of some measures such as washing animals frequently and using HEPA air filters remains uncertain.

Dogs, guinea pigs, mice and rabbits are not as allergenic as cats, and are more easily kept outside, but can still cause annoying and occasionally serious problems. Horse allergy is very serious and even animal hair on clothes may be sufficient to trigger asthma. Great care must be taken to shower and change clothes before returning to a home of a person allergic to horses. Birds may occasionally cause allergic symptoms. This is a different problem to pigeon fancier's lung which is a serious condition and requires complete avoidance.

Mould minimisation

Mould in the home can show as mould, mildew or a musty smell. It is commonly found in bathrooms, refrigerators and in places with little air circulation such as walk-in and built-in wardrobes, and in bedrooms with ensuite bathrooms.

If you are allergic to mould, you may consider:

- Removing visible mould by cleaning with bleach or other mould reduction cleaners.
- Ensuring adequate natural ventilation, including the use of extractor fans.
- Sealing leaks in bathrooms and roofs.
- Clearing overflowing gutters and blocked under floor vents.
- Removing indoor pot plants (which promote mould growth).
- Drying or removing wet carpets.
- Avoiding working with garden compost, mulch or mowing lawns.

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Information
FOR PATIENTS, CONSUMERS AND CARERS

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TREATMENT PLAN FOR Allergic Rhinitis (Hay Fever)

Patient name: _____ Date: / /

Plan prepared by: _____ Signed: _____

ALLERGEN MINIMISATION

☐ Minimising exposure to confirmed allergen/s may assist to reduce symptoms in some people.
For information go to www.allergy.org.au/patients/allergy-treatments/allergen-minimisation

THUNDERSTORM ASTHMA

☐ Try to stay indoors just before, during and just after thunderstorms in pollen seasons if allergic to pollen.
Use preventer treatments such as intranasal corticosteroid sprays or combined intranasal corticosteroid/antihistamine sprays. Consider allergen immunotherapy (see below). If you also have asthma, use asthma preventers regularly.
For information go to www.allergy.org.au/patients/asthma-and-allergy/thunderstorm-asthma

MEDICATIONS

☐ Intranasal corticosteroid spray: _____
☐ 1 or ☐ 2 times/day/nostril for _____ weeks or _____ months or ☐ continuous
☐ Additional instructions: _____
or
☐ Combined intranasal corticosteroid/antihistamine spray:
☐ 1 or ☐ 2 times/day/nostril for _____ weeks or _____ months or ☐ continuous
☐ Additional instructions: _____

Note:
- It is important to use these sprays correctly. See instructions below and directions for use.
- Onset of benefit may take days, so these sprays must be used regularly and should not be stopped every few weeks.
- If significant pain or bleeding occurs contact your doctor.
- Some treatments mentioned above require a prescription.

1. Prime the spray device according to manufacturer's instructions (for the first time or after a period of non-use).
2. Shake the bottle before each use.
3. Blow nose before spraying if blocked by mucus.
4. Tilt head slightly forward and gently insert nozzle into nostril.
5. Aim the nozzle away from the middle of the nose (septum) and direct nozzle into the nasal passage (not towards tip of nose, but in line with the roof of the mouth).
6. Avoid sniffing hard during or after spraying.

☐ Oral non-sedating antihistamine tablet: _____ Dose _____ mL/mg ☐ 1 or ☐ 2 times/day
☐ Additional instructions: _____
☐ Intranasal antihistamine sprays: _____ ☐ 1 or ☐ 2 times/day
☐ Additional instructions: _____
☐ Saline nasal ☐ spray or ☐ irrigation _____ ☐ _____ times/day or ☐ as needed
☐ Use 10 minutes prior if used with intranasal corticosteroid spray
☐ Decongestant: _____ ☐ nasal spray _____ times/day or ☐ tablet
Dose _____ tablets _____ times/day for up to three days (not more than one course/month)
☐ Eye drops or ointments: _____
☐ Other medications: _____

For information and links to animation videos go to www.allergy.org.au/patients/allergic-rhinitis-hay-fever-and-sinusitis

ALLERGEN IMMUNOTHERAPY

If allergen immunotherapy has been initiated by a clinical immunology/allergy specialist, it is important to follow the treatment as prescribed. Contact your doctor if you have any questions or concerns. For information go to www.allergy.org.au/patients/allergy-treatments/immunotherapy

ascia
www.allergy.org.au

Information
FOR PATIENTS, CONSUMERS AND CARERS

Allergic Rhinitis (Hay Fever)

Allergic rhinitis (commonly known as hay fever), affects around 18% of people (children and adults), in Australia and New Zealand. Despite its common name, allergic rhinitis is not caused by hay, and does not result in fever. It is caused by the nose and/or eyes being in contact with environmental allergens, such as pollens, dust mite, moulds and animal dander. People who are sensitive to these allergens may then experience one or more of the following:

Immediate signs or symptoms:

- Runny nose.
- Itchy nose.
- Sneezing.
- Itchy, watery eyes.

Obstructive signs or symptoms:

- Congested nose.
- Snoring.

Some of these symptoms may be similar to those caused by infections (such as colds and flu). However, allergy symptoms tend to persist, unless they are treated correctly.

Symptoms range from mild to moderate (does not affect day to day function), to severe (affects day to day function). They may occur in a particular season (usually due to allergies to grass, weed or tree pollens), or be persistent and present all year round (usually caused by allergies to house dust mites, moulds or animal dander). It is important to note that allergic rhinitis is not caused by a food allergy.

Complications of allergic rhinitis may include:

- Sleep disturbance.
- Daytime tiredness.
- Headaches.
- Poor concentration.
- Recurrent ear infections in children.
- Recurrent sinus infections in adults.
- Asthma which is more difficult to control.

Some people with allergic rhinitis also have asthma. Better control of allergic rhinitis has been shown to result in better asthma control in both adults and children. Untreated allergic rhinitis may also increase the risk of developing asthma.

Allergy testing

If you have allergic rhinitis that affects your day-to-day function, discuss treatment options with your doctor. A referral to a clinical immunology/allergy specialist may be required for allergy testing.

Treatment options – Aeroallergen minimisation

If the allergen/s causing the allergic rhinitis is confirmed, minimising exposure to the allergen/s may reduce symptoms.

they are effective and have few side effects. It is important to use
at can cause problems such as frequent decongestant (unblocking)

about the following medications:

ranasal sprays and eye drops (non-sedating), help to reduce
ting eyes). They are not as effective in controlling severe nasal
e of antihistamines is their flexibility, as you can take them when
when you are well. Antihistamine eye drops can be helpful in
gies.

rays (INCS) have a potent action on inflammation when used
dications). These need to be used regularly and with careful
e used. Different brands of INCS vary in strength and effectiveness,
nd check details with your pharmacist or doctor.

ning an antihistamine and intranasal corticosteroid nasal spray
d advantages of both medications.

dry the nose, but should not be used for more than a few days as
in the nose.

dry the nose, but should be used with caution. They can
ors, trouble sleeping, anxiety or an increase in blood
essure should not take decongestant tablets.

sprays or douches can also be effective in relieving symptoms.

rapy

n as desensitisation, and it reduces the severity of symptoms
T involves the administration of regular, gradually increasing
, by injections or by sublingual tablets, sprays or drops (under the

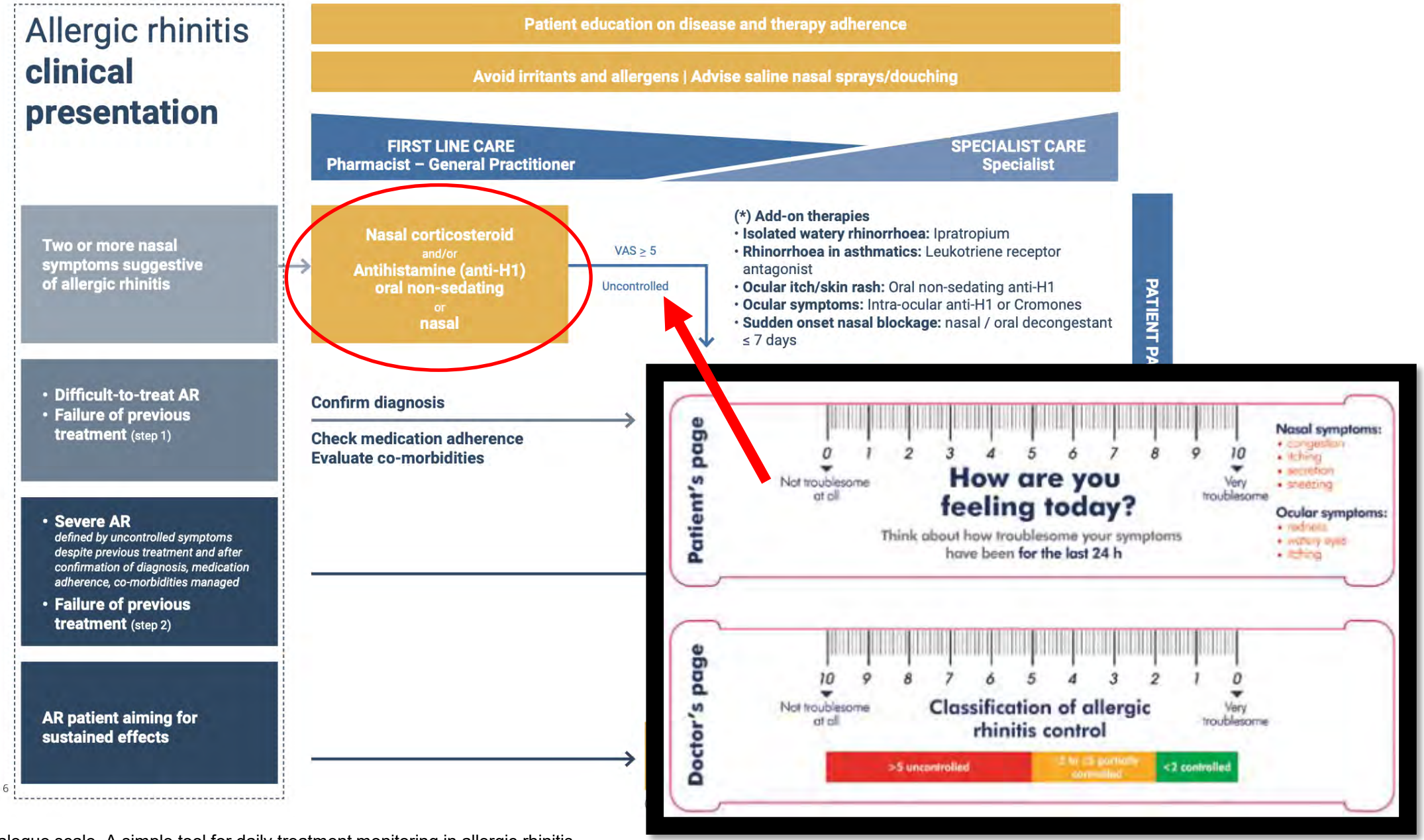
nd is typically offered for people older than five years of age with
reatment that should be initiated by a clinical immunology/allergy

ASCIA is the peak professional body of clinical immunology/allergy specialists in Australia and New Zealand.

ASCIA resources are based on published literature and expert review, however, they are not intended to replace medical advice. The content of ASCIA resources is not influenced by any commercial organisations.

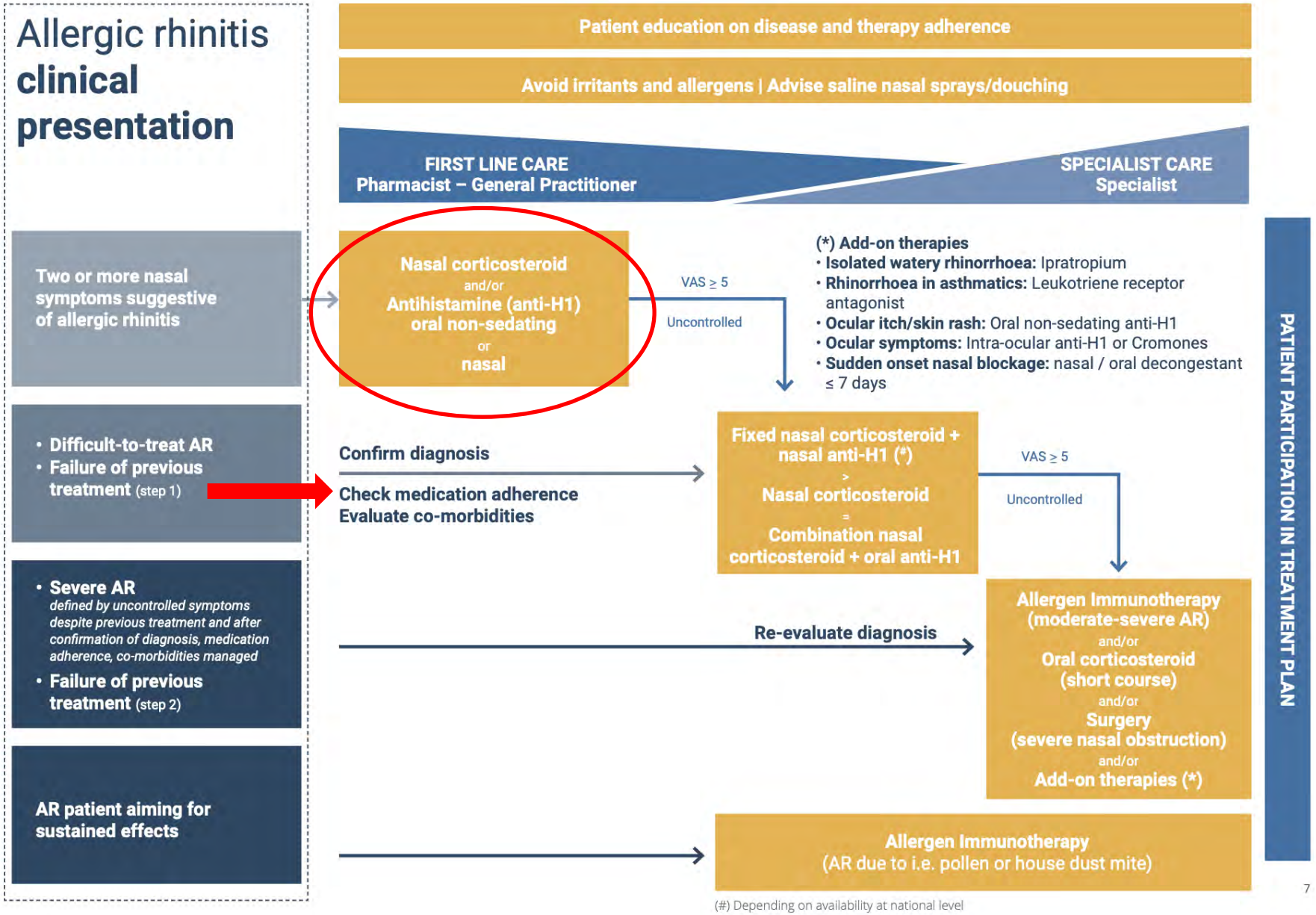
For more information go to www.allergy.org.au

To donate to immunology/allergy research go to www.allergyimmunology.org.au



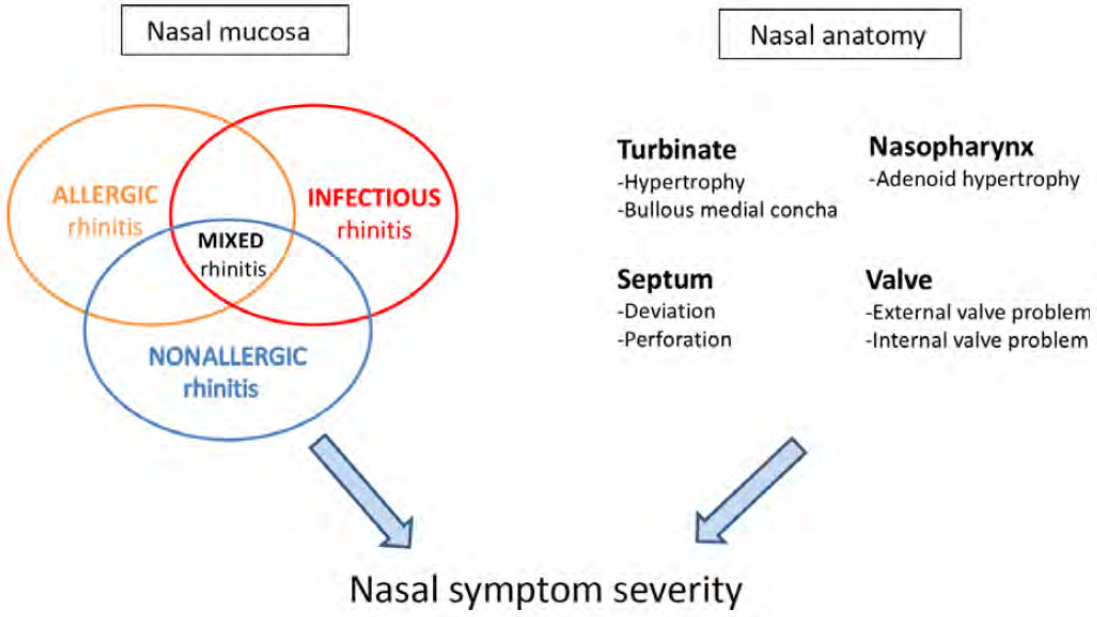
Sybilski, A. J. (2018). Visual analogue scale. A simple tool for daily treatment monitoring in allergic rhinitis. *Pediatria i Medycyna Rodzinna*, *14*(3), 277–281. https://doi.org/10.15557/PiMR.2018.0030

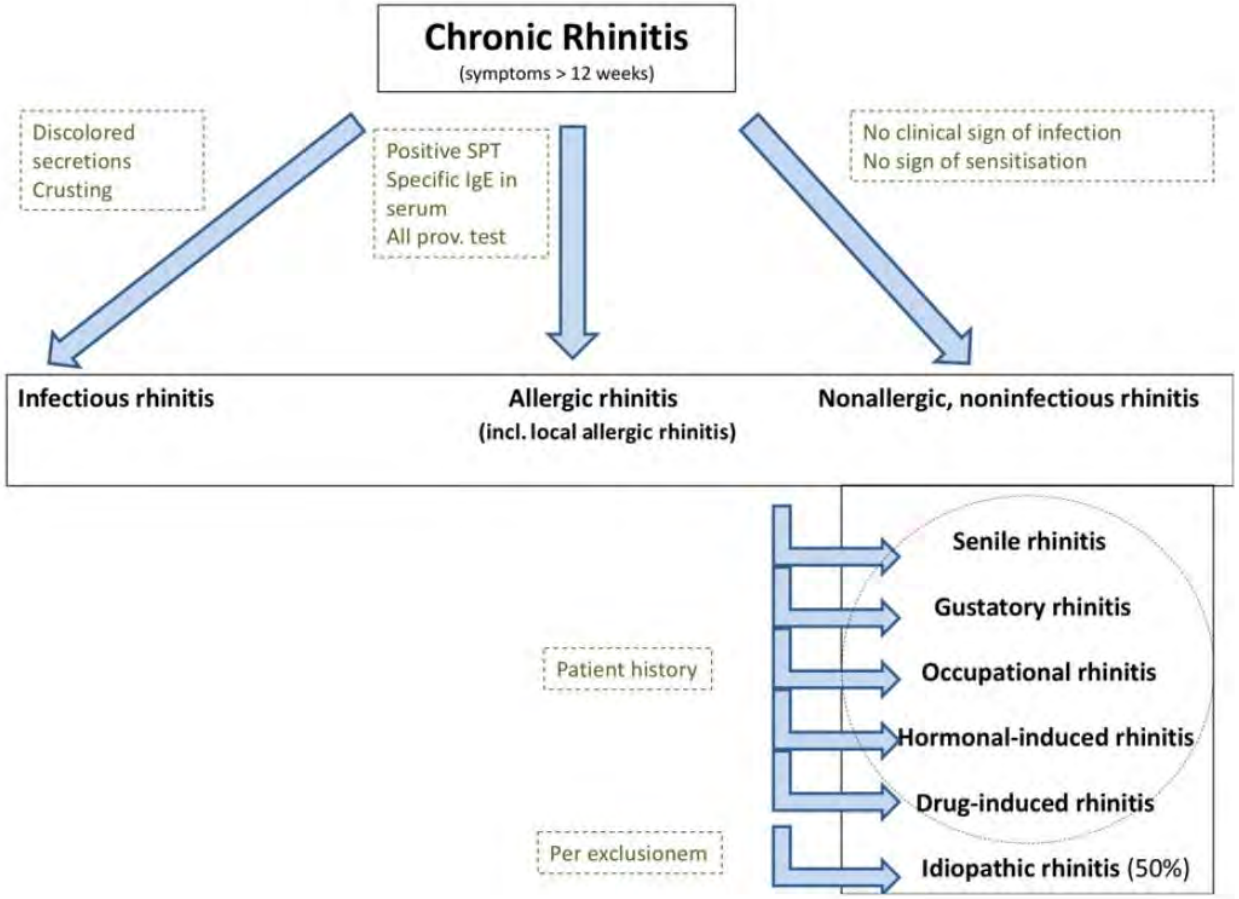
Allergic rhinitis **clinical presentation**



(#) Depending on availability at national level

Other forms of rhinitis



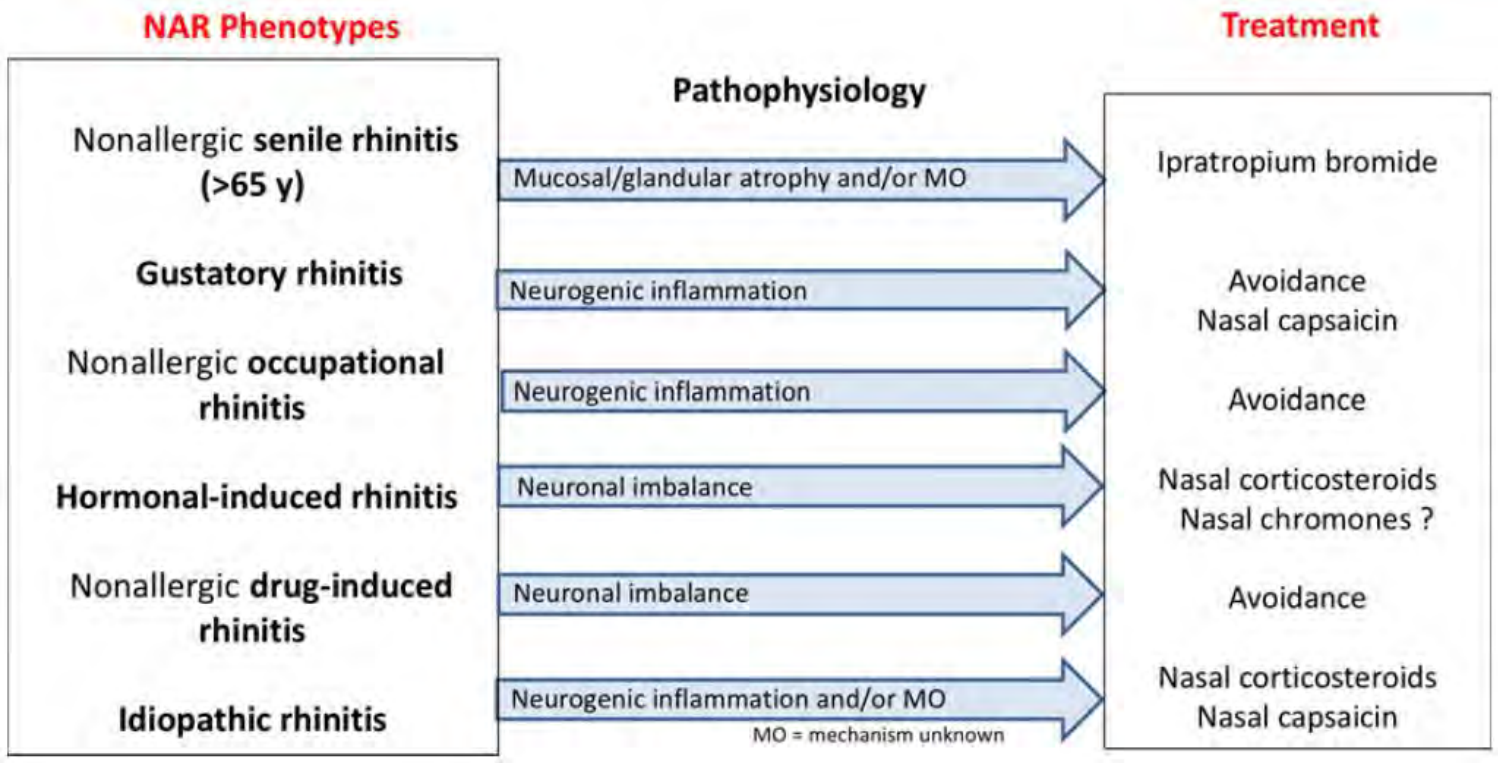


Hellings, P. W.et al (2017). Non-allergic rhinitis: Position paper of the European Academy of Allergy and Clinical Immunology. *Allergy*, *72*(11), 1657–1665. https://doi.org/10.1111/all.13200

Major causes of rhinitis

Allergic rhinitis
Seasonal
Perennial
Nonallergic rhinitis
Vasomotor
Gustatory
Nonallergic rhinitis with eosinophilia syndrome
Mixed rhinitis
CPAP-associated rhinitis
Occupational rhinitis
Rhinitis medicamentosa
Nasal decongestant sprays
Intranasal cocaine
Systemic medication-induced rhinitis
Oral contraceptives
Erectile dysfunction drugs
Some antihypertensives
Aspirin and other NSAIDs (more prevalent among patients with asthma and/or chronic rhinosinusitis with nasal polyposis)
Some antidepressants
Some benzodiazepines
Pregnancy
Atrophic rhinitis
Systemic diseases
Hypothyroidism
Granulomatosis with polyangiitis
Midline granuloma
Sarcoidosis
Cystic fibrosis
Immotile cilia syndromes

CPAP: continuous positive airway pressure; NSAIDs: nonsteroidal antiinflammatory drugs.



Hellings, P. W.et al (2017). Non-allergic rhinitis: Position paper of the European Academy of Allergy and Clinical Immunology. *Allergy*, *72*(11), 1657–1665. https://doi.org/10.1111/all.13200

Other important differentials to consider

Differentials to consider	Key features
Other forms of chronic rhinitis	See previous
Chronic rhinosinusitis/polyposis	Anosmia, facial pressure/pain, muco-purulent discharge
Granulomatous diseases (sarcoid, GPA, EGPA)	External nasal swelling, sinusitis, nose bleeds, septal perforation, collapse of nasal bridge, multi-system involvement
Idiopathic/vasomotor rhinitis	Sudden onset and offset of watery nasal discharge Can be triggered by strong smells or changes in environmental temperature

https://www.allergy.org.au/images/stories/pospapers/ar/ASCIA_HP_Allergic_Rhinitis_2022.pdf

Case - continued

- 19yo M second year university student, grew up in Victoria and moved to Brisbane aged 13
- Lifelong perennial nasal symptoms – worse since moving to QLD
- Background mild asthma, eczema in childhood. Uses salbutamol MDI rarely
- Lives with family. Has a cat at home
- Skin prick testing:
  - ***Dermatophagoides pternonyssinus*** **10mm, pseudopods**
  - ***Dermatophagoides farinae*** **9mm**
  - Bermuda grass 2mm
  - Bahia grass 2mm
  - Johnson grass 2mm
  - Rye grass 3mm
  - **Cat 5mm**
  - Dog 2mm
  - Mould mix 0mm

Case - continued

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- Seen in clinic, discussed allergen minimisation. Commenced daily intranasal corticosteroid and non-sedating antihistamine
- Reviewed 3 months later – symptoms still troubling, resulting in poor sleep and attendance at university.

Case 2

- 19yo M second year university student, grew up in Victoria and moved to Brisbane aged 13
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- Seen in clinic, discussed allergen minimisation. Commenced daily intranasal corticosteroid and non-sedating antihistamine
- Reviewed 3 months later – symptoms still troubling, resulting in poor sleep and attendance at university.

Should we desensitise? What product and allergen should we use?

What is desensitisation/immunotherapy

- Controlled course of allergen exposure leading to modification of the immune response away from the aberrant/inappropriate response to environmental allergen
- Several products available, only venom immunotherapy is medicare funded (NB venom immunotherapy will not be further covered in this talk)
  - Subcutaneous immunotherapy – build up phase followed by monthly injections
    - Aqueous
    - Alum-conjugated
    - Allergoids
  - Sublingual
    - Drops
    - Orally disintegrating tablets
  - Cost varies by product - $850 - $1200 per annum – 3 year course

Efficacy

- 80-90% of patients report good outcomes
- Decreased symptom burden
- Less reliance on medications

- Immunotherapy is not a 'cure' - most patients will still require medications at particular times
- A reasonable expectation is to become a 'normal' person with allergic rhinitis – i.e PRN antihistamines only

Who to consider for allergen immunotherapy for allergic rhinitis

TABLE 1 General considerations for allergen immunotherapy (AIT) for allergic rhino

General indications	Key references
AIT should be considered when all of these criteria are met: • Symptoms strongly suggestive of AR, with or without conjunctivitis • There is evidence of IgE sensitization (positive SPT and/or serum-specific IgE) to one or more clinically relevant allergen • Experience moderate-to-severe symptoms which interfere with usual daily activities or sleep despite regular and appropriate pharmacotherapy and/or avoidance strategies	Dhami[14]
AIT may also be considered in less severe AR where a patient wishes to take advantage of its long-term effect on AR and potential to prevent asthma with grass pollen AIT	Kristiansen[25] Halken[23]
Standardized AIT products with evidence of efficacy in the clinical documentation should be used	Dhami[14]

EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis 2017

Contraindications to immunotherapy

TABLE 2 General contraindications for allergen immunotherapy (AIT) for allergic rhinoconjunctivitis

	Key references	Contextual considerations
The following are considered to be contraindications:		
Uncontrolled or severe asthma	Bernstein[31], Bousquet[29], Calderon[34], Cox[28], CSM 1986[32], Lockey[30], Normansell[33], Pfaar[11]; Pitsios[27]	Weak evidence of risk with uncontrolled asthma, active systemic autoimmune disease, and malignancy from case reports or case series of adverse events with AIT. Taskforce considered that these were contraindications to AIT. Though initiation of AIT is contraindicated during pregnancy, an ongoing AIT is permissible when having been well tolerated by the patient in the past
Active, systemic autoimmune disorders (unresponsive to treatment)	Cabrera[35], Fiorillo[37], Pfaar[11], Sánchez-Morillas[36]; Pitsios[27]	
Active malignant neoplasia	Larenas-Linnemann[39], Pfaar[11]; Wöhrl[38]	
AIT initiation during pregnancy	Metzger[40], Pfaar[11]	
With the following, AIT should only be used with caution when benefits outweigh potential risks in an individual patient:		
Partially controlled asthma	Virchow[41]	One trial with SLIT tablet[41] included some subjects with partially controlled asthma without compromising safety; it is important that confirmatory evidence is acquired.
Beta-blocker therapy (local or systemic)	Cleaveland[44], Hiatt[42], Lang[45]; Pfaar[11]	Weak evidence of risk. May compromise a patient's ability to tolerate an episode of anaphylaxis. This must be considered when deciding whether AIT is appropriate.
Severe cardiovascular diseases, for example, coronary artery disease	Larenas-Linnemann[39]; Linneberg[46]	
Systemic autoimmune disorders in remission or organ specific	Larenas-Linnemann[39], Pitsios[27]	Weak evidence of risk from case reports, case series of adverse events with AIT or expert opinion based on clinical experience. Taskforce considered that careful consideration on a case-by-case basis with discussion between patient and the treating physician is required before deciding whether or not to commence AIT.
Severe psychiatric disorders	Pitsios[27]	
Poor adherence	Pitsios[27]; Pfaar[11]	
Primary and secondary Immunodeficiencies	Larenas-Linnemann[39]; Pitsios[27]	
History of serious systemic reactions to AIT	Calderon[34]; Pfaar 2014[11]	

Most studies exclude >65

EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis 2017

Other considerations

- Adverse effects
  - Non-sedating antihistamine should be taken prior to every injection to minimise adverse effects
  - Large local reaction at injection site is likely to occur
  - Temporary worsening of AR symptoms
  - Exacerbation of asthma symptoms or asthma attack. Do not proceed with injection in a patient with an exacerbation of asthma
  - Anaphylaxis is a rare but possible outcome.

- Patient selection
  - Appropriate patient selection results in the best outcome and the lowest chance of adverse effects
  - Risk factors for poor efficacy;
    - Polysensitisation (particularly to danders when the patient has a pet)
    - Poor compliance (particularly with SLIT)
    - Incorrect diagnosis i.e the patient doesn't actually have allergic rhinitis
    - Co-existent non-allergic rhinitis or CRSwNP

Allergen selection

- The bulk of evidence is for single allergen immunotherapy with house dust mite or grass pollen
- Choose the dominant allergen on the basis of symptoms (perennial (HDM) or seasonal (grass pollen) and skin prick testing results
- Limited evidence for allergen mixes however prescribed commonly
- Beware mixing non-taxonomically related allergens. HDM has enzymatic activity and may break down mixed allergens (not applicable to allergoids)

- Danders;
  - Cat – limited high quality evidence, mixed results
  - Dog – even less evidence than cat
  - Others e.g horse, rat. Extremely limited evidence and can be difficult to source.
  - May be considered in select clinical situations.

- Moulds
  - Diagnostic testing is poorly standardised
  - Extracts/products are of variable quality and deteriorate due to proteolysis
  - Very limited evidence of efficacy

Dhami et al Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis. Allergy. 2017;72:1825–1848.
Coop CA Clin Rev Allerg Immunol (2014)47:289-298

Shared care administration of allergen immunotherapy

ascia
australasian society of clinical immunology and allergy
www.allergy.org.au

TREATMENT PLAN FOR Subcutaneous Allergen Immunotherapy (SCIT)

TO BE COMPLETED BY CLINICAL IMMUNOLOGY/ALLERGY SPECIALIST

Patient name: _____ Date: _____

Date of birth: _____

Referring specialist name: _____ Signature: _____

Contact phone number of referring specialist: _____

Allergen(s): _____ _____ _____ _____

Projected duration of immunotherapy (years): _____ Planned completion date: _____

DOSING SCHEDULE (specialist to attach to this document)

REQUIREMENTS FOR ADMINISTERING SCIT

- Staff to monitor the patient for _____ minutes after injection *(minimum of 30 minutes).*
- 1:1000 adrenaline ampoules, 23G needles, 1mL syringes or adrenaline autoinjector for intramuscular administration of adrenaline.
- Needles for subcutaneous administration of allergen - suggest insulin syringes or 26/27G needles and 1mL syringes.
- Other equipment (IV cannula, IV 0.9% saline, oxygen, sphygmomanometer).
- Equipment to maintain an airway appropriate for supervising doctor's expertise and skill.
- Oral non-sedating antihistamines and oral corticosteroids.

A medical practitioner must be on-site during the administration and entire waiting period.

PATIENT CHECKLIST

- Check patient has been attending on schedule and whether the patient had any reaction following the last injection.
- Check patient and defer injection if:
  - Systemically unwell and/or febrile (>38 °C).
  - Asthma symptoms and/or peak flow _____ L/min (<80% best) prior to injection.
- Do not give injection and contact specialist if:
  - Patient now pregnant and not yet stable on maintenance therapy.
  - Patient commenced on B-blockers (including topical) since treatment initiation.
  - Anaphylaxis with most recent immunotherapy injection.
- Ensure recent weight (kg) available to calculate adrenaline dose in case patient has anaphylaxis.
- Double check (doctor/nurse and patient/guardian) correct allergen, concentration, dose and expiry date.

Missed doses

RECOMMENDED ACTIONS

- **If at any stage you are uncertain about what dose to administer, always call a specialist for advice.**
- **For missed doses during the build-up phase of immunotherapy, the treating specialist should generally be contacted, unless specific advice regarding this has been provided.**

Missed doses during build-up phase (> 14 days since last injection):

Missed 1 dose	☐	Repeat previous dose*	OR ☐	_____
Missed 2 doses	☐	Reduce by one dose*	OR ☐	_____
Missed 3 doses	☐	Go back 2 doses*	OR ☐	_____
Missed 4 doses	☐	Call specialist to discuss		

*Once dose is given, the next dose should be as per the dosing schedule provided by the specialist.

If < 14 days since last injection, give next dose as per schedule.

Missed doses during maintenance phase - select Option A or B::

☐ **OPTION A**

- If less than 6 weeks since last dose and all other criteria meet, administer the usual maintenance dose.
- If more than 6 weeks since the last injection call supervising specialist for advice.

☐ **OPTION B**

- If less than 6 weeks since last dose and all other criteria meet, administer the usual maintenance dose.
- If 6 - 12 weeks since last dose give _____mL (or 2 missed doses)*
- If 12 - 16 weeks since last dose give _____ mL (or 3 missed doses)*
- If more than 16 weeks (4 months since last dose), do not administer. Call specialist to discuss.

* Recommend calling specialist for advice regarding timing and volume of subsequent dosing.

New vial (maintenance dose).

☐ No reduction in dose.

☐ Reduce first injection by_____% and then continue with regular maintenance dose if tolerated.

Large local reaction (> 10 cm).**

☐ No reduction and continue with next scheduled dose.

☐ Repeat same dose at next visit (during up-dosing) and continue with next scheduled dose.

☐ Reduce next injection by_____% and then continue with next scheduled dose.

**If ongoing or repeated problems, contact specialist.

Additional instructions: _____

Subcutaneous vs sublingual immunotherapy

	SCIT	SLIT
Efficacy	Evidence in HDM better	Grass pollen efficacy equal to SCIT HDM tablets equal to SCIT
Safety	More likely systemic reactions or asthma exacerbation	Systemic reactions less likely Local reactions and GI upset can be an issue EoE possible No injections – better for children
Compliance	Requires patient attend a medical practice monthly for injections	Daily dose required Should be separated from food or brushing teeth by 30 minutes
Cost	~$300/per annum cheaper than SLIT	More expensive than SCIT, particularly orally disintegrating tablets
Duration	3 years	3 years

Adapted from: ASCIA AIT Guide (allergy.org.au)

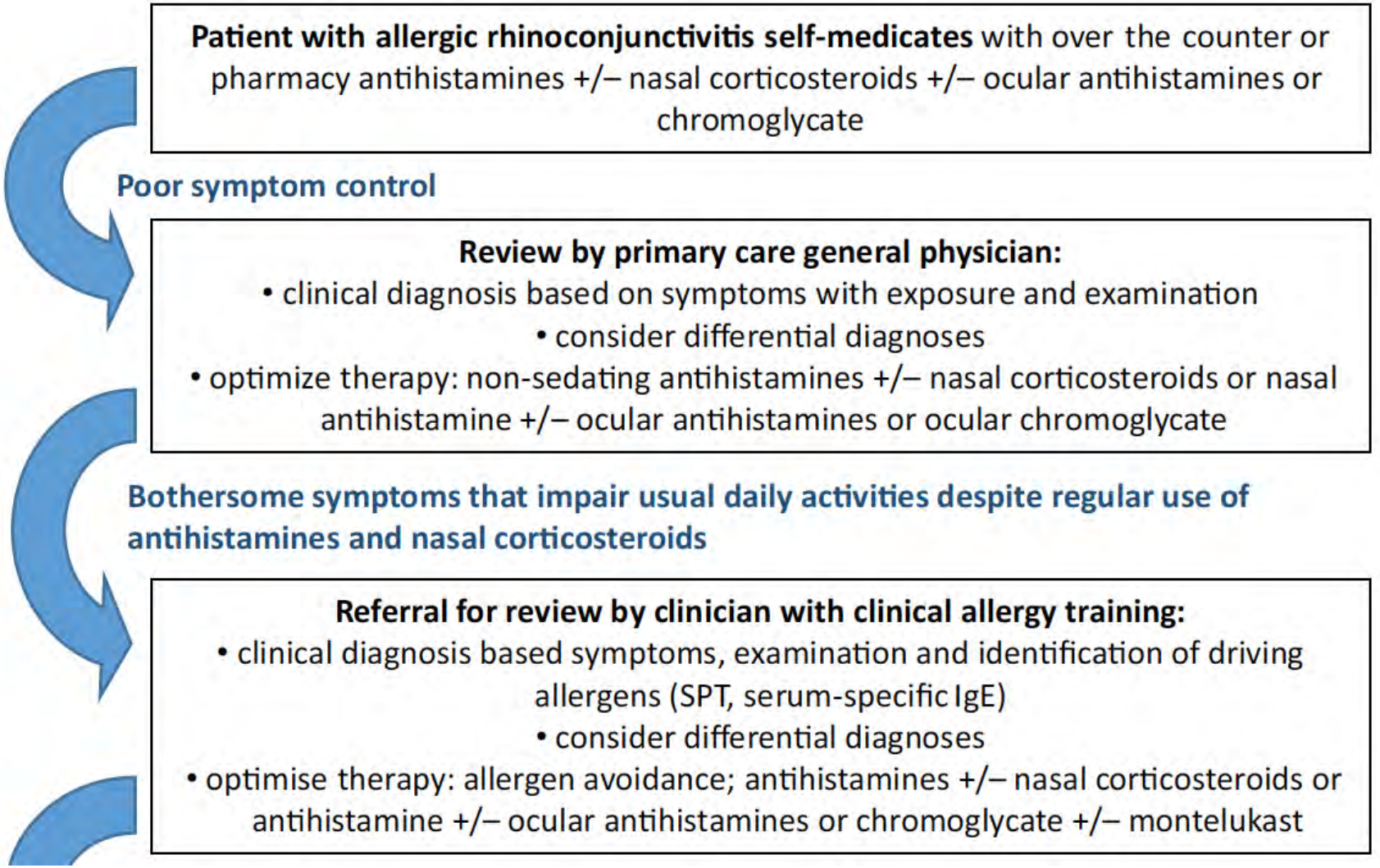
Duration/durability

- Most studies are 1-2 years in duration
- Limited studies demonstrate efficacy for 2 years following 2-3 years of HDM/grass immunotherapy

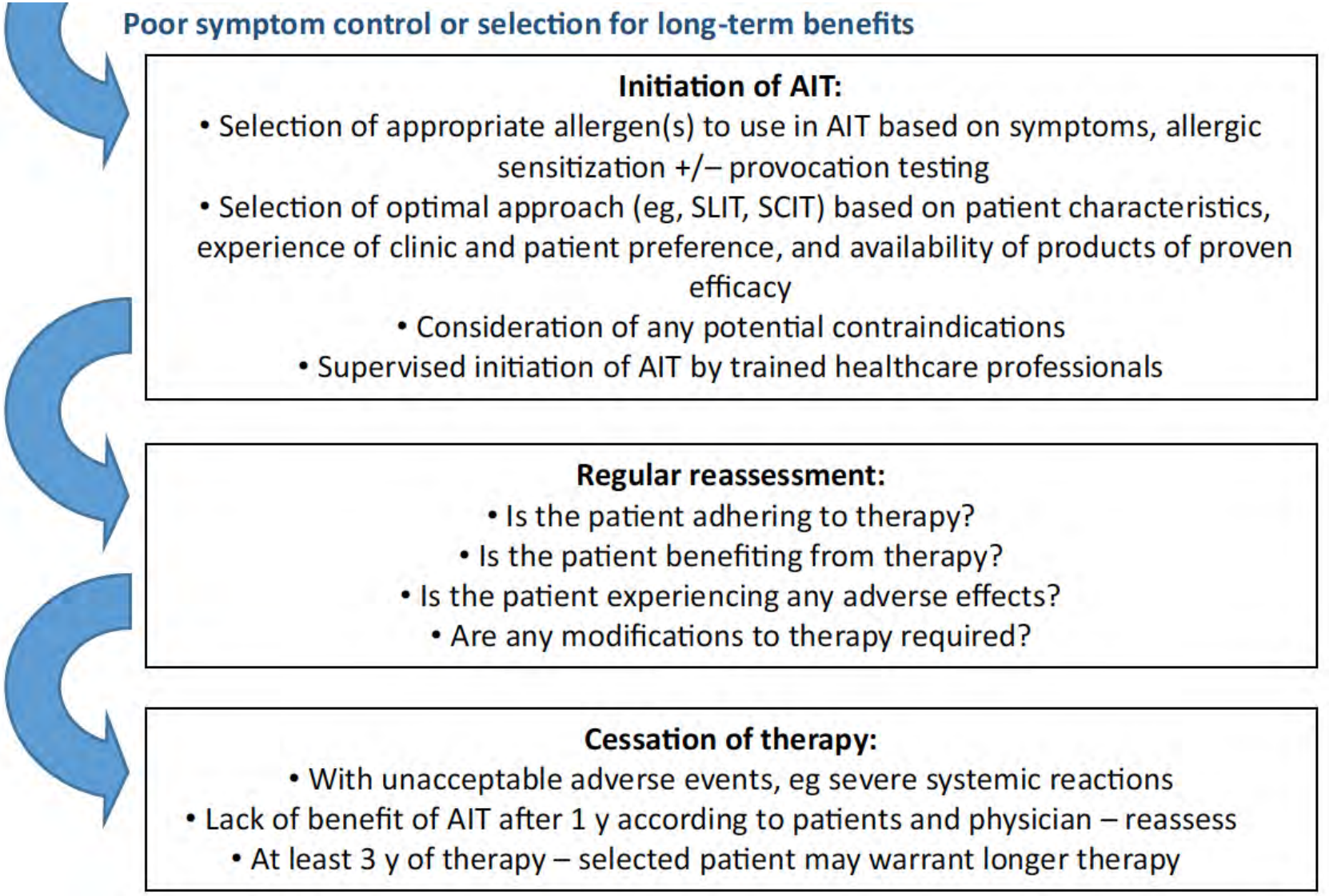
- Up to 12 months for onset of maximal efficacy – most patients begin to notice a subtle improvement at 6 months
- Guidelines recommend minimum of three years
- Or – there is no evidence to continue beyond 3 years

- Generally we tell patients to expect 5-7 years of durability but in reality this is non-evidence based. Results may vary.
- Patients <30 years of age likely to require another course later in life

EAACI flowchart



EAACI flowchart



What about conditions other than allergic rhinitis?

- Asthma:
  - Consider as add-on therapy for asthma that is not controlled by standard therapy, particularly if HDM sensitised.
  - Modestly increased risk of systemic and local adverse effects.

- Atopic dermatitis
  - Conflicting evidence
  - May have positive effects in selected highly sensitised patients
  - May be considered as add-on therapy in patients who have failed other treatments

- Allergic conjunctivitis
  - Most patients have co-existent allergic rhinitis
  - There is limited/no evidence for treating isolated allergic conjunctivitis with allergen immunotherapy

Dhami et al., Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis Allergy. 2017;72:1825–1848.
European Consensus Guidelines for Management of Atopic Eczema (Part 2) 2018

CRSwNP salvage therapy - "biologics"

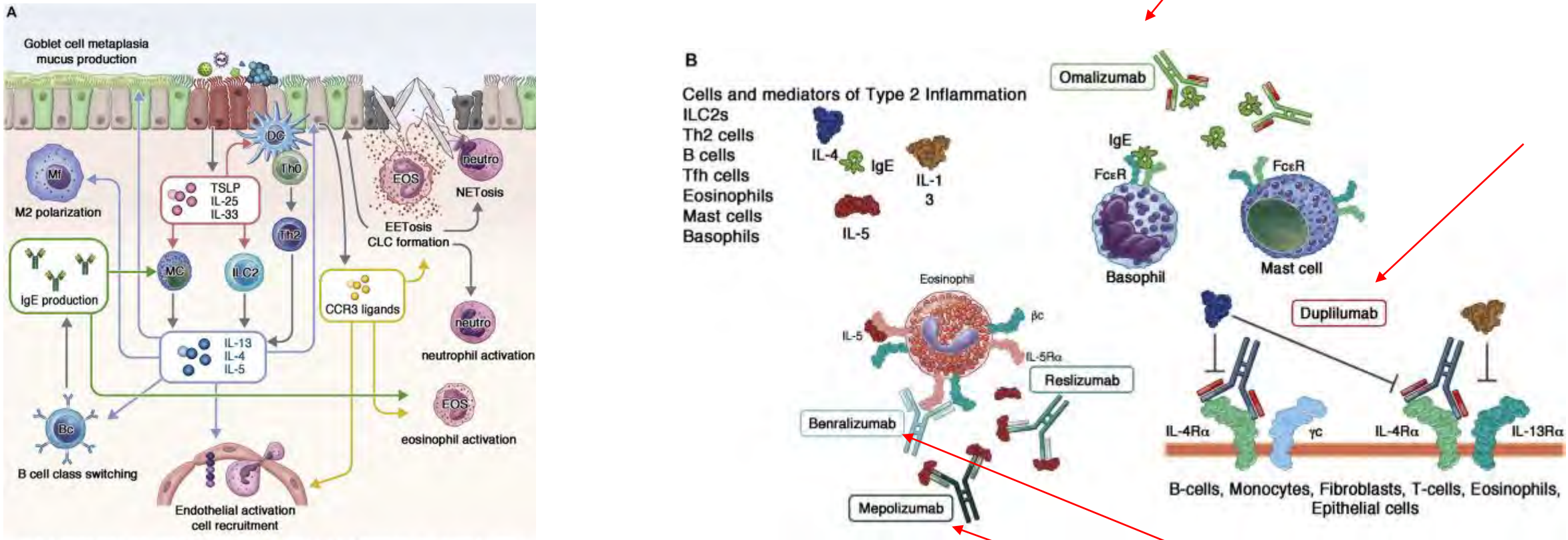
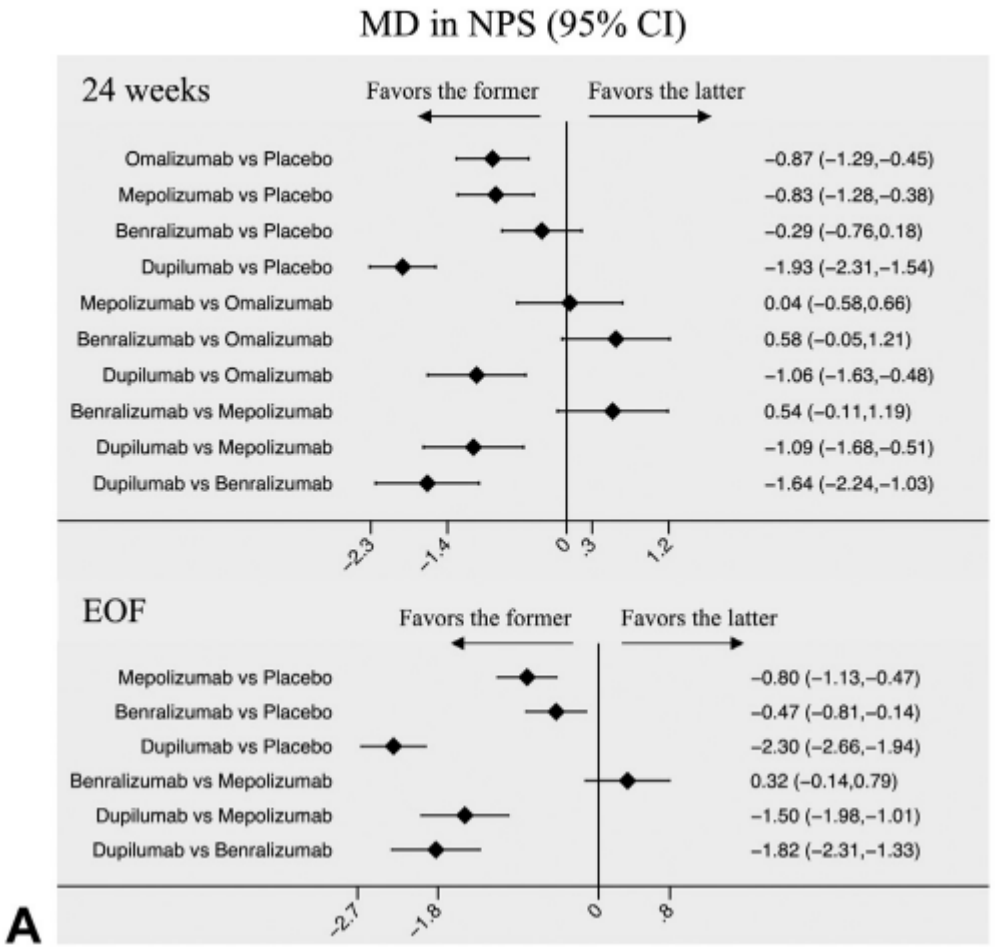


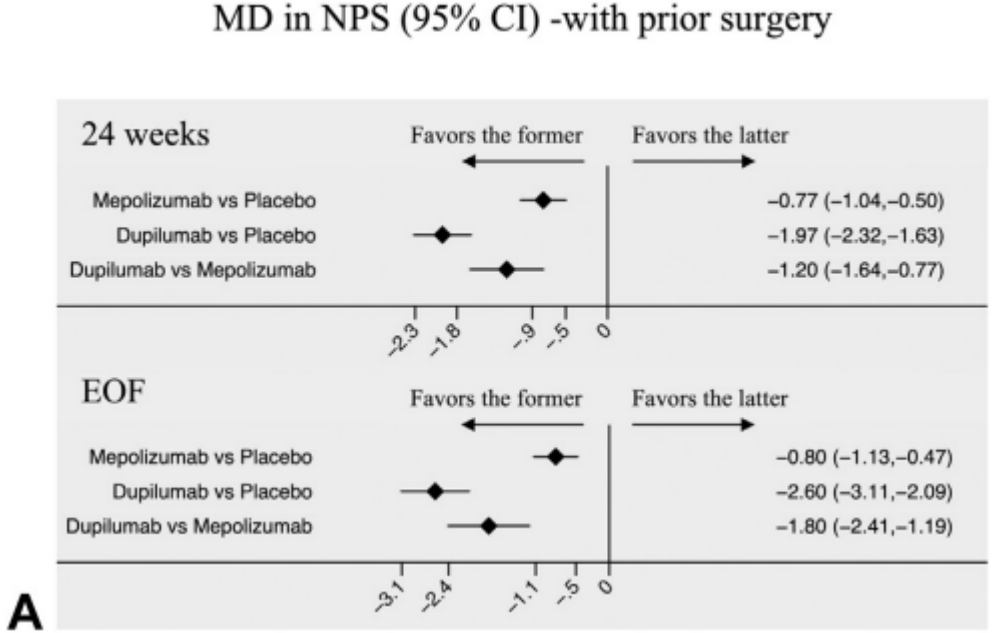
FIG 2. Biologics and their targets in type 2 inflammation in CRSwNP. **A,** Target cytokines in type 2 immune reactions. **B,** Cells and mediators of type 2 inflammation and corresponding biologics. *CCR-3,* C-C motif chemokine receptor 3; *CLC,* Charcot-Leyden-Crystal; *DC,* dendritic cell; *EOS,* eosinophils; *IL-4Rα,* IL-4 receptor alpha; *IL-13Rα,* IL-13 receptor alpha; *neutro,* neutrophils.

Clinical reviews in allergy and immunology

Biologics for chronic rhinosinusitis with nasal polyps

Claus Bachert, MD, PhD,[a,b,c] Nan Zhang, MD, PhD,[a,b] Carlo Cavaliere, MD,[d] Wen Weiping, MD,[a] Elien Gevaert, PhD,[b] and Olga Krysko, PhD[b]
Guangzhou, China, Ghent, Belgium, Stockholm, Sweden, and Rome, Italy





Original Article

Comparison of Different Biologics for Treating Chronic Rhinosinusitis With Nasal Polyps: A Network Analysis

Shiru Cai, BS[a,b,*], Shenglong Xu, BS[a,b,*], Hongfei Lou, MD, PhD[a,b,c], and Luo Zhang, MD, PhD[a,b,c,d] *Beijing, P.R. China*

Cochrane Library

Cochrane Database of Systematic Reviews

Biologics for chronic rhinosinusitis (Review)

Chong LY, Piromchai P, Sharp S, Snidvongs K, Webster KE, Philpott C, Hopkins C, Burton MJ

Biologics in CRSwNP

- Currently only mepolizumab is available for this indication

MEPOLIZUMAB

Source S100 HSD Public

Body System RESPIRATORY SYSTEM > DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES > OTHER SYSTEMIC DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES

▸ Note

▸ ⚠ Authority Required

Code & Prescriber	Medicinal Product Pack (Name, form & strength and pack size)	Max qty packs	Max qty units	No. of repeat	DPMQ	Max Safety Net	General Patient Charge
13237Q (MP)	MEPOLIZUMAB mepolizumab 100 mg/mL injection, 1 mL pen device (PI, CMI)	1	1	5	$1556.10	31.60	$31.60
	Available brands						
	Nucala						

Biologics in

- Currently only

MEPOLIZUMA

Source S10

Body System RES

▸ Note

▸ ⚠ Authority Required

Code & Prescriber		Max Safety Net	General Patient Charge
13237Q (MP)	MEPOLIZ mepolizuma	31.60	$31.60
	Nucala		

SES

13 The patient had, despite optimised nasal polyp therapy, **at least 2** of the following measured within the past 12 months:

☐ bilateral endoscopic nasal polyp score of at least 5 (out of a maximum score of 8, with a minimum score of 2 in each nasal cavity)

Date (DD MM YYYY) Score

and/or

☐ nasal obstruction visual analogue scale (VAS) score greater than 5 (out of a maximum score of 10)

Date (DD MM YYYY) Score

and/or

☐ overall symptom VAS score greater than 7 (out of a maximum score of 10).

Date (DD MM YYYY) Score

14 The patient has:

☐ not received PBS-subsidised treatment with a biological medicine for this condition

or

☐ had a 12 month break in PBS-subsidised treatment with a biological medicine for this condition

15 Will this treatment be used in combination with and within 4 weeks of another PBS-subsidised biological medicine prescribed for either nasal polyps, uncontrolled severe allergic asthma or uncontrolled severe asthma?

No ☐

Yes ☐

16 Did the patient fail to achieve adequate control with optimised nasal polyp therapy, including adherence to intranasal corticosteroid therapy for at least 2 months, and if required, nasal irrigation with saline?

No ☐

Not applicable ☐ Due to contraindication/intolerance to intranasal corticosteroid therapy

Yes ☐ Provide the following details

Intranasal corticosteroid

Prior therapy

Date of commencement (DD MM YYYY)

Duration of therapy

If applicable, nasal irrigation with saline

Prior therapy

Date of commencement (DD MM YYYY)

Duration of therapy

17 Has the patient had a blood eosinophil count greater than or equal to 300 cells per microlitre in the last 12 months?

No ☐

Yes ☐ Provide details

Blood eosinophil count

cells per microlitre

Date (DD MM YYYY)

Biologics in CRSwNP

- Currently only mepolizumab is available for this indication
- If need to teach a patient how to use: National Asthma Council website has broad range of “how to”
- Generally safe and well tolerated
- They are not disease modifying (unknown if earlier introduction would change that)
- In the right individual, can make a dramatic difference – but best selection, timing unknown and costs remain barriers

Useful resources

- Australasian Society of Clinical Immunology and Allergy (ASCIA) - www.allergy.org.au
- National Asthma Council Australia - https://www.nationalasthma.org.au/

- EUFOREA Pocket Guide on Allergic Rhinitis: https://www.euforea.eu/news/allergic-rhinitis-pocket-guide
- EUFOREA Pocket Guide on Chronic Rhinosinusitis: https://www.euforea.eu/news/chronic-rhinosinusitis-pocket-guide