THE ROLE OF PRIMARY CARE

Assessing disease control and management of respiratory allergies
At the end of this module, you should be able to:

1. Assess disease severity and control in allergic rhinitis and asthma
2. Identify the management options of allergic rhinitis and asthma
3. Identify patients eligible for allergy immunotherapy
4. Identify the benefits of allergy immunotherapy in both allergic rhinitis and allergic asthma
“Although the ARIA* classification of disease severity is useful, it is not an optimal guide for making everyday patient management decisions, especially in patients already on therapy”¹

Whilst the concept of control is well-defined in asthma, COPD and other conditions such as glycaemic control in diabetes, it has only recently gained significant attention in the field of allergic rhinitis²

Unlike disease severity, disease control encompasses a complex spectrum of parameters: impairments in everyday life, respiratory function and exacerbations, in addition to symptom severity¹

A simple and validated tool to assess disease severity and control: ARCT – Allergic Rhinitis Control Test – Disease Control¹


*ARIA: Allergic Rhinitis and its Impact on Asthma.
## Simple and validated self-assessment questionnaire for allergic rhinitis control

- Assesses control of AR before treatment and 2 weeks after treatment
- Offers a self-assessment to patients who may only seek medical advice if their AR is not controlled at the end of 2-4 weeks

### ARCT: ALLERGIC RHINITIS CONTROL TEST

### Scores: 5 to 25 (best score)

**Poorly controlled AR < 20 > Well–controlled AR**

Demoly et al. Validation of a self-questionnaire for assessing the control of allergic rhinitis. *Clinical & Experimental Allergy*, 2011 (41) 860–868. Reproduced with permission from Prof Demoly, and Drs Jankowsky, Chassany, Bessah and Allaert.

<table>
<thead>
<tr>
<th>Question</th>
<th>Permanently</th>
<th>Very often</th>
<th>Often</th>
<th>Not often</th>
<th>Never</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>During the last 2 weeks, has your allergic rhinitis had an effect on your professional/personal activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>During the last 2 weeks, has your allergic rhinitis made you irritable?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>During the last 2 weeks, has your allergic rhinitis disturbed your sleep (going to sleep, waking at night)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>During the last 2 weeks, have you needed to use an additional treatment not prescribed by your doctor to treat your allergic rhinitis?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>During the last 2 weeks, how would you assess your allergic rhinitis?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

**Total score**
CASE STUDY: EMILY, 18 YRS OLD, FINISHING HER LAST YEAR OF HIGH SCHOOL

Emily is 18 years old and struggling to keep up at school.

She suffers from allergic rhinitis year-round and recently started to experience breathing difficulties while sleeping, causing her to lose sleep and making it harder for her to concentrate in her classes.

- Spirometry shows no airflow obstruction nor bronchial hyper-reactivity

Her father is allergic to birch tree pollens and her mother is asthmatic.

Emily’s family doctor prescribes a nasal corticosteroid in addition to her usual oral antihistamine. He asks her to return in 2 weeks to assess her progress.
EMILY, 18 YRS OLD, FINISHING HER LAST YEAR OF HIGH SCHOOL

Query

Which simple tool can Emily’s doctor employ to monitor her progress on treatment?

The Allergic Rhinitis Control Test (ARCT) is a simple and validated questionnaire via which her family doctor can monitor her progress before and 2 weeks after starting a new treatment.

✓ Emily’s doctor explains the use of the ARCT self questionnaire and her baseline score is 11

✓ Two and a half weeks later, Emily conducts a self assessment of her control of her AR using the ARCT Questionnaire at home and her score is 12

✓ Emily schedules another visit to her family doctor requesting medical advice given her lack of satisfaction and the limited improvement associated with her symptomatic treatments.

MANAGEMENT OF ALLERGIC RHINITIS

ARIA* Guidelines recommend a combination of patient education, allergen avoidance (when possible), pharmacotherapy, and allergy immunotherapy

*ARIA=Allergic Rhinitis and its Impact on Asthma
**Therapeutic education of the patient is addressed in module 3 of this E-Learning series

### Stepwise Recommendations for Management of Allergic Rhinitis

#### Severity and Frequency of Symptoms Determines Therapy

<table>
<thead>
<tr>
<th>Symptom Severity and Frequency</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild Intermittent</strong></td>
<td>Intranasal steroid, LTRAs*</td>
</tr>
<tr>
<td></td>
<td>Local cromone</td>
</tr>
<tr>
<td></td>
<td>Second-generation non-sedating H&lt;sub&gt;1&lt;/sub&gt; antihistamine</td>
</tr>
<tr>
<td></td>
<td>Intranasal decongestant (&lt;10 days) or oral decongestant</td>
</tr>
<tr>
<td></td>
<td>Allergen and irritant avoidance</td>
</tr>
<tr>
<td><em>LTRAs</em> = leukotriene receptor antagonist</td>
<td></td>
</tr>
</tbody>
</table>

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ALLERGEN AVOIDANCE

☑ Single avoidance measures are ineffective
☑ Use a comprehensive environmental intervention to achieve the greatest possible reduction in personal exposure
☑ Tailor the intervention to patient’s sensitisation and exposure status
☑ Start the intervention as early as possible in the natural history of the disease

ARIA Guidelines 2008
“Although the general consensus is that allergen avoidance should lead to an improvement of symptoms, there is very little evidence to support the use of single physical or chemical methods”

HOW TO AVOID ALLERGENS

<table>
<thead>
<tr>
<th>FOR ANY ALLERGEN</th>
<th>INDOOR ALLERGENS (house dust mites, cat danders…)</th>
<th>OUTDOOR ALLERGENS (pollens)</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Eliminate carpets and rugs in favour of hard flooring</td>
<td>✓ Wash bedding at least once a week (above 60°C)</td>
<td>✓ Stay informed of your local pollen-count to know when to avoid going outdoors</td>
</tr>
<tr>
<td>✓ Choose closed pieces of furniture, such as drawers instead of shelves</td>
<td>✓ Cover pillows, matresses and quilts with house dust mite resistant casings and wash these every 2 months</td>
<td>✓ Avoid activities known to cause exposure to pollen (mowing grass, camping)</td>
</tr>
<tr>
<td>✓ At least once a week, vacuum using a high efficiency particulate air grade filter (HEPA)</td>
<td>✓ Reduce indoor humidity (do not dry clothes on the heater)</td>
<td>✓ Change and wash clothing after being outdoors</td>
</tr>
<tr>
<td></td>
<td>✓ Do not allow pets into the bedrooms</td>
<td>✓ Shower soon after activities where there is high exposure to pollen</td>
</tr>
<tr>
<td></td>
<td>✓ Groom animals regularly outside</td>
<td>✓ Keep car windows closed and consider installing pollen filters in the car</td>
</tr>
</tbody>
</table>

CERTAIN PATIENTS MAY REMAIN UNCONTROLLED DESPITE OPTIMAL PHARMACOTHERAPY

Whilst non-sedating H1-antihistamines and intranasal corticosteroids are recommended as first line treatments, they cannot modify the course of the disease.

Around one third of patients with moderate/severe symptoms are uncontrolled despite optimal pharmacologic treatment.  

Patients with Severe chronic upper airway disease (SCUAD*) have symptoms which are inadequately controlled despite adequate (ie, effective, safe, and acceptable) pharmacologic treatment based on guidelines.

Up to 40% of patient with a new diagnosis of AR want to be cured from their allergy besides symptomatic relief.

* SCUADs include severe uncontrolled AR, non-allergic rhinitis, chronic rhinosinusitis, aspirin-exacerbated respiratory diseases, or occupational airway diseases

BENEFITS OF ALLERGY IMMUNOTHERAPY IN ALLERGIC RHINITIS

✓ Can significantly improve allergic rhinitis symptoms
  - Efficacy on rhinitis symptoms\(^1,2,3\)

✓ Can reduce the need for symptomatic drug therapy
  - Allergic rhinitis patients receiving AIT typically use significantly less rescue medications (e.g. antihistamines, corticosteroids) than patients receiving placebo\(^1,2,3\)

✓ Can be efficacious over the long term
  - Clinical efficacy may persist after discontinuation of AIT\(^3\)

“A particular feature of AIT, unlike usual anti-allergy drugs, is the ability to modify the course of allergic disease”\(^4\)

GINA 2016 advocates that 2 domains of asthma control should be assessed: symptom control and risk factors for adverse outcomes (also called ‘future risk’)

Numerical ‘asthma control’ tools provide scores and cut points to distinguish different levels of symptom control, validated against health care provider assessment:

**Asthma Control Questionnaire (ACQ):**

ACQ score calculated as average of 5, 6 or 7 items with all versions of the ACQ include five symptom questions, ACQ-6 includes reliever use; and in ACQ-7, a score for pre-bronchodilator FEV₁ is averaged with symptom and reliever items. Minimum clinically important difference is 0.5.

Scores range from 0–6 (higher is worse) where a score of 0.0–0.75 is classified as well-controlled asthma; 0.75–1.5 as a ‘grey zone’; and >1.5 as poorly controlled asthma.

**Asthma Control Test (ACT):**

4 symptom/reliever questions plus a patient self-assessed level of control. Minimum clinically important difference: 3 points.

Scores range from 5–25 (higher is better). Scores of 20–25 are classified as well-controlled asthma; 16–20 as not well-controlled; and 5–15 as very poorly controlled asthma.


**ASTHMA MANAGEMENT: STEPWISE APPROACH TO CONTROL ASTHMA SYMPTOMS AND REDUCE RISK**

<table>
<thead>
<tr>
<th>STEP 1</th>
<th>STEP 2</th>
<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PREFERRED CONTROLLER CHOICE</strong></td>
<td><strong>OTHER CONTROLLER OPTION</strong></td>
<td><strong>RELIEVER</strong></td>
<td><strong>MEDICATION CHOICE</strong></td>
<td><strong>ADD-ON TREATMENT</strong></td>
</tr>
<tr>
<td>Consider low dose ICS</td>
<td>Leukotriene receptor antagonists (LTRA)</td>
<td>As-needed short-acting beta₂-agonist (SABA)</td>
<td>Med/high dose ICS, Low dose ICS + LTRA (or + theoph*)</td>
<td>Add tiotropium*†</td>
</tr>
<tr>
<td></td>
<td>Low dose ICS</td>
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<tr>
<td></td>
<td></td>
<td>Med/high ICS/LABA**</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Med/low ICS/LABA</td>
<td>Refer for add-on treatment e.g. tiotropium**†</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>omalizumab mepolizumab*</td>
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</table>

*Not for children <12 years. **For children 6–11 years, the preferred Step 3 treatment is medium dose ICS.

# Low dose ICS/formoterol is the reliever medication for patients prescribed low dose budesonide/formoterol or low dose beclometasone/formoterol for maintenance and reliever therapy.

†Tiotropium by mist inhaler is an add-on treatment for patients with a history of exacerbations (not for children <12 years)


Reproduced for illustrative purposes only.
GINA 2016 states the following in relation to avoidance of indoor allergens:

- Allergen avoidance is not recommended as a general strategy in asthma.
- For sensitized patients, there is no evidence of clinical benefit for asthma with single-strategy indoor allergen avoidance.
- Remediation of dampness or mold in homes reduces asthma symptoms and medication use in adults.
- For patients sensitized to house dust mite and/or pets, there is limited evidence of clinical benefit for asthma with multi-component avoidance strategies (only in children).

**ALLERGIC ASTHMA & ALLERGY IMMUNOTHERAPY**

- **GINA 2016** advocates the treatment of modifiable risk factors to reduce exacerbations and states the following:
  - Allergy immunotherapy may be an option if allergy plays a prominent role, e.g. asthma with allergic rhinoconjunctivitis
  - The efficacy of allergen immunotherapy in asthma is limited

- **Benefits of allergy immunotherapy:**
  - Reduction in symptom scores and medication requirements in adult and paediatric patients with allergic asthma
  - In paediatric asthma and rhinoconjunctivitis, a systematic review of the efficacy and safety of subcutaneous and sublingual immunotherapy concluded that the evidence supports the efficacy of both administration routes for the treatment of asthma and rhinitis in children
  - Improvement in rhinitis symptoms when associated with mild/moderate asthma
  - Reduction of the inhaled corticosteroid dose needed to maintain asthma control

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ALLERGY IMMUNOTHERAPY IS GENERALLY WELL-TOLERATED

✓ Both sublingual (SLIT) and subcutaneous immunotherapy (SCIT) have acceptable safety profiles if administered under the appropriate circumstances

- **SLIT**'s more favorable safety profile allows for administration outside of a medically supervised setting.
  - First dose should be taken under medical supervision

- **SCIT** is recommended only in a medically supervised setting with appropriate staff and equipment to identify and immediately treat systemic reactions or anaphylaxis

✓ Adverse reactions can be local or systemic:

- Local reactions (LRs) are fairly common with both administration routes:
  - With sublingual immunotherapy, most LRs occur shortly after treatment initiation and cease within days to a few weeks without any medical intervention

- Systemic reactions (SRs) are quite rare when AIT is performed according to proper safety recommendations
  - In a 4-year AIT safety survey that included 23.3 million injection visits, incidence of severe SRs approximately 1 in 1 million injections, similar to previous surveys
  - With sublingual immunotherapy, the rate of SRs is significantly lower vs. subcutaneous immunotherapy and severe SRs are relatively uncommon

ALLERGY IMMUNOTHERAPY MAY PREVENT DISEASE PROGRESSION

✓ A recent position paper from the World Allergy Organization (WAO) states...

“The preventive benefits of AIT may be greater if initiated early in the course of allergic disease... where disease progression may be more easily influenced.”

Effective AIT triggers multiple mechanisms, which are sequentially activated

Mechanisms of AIT

Rapid desensitization

Immune tolerance

Early tolerance

Sustained tolerance

Effector cell desensitization
- IgE
- Mast cell and Basophil
- Mediators – Histamine signal

AIT-induced immune tolerance controls:
- The acute phase of the allergic reaction and
- chronic events leading to inflammation and remodeling

Increased Treg/Breg cells
Increased Th1/Th2
Increased IgG4>
Decreased IgE
Decreased tissue inflammation
Decreased mast cells and eosinophils and their mediators in tissues

ALLERGY IMMUNOTHERAPY OFFERS A CHOICE OF ADMINISTRATION ROUTES FOR DIFFERENT PATIENTS

✓ 2 routes of administration are available:

Sublingual immunotherapy (SLIT)
• Tablets or drops
• Self-administered at home after the first dose

Subcutaneous immunotherapy (SCIT)
• Injections
• Requires office visit for each injection

✓ Route selection depends on patients’ needs and preferences¹
  – Patient profile
  – Physician and/or patient preferences
  – Practical considerations

Optimization of administration schedules may help to achieve improved treatment compliance³

WHO ARE CANDIDATES FOR ALLERGY IMMUNOTHERAPY?

✓ Patients with (moderate-severe) rhinitis ± conjunctivitis and/or (mild-moderate) symptoms from the lower airways¹:
  – with demonstrated IgE sensitization and relevant symptoms during the peaks of allergen exposure
  – insufficiently controlled by antihistamines and moderate dose of topical glucocorticosteroids

✓ Patients who do not want to be on constant or long term pharmacotherapy or in whom pharmacotherapy induces undesirable side-effects

✓ Patients who desire “a cure”

✓ In addition to the above, a recent position paper from the World Allergy Organization (WAO)² states that sublingual immunotherapy may be particularly indicated in the following patients:
  – Patients whose allergy is uncontrolled with optimal pharmacotherapy (that is those with severe chronic upper airway disease)
  – Patients who refuse injections

“Sublingual immunotherapy may be considered as initial treatment. Failure of pharmacological treatment is not an essential prerequisite for the use of sublingual immunotherapy.”²

WHO ARE NOT CANDIDATES FOR ALLERGY IMMUNOTHERAPY?

✓ Age <5 years
✓ Severe or poorly controlled asthma
✓ Significant CV disease
  - E.g., Unstable angina, recent myocardial infarction, significant arrhythmia, uncontrolled hypertension
✓ Malignant diseases

Note: Chronic nasal inflammatory responses and nasal polyps are not contraindications

A 2015 position paper on clinical contraindications to AIT by the European Academy of Allergology and Clinical Immunology (EAACI) proposes that:

- Autoimmune disorders in remission are a relative contraindication and active forms are an absolute contraindication
- β-blockers are a relative contraindication as patients may be at increased risk of more severe systemic reactions
- Angiotensin-converting enzyme inhibitors are not a contraindication

JUDITH, 33 YEARS OLD, ACTIVE WOMAN

✓ Personal information
- 33 years young woman living in Germany
- International journalist
- Single, no child, no pets

✓ Clinical history
- For 5 years, rhinitis symptoms (frequent sneezing salvos, rhinorrhea, itchy nose and throat, itchy and red eyes, fatigue) occurring from around end of May peaking at the end of July until symptoms disappear towards end of September
- She suffers from fatigue and irritability at work
- Cromoglycate eye drops
- Nasal corticosteroids (which she presumably does not take)
- Last year, for the first time, she complained of breath difficulties with diurnal wheezing after a week-end outdoors during the season
- Inhaled salbutamol
At visit, Judith complains of symptoms worsening compared to her symptoms at the end of May which has prompted her to see her family physician.

Judith expresses her frustration with her long term use of her oral H1-antihistamines and sees little ‘end in sight’

Clinical Exam @ July 2015:
- Normal clinical exam:
  - No congested nasal mucosa and watery secretions
  - No red conjunctiva
  - No wheeze

Her physician uses the ARCT Questionnaire and her score is 8 = poorly controlled AR
Her physician considers the pollen calendar in Germany:

Suspected seasonal allergic rhinitis to grass pollen: referral to allergy specialist for diagnosis and treatment

http://www.pollenstiftung.de
JUDITH, 33 YEARS OLD, ACTIVE WOMAN

The allergy specialist, who is also a pulmonologist, conducts skin prick tests, lung function test and anterior rhinoscopy

<table>
<thead>
<tr>
<th>INITIAL DIAGNOSTIC RESULTS</th>
<th>CHEST &amp; NOSE EXAM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Skin prick tests:</strong></td>
<td></td>
</tr>
<tr>
<td>✓ Histamine</td>
<td></td>
</tr>
<tr>
<td>✓ Negative control</td>
<td>✓ Lung Function Test: normal</td>
</tr>
<tr>
<td>✓ Grass pollen</td>
<td>✓ Anterior rhinoscopy: normal</td>
</tr>
<tr>
<td>✓ Cat</td>
<td></td>
</tr>
<tr>
<td>✓ Cypress</td>
<td></td>
</tr>
<tr>
<td>✓ Parietaria</td>
<td></td>
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<tr>
<td>✓ Dpte, Dfar mites</td>
<td></td>
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<tr>
<td>✓ Birch</td>
<td></td>
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<tr>
<td>✓ Alternaria</td>
<td></td>
</tr>
<tr>
<td>✓ Olive</td>
<td></td>
</tr>
</tbody>
</table>

Sensitized to grass pollen and cat but allergic to grass pollen, in correlation with clinical symptoms
JUDITH, 33 YEARS OLD, ACTIVE WOMAN*

Diagnosis:

Grass pollen induced allergic rhinitis with mild asthma

*Judith's case does not represent an actual patient
IS AIT INDICATED FOR JUDITH?

✓ Judith satisfies the indication for AIT:
  - IgE sensitization to clinically relevant allergens: grass pollen induced allergic rhinitis with mild asthma
  - Allergic rhinitis symptoms insufficiently controlled by antihistamines and topical medications
  - Does not wish to be on long-term pharmacotherapy

<table>
<thead>
<tr>
<th>ALLERGEN AVOIDANCE</th>
<th>AIT OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subcutaneous immunotherapy (Injections)</td>
</tr>
<tr>
<td>YOUR CHOICE</td>
<td>×</td>
</tr>
<tr>
<td>PATIENT’S PREFERENCE</td>
<td>×</td>
</tr>
</tbody>
</table>

Prescription:
Sublingual immunotherapy for pollen induced allergic rhinitis starting next January on a pre-coseasonal scheme

In January, Judith started a sublingual grass pollen immunotherapy and after a few months of treatment she felt better during the grass pollen season compared to the previous year

Considerations:
■ Lifestyle (Duration of treatment & convenience)
■ Polysensitization status
■ Mild Asthma co-morbidity
■ Desire to avoid injections if possible
Certain patients may remain uncontrolled despite optimal pharmacotherapy

Unlike symptomatic treatments, AIT has the ability to modify the natural course of the disease

Preventive benefits of AIT may be greater if initiated early in the course of allergic disease where disease progression may be more easily influenced

2 routes of administration are available: sublingual and subcutaneous immunotherapy

– Route selection depends on patients’ needs and preferences

Demonstrated efficacy in allergic rhinitis and allergic asthma