Clinical Practice Guidelines:
Allergic rhinitis

These guidelines were adapted mainly from "Clinical Practice Guideline: Allergic Rhinitis" developed by the American academy of Otolaryngology-Head and neck surgery Foundation in 2015 [(1)] and "International consensus statement on allergy and rhinology: allergic rhinitis- executive summary" published in the International Forum of Allergy & Rhinology in 2018 [(2)]

Aknowledgement

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Abbreviations

AR: Allergic rhinitis
INC: Intranasal corticosteroid
LTRA: Oral leukotriene receptor antagonist
PAR: Perennial allergic rhinitis
RCT: andomized controlled trial
SAR: Seasonal allergic rhinitis

Glossary

Allergic rhinitis (AR): Disease caused by an IgE-mediated inflammatory response of the nasal mucous membranes after exposure to inhaled allergens. Symptoms include rhinorrhea (anterior or posterior nasal drainage), nasal congestion, nasal itching, and sneezing.

Seasonal allergic rhinitis (SAR): Disease caused by an IgE-mediated inflammatory response to seasonal aeroallergens. The length of seasonal exposure to these allergens is dependent on geographic location and climatic conditions.

Perennial allergic rhinitis (PAR): Disease caused by an IgE-mediated inflammatory response to year-round environmental aeroallergens. These may include dust mites, mold, animal allergens, or certain occupational allergens.

Intermittent allergic rhinitis: Disease caused by an IgE-mediated inflammatory response and characterized by frequency of exposure or symptoms (<4 days per week or <4 weeks per year).
Persistent allergic rhinitis: Disease caused by an IgE-mediated inflammatory response and characterized by persistent symptoms (>4 days per week and >4 weeks per year).
Episodic allergic rhinitis: Disease caused by an IgE-mediated inflammatory response that can occur if an individual is in contact with an exposure that is not normally a part of the individual's environment. (ie, a cat at a friend's house).

Scope

This Guideline is concerned with diagnosis and treatment decision of allergic rhinitis, and reduce harmful or unnecessary variations in care. The guideline is intended to be applicable for both pediatric and adult patients with AR. Children under the age of 2 years were excluded because rhinitis in this population may be different than in older patients and is not informed by the same evidence base.

Executive Summary

- **PATIENT HISTORY AND PHYSICAL EXAMINATION:** Clinicians should make the clinical diagnosis of AR when patients present with a history and physical examination consistent with an allergic cause and 1 or more of the following symptoms: nasal congestion, runny nose, itchy nose, or sneezing. Findings of AR consistent with an allergic cause include, but are not limited to, clear rhinorrhea, nasal congestion, pale discoloration of the nasal mucosa, and red and watery eyes.
- **ALLERGIC TESTING:** Clinicians should perform and interpret, or refer to a clinician who can perform and interpret, specific IgE (skin or blood) allergy testing for patients with a clinical diagnosis of AR who do not respond to empiric treatment, or when the diagnosis is uncertain, or when knowledge of the specific causative allergen is needed to target therapy.
- **IMAGING:** Clinicians should not routinely perform sinonasal imaging in patients presenting with symptoms consistent with a diagnosis of AR.
- **ENVIRONMENTAL FACTORS:** Clinicians may advise avoidance of known allergens or may advise environmental controls in AR

patients who have identified allergens that correlate with clinical symptoms.

- **CHRONIC CONDITIONS AND COMORBIDITIES:** Clinicians should assess patients with a clinical diagnosis of AR for, and document in the medical record, the presence of associated conditions such as asthma, atopic dermatitis, sleep-disordered breathing, conjunctivitis, rhinosinusitis, and otitis media.
- **PHARMACOLOGIC THERAPY:**
  - A- TOPICAL STEROIDS: Clinicians should recommend intranasal steroids for patients with a clinical diagnosis of AR whose symptoms affect their quality of life.
  - B- ORAL ANTIHISTAMINES: Clinicians should recommend oral second-generation/less sedating antihistamines for patients with AR and primary complaints of sneezing and itching.
  - C- INTRANASAL ANTIHISTAMINES: Clinicians may offer intranasal antihistamines for patients with seasonal, perennial, or episodic AR.
  - D- ORAL LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRAs): Clinicians should not offer LTRAs as primary therapy for patients with AR.
  - E- SALINE NASAL WASH: Saline nasal wash is recommended as part of the treatment strategy for AR.
  - F- ORAL CORTICOSTEROIDS: Recommendation against the routine use of oral corticosteroids for AR.
  - G- CROMOLYN: Disodium chromoglycate (DSCG) may be considered for the treatment of AR, particularly in patients known triggers and who cannot tolerate INCSs.
  - H- INTRANASAL ANTICHOLINERGIC: Ipratropium bromide nasal spray may be considered as an adjunct medication to INCSs in PAR patients with uncontrolled rhinorrhea.
  - I- OMALIZUMAB: Strong recommendation against use in treatment of allergic rhinitis alone
- **COMBINATION THERAPY:** Clinicians may offer combination pharmacologic therapy in patients with AR who have inadequate response to pharmacologic monotherapy.

- **PHARMACOLOGIC THERAPY OF ALLERGIC RHINITIS ASSOCIATED WITH BRONCHIAL ASTHMA:**
  - Use of systemic corticosteroid is not recommended for routine use in AR with comorbid asthma.
  - Omalizumab: Recommended for those patients with clear IgE-mediated allergic asthma with coexistent AR who fail conventional therapy.
- **IMMUNOTHERAPY:** Clinicians should offer, or refer to a clinician who can offer, immunotherapy (sublingual or subcutaneous) for patients with AR who have inadequate response to symptoms with pharmacologic therapy.
- **INFERIOR TURBINATE REDUCTION:** Clinicians may offer, or refer to a surgeon who can offer, inferior turbinate reduction in patients with AR with nasal airway obstruction and enlarged inferior turbinates who have failed medical management.
- **HERBAL THERAPY:** No recommendation regarding the use of herbal therapy for patients with AR.

Introduction

Allergic rhinitis (AR) is one of the most common diseases affecting adults and children. It can impair quality of life and, through loss of work and school attendance. Various diagnostic tests and treatments are used in managing patients with this disorder, yet there is considerable variation in their use. This clinical practice guideline was undertaken to optimize the care of patients with AR by addressing quality improvement opportunities through an evaluation of the available evidence and an assessment of the harm-benefit balance of various diagnostic and management options.

Purpose

The primary purpose of this guideline is to address quality improvement opportunities for all clinicians, in any setting, who are likely to manage patients with AR, as well as to optimize patient care, promote effective diagnosis and therapy, and reduce harmful or unnecessary variations in care. The guideline is not intended to replace individualized patient care or clinical judgment.

The target audience

The guideline is intended for all clinicians who are likely to diagnose and manage patients with allergic rhinitis, and it applies to any setting in which allergic rhinitis would be identified, monitored, or managed.

Methods

A comprehensive search for guidelines was undertaken to identify the most relevant guidelines to consider for adaptation.

inclusion/exclusion criteria followed in the search and retrieval of guidelines to be adapted:

- *Selecting only evidence-based guidelines (guideline must include a report on systematic literature searches and explicit links between individual recommendations and their supporting evidence)*
- *Selecting only national and/or international guidelines*
- *Specific range of dates for publication (using Guidelines published or updated 2015 and later)*
- *Selecting peer reviewed publications only*
- *Selecting guidelines written in English language*
- *Excluding guidelines written by a single author not on behalf of an organization in order to be valid and comprehensive, a guideline ideally requires multidisciplinary input*
- *Excluding guidelines published without references as the panel needs to know whether a thorough literature review was conducted and whether current evidence was used in the preparation of the recommendations*

The following characteristics of the retrieved guidelines were summarized in a table:

- *Developing organisation/authors*
- *Date of publication, posting, and release*
- *Country/language of publication*
- *Date of posting and/or release*
- *Dates of the search used by the source guideline developers*

All retrieved Guidelines were screened and appraised using AGREE II instrument (www.agreetrust.org) by at least two members. the panel decided a cut-off point or rank the guidelines (any guideline scoring above 50% on the rigour dimension was retained)

Evidence assessment

According to WHO handbook for Guidelines we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations. GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations. Detailed information on GRADE is available through the GRC secretariat and on the following sites:

■ *GRADE working group: http://www.gradeworkingroup.org*
■ *GRADE online training modules: http://cebgrade.mcmaster.ca/*
■ *GRADE profile software: http://ims.cochrane.org/revman/gradepro*

Table 1 Quality of evidence in GRADE

Quality level	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

Table 2 Significance of the four levels of evidence

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect	Any estimate of effect is very uncertain

Table 3 Factors that determine How to upgrade or downgrade the quality of evidence

Downgrade in presence of	Upgrade in presence of
Study limitations -1 Serious limitations -2 Very serious limitations	Dose-response gradient +1 Evidence of a dose-response gradient
Consistency -1 Important inconsistency	Direction of plausible bias +1 All plausible confounders would have reduced the effect
Directness -1 Some uncertainty -2 Major uncertainty	Magnitude of the effect +1 Strong, no plausible confounders, consistent and direct evidence
Precision -1 Imprecise data	+2 Very strong, no major threats to validity and direct evidence
Reporting bias -1 High probability of reporting bias	

The strength of the recommendation

The strength of a recommendation communicates the importance of adherence to the recommendation.

Strong recommendations

With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted as policy.

Conditional recommendations

These are made when there is greater uncertainty about the four factors above or if local adaptation has to account for a greater variety in values and preferences, or when resource use makes the intervention suitable for some, but not for other locations. This means that there is a need for substantial debate and involvement of stakeholders before this recommendation can be adopted as policy.

When not to make recommendations

When there is lack of evidence on the effectiveness of an intervention, it may be appropriate not to make a recommendation.

Recommendations

1- PATIENT HISTORY AND PHYSICAL EXAMINATION: Clinicians should make the clinical diagnosis of AR when patients present with a history and physical examination consistent with an allergic cause and 1 or more of the following symptoms: nasal congestion, runny nose, itchy nose, or sneezing. Findings of AR consistent with an allergic cause include, but are not limited to, clear rhinorrhea, nasal congestion, pale discoloration of the nasal mucosa, and red and watery eyes.

Strong recommendation

Moderate quality evidence (Observational studies) [3-6]

2- ALLERGY TESTING:

Clinicians should perform and interpret, or refer to a clinician who can perform and interpret, specific IgE (skin or blood) allergy testing for patients with a clinical diagnosis of AR who do not respond to empiric treatment, or when the diagnosis is uncertain, or when knowledge of the specific causative allergen is needed to target therapy.

Strong recommendation

High quality evidence (RCTs and systematic reviews) [7-15]

3- IMAGING:

Clinicians should not routinely perform sinonasal imaging in patients presenting with symptoms consistent with a diagnosis of AR.

Strong recommendation against

Moderate quality evidence (Observational studies) [16,17]

4- ENVIRONMENTAL FACTORS:

Clinicians may advise avoidance of known allergens or may advise environmental controls (eg, removal of pets; the use of air filtration systems, bed covers, and acaricides [chemical agents that kill dust mites]) in AR patients who have identified allergens that correlate with clinical symptoms.

Conditional recommendation

Moderate quality evidence (Randomized controlled trials and observational studies) [18-23]

5- CHRONIC CONDITIONS AND COMORBIDITIES:

Clinicians should assess patients with a clinical diagnosis of AR for, and document in the medical record, the presence of associated conditions such as asthma, atopic dermatitis, sleep-disordered breathing, conjunctivitis, rhinosinusitis, and otitis media.

Conditional recommendation

Moderate quality evidence (Randomized controlled trials with some heterogeneity) [24-31]

6- PHARMACOLOGIC THERAPY:

A- TOPICAL STEROIDS:

Clinicians should recommend intranasal steroids for patients with a clinical diagnosis of AR whose symptoms affect their quality of life.

Strong recommendation

High quality evidence (RCTs with minor limitations) [32-39]

B- ORAL ANTIHISTAMINES:

Clinicians should recommend oral second-generation/less sedating antihistamines for patients with AR and primary complaints of sneezing and itching.

Strong recommendation
High quality evidence (RCTs with minor limitations) [40-48]

C- INTRANASAL ANTIHISTAMINES:

Clinicians may offer intranasal antihistamines for patients with seasonal, perennial, or episodic AR.

Conditional recommendation
High quality evidence (RCTs and observational studies) [49-53]

D- ORAL LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRAs):

Clinicians should not offer LTRAs as primary therapy for patients with AR.

Strong recommendation against
High quality evidence (RCTs and systematic reviews) [54-57]

E- SALINE NASAL WASH:

Saline nasal wash is recommended as part of the treatment strategy for AR.
Strong recommendation
High quality evidence (RCTs and systematic reviews) [58-64]

F- ORAL CORTICOSTEROIDS :

Recommendation against the routine use of oral corticosteroids for AR. Although not recommended for routine use in AR, certain clinical scenarios warrant the use of short courses of systemic corticosteroids after a discussion of the risks and benefits with the patient. This may include patients with significant nasal obstruction that would preclude penetration of intranasal agents (INCSs or antihistamines). In these cases, a short course of systemic oral corticosteroids could improve congestion and facilitate access and efficacy of the topical agents.
Conditional recommendation against
Moderate quality evidence (RCTs) [65-68]

G- CROMOLYN :

Disodium chromoglycate (DSCG) may be considered for the treatment of AR, particularly in patients known triggers and who cannot tolerate INCSs.

Conditional recommendation

Low quality evidence [69-72]

H- INTRANASAL ANTICHOLINERGIC :

Ipratropium bromide nasal spray may be considered as an adjunct medication to INCSs in PAR patients with uncontrolled rhinorrhea.

Conditional recommendation

Low quality evidence [73-75]

I- OMALIZUMAB:

Stronge recommendation against the use of Omalizumab as monotherapy in the treatment of AR. Omalizumab may be used for patients with clear IgE mediated asthma with cpexistent allergic rhinitis who fail conventional therapy. Omalizumab is not currently approved by the FDA for AR treatment. Also as an expensive treatment, cost should be taken into consideration.

Strong recommendation against use in treatment of allergic rhinitis alone

High quality evidence (RCTs and systematic reviews)[76-78]

7- COMBINATION THERAPY:

Clinicians may offer combination pharmacologic therapy in patients with AR who have inadequate response to pharmacologic monotherapy.

Conditional recommendation

Moderate quality evidence (RCTs and observational studies)

There is strong evidence supporting the use of some combinations and the ineffectiveness of other combinations:

- Intranasal Steroids and Intranasal Antihistamines

The combination of INS and intranasal antihistamine is more effective than INS or intranasal antihistamine monotherapy

for AR. [79-81]

- Intranasal Steroids and Oral Antihistamines:

When patients have no response to INS or incomplete control of nasal symptoms with an INS, oral antihistamines should not be routinely used as additive therapy. [82-84]

- Oral Antihistamines and Oral Decongestants:

Oral antihistamines and oral decongestant combinations control AR symptoms better than either oral antihistamine or oral decongestant alone. Oral decongestant use is not recommended for patients under 4 years of age, and the extended release, 120-mg, 12-hour dose is not recommended for patients under 12 years of age. There is recommendation against long-term use given the significant side effect profile of oral decongestants. [85-88]

- Oral Antihistamines and Leukotriene Receptor Antagonists:

There is conflicting evidence as to whether combined treatment with oral antihistamine and LTRA is superior to either as single treatment, and therefore routine use of combined therapy is not recommended. Combination of oral antihistamine and LTRA is either inferior to or less likely equivalent to INS monotherapy in control of AR symptoms. Combination therapy with LTRA and oral antihistamine is an option for management of AR, particularly in patients with comorbid asthma or those who do not tolerate INCSs and symptoms are not well-controlled on oral antihistamine monotherapy. [89-95]

- Intranasal Steroids and Leukotriene Receptor Antagonists:

LTRAs should not routinely be used as additive therapy for patients benefiting from INS for AR. [96-100]

- Intranasal Steroids and Intranasal Oxymetazoline:

The combination of INS and intranasal oxymetazoline is more effective in controlling AR symptoms than either monotherapy. Short-term use (<3 days) of this combination in cases of severe nasal congestion is recommended. [101-103]

8- PHARMACOLOGIC THERAPY OF ALLERGIC RHINITIS ASSOCIATED WITH BRONCHIAL ASTHMA:

Asthma association with AR and nonallergic rhinitis: Most patients with asthma also have rhinitis, and 10%-40% of rhinitis patients have asthma. IgE mediated inflammation may involve both the upper and lower airways, supporting the unified airway concept.
Rhinitis as a risk factor for asthma: Rhinitis, both allergic and nonallergic, is a risk factor for developing asthma. Asthma and AR also share common risk factors, such as allergen sensitization.
Pharmacotherapy: was reviewed in the treatment of AR with coexisting asthma. Recommendations are as follows:

- Use of pharmacotherapy other than systemic steroids: Recommended for optimal control of AR, with potential additional benefit for coexistent asthma, although not recommended for primary intent of asthma treatment.
- Use of systemic corticosteroid is not recommended for routine use in AR with comorbid asthma due to an unfavorable risk-benefit profile, although certain situations may indicate a short course (eg, acute asthma exacerbation).
- Omalizumab: Recommended for those patients with clear IgE-mediated allergic asthma with coexistent AR who fail conventional therapy. The significant additional cost of this therapy should be considered in its evaluation.

Strong recommendation
High quality evidence (RCTs and Systematic reviews) [104-106]

9- IMMUNOTHERAPY:

Clinicians should offer, or refer to a clinician who can offer, immunotherapy (sublingual or subcutaneous) for patients with AR who have inadequate response to symptoms with pharmacologic therapy.
Strong recommendation
High quality evidence (RCTs and observational studies) [107-113]

10- INFERIOR TURBINATE REDUCTION:

Clinicians may offer, or refer to a surgeon who can offer, inferior turbinate reduction in patients with AR with nasal airway obstruction and enlarged inferior turbinates who have failed medical management.
Conditional recommendation
Moderate quality evidence (Observational studies) [114-117]

11- HERBAL THERAPY:
No recommendation regarding the use of herbal therapy for patients with AR, based on limited knowledge of herbal medicines and concern about the quality of standardization
and safety.
No recommendation
Low quality evidence [118-125]

Clinical Indicators for Monitoring

1- **Allergic testing:**

Clinicians should perform and interpret, or refer to a clinician who can perform and interpret, specific IgE (skin or blood) allergy testing for patients with a clinical diagnosis of AR who do not respond to empiric treatment, or when the diagnosis is uncertain, or when knowledge of the specific causative allergen is needed to target therapy.

2- **Imaging:**

Clinicians should not routinely perform sinonasal imaging in patients presenting with symptoms consistent with a diagnosis of AR.

3- **Comorbidities:**

Clinicians should assess patients with a clinical diagnosis of AR for, and document in the medical record, the presence of associated conditions such as asthma, atopic dermatitis, sleep-disordered breathing, conjunctivitis, rhinosinusitis, and otitis media.

4- **Pharmacologic therapy**:

Clinicians should not recommend the routine use of oral corticosteroids for AR, and should not use Omalizumab in treatment of allergic rhinitis alone.

These indicators cover aspects such as documentation, diagnostic procedures, treatment decisions, and patient education, providing a comprehensive approach to monitoring physician adherence to the clinical guidelines.

Updating the guideline

To keep these recommendations up to date and ensure its validity it will be periodically updated. This will be done whenever a strong new evidence is available and necessitates updation.

Research Needs

1- Controlled trials are needed comparing surgical versus medical management of inferior turbinate hypertrophy with nasal congestion in patients with AR. In addition, there is a need for further research regarding the role of septoplasty in the treatment of AR.

2- Research is needed to determine the relationship between AR and comorbid conditions such as otitis media and sinusitis. In addition, research is needed to determine the effect of AR treatment on comorbid conditions and the effect of treatment for comorbid conditions on AR.

3- More research, including basic and/or translational trials, is needed to evaluate novel forms of immunotherapy such as peptide vaccines, DNA conjugated vaccines, intradermal injections, and intralymphatic injections. These are all strategies that are hypothesized to reduce the allergenicity of extracts while maintaining or enhancing the beneficial effect on the immune system.

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