Complete Summary

GUIDELINE TITLE

Allergic rhinitis and its impact on asthma.

BIBLIOGRAPHIC SOURCE(S)

Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001 Nov;108(5):S147-334. [2776 references]

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
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CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY

SCOPE

DISEASE/CONDITION(S)

Allergic rhinitis and asthma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Diagnosis
Management
Prevention
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Infectious Diseases
Internal Medicine
Nursing
Otolaryngology

Pediatrics
Preventive Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Health Plans
Managed Care Organizations
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To update clinicians´ knowledge of allergic rhinitis
- To highlight the impact of allergic rhinitis on asthma
- To provide an evidence-based approach to diagnosis
- To provide an evidence-based approach to treatment
- To provide a stepwise approach to the management of the disease

TARGET POPULATION

Patients of all ages in all geographic locations who have allergic rhinitis and asthma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. General medical, environmental, occupational, personal, and family history
2. Examination of the nose, including anterior rhinoscopy, nasal endoscopy, and intranasal anaesthesia
3. Skin tests (immediate hypersensitivity skin tests), including scratch tests, prick and puncture tests (SPT), intradermal skin tests
4. Techniques to accurately measure serum specific IgE, including RAST (radioallergosorbent test) and new techniques using either radio- or enzyme-labeled anti-IgE
5. Nasal challenge with allergens or nonspecific agents
6. Nasal airway assessment using rhinomanometry, nasal inspiratory or expiratory peak flow
7. Imaging studies, e.g., computerised tomography (CT), magnetic resonance imaging (MRI)
8. Evaluation for asthma with measurement of lung function using forced expiratory volume in 1 second (FEV_1) and peak expiratory flow (PEF)

Management/Treatment/Prevention

1. Allergen avoidance

- Dust mite control including use of acaricides to clean carpets and vacuum cleaners with integral HEPA filter
- Reduction of occupational exposure to allergens (e.g., latex)

2. Medication
    - Second-generation oral H1-antihistamines such as acrivastine, astemizole, cetirizine, ebastine, emedastine, fexofenadine, levocabastine, loratadine, mequitazine, mizolastine, terfenadine, ketotifen, oxatomide
    - Intranasal and ocular administration of H1-antihistamines such as azelastine and levocabastine
    - Intranasal glucocorticosteroids such as beclomethasone, budesonide, flunisolide, fluticasone propionate, mometasone furoate, and triamcinolone acetonide
    - Systemic glucocorticosteroids such as prednisolone and methylprednisolone
    - Chromones such as disodium cromoglycate (cromolyn, DSCG) and nedocromil sodium and N-acetyl-aspartyl glutamic acid (NAAGA)
    - Decongestants such as alpha1-adrenergic agonists (e.g., phenylephrine), alpha2-adrenergic agonists (e.g., oxymetazoline, xylometazoline, naphazoline), noradrenaline releasers (e.g., ephedrine, pseudoephedrine, amphetamines), drugs preventing the re-uptake of noradrenaline (e.g., cocaine, tricyclic antidepressants, phenylpropanolamine)
    - Topical anti-cholinergics such as ipratropium bromide
    - Anti-leukotrienes such as zileuton, zafirlukast, and montelukast
    - Nasal douching
    - Surgical treatment of turbinate hypertrophy, cartilaginous or bony obstruction of the nasal airways, or secondary and independent sinus disease
3. Immunotherapy
    - With unmodified vaccines, vaccines modified chemically (e.g., formaldehyde allergoids), and vaccines modified by absorption onto different carriers (so-called depot-vaccines) including birch and Betulaceae pollen, grass pollen, ragweed pollen, Parietaria pollen, house dust mites, and cat
    - By nasal, sublingual-swallow, and oral routes
4. Education
    - Nature of the disease
    - Treatment options
    - Potential side effects
    - Complications of rhinitis
    - Realistic expectations
5. Considered, but not recommended:
    - Diagnostics including IgG and IgG4 measurement, peripheral blood activation markers such as histamine release/CysLT release or basophil degranulation tests, nasal specific IgE, nasal microsuction, measurement of nitric oxide, rhinostereometry, acoustic rhinometry, head-out body/whole body plethysmography, oscillometry, bacteriology (swabs taken blindly from the nose), plain sinus radiographs, mucociliary function, olfaction assessment
    - Non-sedating first-generation antihistamines such as brompheniramine, clemastine, chlorpheniramine
    - Oral anti-allergic drugs such as pemirolast

    - Alternative therapies such as homeopathy, acupuncture, chiropractic, herbal remedies, ayurvedic medicine, yoga
    - Antibiotics
    - Combination oral antihistamines and decongestants
    - Humanised monoclonal antibodies against IgE
    - Inhibition of eosinophilic inflammation
    - Inhibition of allergic inflammation
6. Specific immunotherapy with recombinant allergens, peptide vaccines, using IL-12 as an adjuvant, with bacterial or mycobacterial products to stimulate Th1 response, with plasmid DNA encoding of antigen, with house dust, or Candida albicans
7. Avoidance of ubiquitous environmental allergens including dogs and cats, cockroaches, pollen, moulds, and foods

MAJOR OUTCOMES CONSIDERED

- Prevalence of allergic rhinitis
- Changes in the prevalence of seasonal allergic rhinitis
- Symptoms of allergic rhinitis
- Sensitivity and specificity of diagnostic tests
- Side effects of treatment
- Response of symptoms (sneezing, rhinorrhea, nasal obstruction, nasal itch, eye symptoms) to treatment
- Quality of life
- Cost-effectiveness of treatments

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

In the present document, an extensive Medline search was carried out from 1966 to 31-12-1999 using PubMed® concerning the following items:

- rhinitis
- all treatment options
- all diagnosis options
- for medications, the generic name of all known medications (for rhinitis) was used with the key words "placebo-controlled". When no placebo-controlled studies were available, the authors used the key words "controlled".

For treatment options, a search with EMBASE® (Excerpta Medica) was also carried out to find papers not referenced on Medline.

A search of randomised rhinitis trials was done using the Cochrane Library database (12-1999). The search included the Cochrane Database of Systematic Reviews (CDSR) and the Database of Reviews of Effectiveness (DARE).

NUMBER OF SOURCE DOCUMENTS

More than 2,000

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Category of evidence:

Ia: Evidence for meta-analysis of randomised controlled trials

Ib: Evidence from at least one randomised controlled trial

IIa: Evidence from at least one controlled study without randomisation

IIb: Evidence from at least one other type of quasi-experimental study

III: Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies

IV: Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The literature of each of the chapters was extensively reviewed by at least the chairmen and two members of the panel. A full consensus was reached on all of the material presented in this position paper.

The statement of evidence for the development of these guidelines has followed World Health Organization (WHO) rules and is based on Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. BMJ 1999 Feb 27;318(7183):593-6 (Review). The statements of evidence for the different treatment options of allergic rhinitis have been examined by the report panel. However, a slight modification has been proposed since:

- for most interventions, placebo-controlled studies are available,
- there is evidence that neither physician nor patient can easily distinguish between an effective and an ineffective procedure for allergic disease without performing a proper trial. Although these considerations were issued for

allergen specific immunotherapy, it seems that they also apply to other treatments of allergic rhinitis.

Thus, for double-blind studies with a placebo group, the level of evidence was classified as A, and as A* for double blind studies without a placebo group.

For each intervention, the highest level of evidence was set from Ia to IV depending on the available studies published in papers indexed in Medline and Embase.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A full consensus was reached on all of the material presented in the guideline.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of recommendations:

A. Directly based on category I evidence (A* for recommendations based on double-blind studies without a control group)
B. Directly based on category II evidence or extrapolated recommendation from category I evidence
C. Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D. Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence

COST ANALYSIS

The guideline developers provide a chapter on the economic impact of asthma and rhinitis. The costs of illness for asthma, the costs of illness for rhinitis, the cost-effectiveness of various interventions in the care of persons with asthma and rhinitis, and the policy implications are reviewed. Refer to the original guideline document (chapter 12) for details.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Summary of Major Recommendations

1. Allergic rhinitis is a major chronic respiratory disease due to its:
    - prevalence,
    - impact on quality of life,
    - impact on work/school performance and productivity,
    - economic burden,
    - links with asthma.
2. In addition, allergic rhinitis is associated with sinusitis and other co-morbidities such as conjunctivitis.
3. Allergic rhinitis should be considered as a risk factor for asthma along with other known risk factors.
4. A new subdivision of allergic rhinitis has been proposed:
    - intermittent
    - persistent
5. The severity of allergic rhinitis has been classified as "mild" or "moderate/severe" depending on the severity of symptoms and quality of life outcomes.
6. Depending on the subdivision and severity of allergic rhinitis, a stepwise therapeutic approach has been proposed.
7. The treatment of allergic rhinitis combines:
    - allergen avoidance (when possible),
    - pharmacotherapy,
    - immunotherapy.
8. The environmental and social factors should be optimised to allow the patient to lead a normal life.
9. Patients with persistent allergic rhinitis should be evaluated for asthma by history, chest examination and, if possible and when necessary, the assessment of airflow obstruction before and after bronchodilator.
10. Patients with asthma should be appropriately evaluated (history and physical examination) for rhinitis.
11. A combined strategy should ideally be used to treat coexistent upper and lower airway diseases in terms of efficacy and safety.

Specific Recommendations

Diagnosis and Assessment of Severity

History

History should take into account some associated symptoms common in patients with rhinitis. They include:

- loss of smell (hyposmia or anosmia),
- snoring, sleep problems,
- post nasal drip or chronic cough, in particular if sinusitis is present,
- sedation, which may be caused by rhinitis,

- questions on asthma and conjunctivitis.

The history includes a full-length questionnaire:

- The frequency, severity, duration, persistence or intermittence and seasonality of symptoms should be determined.
- It is important to assess their impact on the patients' quality of life in terms of impairment of school/work performance, interference with leisure activities and any sleep disturbances.
- Potential allergic triggers should be documented including exposure in the home, workplace and school. Any hobbies which may provoke symptoms should also be noted.
- An occupational history should be obtained.
- The effects of previous allergen avoidance measures should be noted, bearing in mind that up to 3-6 months of vigorous cleaning may be needed to eradicate mites, cat dander and other relevant allergens from the home.
- Response to pharmacological treatment and previous immunotherapy should be recorded in terms of improvement and side effects.
- Compliance with treatment and patients' fears about treatment should be explored, particularly if the response to treatment has been below that expected.
- Drugs affect skin tests and it is always necessary to ask patients about the drugs they have taken.

Examination of the Nose

In patients with mild intermittent allergic rhinitis, a nasal examination is optimal. All patients with persistent allergic rhinitis need a nasal examination. Nasal examination should describe:

- the anatomical situation in the nose (e.g., the septum, the size of the inferior turbinate and if possible the structures in the middle meatus),
- the colour of the mucosa,
- the amount and aspect of the mucus.

Anterior rhinoscopy, using a speculum and mirror, gives information which is sometimes limited, but it remains an appropriate method for studying the major modifications observed in most cases of allergic rhinitis.

Nasal endoscopy can find nasal and sinus pathology that might easily be missed with routine speculum and nasopharyngeal examination. Ear, nose, and throat (ENT) examination in the clinic is now considerably facilitated by the use of rigid Hopkins rods or flexible fibre-optic endoscopes.

The administration of intranasal anaesthesia is recommended at initial assessment. Specific attention is paid to abnormality within the middle meatus and nasopharynx.

Refer to the original guideline document for typical findings during examination of the nasal mucosa in patients with allergic rhinitis.

Allergy Diagnosis

Skin Tests

- Immediate hypersensitivity skin tests are widely used to demonstrate an IgE-mediated allergic reaction of the skin and represent a major diagnostic tool in the field of allergy. If properly performed, they yield useful confirmatory evidence for a diagnosis of specific allergy. As there are many complexities for their performance and interpretation, it is recommended that they should be carried out by trained health professionals. Delayed hypersensitivity tests provide little information.
- Scratch tests should not be used any longer because of poor reproducibility and possible systemic reactions.
- Prick and puncture tests (SPT) are usually recommended for the diagnosis of immediate type allergy. Skin prick tests should be 2 cm apart.
- In some instances, (e.g., weak allergen solution), intradermal skin tests may be employed for allergy diagnosis.
- As a general rule, the starting dose of intracutaneous extract solutions in patients with a preceding negative prick test should range between 100 and 1,000 fold dilutions of the concentrated extract used for prick-puncture tests.
- It does not seem that intradermal skin tests are required for the diagnosis of inhalant allergy when standardised extracts are available.

Refer to the original guideline document for information on the use of negative and positive control solutions, grading of skin tests and criteria of positivity, factors affecting skin testing, and interpretation of skin tests.

IgE

- The measurement of total serum IgE is barely predictive for allergy screening in rhinitis and should no longer be used as a diagnostic tool.
- In contrast to the low predictive value of total serum IgE measurements in the diagnosis of immediate type allergy, the measurement of allergen-specific IgE in serum is of importance.

Refer to the original guideline document for information on measuring serum specific IgE, including methods used in measuring, factors affecting measurement, and the significance of measurement.

Nasal Challenge

- Indications for nasal challenge tests:
    - Allergen provocations
        - When discrepancies between history of allergic rhinitis and tests or between tests are present (e.g., in cases of diagnostic doubt)
        - For diagnosis of occupational allergic rhinitis
        - Before immunotherapy for allergic rhinitis. Although it is still not very common to use nasal provocation before starting immunotherapy, it has been considered that a laborious long-lasting therapy is justified by a proper diagnosis. This holds true particularly in the case of perennial allergic rhinitis.

        - For research
    - Lysine-aspirin: Nasal provocation is recommended as a substitute for oral provocation in aspirin intolerance. Whenever such a nasal provocation is negative, an oral test is still required.
    - To test non-specific hyperreactivity: nasal provocation with non-specific stimuli (histamine, methacholine, cold dry air, etc.) is not relevant for daily clinical practice and diagnosis but can be used in research.
- Recommendations for the performance of nasal challenge tests:
    - Provoking agent
        - Use solutions at room temperature
        - Standardised extracts
        - Isotonic solutions buffered to a pH of about 7
        - Use control solutions
- Deposition into the nose
    - Meter-dose pump spray
    - Paper disks
- Assessment of the nasal response: symptom scores are combined with objective measures
    - Counting sneezes or attacks of sneezes
    - Measuring volume or weight of nasal secretion
    - Changes of nasal patency, airflow or airflow resistance
- Methods to evaluate nasal patency, airflow and airflow resistance
    - The most important techniques are: rhinomanometry, acoustic rhinometry, rhinostereometry, nasal inspiratory or expiratory peak flow
    - Less common methods are: rhinostereotomy, head-out body plethysmography and oscillometry

Refer to the original guideline document for additional information on performing nasal challenge tests.

Also refer to the original guideline document for recommendations on interpretation of tests, including correlation between skin and specific IgE tests, diagnosis of inhalant allergy, diagnosis of food allergy, and diagnosis of occupational allergy.

Other ENT Diagnosis

Bacteriology

Routine swabs taken blindly from the nose and nostril are not diagnostically helpful. This may not be the case if the swabs are taken endoscopically.

Imaging

- Plain sinus radiographs are not indicated for the diagnosis of allergic rhinitis or sinusitis.
- Computerised tomography (CT) has become the principal radiological investigation for major sino-nasal disorder but is of limited use in the diagnosis of allergic rhinitis. Computerised tomography scans can be carried out after receiving specialist advice:

    - To eliminate other conditions,
    - To exclude chronic sinusitis,
    - To eliminate complications from rhinitis,
    - In patients who do not respond to treatment,
    - In patients with unilateral rhinitis.
- Magnetic resonance imaging (MRI) is rarely indicated as a diagnostic tool. However, there are circumstances where magnetic resonance imaging is useful, in particular in fungal sinusitis.

Mucociliary function

Tests for mucociliary clearance or ciliary beat frequency have little relevance in the diagnosis of allergic rhinitis, but are relevant in the differential diagnosis of chronic rhinorrhea in children.

Nasal airway assessment

Nasal inspiratory or expiratory peak flow, rhinomanometry or acoustic rhinometry may be used.

Olfaction

Although olfaction is often impaired in allergic rhinitis and methods for assessing olfaction are available, these are not generally used for the diagnosis of allergic rhinitis.

Diagnosis of Asthma

Guidelines for recognizing and diagnosing asthma have been published by the Global Initiative for Asthma (GINA) and are recommended by ARIA.

The diagnosis of asthma may be difficult due to the transient nature of the disease and the reversibility of the airflow obstruction spontaneously or after treatment. Key indicators for diagnosing asthma are presented below:

Key Indicators for Diagnosing Asthma

Consider asthma if any of the following are present:

- Wheezing - high-pitched whistling sounds when breathing out--especially in children. (A normal chest examination does not exclude asthma.)
- History of any of the following:
    - Cough, worse particularly at night
    - Recurrent wheezing
    - Recurrent difficult breathing
    - Recurrent chest tightness

  Note: Eczema, hay fever or family history of asthma or atopic diseases are often associated with asthma, but they are not key indicators.

- Symptoms occur or worsen at night, awakening the patient.

- Symptoms occur or worsen in the presence of:
    - Exercise
    - Viral infection (common cold)
    - Animals with fur
    - Domestic dust mites (in mattresses, pillows, upholstered furniture, carpets)
    - Smoke (tobacco, wood)
    - Pollen
    - Changes in temperature
    - Strong emotional expression (laughing or crying hard)
    - Aerosol chemicals
    - Drugs (aspirin, beta blockers)
- Reversible and variable airflow limitation as measured by using a peak expiratory flow (PEF) meter or forced expiratory volume in 1 second (FEV_1) in any of the following ways:
    - PEF or FEV_1 increases more than 12% 15 to 20 minutes after inhalation of a short-acting beta2-agonist, or
    - PEF or FEV_1 varies more than 20% from morning measurement upon arising to measurement 12 hours later in patients taking a bronchodilator (more than 10% in patients who are not taking a bronchodilator), or
    - PEF or FEV_1 decreases more than 15% after 6 minutes of running or exercise.

Refer to the original guideline document for additional information on measurement of lung function and special considerations in difficult groups (e.g., infants and young children, tobacco smokers, the elderly). Table 15 in the original guideline gives the advantages and drawbacks of different methods for measuring lung function.

Assessment of Severity of Rhinitis

For rhinitis, there is no accepted measure of nasal obstruction. The nasal inspiratory peak flow (NIPF) has been extensively studied but results are not consistent among the different studies. Moreover, the correlation between the objective measurement of nasal resistance and subjective reports of nasal airflow sensation is usually poor.

Management Recommendations

Definitions for the category of evidence (Ia-IV) and strength of recommendation (A-D) for management recommendations are given at the end of the Major Recommendations section.

Allergen Avoidance

Allergen avoidance, including house dust mites, should be an integral part of a management strategy.

Measures for reducing house dust mite allergen exposure:

Essential

- Encase mattress, pillow and quilt in impermeable covers
- Wash all bedding weekly in a hot cycle (55-60 degrees C)

Optimal

- Replace carpets with linoleum or wooden flooring
- If carpets cannot be removed, treat with acaricides and/or tannic acid
- Minimise upholstered furniture/replace with leather furniture
- Keep dust accumulating objects in closed cupboards
- Use a vacuum cleaner with integral HEPA filter and double thickness bags
- Replace curtains with blinds or easily washable (hot cycle) curtains
- Hot wash/freeze soft toys

<u>Occupational agents</u>

- The early identification of occupational sensitisers and the removal of sensitised patients from any further exposure are important aspects of the management of occupational rhinitis.
- Prevention of latex allergy is essential.

  (Level of evidence = IV; Strength of recommendation = D for adults and children with perennial rhinitis or adults and children with latex allergy.)

Medication

Oral H1 antihistamines

- Old-generation H1 antihistamines are effective and may be the only molecules available in some developing countries. But because of their more favourable risk/benefit ratio and enhanced pharmacokinetics, new H1-antihistamines should be considered as a first-choice treatment for allergic rhinitis when they are available and affordable. However, in some countries, not all molecules are available and the choice may be restricted. The anti-allergenic activities exerted by some drugs would suggest that long-term use is preferable to an "on demand" regimen, especially in persistent disease. In perennial allergic rhinitis, when obstruction is the predominant symptom, intranasal glucocorticosteroids should either be added to a H1-antihistamine or used as a first choice drug.

  (Level of evidence = Ib; Strength of recommendation = A for adults and children with seasonal or perennial allergic rhinitis.)

Intranasal or intraocular (topical) H1 antihistamines

- Topical H1-antihistamines have a rapid onset of action (less than 15 minutes) at low drug dosage, but they act only on the treated organ. Topical H1-antihistamines usually require bi-daily (BID) administrations to maintain a satisfactory clinical effect. Their use may therefore be recommended for mild

organ-limited disease, as an "on demand" medication in conjunction with a continuous one.

(Level of evidence = Ib; Strength of recommendation = A for adults and children with seasonal or perennial allergic rhinitis.)

Intranasal corticosteroids

- A recent meta-analysis has demonstrated that intranasal glucocorticoids are more efficacious in reducing the symptoms of allergic rhinitis than antihistamines. The advantage was most obvious for nasal blockage. However, in clinical practice, compliance, drug preference, drug availability and potential side effects should be considered.
- Because intranasal glucocorticosteroids are more effective in moderate to severe rhinitis and can suppress many stages of the allergic inflammatory disease, the therapeutic risk/benefit ratio has to be considered. Generally, the groups of patients with persistent allergic rhinitis who usually suffer from nasal blockage are better managed with intranasal glucocorticosteroids. When symptoms are mild or only intermittent, an H1-antihistamine is a good choice. The balance between intranasal glucocorticosteroids and H1-antihistamines has to be individualised.
- In conclusion, intranasal glucocorticosteroids should be regarded as a highly effective first-line treatment for patients suffering from allergic and non-allergic rhinitis with moderate to severe and/or persistent symptoms. Even though intranasal glucocorticosteroids may be less effective in non-allergic rhinitis, they are worth trying.

  (Level of evidence = Ib; Strength of recommendation = A for adults and children with seasonal or perennial allergic rhinitis.)

Systemic glucocorticosteroids

- Systemic glucocorticosteroids are never the first line of treatment for allergic rhinitis. They can be used as a last resort of treatment when other treatments are ineffective. Oral glucocorticoids have the advantage over depot injections that treatment adjustments can follow the pollen count. Systemic glucocorticoids, in contrast to intranasal treatment, reach all parts of the nose and paranasal sinuses, therefore short courses in patients with severe perennial rhinitis or nasal polyposis can be helpful.
- Systemic glucocorticosteroids should be avoided in children, pregnant women and patients with known contraindications.

  (Level of evidence = Ib; Strength of recommendation = A for adults with seasonal allergic rhinitis.)

Intranasal or intraocular chromones

- In placebo-controlled trials, disodium cromoglycate (DSCG) 4 times daily has been shown to be effective in allergic rhinitis and conjunctivitis, although less effective than H1-antihistamines or intranasal glucocorticosteroids.

- Nedocromil sodium has also been shown to be effective in allergic rhinitis and conjunctivitis and has the advantage of a BID dosing regimen.
- In adults, chromones are not a major therapeutic option in the treatment of allergic rhinitis, although they maintain a valued place for the treatment of allergic conjunctivitis.
- In children and pregnant women, chromones can be recommended in view of their excellent safety profile.

  (Level of evidence = Ib; Strength of recommendation = A for adults and children with seasonal allergic rhinitis and adults with perennial allergic rhinitis.)

Decongestants

- In general, because of the risk of rhinitis medicamentosa, the use of intranasal decongestants should be limited to a duration of less than 10 days.
- Short courses of intranasal decongestants can be useful to promptly reduce severe nasal blockage while co-administering other drugs.
- Decongestants should be used with care in children under one year of age because of the narrow range between therapeutic and toxic doses.
- Furthermore, it is advised not to prescribe pseudoephedrine to patients over 60 years of age, to pregnant women and, in general, to patients suffering from hypertension, cardiopathy, hyperthyroidism, prostatic hypertrophy, glaucoma and psychiatric disorders as well as to those taking beta-blockers or monoamine oxidase (MAO) inhibitors.

  (Oral Decongestants with H1 antihistamine: Level of evidence = Ib; Strength of recommendation = A for adults and children with seasonal allergic rhinitis and for adults with perennial allergic rhinitis.) (Oral and Nasal Decongestants – no data)

Topical anti-cholinergics

- Studies performed in perennial allergic rhinitis demonstrated that ipratropium bromide only improves nasal hyper-secretion. (No data are available for seasonal rhinitis.)
- Since patients with perennial rhinitis usually suffer also from nasal congestion, itching and sneezing, other drugs are preferable as first-line agents to ipratropium in the vast majority of cases of allergic rhinitis.
- However, the ipratropium bromide nasal spray alone should be considered in patients for whom rhinorrhea is the primary symptom.
- Its use in combination with an intranasal glucocorticosteroid or an H1-antihistamine may be considered in patients where rhinorrhea is the predominant symptom, or in patients with rhinorrhea who are not fully responsive to other therapies.
- Moreover, ipratropium may be used in patients with or without allergic rhinitis who suffer from rhinorrhea when in contact with cold air.
- In elderly patients, ipratropium may be of interest in the treatment of isolated rhinorrhea.

  (Level of evidence = Ib; Strength of recommendation = A for adults and children with perennial allergic rhinitis.)

Anti-leukotrienes

- In seasonal allergic rhinitis, the combination of a CysLT receptor antagonist, montelukast and loratadine showed that symptoms of rhinitis and conjunctivitis were more effectively treated with the combination of these drugs as opposed to any one of them alone or with the placebo.

  (Level of evidence = Ib; Strength of recommendation = A for adults with seasonal allergic rhinitis.)

Treatments with a lack of demonstrable efficacy (homeopathy, acupuncture, chiropractic, traditional medicine and phytotherapy, other alternative therapies)

- None of the methods used in alternative medicine can be supported scientifically to be clinically effective. The public should be warned against methods of diagnosis and treatment which may be costly and which have not been validated. Properly designed randomized clinical trials are required to assess the value of these forms of treatment.

  (Level of evidence = Ib, DB only for homeopathy; strength of evidence A* for homeopathy; no data for other interventions.)

Antibiotics

- In non-complicated rhinitis, antibiotics are not a recommended treatment.

Nasal douching

- Nasal douching with a traditional alkaline nasal douche or a sterile seawater spray was shown to improve symptoms of rhinitis.

Surgery

Indications for surgical intervention are:

- drug-resistant inferior turbinate hypertrophy,
- anatomical variations of the septum with functional relevance,
- anatomical variations of the bony pyramid with functional/aesthetic relevance,
- secondary or independently developing chronic sinusitis,
- different forms of nasal unilateral polyposis (choanal polyp, solitary polyp, allergic fungal sinusitis) or therapy-resistant bilateral nasal polyposis,
- fungal sinus disease (mycetoma, invasive forms) or other pathologies unrelated to allergy (cerebro-spinal fluid leak, inverted papilloma, benign and malignant tumours, Wegener's disease, etc.).

Induction of aspirin tolerance

- In order to prevent life-threatening reactions, patients with aspirin-intolerant rhinitis/asthma should avoid aspirin, all products containing aspirin and other analgesics that inhibit cyclooxygenase (COX). The education of physicians and patients regarding this matter is extremely important.

- The patient should obtain a list of drugs that are contraindicated, preferably with both the generic and trade names. If necessary, these patients can take acetominophen or paracetamol; it is safer not to exceed a dose of 1000 mg. Sodium salicylate, benzydamine, azapropazone, and dextropropoxyphene can be administered.

Refer to the original guideline document for details regarding induction of aspirin tolerance.

Specific Immunotherapy (SIT)

- In order to make the patient as symptom-free as possible, immunotherapy is indicated as a supplement to allergen avoidance and as a drug treatment in patients with rhinitis predominantly induced by dominating allergens.
- Immunotherapy should be initiated early in the disease process to reduce the risk of side effects and to prevent the further development of severe disease. Arguments for specific immunotherapy are:
    - Insufficient response to conventional pharmacotherapy,
    - side effects from drugs
    - rejection of drug treatment.
    - Injection (subcutaneous) specific immunotherapy may be used in severe or prolonged allergic rhinitis (eventually associated with asthma),
    - Local (intranasal and sublingual-swallow) specific immunotherapy may be considered in selected patients with systemic side effects and with refusal to injection treatment.

  Subcutaneous SIT in asthma or rhinitis + conjunctivitis (Level of evidence =1a, Ib; Strength of recommendation = A for adults and children with seasonal or perennial allergic rhinitis.)

  Local Specific Immunotherapy (Sublingual and Nasal SIT) – Very high dose (Level of evidence = Ib; Strength of recommendation = A for adults and children with seasonal allergic rhinitis and adults with perennial allergic rhinitis.)

  Refer to the original guideline document for details regarding the management of pediatric, pregnant, and elderly patients.

Education

- It is important to educate both the patient and relevant family members regarding the nature of the disease and available treatments. This should include general information regarding the symptoms, causes and mechanisms of rhinitis.
- In addition, education about means of avoidance, immunotherapy and drug therapy must be provided. It is vital that patients understand the potential side effects of therapy, especially drug side effects, in order to insure that they do not abruptly discontinue beneficial therapy but rather communicate adverse events to their physician so they can deal with them in a manner best for the patient.

- It is also important to provide patients with education about the complications of rhinitis including sinusitis and otitis media, and about comorbid conditions such as nasal polyps. They should be aware of how such complications are recognised and how they are treated.
- Patients need to be aware of the potential negative impact of rhinitis on the quality of life and potential benefits of complying with therapeutic recommendations.
- Patients must also have realistic expectations for the results of therapy and should understand that complete cures do not usually occur in the treatment of any chronic disease, including rhinitis.

Developing Countries

Refer to the original guideline document for details regarding recommendations for developing countries.

Definitions:

Category of evidence:

Ia: Evidence for meta-analysis of randomised controlled trials

Ib: Evidence from at least one randomised controlled trial

IIa: Evidence from at least one controlled study without randomisation

IIb: Evidence from at least one other type of quasi-experimental study

III: Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies

IV: Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

Strength of recommendations:

A. Directly based on category I evidence (A* for recommendations based on double-blind studies without a control group)
B. Directly based on category II evidence or extrapolated recommendation from category I evidence
C. Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D. Directly based on category IV evidence of extrapolated recommendation from category I, II, or III evidence.

CLINICAL ALGORITHM(S)

Algorithms are provided for management of allergic rhinitis.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Type of evidence is identified and graded for selected recommendations (See the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved diagnosis and cost-effective management of allergic rhinitis
- Improved recognition that asthma and rhinitis are common co-morbidities
- Improved respiratory function and quality of life for patient with allergic rhinitis and asthma

Subgroups Most Likely to Benefit:

- Specific immunotherapy is more effective in children and young adults than in later life.
- Patients with allergic triggers by a specific allergen are more likely to benefit from specific immunotherapy.

POTENTIAL HARMS

- Intradermal Skin Tests - Systemic reactions can rarely occur
- Oral Challenge for Aspirin-induced Rhinitis and Asthma - Severe systemic reactions
- Acaricides (for carpet cleaning) - Adverse reactions
- Intranasal drugs - Irritant or cilia toxic effect from added preservative
- Intranasal vasoconstrictor - Rhinitis medicamentosa
- Intranasal ipratropium bromide - Nasal dryness and blood tinged mucus
- H1-antihistamines - Sedation, central nervous system (CNS) depression, central nervous system stimulation, appetite stimulation and consequent weight gain, cardiac side effects--torsade de pointes, dry mouth, altered taste perception
- Topical H1-antihistamines - Short lasting perversion of taste
- Intranasal glucocorticosteroids - Local side effects such as crusting, dryness, and minor epistaxis, rare septal perforations, contact allergic reactions, possible effect on growth
- Decongestants - Nasal burning, stinging, dryness or mucosal ulcerations and even septal perforations may occur after the use of intranasal decongestants. A prolonged use (>10 days) of intranasal vasoconstrictors may lead to tachyphylaxis, a rebound swelling of the nasal mucosa and to "drug induced rhinitis" (rhinitis medicamentosa). Systemic side effects are not uncommon with these oral drugs and include irritability, dizziness, headaches, tremor and insomnia. Tachycardia, especially in susceptible subjects such as pregnant women, and hypertension may occur, as well as some less common effects such as visual hallucinations.
- Benzalkonium chloride (a preservative in intranasal decongestants) induces intranasal side effects.

- Topical anti-cholinergics - Nasal dryness, irritation and burning are the most prominent effects, followed by a stuffy nose, dry mouth and headache
- Subcutaneous immunotherapy - Systemic allergic reactions
- Intranasal specific immunotherapy - Asthma (probably caused by an incorrect administration of allergen vaccine)
- Sublingual specific immunotherapy - Asthma, urticaria, and gastrointestinal complaints

Subgroups Most Likely to be Harmed:

- Intradermal skin tests - Patients treated with beta-blocking agents
- Acaricides - Asthmatics
- Intranasal drugs - Patients with rhinitis-induced hyper-responsiveness
- H1-antihistamines - Elderly patients present a greater risk for central nervous system side effects and old-generation antihistamines should not be used.
- Patients with underlying hepatic or cardiac disease should not take astemizole or mizolastine
- Intranasal glucocorticosteroids - Risk of nasal perforation is greatest in the first 12 months of treatment and the majority of cases involves young women. The direction of the spray (towards the septum) could have an influence, and patients should always be advised to aim away form the septum.
- Reduced growth was noted in 6- to 9-year-old children using glucocorticosteroids.
- Decongestants - Most of these side effects are dose-dependent. Therefore, care should be exercised when giving the drugs to patients with cardiovascular diseases such as hypertension and myocardial ischaemia due to the systemic vasoconstrictor effects. Patients with glaucoma or hyperthyroidism and elderly men with urinary retention due to prostate enlargement are also at risk with oral sympathomimetic decongestants. These agents should also be used with caution in pregnant women, as the medication will be transferred to the foetus via the systemic circulation.
- Subcutaneous immunotherapy - Asthma patients are more at risk of systemic allergic reactions.
- Sublingual specific immunotherapy - Side effects are most common in children.

CONTRAINDICATIONS

CONTRAINDICATIONS

Specific immunotherapy is contraindicated in patients with: serious immunopathological and immunodeficiency diseases, malignancy, severe psychological disorders, treatment with beta-blockers, even when administered topically, poor compliance, severe asthma uncontrolled by pharmacotherapy and/or patients with irreversible airways obstruction (FEV_1 is consistently under 70% of predicted values after adequate pharmacological treatment), significant cardiovascular diseases which increase the risk of side effects from epinephrine, and children under 5 years of age unless there are specific indications.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The ARIA Paper is not intended to be a standard of care document for individual countries. It is provided as a basis for physicians and organisations involved in the treatment of allergic rhinitis and asthma in various countries to develop relevant local standard of care documents for their patients.
- The panel recognised that the suggestions it puts forward are valid for the majority of patients within a particular classification but that individual patient responses to a particular treatment may differ from the suggested therapy.
- It is assumed that a correct diagnosis is achieved before treatment.
- The guidelines do not take the cost of treatment into account.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Allergic rhinitis and its impact on asthma. J Allergy Clin Immunol 2001 Nov;108(5):S147-334. [2776 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

Allergic Rhinitis and its Impact on Asthma Workshop Group - Independent Expert Panel

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Allergic Rhinitis and its Impact on Asthma (ARIA) Workshop Group

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Disclosure of potential conflict of interest forms were collected from each of the 37 contributing authors. Authors noted instances of financial or other interests concerning the subject matter contained in this publication. Twenty-two of the authors had no conflict of interest. Of the remaining, 12 were on the advisory boards or served as consultants to pharmaceutical firms and 12 had done or were doing research supported by the pharmaceutics industry.

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All India Rhinology Society - Medical Specialty Society
Allergy and Immunology Society of Thailand - Medical Specialty Society
Allergy Society of South Africa
American Academy of Allergy, Asthma and Immunology - Medical Specialty Society
American College of Allergy, Asthma and Immunology - Medical Specialty Society
Argentine Association of Allergy and Immunology (Not stated) - Medical Specialty Society
Asia Pacific Association of Allergology and Clinical Immunology - Medical Specialty Society
Asociacion Argentina de Medicina Respiratoria - Medical Specialty Society
Belgian Society for Allergology and Clinical Immunology - Medical Specialty Society

Brazilian Society of Pediatrics - Professional Association
British Association of Otorhinolaryngologists - Head and Neck Surgeons - Medical Specialty Society
British Society for Allergy and Clinical Immunology - Medical Specialty Society
British Thoracic Society
Bulgarian Society of Allergology - Medical Specialty Society
Danish Society for Allergology - Medical Specialty Society
Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie - Medical Specialty Society
ENT India - Medical Specialty Society
European Academy of Allergy and Clinical Immunology - Medical Specialty Society
European Federation of Asthma and Allergy Associations - Medical Specialty Society
European Respiratory Society - Professional Association
European Rhinology Society - Medical Specialty Society
German Society for Allergology and Clinical Immunology - Medical Specialty Society
Hong Kong College of ENT - Professional Association
Indonesian Otorhinolaryngology Head and Neck Surgery Society - Medical Specialty Society
International Union Against Tuberculosis and Lung Disease - Private Nonprofit Organization
Italian Society of Respiratory Medicine - Medical Specialty Society
Japan Allergy Foundation - Private Nonprofit Organization
Japan Rhinology Society - Medical Specialty Society
Japan Society of Allergy and Immunology in Otolaryngology - Medical Specialty Society
Japanese Society of Allergology - Medical Specialty Society
Korean Rhinologic Society - Medical Specialty Society
Latin American Society of Pediatric Allergy, Asthma and Immunology - Medical Specialty Society
Malaysian Society of Otorhinolaryngology - Head and Neck Surgeons - Medical Specialty Society
National Asthma Campaign - Private Nonprofit Organization
Netherlands Society of Allergology - Medical Specialty Society
Philippine ENT Society - Medical Specialty Society
Philippine Society of Allergy, Asthma & Immunology, Inc. - Private Nonprofit Organization
Polish Society of Allergology - Medical Specialty Society
Rhinology Society of the Philippines - Medical Specialty Society
Rhinology Society of Turkey - Medical Specialty Society
Royal Belgian Society for Oto-rhino-laryngology, Head and Neck Surgery - Medical Specialty Society
Singapore ENT Society - Medical Specialty Society
Sociedade Portuguesa de Alergologia e Imunologia Clinica - Medical Specialty Society
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Society
South African Thoracic Society - Medical Specialty Society
Spanish Society of Allergology and Clinical Immunology - Medical Specialty Society
Thai Rhinologic Society - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies of ARIA documents and resourses available from the Allergic Rhinitis and its Impact on Asthma (ARIA) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Allergic Rhinitis and its Impact on Asthma (ARIA) Pocket Guide. Electronic copies available from the ARIA Web site.
- ARIA Teaching Slides (Power Point Download). Electronic copies available from the ARIA Web site.

PATIENT RESOURCES

None available

NGC STATUS

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