

Management of Allergic Rhinitis and How it Relates to Asthma

Saturday, June 18, 2011
Madrid I ~ 11:10am - 11:55am

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Objectives

- Understand the pathophysiology, classification, and characteristics of allergic rhinitis
- Compare and contrast USA guidelines and ARIA guidelines for diagnosis and Rx
- Be able to describe the Rx options available in USA
- Decide if there is a correlation between rhinitis and asthma
- Consider the consequences of vaccine refusal
- Investigate strategies for counseling parents about vaccine safety

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**Management of Allergic
Rhinitis & How it Relates to
Asthma**

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Tulsa, Oklahoma



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SPEAKER DECLARATION

Warren Filley, MD declares the following affiliations:

- Employment: Oklahoma Allergy & Asthma Clinic
- Speakers Bureau: GSK, Teva

Allergic Rhinitis

Causes significant illness in the USA

- Second leading cause of chronic disease in the US
 - Affecting approximately 40-60 million people in the US (1 person/4 households)
 - > 50% suffer with symptoms for longer than 10 years
 - Up to 40% of children
- As many as 3.8 million missed days/year, including work and school
- Is a chronic inflammatory condition
- However often dismissed as a “nuisance disorder”

Maple et al. Otolaryngol - JNS 2007;136:S107-24
ARIA/WHO Guidelines & US Practice Parameters

Prevalence of Allergic Rhinitis in Children

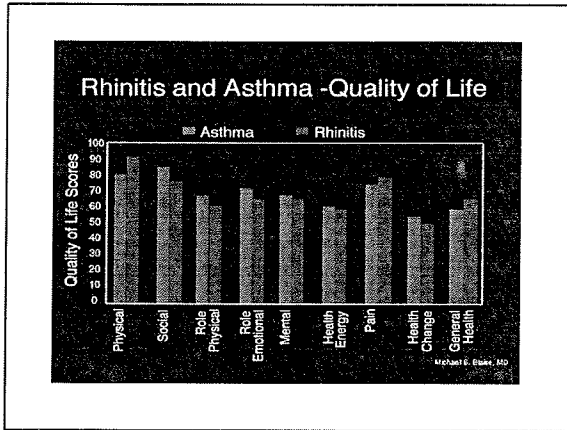
Prevalence	Data Collection
9%	Community based (Seattle, Wash) (5-8 years of age) ¹
20%	US national survey (NHANES III) (6-11 years of age) ²
42%	Community based (Tucson, Ariz) (6 years of age) ³

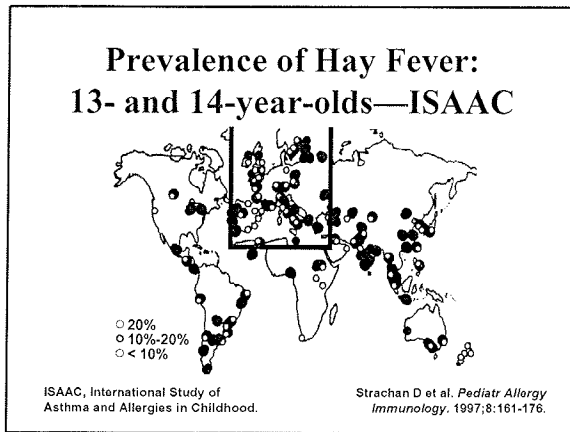
1. Arrighi HM et al. *J Allergy Clin Immunol.* 1995;95(1, pt 2):192.
2. Ma X et al. *Am J Respir Crit Care Med.* 2000;161(3):A326.
3. Wright AL et al. *Pediatrics.* 1994;94:895-901.

Burden of Allergic Rhinitis

Category	Patients Affected, %
Daily Activities	96
Work Productivity	91
Classroom Productivity	93
Missed Work Time	23
Missed Classroom Time	23

N=1,885.
Adapted from Tanner LA et al. *Am J Manag Care.* 1999;5(suppl):S235-S247, reprinted by permission of *The American Journal of Managed Care.* Copyright 2003. All rights reserved.





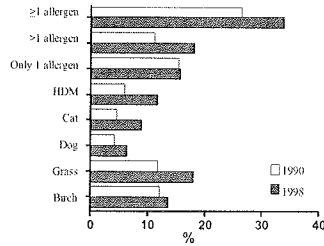
Increase in Prevalence of Rhinitis With Age in Denmark

- Study 1: children 7 to 17 years of age were studied at 6-year interval¹
 - Rhinitis increased from 15% to 22%
 - Often linked with IgE sensitization
- Study 2: adults 15 to 41 years of age were studied at 8-year interval²
 - Rhinitis increased from 25% to 32%
 - Often linked with IgE sensitization

1. Ulrik CS et al. *Allergy*. 2000;55:1019-1024.
2. Linneberg A et al. *J Allergy Clin Immunol*. 2000;106:247-252.

Increasing Prevalence of Specific IgE in an Adult Population

- 15- to 41-year-old adults
- Same subjects studied 8 years apart
- Increase in rhinitis symptoms associated with increase in IgE



Linneberg A et al. *J Allergy Clin Immunol.* 2000;106:247-252.

Rhinitis

- Rhinitis is an inflammation of the mucous membranes of the nose
- Characteristic nasal symptoms:
 - Congestion
 - Sneezing
 - Itching
 - Postnasal drip
 - Rhinorrhea
- Rhinitis can be allergic, nonallergic, or both

American Academy of Allergy, Asthma, and Immunology. The Allergy Report. <http://www.aaaai.org/>. Accessed April 13, 2005.

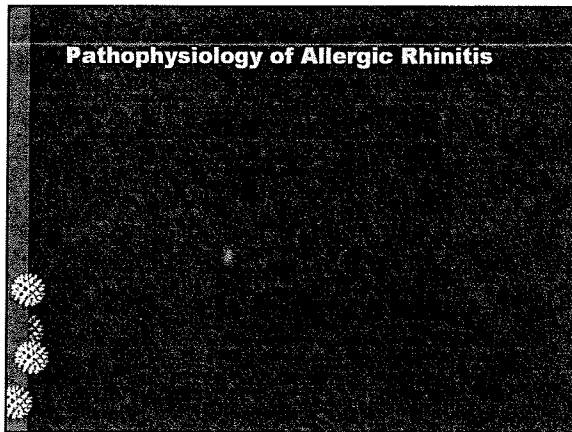
Allergic History

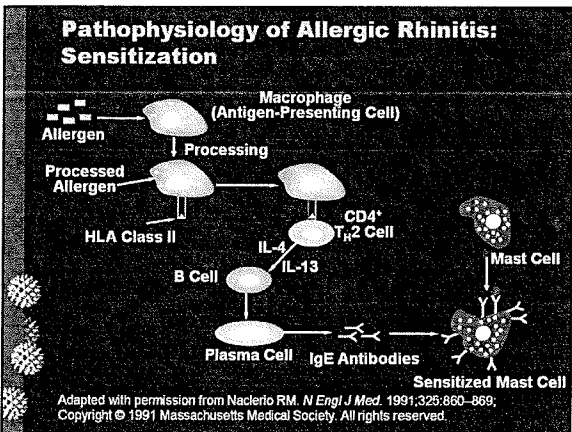
- Symptoms relating to pollen & animal exposure have been shown to have positive predictive value for allergic rhinitis diagnosis¹
- Quality of life questions (2,4) should include symptoms of:
 - Fatigue
 - Learning & attention problems
 - ↓ concentration at school *
 - Sleep disturbances *
 - Absenteeism & Presenteeism at school *

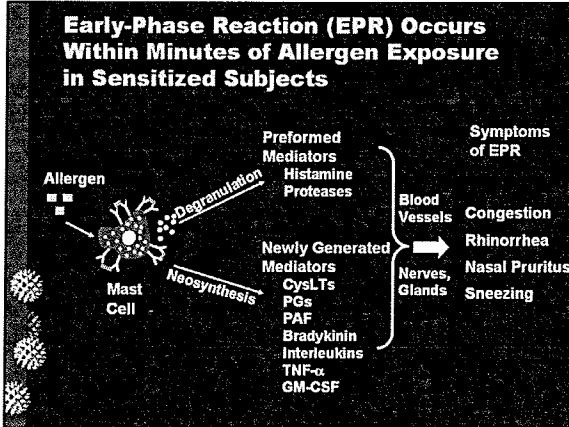
* Improvement measured after treatment
 1. Gendri, 2004. 2. Verman, 1993. 3. Mohr, 2001. 4. Shergin, 2001. 5. Burger, 2004

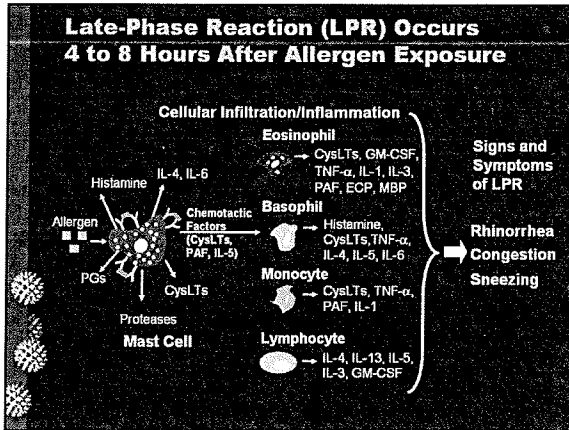
Conditions that Mimic Rhinitis

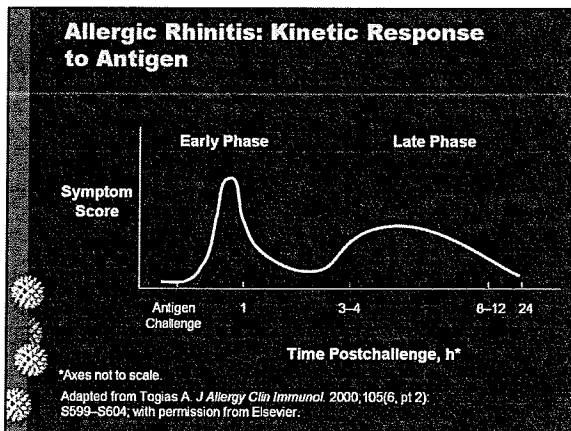
Nasal polyps	Choanal atresia
Structural/mechanical dyskinesia	Ciliary
Adenoidal hypertrophy reflux	Pharyngealnasal
Trauma	Acromegaly
Foreign body	CSF rhinorrhea
Tumors – benign/malignant	Cleft palate











In 2008 two Evidence-based updates on Allergic Rhinitis were Published

ARIA/WHO Guidelines
&
US Practice Parameters for the
Diagnosis & Management of Rhinitis

Classification of Rhinitis
2008 US Rhinitis Practice Parameters

- Allergic rhinitis
 - Seasonal
 - Perennial
 - Perennial with seasonal exacerbation
 - Episodic (after a sporadic exposure)
- Nonallergic rhinitis
 - Perennial nonallergic rhinitis (idiopathic/vasomotor)
 - Infectious
 - Rhinitis medicamentosa (drug induced)
 - Hormonal
 - Anatomical
 - Gustatory
 - Nonallergic with eosinophils (NARES)
 - Atrophic
 - Occupational

Wallace DV & Dykewicz PE. The Diagnosis & Management of Rhinitis: An updated Practice Parameter. J Allergy Clin Immunol. 2008;122:S4-S44

ARIA

**World Health Organization
Initiative on
Allergic Rhinitis
and Asthma**

**Jean Bousquet, Chair
France**

The Need for Guidelines

- Allergic rhinitis is a worldwide health problem
- It can affect the social life of patients
- Guidelines increase the control of rhinitis



ARIA

The Classifications "*Seasonal*" and "*Perennial*" Allergic Rhinitis have been changed to "*Intermittent*" and "*Persistent*" Allergic Rhinitis to bring descriptions into compliance with those for asthma.

ARIA Classification (in Untreated Patients)

Intermittent • Symptoms < 4 days per week • or Symptoms < 4 weeks	Persistent • > 4 days per week • and > 4 weeks
Mild Normal sleep & no impairment of daily activities, sport, leisure & normal work and school & no troublesome symptoms	Moderate-severe <i>One or more items</i> • Abnormal sleep • Impairment of daily activities, sport, leisure • Abnormal work and school • Troublesome symptoms

Appropriate Medications for Disease Severity and Symptoms

- Categories based on ARIA guidelines
 - Mild disease
 - Antihistamines
 - Antihistamine/decongestant combinations
 - Intranasal cromolyn sodium
 - Moderate/severe disease
 - Intranasal corticosteroids
 - Antihistamine/decongestant combinations
 - Immunotherapy

ARIA, Allergic Rhinitis and Its Impact on Asthma.

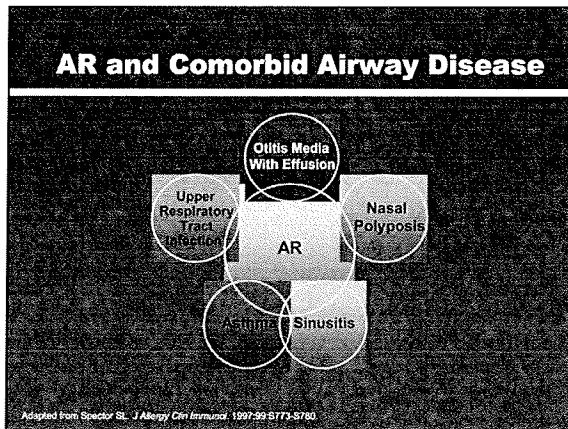
ARIA Recommendations

- Patients with persistent allergic rhinitis should be evaluated for asthma by history, chest examination and, if possible and when necessary, assessment of airflow obstruction before and after bronchodilator
- History and examination of the upper respiratory tract for allergic rhinitis should be performed in patients with asthma
- A strategy should combine the treatment of both the upper and lower airway disease in terms of efficacy and safety

RHINITIS ASSOCIATED WITH A NUMBER OF CHRONIC CONDITIONS

- Asthma
- Eustachian Tube Dysfunction & Otitis Media
- Rhinosinusitis
- Nasal Polyposis
- Allergic Conjunctivitis
- Atopic Dermatitis

The Allergy Report 2002
21 Medical Associations, Governmental Agencies, and Lay Organizations



THE RELATIONSHIP BETWEEN ALLERGIC RHINITIS AND BRONCHIAL ASTHMA

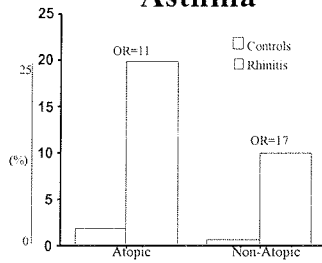
- Nasal allergy is a predisposing risk factor for asthma.
- Treatment of allergic rhinitis may improve asthma symptoms, airway caliber, bronchial hyper-responsiveness.
- Nasal disease can influence pulmonary function via direct and indirect mechanisms.
- Consider nasal disease in all patients with asthma.

Cummings J. Curr Opin Pulm Med. 5(1):35-7 January 1999

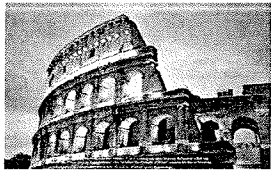
THE LINK BETWEEN ALLERGIC RHINITIS & ASTHMA IS EVIDENT

- More than 70% of asthmatic patients report nasal symptoms.
Pederson et al. Allergy 1983;31(1):25-9
- Approximately 20% of hay fever patients develop asthma.
Reckemann et al. NEJM 1952; 246(21):815-23
Linnar et al. Acta Paediatr 1992;81(2):100-2

Perennial Rhinitis: An Independent Risk Factor for Asthma



Leynaert B et al. *J Allergy Clin Immunol.* 1999;104:301-304.

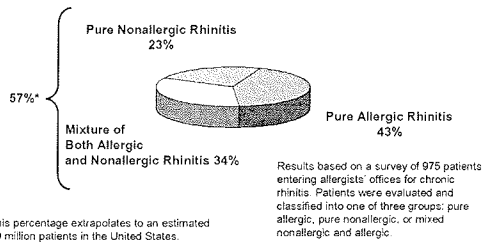


“IF YOU PURGE THE NOSE OF SECRETIONS, YOU WILL IMPROVE THE FUNCTION OF THE LUNGS.”

Galen
129-210 AD

In Chronic Rhinitis, Nonallergic Rhinitis Is a Major Causative Factor

National Rhinitis Classification Task Force Survey Results



Berger et al. *J Managed Care Pharmacy* 2001,7(suppl):4-13.

**INFLAMMATORY COMPONENTS
COMMON TO ALLERGIC
RHINITIS & ASTHMA**

- Inflammatory Cells
 - Mast Cells
 - Eosinophils
 - TH2 Lymphocytes
- Inflammatory Mediators
 - Histamine
 - Leukotrienes
 - Proinflammatory Cytokines

The Allergy Report 2002
21 Medical Associations, Governmental Agencies, and Lay Organizations

**SO THERE IS A RELATIONSHIP
BETWEEN
ASTHMA & ALLERGIC RHINITIS**



**ALLERGIC RHINITIS -
DIAGNOSIS**

- History and physical is most important.
- Confirm suspicions with specific allergy skin tests as the most cost effective method.
- Look for eosinophilia in the blood and nasal secretions.
- Associated diseases of asthma and sinusitis are common.

**Management of Allergic Rhinitis:
Principal Components**

- **Environmental control measures**
 - Avoidance of allergens/triggers
- **Pharmacotherapy**
 - Relief of symptoms
- **Immunotherapy**
 - Prevention or reduced reaction to allergens
 - Control of symptoms of allergic rhinitis
- **Education**
 - Patients and/or caregiver education to improve compliance

Dykewicz MS et al. *Ann Allergy Asthma Immunol*. 1998;81:478-518.

Proper Treatment of Allergic Rhinitis can:

- Help contain costs by reducing absenteeism and presenteeism
- Decrease associated complications of allergic rhinitis
- Avoid costly side effects of OTC medications

ENVIRONMENTAL CONTROL

- First step in treatment
- Not always easy
- A cornerstone of therapy
- May not be fully effective

TREATMENT STATISTICS

- Only 12% of rhinitis patients seek medical help.
- 98% who seek help first present to a primary care physician.¹
- Empiric treatment with antihistamines alone will have a 50% failure rate.
- Patients often dictate their preference for delivery route and medication type.²

- 1 Rachelefsky, G. Ann Allergy Asthma Immunol 1999;82:296-305
- 2 Ledford, D. Allergy & Asthma Proceedings. 2003;24(3):155-162

Allergic Rhinitis: OTC Pharmacotherapy

- Intranasal decongestants
- Nasal saline rinse
- Oral antihistamines
- Oral decongestants
- Intranasal cromolyn sodium

American Academy of Allergy, Asthma and Immunology. The Allergy Report <http://www.aaaai.org/> Accessed April 13, 2010

Allergic Rhinitis: Prescription Pharmacotherapy

- Antihistamines
 - Intranasal & Systemic
- Corticosteroids
 - Intranasal & Systemic
- Anticholinergics
 - Intranasal & Systemic
- Anti-Leukotriene receptor antagonists
- Decongestants

American Academy of Allergy, Asthma and Immunology. The Allergy Report <http://www.aaaai.org/> Accessed April 13, 2010

Medications for Management of Allergic Rhinitis

Based on evidence presented in ARIA Guidelines and US Rhinitis Practice Parameters
 (Bousquet, et al., 2008 & Wallace et al., 2008)

KEY: ++ Substantial benefit; + Modest benefit; +/- Little/no benefit; - No benefit

Medication Class	Sneezing	Itching	Congestion	Rhinorrhea	Eyes	Inflammation
Oral antihistamines	++	++	+/-	++	+	+
Intranasal antihistamines	++	++	+	++	+/-	+
Intraocular antihistamines	-	-	-	-	++	-
Intranasal corticosteroids	++	++	++	++	+	++
Oral corticosteroids	+++	+++	+++	+++	+++	+++

Medications for Management of Allergic Rhinitis

Based on evidence presented in ARIA Guidelines and US Rhinitis Practice Parameters (Bousquet, et al., 2008 & Wallace et al., 2008)

KEY: ++ Substantial benefit; + Modest benefit; +/- Little/no benefit; - No benefit

Medication Class	Sneezing	Itching	Congestion	Rhinorrhea	Eyes	Inflammation
Leukotriene receptor antagonists	+/-	+/-	-	+/-	+/-	+
Decongestants (oral and intranasal)	-	-	++	-	-	-
Cromolyn sodium	+	+	-	+	+	+
Intraocular Cromolyn sodium	-	-	-	-	+	-
Intranasal anticholinergic	-	-	-	++	-	-

PHARMACOTHERAPY FOR ALLERGIC RHINITIS

ANTI-HISTAMINES

- First generation - sedative OTC & Rx
- Second generation - "non-sedative" (claritin, zyrtec) OTC
- Third generation - active metabolites of second generation
 - Fexofenadine (Allegra) OTC
 - Desloratadine (Clarinex) Rx
 - Levocetirizine (Xyzal) Rx, generic
- Topically active - Azelastine (Astelin) Rx
- Olopatadine (Patanase) Rx

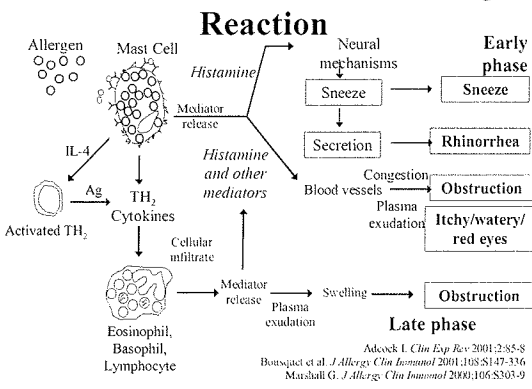
Age Limits of Newer Antihistamines

- Fexofenadine (Allegra) 2 years
- Loratadine (Claritin) 2 years
- Desloratadine (Clarinex) 6 months
- Cetirizine (Zyrtec) 6 months
- Levocetirizine (Xyzal) 6 years
- Azelastine (Astepro) 5 years
- Olopatadine (Patanase) 12 years

Antihistamines

- Both guidelines consider them first-line treatments
- Are safe
- Second-generation non-sedative antihistamines are preferred
- May be given orally or intranasally
- Do not treat congestion/obstruction very well

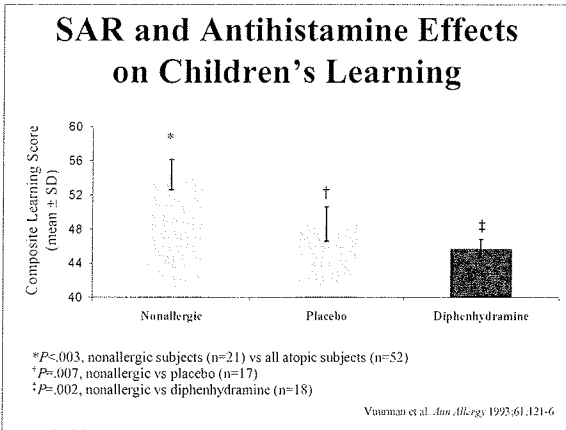
Role of Histamine in Nasal Allergic Reaction

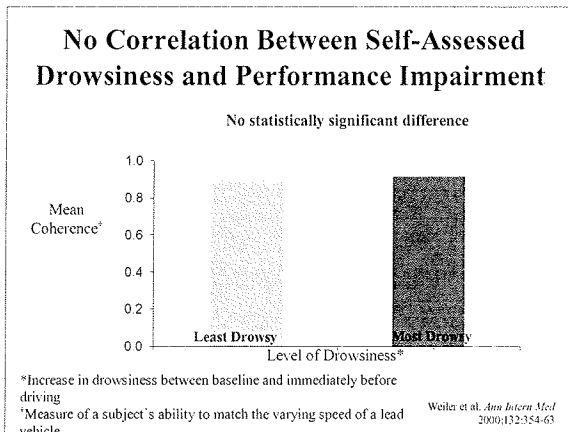


ANTI-HISTAMINES AND ACADEMIC PERFORMANCE

- Children with allergic rhinitis have significantly worse academic scores than non-allergic children.
- Treatment with non-sedative second generation antihistamines increased performance to near normal.¹
- Treatment with first generation sedative antihistamines worsened performance even further.²

- 1 Bender, et al. *Pediatr Asthma Allergy Immunol.* 1998;12: 1-11
- 2 Vaerman, et al. *Ann Allergy.* 1993;71:121-126





**TREATMENT OF RHINITIS
BENEFITS ASTHMA**

- Oral antihistamines with or without decongestants improve symptoms and pulmonary functions in patients with both diseases.

- Grant et al (cetirizine) JACI 1995; (95):923-932
- Corren et al (loratadine) JACI 1997; (100): 781-788

DECONGESTANTS

- Only relieve the congestion.
- Topicals are associated with rebound reorganization (rhinitis medicamentosa).
- Oral products associated with hypertension, CNS stimulation, tachycardia, or even arrhythmias.
- Therefore often contraindicated in older adult patients.

ANTICHOLINERGICS

- Examples
 - Atropine
 - Methscopolamine
 - Ipratropium
- Side effects
 - Excessive dryness of mouth
 - Tachycardia
 - Blurring of vision

IPRATROPIUM BROMIDE

- Blocks hypersecretion by competing with acetylcholine for binding sites.
- Topically active as a nose spray.
- Effective for rhinorrhea of both allergic and non-allergic causes.
- Better tolerated than oral anticholinergics.

CROMOLYN SODIUM

- Available OTC.
- Extremely safe.
- Short half life - dosed QID.
- Mast cell stabilizer.
- Pretreatment blocks both early and late allergic responses.
- Main efficacy is with mild disease.
- Regular usage (QID) can reduce the severity and frequency of rhinitis attacks.

Intranasal Steroids (INS)

- Both guidelines consider these the “Gold Standard”
- Consistently outperforms all other pharmacological treatments
- Best for moderate-severe persistent symptoms
- Once symptoms stabilize dose should be reduced to reduce side effects

INTRANASAL CORTICOSTEROIDS FOR ALLERGIC RHINITIS: HOW DO DIFFERENT AGENTS COMPARE?

- Corticosteroids compared:
 - Mometasone
 - Beclomethasone
 - Budesonide
 - Fluticasone
 - Triamcinolone
 - Betamethasone
 - Dexamethasone

Corren J., J. Allergy Clin. Immunology 104 (4PT.1): S144-9, October 1999

INTRANASAL CORTICOSTEROIDS FOR ALLERGIC RHINITIS: HOW DO DIFFERENT AGENTS COMPARE?

- Mometasone Furoate and Fluticasone Propionate.
 - Higher topical potency than older compounds.
 - Higher lipid solubility than older compounds.
 - Lower systemic bio-availability than older compounds.
 - Less potential for systemic side effects than older compounds.
- In clinical usage all, however, appear equally effective.

Corren, J., J. Allergy Clin. Immunology 104 (4PT.1): S144-9, October 1999

INTRANASAL CORTICOSTEROIDS FOR ALLERGIC RHINITIS: HOW DO DIFFERENT AGENTS COMPARE?

- Commonly held belief that it takes weeks to relieve symptoms is incorrect.
- Studies support as-needed use of drugs.
- Clinical improvement within 1-2 days documented.

Corren, J., J. Allergy Clin. Immunology 104 (4PT.1): S144-9, October 1999

AS-NEEDED USE OF FLUTICASONE PROPRIONATE NOSE SPRAY REDUCES SYMPTOMS OF SEASONAL ALLERGIC RHINITIS

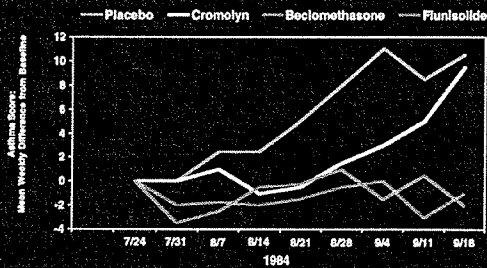
- QOL significantly improved for:
 - Sleep
 - Non-nose/eye symptoms
 - Activities
 - Nasal symptoms
 - Practical domains
 - Overall quality of life

Jen, A., et al. Journal Allergy Clin. Immunology, 105: 732-738, 2000

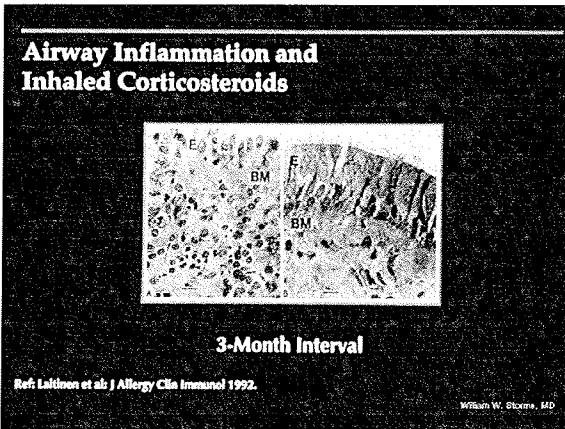
TREATMENT OF RHINITIS BENEFITS ASTHMA

- Use of nasal steroids can improve various aspects of asthma.
 - Henriksen & Wenzel (budesonide) Am Rev Respir Dis 1984; (130): 1014-1018
 - Welsh (beclomethasone, flunisolide, cromolyn) Mayo Clin Proc 1987; (62):125-134
 - Watson, et al JACI 1993; (91):97-101
 - Corren (beclomethasone) JACI 1992; (90):250-256
 - Wood & Eggleston Am Rev Respir Crit Care Med 1995; (151):315-320
 - Foregi et al (fluticasone) JACI 1996; (98):274-282

Treating Seasonal Allergic Rhinitis— Effect on Asthma Symptoms



Alan Lusk, MD



INH Age Limits

- Beclomethasone (Beclvent) 6 years
- Budesonide (Rhinocort Aqua) 6 years
- Ciclesonide (Omnaris) 12 years
- Flunisolide (Nasalide) 6 years
- Fluticasone propionate (Flovent) 4 years
- Fluticasone furoate (Veramyst) 2 years
- Mometasone (Nasonex) 2 years
- Triamcinolone (Nasacort AQ) 2 years

LEUKOTRIENE RECEPTOR ANTAGONISTS (LTRAs)

- Developed to counter cysteinyl leukotrienes (proinflammatory mediators)
- Inhibit the binding of leukotrienes to their receptors
- FDA approved for allergic rhinitis (2003) Previously approved for asthma
- Some clinical trials support use in allergic rhinitis therapy while others show no difference between LTRAs and antihistamines
- Not as effective as INH
- FDA requires warning label for neuropsychiatric events (6-12-09)

1. Malmqvist, JACI 2004;114:151-155; Abstract S19. 2. Filipiak, Allergy 2004;59: Abstract a EAACI. 3. Mellors, JMAI 2004;16:917-922

EFFECTS OF LEUKOTRIENES

- When placed directly in the nose they clearly cause nasal congestion and to a certain extent nasal drainage.
- They do not cause sneezing and itching on direct placement in the nose.
- Conflicting data on the additive effects with antihistamines.
- No studies combined with topical steroids.
- Reasonable to try in patients who respond to nothing else.

Robert Nathan, M.D.
University of Colorado Health Sciences Center

IMMUNOTHERAPY

- Used since the early 1900's. 100th anniversary in 2011
- Only Rx which alters the natural course of the disease process.
- Reduces allergy inflammation by altering the body's immune response.
- ↓ IgE, ↑ IgG, ↑ suppressor T cells, ↓ CD4 & CD8 T cells.
- Shift lymphocyte response from TH2 to TH1.
- Response specific to the allergens used.
- Efficacy demonstrable in numerous clinical trials.
- Duration of efficacy continues after cessation of therapy.

Subcutaneous Immunotherapy (SCIT or SIT) vs Sublingual Immunotherapy (SLIT)

- Subcutaneous is the "gold standard" therapy used for 100 years
- Sublingual is currently only approved for use in Europe and represents 45% of all immunotherapy given there
- Sublingual is not approved by the FDA in USA and there are no payment codes for it
- Although shown to be efficacious sublingual is not as effective as subcutaneous with multiple allergens

Allergy Immunotherapy for Allergic Rhinitis

- May prevent the development of new allergic sensitization (2,4)
- May reduce the risk of developing asthma (4,9)
- Is the only treatment that can potentially modify the disease process (10-12)
- May be continued during pregnancy without dose escalation to minimize inducing a systemic reaction (1)

• 1 Cox, 2007 2 Pirello-D'Ambrosio, 2001 3 Pajus, 2001 4 Des Roches, 1997 5 Jacobsen, 2001
• 6 Niggemann, 2006 7 Polosa, 2005 8 Polosa, 2004 9 Cox, 2007 10 Rodrigo, 2006
• 11 Gafley, 1988 12 Deckhorn, 1992

LONG-TERM CLINICAL EFFICACY OF GRASS-POLLEN IMMUNOTHERAPY

- A well conducted, placebo-controlled, randomized study.
- 3-4 years of therapy produced significant reduction in symptoms versus placebo.
- This improvement was maintained for at least 3 years after discontinuation of therapy.

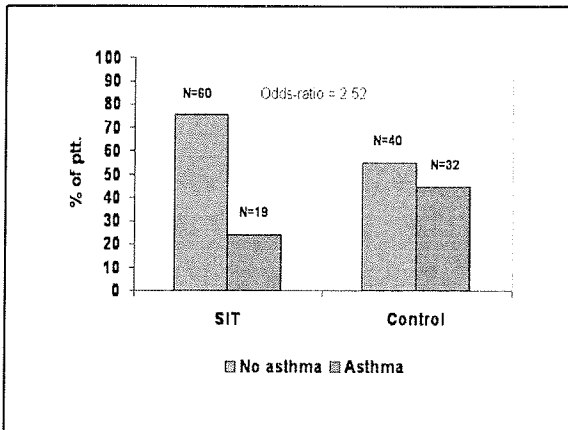
S.R. Durham, M.D., et al.
NEJM 1999; 341:468-475

POLLEN IMMUNOTHERAPY REDUCES THE DEVELOPMENT OF ASTHMA IN CHILDREN WITH SEASONAL RHINOCONJUNCTIVITIS

(The PAT-Study)

- 205 Children 6-14 year old
- Control group or 3 years immunotherapy
- At inclusion none reported asthma with need for daily medications.
- At inclusion 20% reported mild asthma symptoms during the pollen season.
- Grass or birch pollen sensitive.
- Immunotherapy group had 1/2 the rate of asthma onset as the control.

Moller et al
Sweden, Norway, Denmark, Finland, Austria, Germany
JACI 2002; 109(2):251-256



HELP FOR THE PROBLEM PATIENT

Salt water rinses prior to the use of intranasal corticosteroid sprays will clear the nose of secretions and increase the effectiveness of the steroid spray.



CONCLUSIONS

- Allergic diseases increasing worldwide.
- Newer classifications and recommendations (ARIA & US Practice Parameters) will help to recognize and treat the disease process better.
- There is a relationship between asthma and rhinitis.
- Numerous excellent treatments are available.
- Treatment of the nose can improve asthma.
- Treatments should be individually tailored.
- When symptoms persist despite treatments do not hesitate to ask for help.
