Allergen immunotherapy for asthma

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สาขาวิชาโรคภูมิแพ้และอิมมูโนวิทยา

ภาควิชาอายุรศาสตร์

คณะแพทยศาสตร์ศิริราชพยาบาล

Current available treatment

Specific immunotherapy

Allergic rhinitis

- Antihistamine
- Nasal steroid
- Leukotriene modifier

Allergic asthma

- Inhaled steroid
- ICS+LABA
- Leukotriene modifier
- Theophylline-SR
- Anti-IgE

Definition

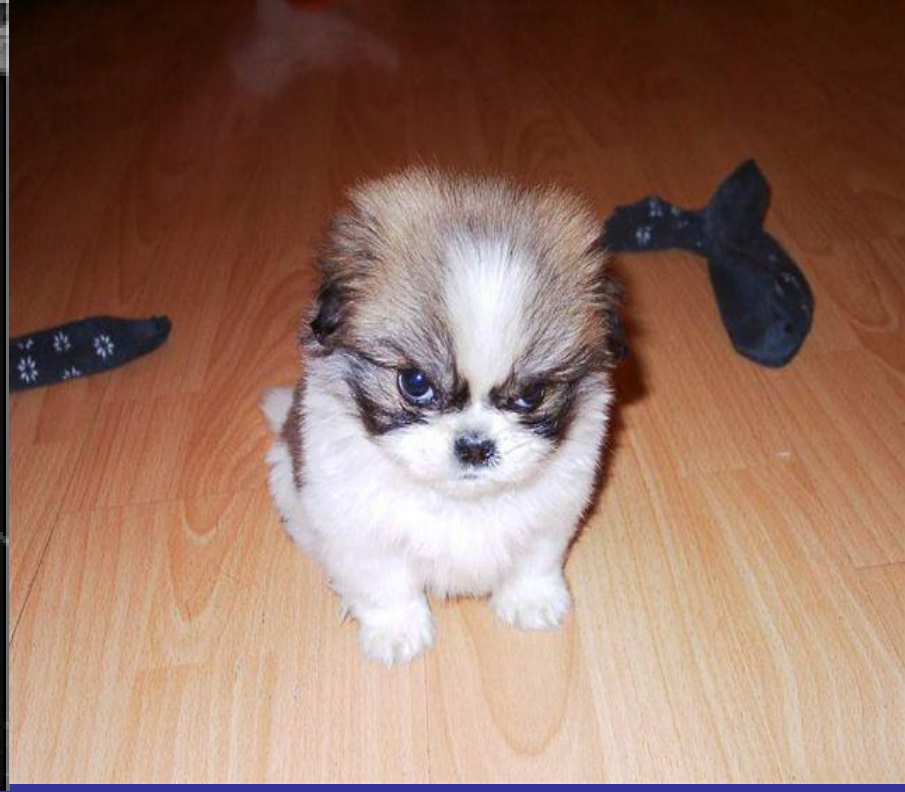
- The repeated administration of specific allergens to patients with IgE-mediated conditions for the purpose of providing protection against the allergic symptoms and inflammatory reactions associated with natural exposure to allergens.

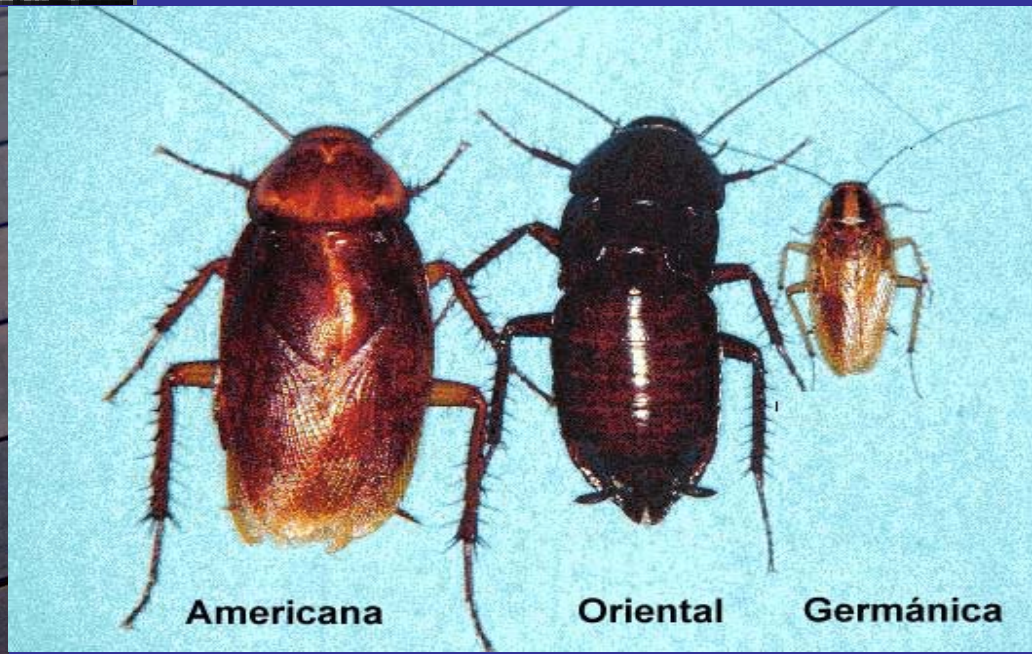
Allergen extract

Allergen vaccine

A WHO position paper. Bousquet J. J Allergy Clin Immunol 1998;102:558-62


100µm F4 L0
X250 39mm




Americana
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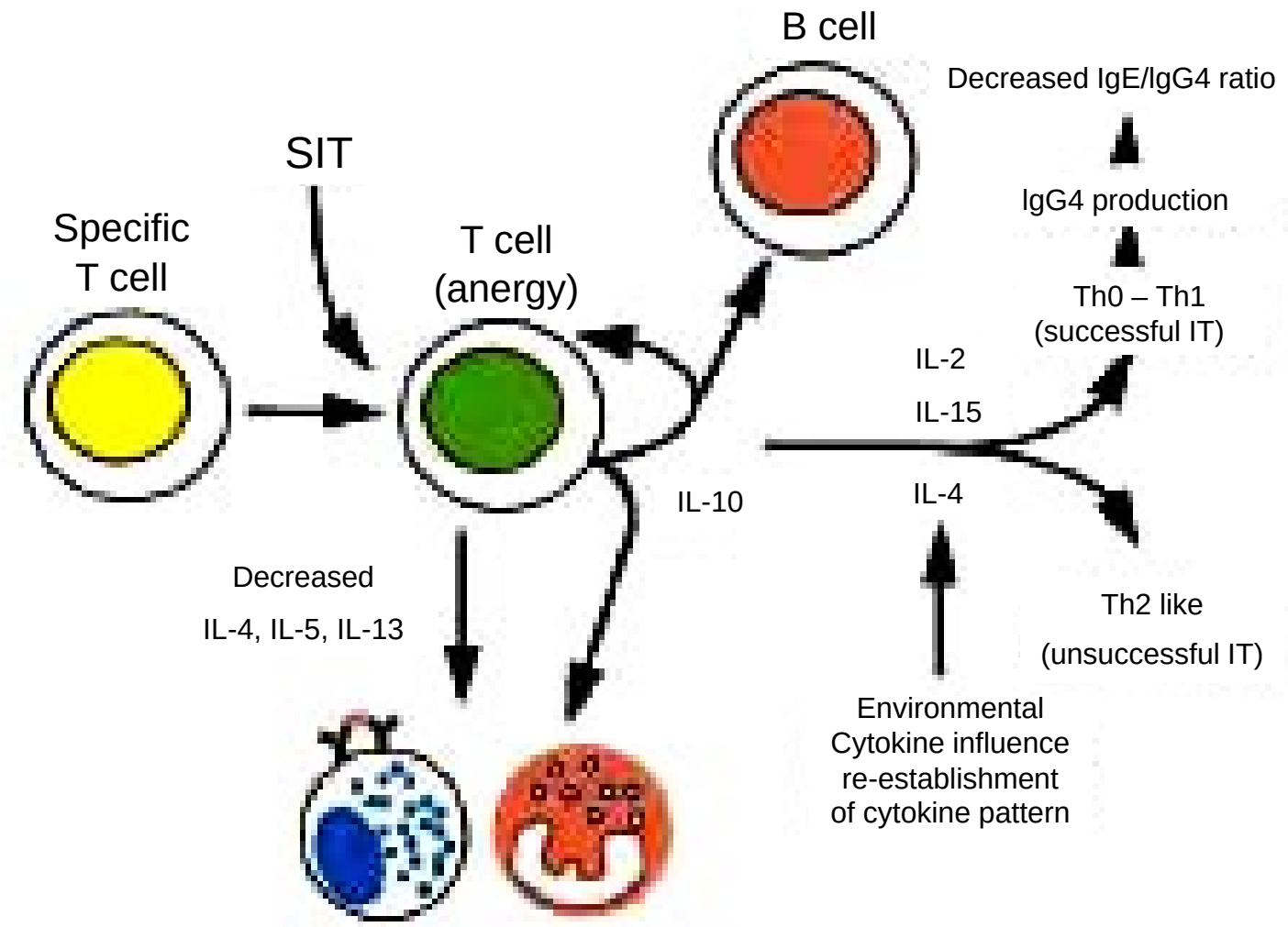
Allergy skin testing



Akdis and Blaser. The FASEB Journal. 1999;302:203-9.

Indication

- Symptoms of **AR and/or asthma** after natural exposure to aeroallergens and demonstrable evidence of clinically **relevant specific IgE**.

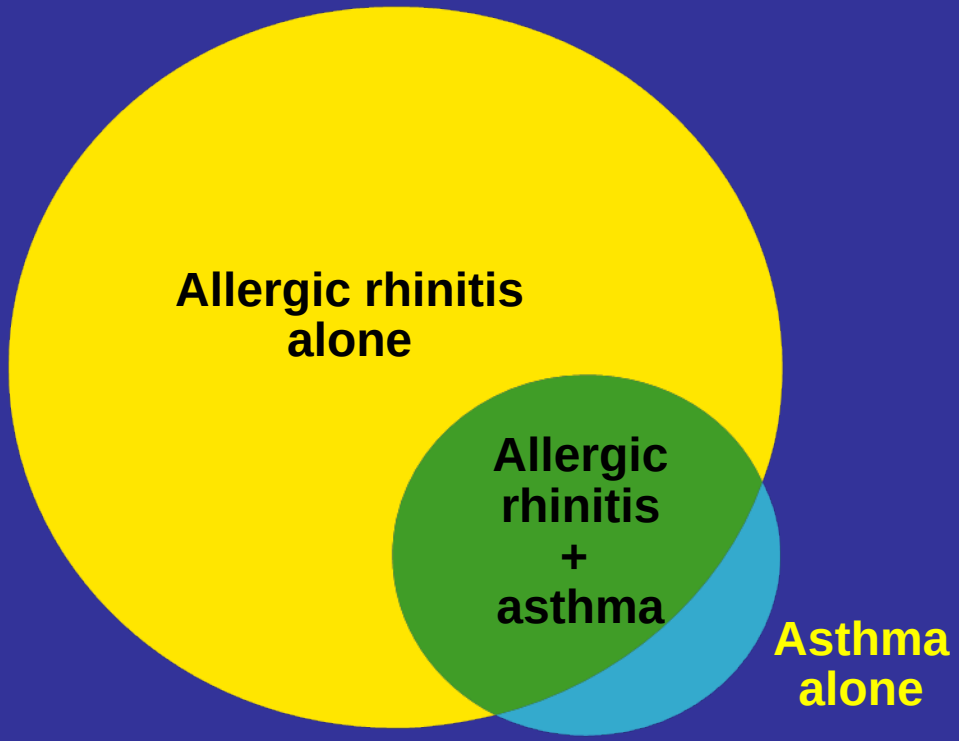
+

- Poor response to allergen avoidance and pharmacotherapy.
- Unacceptable adverse effects of medications.
- Wish to reduce or avoid long term pharmacotherapy and the cost of medication.
- Coexisting allergic rhinitis and asthma

Cox L. J Allergy Clin Immunol 2007;120:s25-85.

Most Patients with Asthma Have Allergic Rhinitis

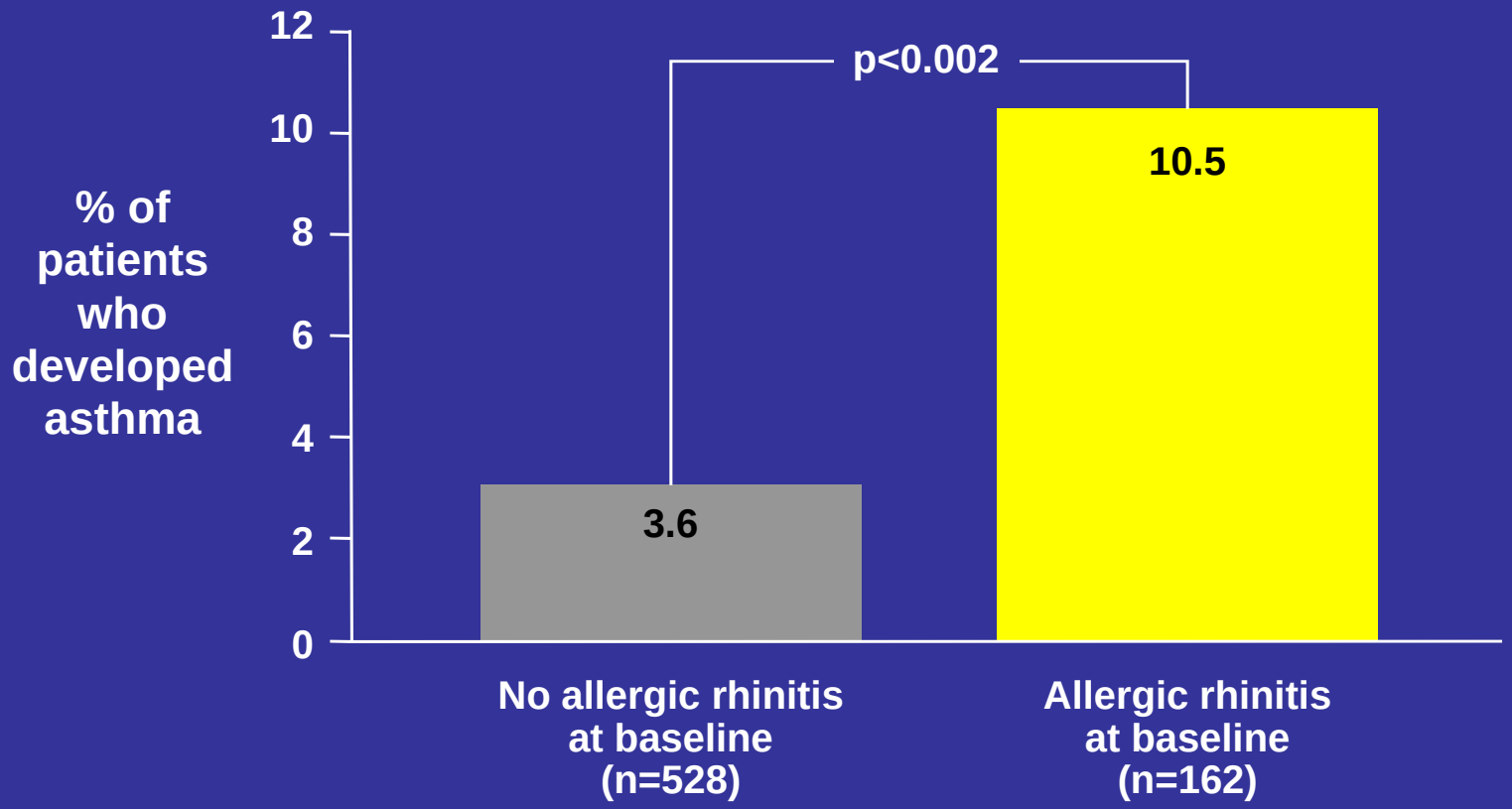
Approximately **80%** of asthmatics have allergic rhinitis



Adapted from The Workshop Expert Panel. *Management of Allergic Rhinitis and its Impact on Asthma (ARIA) Pocket Guide. A Pocket Guide for Physicians and Nurses.* 2001; Bousquet J and the ARIA Workshop Group *J Allergy Clin Immunol* 2001;108(5):S147-S334; Sibbald B, Rink E *Thorax* 1991;46:895-901; Leynaert B et al *Am J Respir Crit Care Med* 2000;162:1391-1396.

Allergic Rhinitis Is a Risk Factor for Asthma

- Allergic rhinitis increased the risk of asthma ~**3**-fold



23-year follow-up of college freshmen undergoing allergy testing; data based on 738 individuals (69% male) with average age of 40 years.

Adapted from Settipane RJ et al *Allergy Proc* 1994;15:21-25.

Effectiveness on allergic rhinitis

- Meta-analysis of prospective, randomized, double-blind, placebo-controlled studies
- All studies of SIT in allergic rhinitis between 1966-1996 were identified.
- **16** studies involving **759** patients with allergic rhinitis.

Ross RN. Clin Ther 2000; 22:342-50.

Effectiveness on allergic rhinitis

- Improve symptoms of allergic rhinitis

  (OR 1.81, 95%CI 1.48-2-23).

- Improve symptom-medication score

  ($P < 0.05$).

Ross RN. Clin Ther 2000; 22:342-50.

Effectiveness on asthma

- 75 RCT with a total of 3,188 patients with asthma
- Significant improvement of asthma symptoms, medication use and BHR.
- No consistent effect on lung function.

Abramson MJ. Cochrane Database Syst Rev 2003:CD001186.9

SIT for asthma: systematic reviews

- 88 RCTs were included.
- 42 SIT for mite, 27 for pollens,10 for animal dander, and 6 for multiple allergens.
- Only 16 trials were assessed as clearly adequate.

Cochrane Database Syst Rev 2010,Aug:CD001186.

SIT for asthma: systematic reviews

- Significant improvement in asthma symptom score.
- Treat 3 pts. to avoid 1 deterioration in asthma symptom.
- Treat 4 pts. to avoid 1 requiring increased medication.
- Reduce BHR.
- No consistent effect on lung function
- 16 pts with SIT, 1 local reaction.
- 9 pts with SIT, 1 systemic reaction.

Cochrane Database Syst Rev 2010,Aug:CD001186.

Effectiveness of SLIT on asthma

- Meta-analysis including 25 RCT with 1706 patients with asthma.
- SLIT is beneficial for asthma, albeit the magnitude is not large.
- Safer than subcutaneous route.

Calamita Z. Allergy 2006:61;1162-72.

Effect of SIT added to drug treatment

- A double-blinded RCT in 72 patients with mild to moderate asthma, allergic to HDM.
- ↓ patients requiring rescue β_2 agonist.
- ↑ morning PEF.
- No benefit on the dose of inhaled steroid, asthma symptoms, lung volumes and BHR.

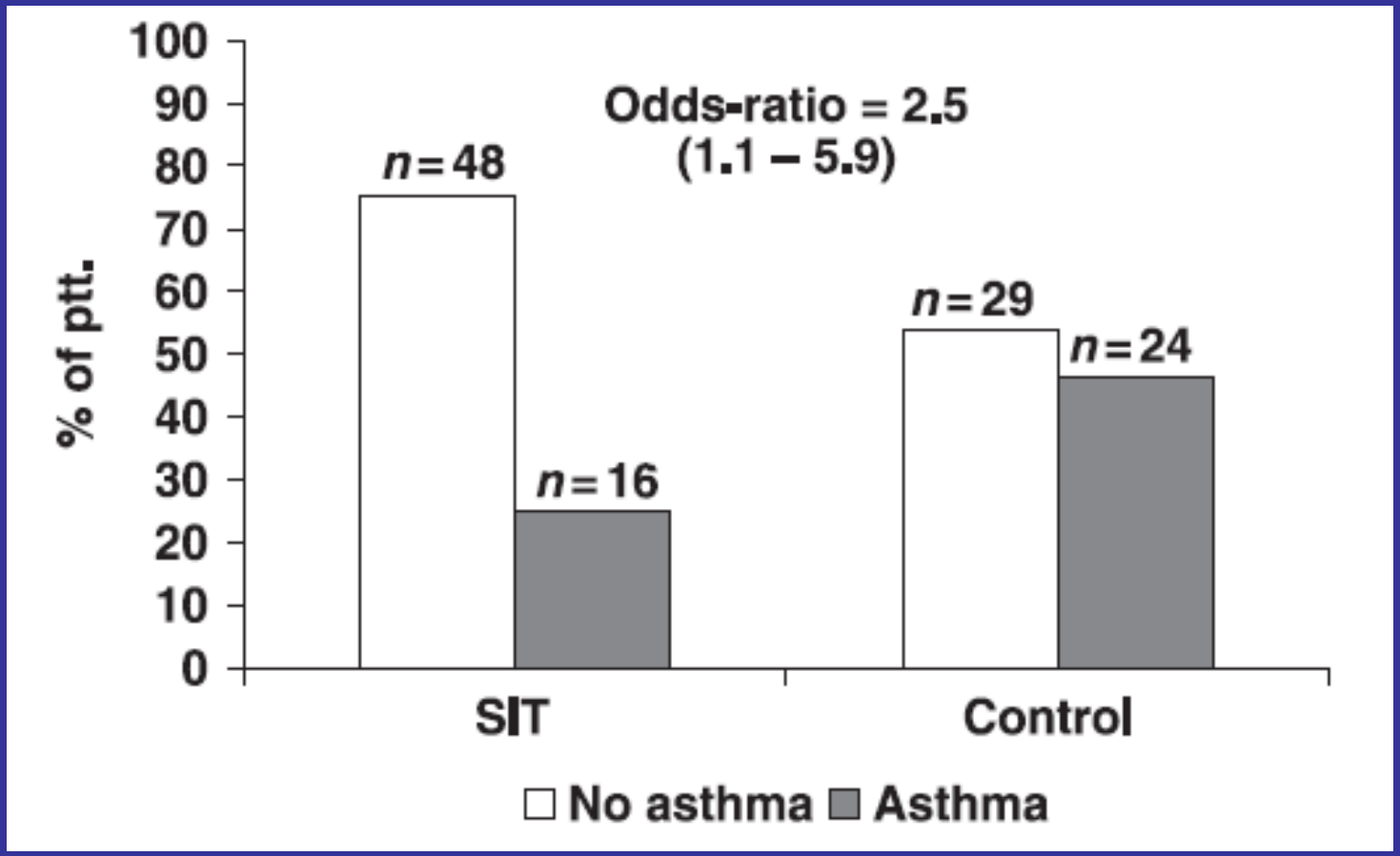
Maestrelli P. J Allergy Clin Immunol 2004;113:643-9.

SIT prevents asthma

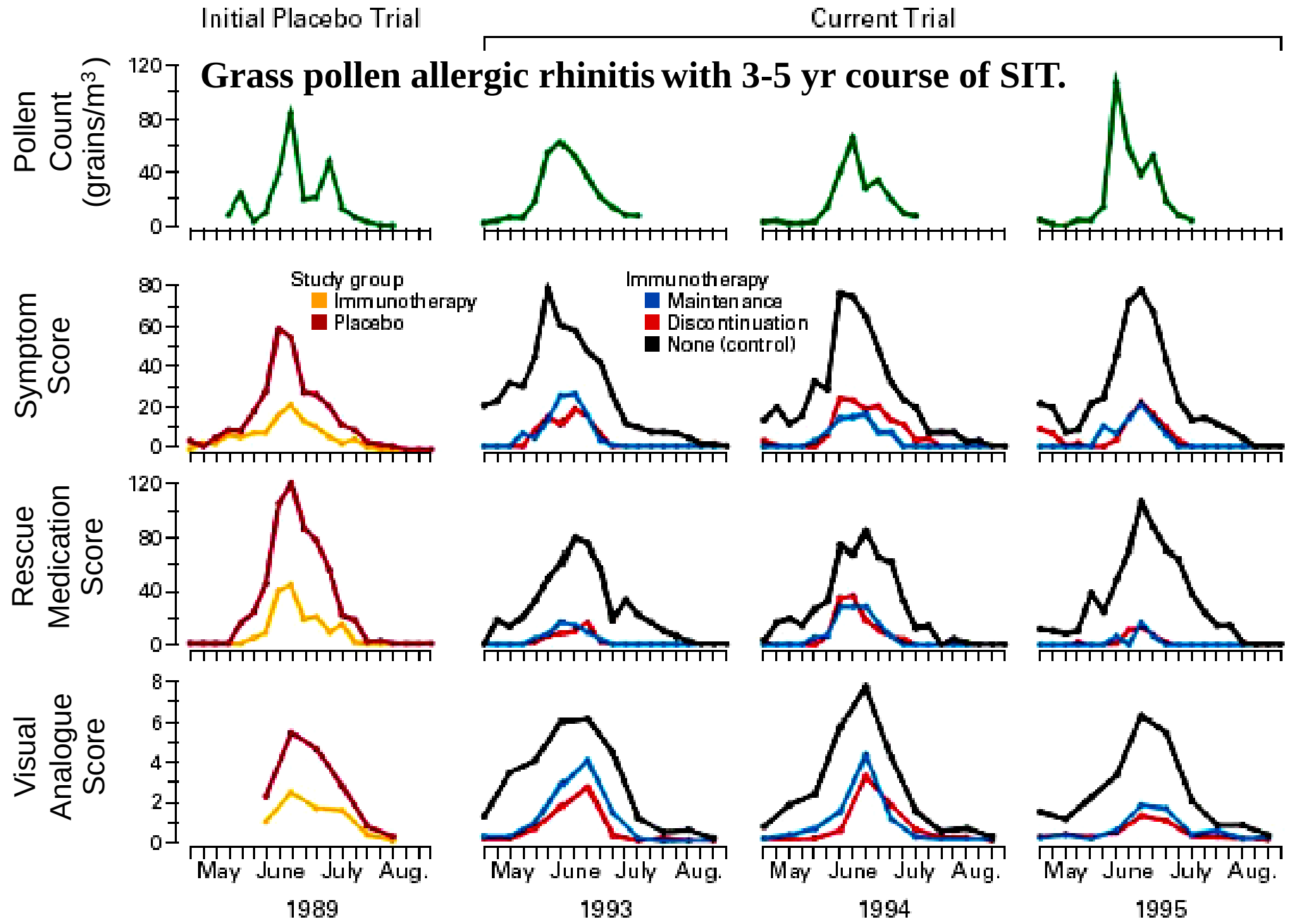
- 147 subjects with allergic rhinitis, aged 16-25 yr. with grass pollen allergy were followed up for 10 yr after 3-yr course of SIT.
- 3-yr course of SIT have long-term clinical effects.
- Less actively treated subjects had developed asthma (OR 2.5).

Jacobsen L. The Preventive Allergy Treatment study (PAT). Allergy 2007:62;943-8.

SIT prevents asthma



Jacobsen L. The Preventive Allergy Treatment study (PAT). Allergy 2007:62;943-8.



Durham SR, et al. N Engl J Med 1999;341:468-75.

SIT prevents new sensitization

- 147 children with rhinitis and/or asthma monosensitized to dust mite were recruited.
- 85 underwent SIT, and 62 on medication.
- 25% in SIT, 53% in control developed new sensitization.

Inal A. J Investig Allergol Clin Immunol 2007;17:85-91.

Summary

- Specific immunotherapy (SIT) has a role in selected asthma patients.
- SIT prevents new sensitization and asthma in adulthood.
- Effect of SIT lasts for several years after 3-5 yr-course of treatment.


Thank You

Safety

- Systemic reactions

  -conventional schedule: <1%

  -rush immunotherapy

- Systemic reactions usually occur within 30 mins.

Cox L. J Allergy Clin Immunol 2007;120:s25-85.

Risk factors for systemic reactions

- Uncontrolled diseases

  -uncontrolled asthma

  -cardiovascular diseases

- FEV_1 <70% of predicted.
- Taking β-blocker.

Cox L. J Allergy Clin Immunol 2007;120:s25-85.

Allergen extract/vaccine

- Standardized extract

  -Cat hair or pelt

  -Mite

  -Grass

  -Ragweed

- Non- Standardized extract

  -Dog, other pollens, cockroach, mold

Cox L. J Allergy Clin Immunol 2007;120:s25-85.

How to do SIT

- Serial dilutions

  1:1,000→1:100 →1:10 →Full strength (maintenance)

- Clear labeling
- Evaluate at 1-yr after starting treatment

Cox L. J Allergy Clin Immunol 2007;120:s25-85.

How to do SIT

- If not effective, consider:

  1) still expose to allergens

  2) still expose to non-allergenic trigger

  3) type or dose of allergens is not appropriate

Cox L. J Allergy Clin Immunol 2007;120:s25-85.

Effectiveness on asthma

- Meta-analysis of prospective, randomized, double-blind, placebo-controlled studies
- All studies of SIT in asthmatics between 1966-1998 were identified.
- **24** studies involving **962 asthmatics.**

Ross RN. Clin Ther 2000; 22:329-41.

Effectiveness on asthma

- SIT compared to placebo

  -Improve symptoms of asthma (OR 2.76, 95%CI 2.22-3.42).

  -Improve pulmonary function (OR 2.87, 95%CI 1.82-4.52).

  -Protection against bronchial challenge (OR 2.0, 95%CI 1.46-2.72).

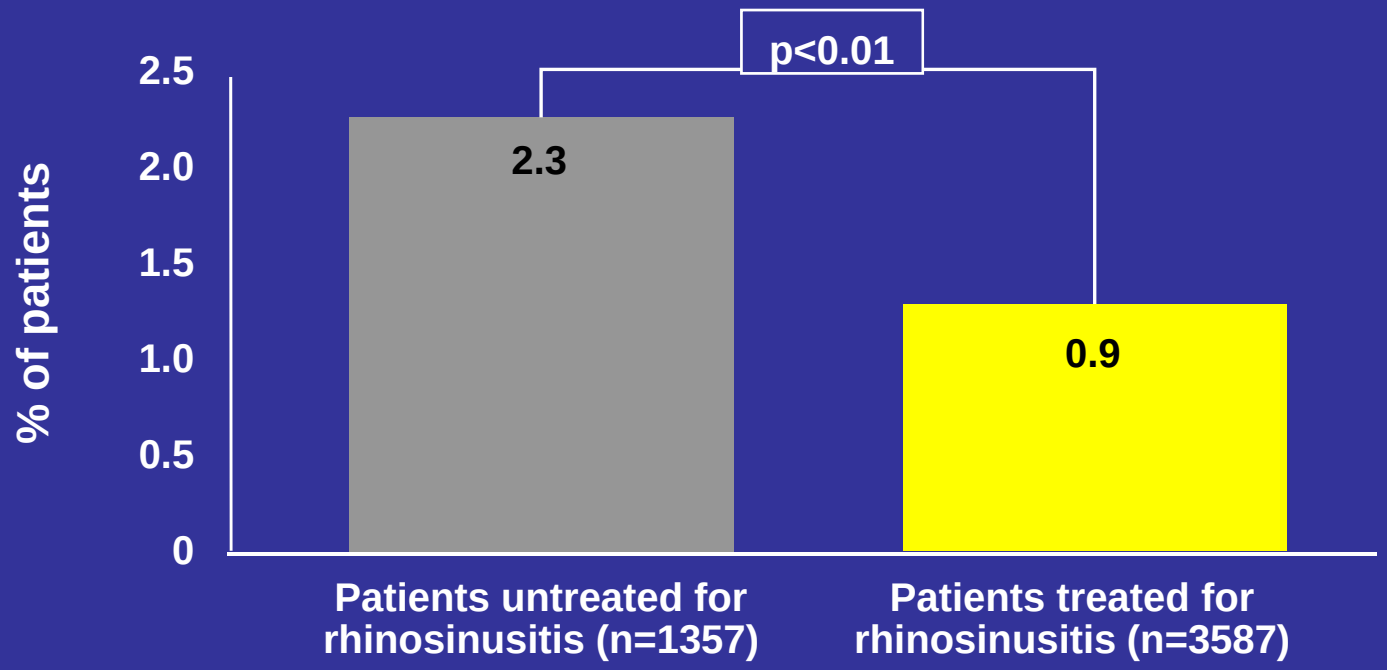
Ross RN. Clin Ther 2000; 22:329-41.

Summary of mechanisms

- A shift from Th2 to Th1
- Immunologic tolerance
- Decrease of specific IgE
- Increase of IgG blocking antibody

Treating Rhinosinusitis Decreased Asthma-Related Resource Utilization

- 61% fewer hospitalizations in treated patients



Retrospective cohort study of costs over a period of up to one year incurred by patients 12 to 60 years of age with both allergic rhinitis and asthma.

Adapted from Crystal-Peters J et al *J Allergy Clin Immunol* 2002;109(1):57-62.