METHODS. After an 8-week evaluation to assess baseline symptoms, patients were randomized to 1 of 4 parallel treatment groups. One group was treated with pharmacotherapy, while the other 3 received immunotherapy administered in 1 of the 3 following regimens: (1) 16-week induction with weekly in-clinic SCIT using a glycerinated solution of HDM extract, followed by maintenance with monthly in-clinic SCIT (SCIT alone); (2) 1-month induction with SLIT using extract adsorbed onto aluminum hydroxide, given 3 times per week at home with gradually increasing doses, followed by maintenance at the maximum dose (SLIT alone); or (3) 16-week induction phase using SCIT (described earlier), followed by maintenance with in-home self-administered SLIT (SCIT plus SLIT). During clinic visits at –1, 0, 1, 4, 12, and 18 months, physicians assessed clinical status by recording frequency of asthma attacks, corticosteroid use, symptoms scores, and medications scores. Blood drawn at each of these visits was evaluated for total serum IgE and for HDM-specific levels of IgE and IgG4 antibodies. Additionally, supernatants from culture of peripheral blood mononuclear cells (isolated from whole blood drawn at each visit) were analyzed for HDM-specific interferon (IFN)-γ, transforming growth factor (TGF)-β, interleukin (IL)-5, IL-10, IL-13, and IL-17 cytokines.

RESULTS. Fifty patients completed the study protocol. Immunotherapy for the SCIT alone, SLIT alone, and SCIT plus SLIT groups proved effective in the treatment of asthma and allergic rhinitis. Improved symptoms scores correlated with increases in T-helper 1 (Th1) cytokines (IFN-γ), regulatory T-cell cytokines (TGF-β and IL-10), and ratio of Th1 to Th2 cytokines (IFN-γ/IL-5). For patients in the SCIT alone and SCIT plus SLIT groups, improvement in symptom scores was greater and earlier in onset; this correlated with significant increases in IgG4 levels (blocking antibodies). Interestingly, improvement in scores for allergic rhinitis was only significant in the combined SCIT plus SLIT group. Adverse effects were observed in only 2 patients, both in the SCIT group.

CONCLUSIONS. In this prospective, randomized, controlled study, a novel combination of SCIT for induction and SLIT for maintenance was as effective in reducing symptoms as SCIT alone. Additionally, as expected, both SCIT alone and SCIT plus SLIT were found to be more effective that SLIT alone. This combination regimen also had the advantage of allowing patients to receive SLIT in place of SCIT during maintenance phase, thus avoiding the monthly office visits and injections following the initial 16-week induction on SCIT.

REVIEWER COMMENTS. While SCIT has been shown to be more effective in reducing allergic symptoms than SLIT, SCIT remains unappealing to many pediatric patients because of its poorer safety profile, uncomfortable injections, and in-clinic administration, requiring school absences for patients and work absences for parents. This study offers a promising, novel regimen that will allow patients to avoid the less-appealing aspects of SCIT for the maintenance phase of their course of immunotherapy. Additionally, this study made important conclusions about cytokine responses to immunotherapy and how these correlate with symptoms. Further study should focus on long-term outcomes from this novel regimen to establish its utility in pediatric patients.

Evidence of Effect of Subcutaneous Immunotherapy in Children: Complete and Updated Review From 2006 Onward


PURPOSE OF THE STUDY. To review the literature regarding the use of subcutaneous immunotherapy (SCIT) in the treatment of atopic children.

STUDY POPULATION. Both MEDLINE and EMBASE were searched using the keywords (immunotherapy* or desensit*) and allerg* and (child* or pediatr*). The time period of January 2006 to April 2011 was used. The authors also searched references from published trials or recent reviews.

METHODS. Articles that included patients aged 3 to 18 years were included. The patients were proved to have allergic sensitization in the form of respiratory allergy with symptoms of asthma, allergic rhinitis (either seasonal or perennial), or rhinoconjunctivitis. Information regarding clinical efficacy in terms of symptoms, safety of SCIT, and immunologic outcome data was obtained. The quality of the evidence was rated from very low to high.

RESULTS. Of 109 possible candidate articles, 31 articles were included in the analysis. High-quality evidence for SCIT using grass pollen exists for improved symptoms and reduced medication scores up to 7 years after termination of treatment. Moderate evidence that SCIT for grass pollen prevented asthma in children with rhinitis only at the start of the study also exists. Alternaria SCIT improved quality of life, symptom-medication scores, and medication scores. For SCIT with house dust mite, high-quality evidence showed improvement in asthma symptoms and medication scores and reduced visits to the emergency department. Improvements in skin test reactivity were seen with both grass pollen and house dust mite.

CONCLUSIONS. Pediatric patients with allergy benefit from treatment with SCIT using house dust mite, Alternaria, and grass pollen.
Revue Comments. This review supports the use of subcutaneous immunotherapy in the treatment of pediatric patients with respiratory allergy. While the results of a large randomized trial of pediatric patients with asthma brought into question the benefit of SCIT, this review reassures clinicians that evidence, ranging from low to high quality, exists to support the treatment of atopic respiratory disease in children. Since environmental avoidance is not always possible, the information regarding the benefit of immunotherapy is essential in the pediatric patient population.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2012-2183

Vivian Hernandez-Trujillo, MD
Miami, FL

Microbiome, Mucosal Immunology, and Immunomodulation

Exogenous Stimuli Maintain Intraepithelial Lymphocytes Via Aryl Hydrocarbon Receptor Activation

Purpose of the Study. Intraepithelial lymphocytes (IELs) are immune cells with unique but incompletely understood properties related to epithelial barrier defense. This study builds off the authors’ previous work with specialized T-cell populations and investigates how these interesting cells develop and function.

Study Population. Studies were performed in mice.

Methods. The authors used gene expression studies and transgenic mouse models to characterize factors involved with IEL development, survival, and function in the gastrointestinal tract.

Results. In contrast to other lymphocyte populations, IELs were found to express high levels of a transcription factor known as aryl hydrocarbon receptor (Ahr). In Ahr-deficient mice, IELs developed and were recruited normally to the intestines and skin, but their survival was markedly diminished and they eventually disappeared as the animals matured. Previous studies had shown Ahr to bind to plant-derived nutrients found naturally in cruciferous vegetables, and therefore the authors investigated whether diet affected Ahr signaling and, consequently, IEL development. Feeding wild-type mice a synthetic diet devoid of Ahr ligands resulted in the disappearance of intestinal IELs similar to that seen in transgenic mice lacking Ahr expression; and the IELs returned when a single specific Ahr ligand was added to the synthetic diet. Finally, IELs appeared to be important for intestinal health, since their absence was associated with increased intestinal bacterial burdens, resulting in abnormal immune activation and increased susceptibility to chemical-induced colitis.

Conclusions. Diet-derived compounds activate Ahr-signaling pathways to maintain proper intestinal immune function.

Reviewer Comments. This article presents another reason to eat your vegetables: proper functioning of the intestinal immune system. The authors demonstrate that specific dietary compounds found in cruciferous vegetables like broccoli, cauliflower, and cabbage are essential for the survival of IELs, which maintain the delicate balance between immune reactivity and tolerance to the intestinal microbiota. These provocative findings provide a potential mechanism by which diets low in fruits and vegetables may predispose people to immune dysregulation and the occurrence of intestinal inflammatory diseases. Furthermore, this article highlights how the environment can have dramatic effects on immune system development and function.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2012-2183

Timothy P. Moran, MD, PhD
Brian P. Vicker, MD
Durham, NC

Infant B Cell Memory Differentiation and Early Gut Bacterial Colonization

Purpose of the Study. To determine whether early intestinal bacterial colonization patterns are associated with B-cell activation and maturation.

Study Population. The study evaluated 65 healthy Swedish infants (33 boys and 32 girls) born at term in rural areas in southwest Sweden. These infants were part of a prospective newborn/infant cohort that was followed to investigate the relationship between intestinal bacterial colonization and pattern and maturation of the immune system.

Methods. Cord blood samples from newborn children and peripheral blood samples from children at 3 to 5 days, 1 month, 4 months, 18 months, and 36 months of age were obtained. Phenotypic characterization of the circulating B cells by flow cytometry was performed within 72 hours after venipuncture. Fecal samples were obtained at 1, 2, 4, and 8 weeks of age and cultured quantitatively for major groups of aerobic and anaerobic bacteria.

Results. At both 4 months and 18 months of age, children colonized with Escherichia coli and/or bifidobacteria during the first 8 weeks of life had significantly higher numbers of CD27+ memory B cells than did noncolonized children. Early colonization with Staphylococcus aureus was associated with low numbers of CD27+ memory B cells at 4 months of age.
Evidence of Effect of Subcutaneous Immunotherapy in Children: Complete and Updated Review From 2006 Onward

Vivian Hernandez-Trujillo

Pediatrics 2012;130;S45
DOI: 10.1542/peds.2012-2183

Updated Information & Services
including high resolution figures, can be found at:
/content/130/Supplement_1/S45.full.html

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Allergy/Immunology
/cgi/collection/allergy:immunology_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
/site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2012 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™
Evidence of Effect of Subcutaneous Immunotherapy in Children: Complete and Updated Review From 2006 Onward

Vivian Hernandez-Trujillo

*Pediatrics* 2012;130:S45

DOI: 10.1542/peds.2012-2183WWW

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/130/Supplement_1/S45.full.html