Sublingual Immunotherapy: An Alternative to Allergy Shots

by Diego Saporta, MD

Introduction

Allergies occur because of a dysfunction of the immunological system (in a simplified explanation, there is a predominance of a Th2 response) wherein exposure to an antigen stimulates liberation of pro-inflammatory molecules and eventually a multitude of chemicals ultimately responsible for the production of the allergy symptoms.

Management of nasal allergies is based upon pharmacotherapy, modification of the sufferer's environment, and immunotherapy. While pharmacotherapy will prevent these chemicals from reaching the target cell receptors and therefore from eliciting symptoms, and while environmental modification maneuvers will sometimes decrease symptoms by decreasing exposure to the offending antigen, immunotherapy is the only treatment capable of modifying the immunological response, as it will lead into a change in the immunological system (favoring a Th1-type of response). As a result, the patient will become less reactive or nonreactive.

Therefore while medications will offer at best a positive effect while being administered, and environmental modifications will in the best case decrease symptoms by minimizing exposure, immunotherapy is the only treatment modality that can modify the dysfunctional immunological system into a functional one, capable of tolerance to the allergens that elicited the symptoms. In other words, immunotherapy will produce a shift from a Th2 system (proallergenic) to a Th1 (nonreactive).

Immunotherapy implies the administration of small but increasing doses of antigen that will slowly produce the above changes so that the patient will stop reacting to the offending antigen. When properly administered, immunotherapy will lead into a long-term effect after discontinuation. The usual route for immunotherapy administration (and the one most commonly known by both doctors and patients) is the subcutaneous route; that is, subcutaneous injection immunotherapy (SCIT), usually referred as "allergy shots."

SCIT is not the only route for the administration of immunotherapy, as there are alternate routes such as nasal, bronchial, oral, and sublingual. Bronchial immunotherapy leads into a significant number of adverse reactions. Nasal immunotherapy has only a few reports that support its use. Oral immunotherapy (that implies swallowing the antigen without previous exposure to the oral mucosa) has not proved to be very effective.[1]

Sublingual immunotherapy (SLIT) is the only alternative immunotherapy modality that has been extensively studied, and it has clearly been proved to be extremely safe and effective. There is a voluminous body of literature (including many papers with category A evidence – acquired from double-blind, placebo-controlled studies) that establish SLIT as a valid, effective, and safe immunotherapy treatment modality.

Historical Perspective

While most of the literature being published at this time is of European origin, and while there is a perception that SLIT is a rather "recent discovery," the oral route for immunotherapy administration has been in use for many decades.[2] The first article about oral immunotherapy was published in 1900 by H.H. Curtis, "The Immunizing Cure of Hay Fever."[3] The author describes his experience of "the last 25 years"; therefore, we can easily accept that oral immunotherapy has been in use since the late 1800s.

In 1911 there was a landmark paper by Leonard Noon about injection immunotherapy; therefore, the use of oral vaccines may precede the use of injections, but it is probably a safe assumption to consider that both modalities have been around since early in the development of the field of allergy.[4]

Sublingual (SL) vaccines were widely used in the US for many years. Early literature includes many papers by authors such as Hansel, Dickey, Pfeiffer, Ruddy, and Waickman.[5–10] Hansel cites Black, who in 1928 reported on the successful management of pollen allergy by SL vaccines. Hansel postulated (well ahead of his time) that the sublingual mucosa had immunological properties, and he also stated that the sublingual method would supplant the intradermal method. A course called "Sublingual Therapy in Allergy" was offered at the American Academy of Otolaryngic Allergy (AAOA) from 1963 to 1980.[6] In those early days, SLIT was available

not only as drops, but also as rapidly dissolving tablets that only recently have been introduced in Europe.[5,11]

For reasons that are not clear, and contrary to Hansel's prediction, the use of SLIT in the US decreased markedly. In 1976 Ruddy already stated that despite SLIT's having been available for many years, it had not been adopted by the allergy practitioners.[8] The lack of understanding at that time of its mechanism of action and the rather anecdotal nature of the reports contributed perhaps to this treatment modality's falling in almost complete disregard.[12] Eventually, the use of sublingual vaccines almost "vanished" in the US (an exception is American Academy of Environmental Medicine, where Frank Waickman offered courses on sublingual treatments for years). With the exception of a few publications by David Morris, MD, no more articles about SL treatments were published in the US after the 1980s. Most of the general allergists and ENT-allergists used only SCIT.

The same was true for Europe until the mid-1980s: In 1986 the British Committee for the Safety of Medicines published a report about a series of deaths as a consequence of the administration of SCIT. This in turn led to strict governmental regulations that made the administration of injection-immunotherapy extremely difficult.[1] While subsequent analysis of the problem found that the deaths occurred as a consequence of avoidable human error (as the injections were given in non-allergists' offices; in other words, the allergist had sent the treatment vials to the primary care physician's office), the consequences still were the significant drop in the use of injectable vaccines. This decrease spread all over Europe. European practitioners sought alternate routes for the administration of immunotherapy, and that is how the SL route was "discovered" or rather rediscovered and therefore used once again.

The use of SLIT soon became well accepted. In 1998 the World Health Organization (WHO) stated that SLIT was a viable alternative to SCIT, and in 2001 the ARIA group stated that SLIT was an effective immunotherapy modality not only for adults but also for children.[1,13,14] (ARIA stands for Allergic Rhinitis and its Impact in Asthma, and is a group of experts who establish guidelines for the management of those conditions). In the subsequent years, many papers were published that adhered to the strictest rules of evidence-based medicine so that there are numerous papers in the "modern" world's literature based on category A type of evidence (from double-blind, placebo-controlled studies). This led to a rather quick acceptance by the European allergy/medical community of the sublingual route as an alternative for the administration of immunotherapy that was both safe and effective. The dosages used nowadays in Europe are higher than those used by the early US practitioners, and studies that compare doses of SLIT versus SCIT consistently find the dose of SLIT several times higher than SCIT, sometimes many times higher.[1]

In the European literature, there are multiple publications on this subject, too many to list here, including clinical papers, research papers, review articles, and several meta-analyses, and there is extensive research being done about the issues of efficacy, safety, and mechanism of action.

Efficacy

The efficacy is evaluated in the same way as with SCIT: Researchers will follow changes in the symptom scores, medication scores, quality of life questionnaires; also changes in the immunological parameters, in the dose necessary for a provocation test, and sometimes in the functional respiratory parameters.

In 2005 the first meta-analysis by Wilson et al. was published, and it was determined that SLIT led into a significant reduction in symptom and medication scores; it was effective for adults and children.[15] SLIT should therefore be considered effective for the management of allergic rhinitis. In 2006 other meta-analyses were published that determined that SLIT is effective for the management of asthma (there were good results but not statistically significant), and in the treatment of children with asthma (this one showing a statistically significant improvement). In 2009, a review article was published that shows statistically significant improvement in symptom and medication scores for rhinitis and asthma in children with pollen allergy.[16–18]

Safety

The concept of safety emanates from the analysis of the reported side effects of this treatment modality. Since early in the literature (including the early American literature) there is a consensus that SLIT is a safe treatment modality.[1,6,19,20]

With injections, there is a possibility of eliciting local or systemic reactions. Local reactions imply mainly pain and swelling at the injection site (that on occasion can be considerable) or systemic reactions including urticaria, angioedema, and the feared risk of laryngeal or bronchial involvement with the possibility of severe bronchospasm. Rarely this type of severe reaction to shots can lead into irreversible bronchial obstruction or cardiovascular collapse, and therefore death. While the risk of such a reaction is low, it is by no means zero.[21,22] In the AAAI survey, it was estimated that fatal reactions occurred in 1 per 2.5 million injections, with an average of 3.4 deaths per year.[22] The majority of these deaths occurred in asthmatic patients.

When using SL drops, there is a possibility of eliciting minor reactions that in the European literature have been called adverse events (AE).[1,20] These include itching or burning sensation of the peri-oral area, face, or rarely diffuse; minor swelling of the lip, tongue or other parts of the oral mucosa; headaches; and GI symptoms, mainly abdominal pain. There is also the possibility of developing systemic reactions including rhinitis, conjunctivitis, or asthma attacks.[33]

In studies where the safety of SLIT was compared with that of SCIT, it

➤

➤

was found that the reactions in the SLIT group were consistently less significant.[33] In 66 studies reviewed, there were no life-threatening reactions.[33] In the last few years, case reports of severe reactions after SLIT administration have been published that included urticaria, angioedema, and bronchospasm, but to this date no case of mortality has ever been reported after SLIT administration.[23–26] According to published literature, it is clear that SLIT is safer and better tolerated than SCIT. The fact that SLIT can elicit severe reactions should come as no surprise, as Pfeiffer already had described in the US a SL provocation test; therefore, it is clear that oral administration of antigens can and will provoke symptoms if precautions are not taken.[27]

Some articles suggest that the AE will disappear with the continued use of SLIT and that there is no difference in AEs regardless of the aggressiveness of the escalation phase of the treatment.[1,28,29] This type of conclusion is, in my opinion, a dangerous one, as it can lead the practitioner to think that one is working with a completely safe technique, and while it is certainly safer than the injectable route, the allergy practitioner would be wise to always know that a reaction can be elicited and that it is better to decrease the dose or even interrupt the treatment if even a minor AE occurs. A judicious slow advancement of the dose appears always warranted in any type of immunotherapy. It is also prudent to train the patients in the use of an adrenaline autoinjector because, as stated above, although very safe, symptom provocation can occur after SLIT administration. Even if this is an infrequent event, provoked symptoms can be severe.

Mechanism of Action

While it is accepted that SCIT leads into a change of the immune response from a Th2 response (with IL-5 and IL-13, eosinophils, and IgE) to a Th1 response (characterized for the absence of eosinophils and an IgG antibody response), it is not completely clear how sublingual immunotherapy works.[15] Contrary to common assumptions, the allergens presented sublingually are not absorbed; in other words, the allergen does not enter into the blood circulation, but rather is "captured" by the local dendritic cells and kept in the oral mucosa for many hours after a brief exposure.[30,31] Oral mucosa dendritic cells can process antigens applied to the mucosal surface (becoming antigen presenting cells).[32] IL-10 and TGF-beta are secreted, leading to the production of regulatory T cells and the establishment of immune tolerance.[15,33] Many patients receiving SLIT show immunologic changes similar to those on SCIT, such as an increase in allergen-specific IgG4.[33] It could be speculated that production of T_{reg} cells underlies the response to both types of immunotherapy.

SLIT vs. SCIT

When addressing two similar treatment modalities, there is the obvious question of which one is better. In comparing SCIT with SLIT, a review of the literature reveals only a few articles that directly address this issue.[34–39] In four of these reports, SCIT and SLIT are found to be equally effective. [35–38] In one report, SCIT is found to have better results, and one report finds both equally effective for allergic rhinitis patients but SCIT more effective for asthmatic patients.[34,39]

In my own experience, SLIT and SCIT appeared to be of similar efficacy, but I have further studied this issue by comparing results of 50 patients treated with shots (SCIT) versus 43 patients treated with SLIT.[40] The results of this study were presented at the 2009 AAOA annual meeting.[41] After a statistical analysis, I found that while both treatment modalities led to a statistically significant symptom improvement (mostly with a $p < 0.001$), the comparison of the results was not statistically significant (except for cough that improved better with SCIT [$p = 0.037$] and wheezing that improved more with SLIT [$p = 0.024$]), which suggests that the results obtained with one treatment modality are similar to the results obtained with the other treatment modality (as observed in daily practice).

Choosing one treatment modality over the other depends on multiple factors, but the list below can summarize why SLIT could be chosen as the more preferable treatment modality:

- Personal preference
- Fear of needles
- Busy schedule: Given the safety profile, SLIT could be considered as the ideal home-immunotherapy treatment. Even though some allergists allow patients to self-administer shots, this is a potentially dangerous practice.[42]
- Economical considerations. SLIT may offer savings in time and money as there is no need to travel to and from doctor's office and there are no co-pays.
- SLIT obviously will not have local arm reactions that are sometimes painful and are rather common in patients on SCIT; therefore, it may be easier to comply with.
- Easy program to follow. As stated, this is a home-based treatment. If patient needs to travel or be absent for a relatively long period of time, he can carry the SLIT bottle(s) rather than interrupting immunotherapy treatment. Obviously, SLIT offers an advantage to patients who, due to distance or other conditions, cannot easily travel to the allergist's office. Even though SCIT is often not advised for old or debilitated patients, this group is frequently symptomatic, commonly with a persistent nasal obstruction (mainly related to indoor allergens such as dust mites, animal dander, and others) that prevents a restful sleep and therefore deeply affects quality of life.
- When the diluent used is glycerin, the SLIT bottle does not need to

be refrigerated, as the antigens will not lose activity for a very long time. For patients who go on vacation or relocate, the SLIT bottle can "travel" with them. Therefore, in those circumstances, SLIT offers an alternative to discontinuing treatment. We found that avoiding the need for refrigeration helps our patients to comply with the treatment, as the bottle is kept "in view," reminding them to take the drops.

- SLIT can safely be used for the difficult-to-treat patient, such as the asthmatic patient or the very young patient.[43,44] Present immunotherapy guidelines advise not to treat patients younger than 5 years old, as there is evidence that below that age, reactions occur more frequently.[45,46] On the other hand, given the relationship between nasal allergies and asthma development, specific immunotherapy should be started early in the disease process, therefore during early childhood for many patients.[44,47] Young children have been successfully treated with SLIT. Agostinis et al. have treated children almost 2 years old (1 year and 11 months).[48] I have successfully treated a handful of children under age 2.

Present Situation in the US

There is a growing interest in the US about the use of SLIT for the management of allergic conditions. The main allergy academies are offering yearly courses or presentations related to SLIT. Reviews have been published in our country.[33,49] A joint task force was formed by the American College of Allergy, Asthma and Immunology (ACAAI) and the American Academy of Allergy Asthma and Immunology (AAAAI), and a comprehensive report of the topic was published in 2006.[33]

SLIT is not approved by the FDA. It constitutes an off-label use of allergenic extracts and is not reimbursed by most insurance carriers. Even though SLIT has been clearly demonstrated in the European countries to be safe and effective, the FDA requires the proof to be provided in the US. Greer Labs conducted a clinical experiment with sublingual allergens, finding a decrease in allergy symptoms, and Alk Abello Lab is conducting studies on the effect of a grass-allergy tablet, finding results similar to the ones obtained in Europe.[50,51]

My Experience with SLIT

I started working with SL vaccines in 2003. In 2005 I presented a protocol for SLIT administration at the 64th AAOA Annual Meeting (later published in 2007).[40]

In my hands, this protocol has proved to be extremely efficacious. Using it has enabled me to successfully manage cases of nasal allergies with or without asthma, in adults or pediatric patients (including very young patients to whom it is difficult and even dangerous to give injections).

In 2007 I presented a paper at the Pan American Allergy Society, where I showed that SLIT was effective for the management of asthma, and this information was later on published in this magazine.[44] In 2009 I presented a paper at the AAOA Annual meeting comparing the effectiveness of the SCIT and SLIT, and after a statistical analysis for the results it was found that both treatments are equally effective.

Therefore, my experience is in agreement with the results of the European literature; namely:

- SLIT is efficacious and very safe.
- It can be used for the management of nasal allergies with or without asthma.
- It can be used in adults and children, even very young children.

It is my opinion that:

- given the risks of injection immunotherapy mainly for asthmatics, SLIT should be considered the first option for the management of the asthmatic patient, and

➤

Health Writers Group

A book is still the best way to affirm your expertise and reach a larger audience.

Our services are tailored to the busy clinician. On a recent book project, Health Writers Group collaborated with the authors to describe a leading-edge type of cancer therapy used in Europe. The next step in developing their book was to perform a thorough literature review, to document the research in language that consumers would understand. This provided a wealth of evidence from the scientific community confirming the safety and efficacy of their approach. We were able to develop the book sufficiently to warrant publication by an imprint of a major New York publisher.

- **Books & Chapters**
- **Articles & White Papers**
- **Proposals & Reports**
- **Manuals**
- **Research & Analysis**
- **Web Copy & Blogs**

For a free consultation call 415.922.6234
info@WritersGroupInc.com Website: www.HealthWritersGroup.com

➤

- SLIT is the ideal modality for the management of the very young patient.

Several European authors also think along those lines. It is well established that a child with nasal allergies has a high probability of developing asthma in the few years subsequent to the diagnosis of allergies (20%–50%), and immunotherapy is the only treatment that can prevent such a progression.[52–54]

Summary

We have reviewed the history of sublingual immunotherapy, a very old treatment modality that is being used extensively in Europe for the last 20 years, and interest in its use is growing in the US. It is an effective, extremely safe, and very easy-to-use immunotherapy modality. Given the danger and difficulties in administering immunotherapy to the very young child and the asthmatic patient, SLIT should be considered as the main treatment modality in these cases.

Notes

1. Canonica GW, Passalacqua G. Non injection routes for immunotherapy. *J Allergy Clin Immunol*. 2003:437–448.
2. Frati F, Moingeon P, Marcucci F, et al. Mucosal immunization application to allergic disease: sublingual immunotherapy. *Allergy Asthma Proc*. 2007;28:35–39.
3. Curtis HH. The immunizing cure of hay fever. *Med News*. 1900;77:16.
4. Noon L. Prophylactic inoculation against hay fever. *Lancet*. 1911;1:1572–1573.
5. Hansel FK. Sublingual testing and therapy. A comparison with injectable methods. *Trans Am Soc Ophthalmol Otolaryngol Allergy*. 1972;11:93–103.
6. Dickey LW. Sublingual antigen testing and therapy for inhalants, foods and petrochemicals. In: Dickey L, ed. *Clinical Ecology*. Springfield, IL: Charles C. Thomas. 1976:544–553.
7. Pfeiffer GO. Sublingual procedures. *Trans Am Soc Ophthalmol Otolaryngol Allergy*. 1970;11:104.
8. Ruddy LW. Why sublingual therapy in otolaryngologic allergy. *Trans Am Soc Ophthalmol Otolaryngol Allergy*. 1976;17(1):93–102.
9. Waickman FJ. Pediatric allergy. *Trans Am Soc Ophthalmol Otolaryngol Allergy*. 1965;6:39.
10. Hansel FK. *Allergy of the Nose and Paranasal Sinuses*. St. Louis: CV Mosby Co. 1936:755.
11. Kleine-Tebbe J, Ribel M, Herold DA. Safety of a SQ-standardized grass allergen tablet for sublingual immunotherapy: a randomized, placebo-controlled trial. *Allergy*. 2006;61:181–184.
12. Bellanti JA, Settipane RA. Sublingual immunotherapy: A procedure whose time has come? *Asthma Allergy Proc*. 2007;28(1):1–2.
13. Bousquet J, ARIA Workshop Group. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol*. 2001;108 (Suppl 5).
14. Bousquet J. The new ARIA guidelines: putting science into practice. *Clin Exper Allerg Rev*. 2002; 2:38–43.
15. Wilson DR, Torres Lima R, Durham SR. Sublingual immunotherapy for allergic rhinitis: systematic review and meta-analysis. *Allergy*. 2005;60:4–12.
16. Calamita Z, Saconato H, Pelá AB, Atallah AN. Efficacy of sublingual immunotherapy in asthma: systematic review of randomized-clinical trials using the Cochrane Collaboration method. *Allergy*. 2006 Oct;61(10):1162–1172.
17. Penagos M, Passalacqua G, Compalati E, et al. Metaanalysis of the efficacy of sublingual immunotherapy in the treatment of allergic asthma in pediatric patients, 3 to 18 years of age. *Chest*. 2008 Mar;133(3):599–609. Epub 2007 Oct 20.
18. Larenas-Linnemann D. Sublingual immunotherapy in children: complete and updated review supporting evidence of effect. *Curr Opin Allergy Clin Immunol*. 2009 Apr;9(2):168–176.
19. Gidaro GB, Marcucci F, Sensi L, et al. The safety of sublingual-swallow immunotherapy: an analysis of published studies. *Clin Exp Allergy*. 2005 May;35(5):565–571.
20. Andre C, Vatrinet C, Galvain S, et al. Safety of sublingual-swallow immunotherapy in children and adults. *Int Arch Allergy Immunol*. 2000;121:220–234.
21. Reid MJ, Lockey RF, Turkeltaub PC, Platts-Mills TA. Survey of fatalities from skin testing and immunotherapy 1985–1989. *J Allergy Clin Immunol*. 1993 Jul;92(1 Pt 1):6–15.
22. Bernstein DI, Wanner M, Borish L, Liss GM. Twelve-year survey of fatal reactions to allergen injections and skin testing: 1990–2001. *J Allergy Clin Immunol*. 2004 Jun;113(6):1129–1136.
23. Dunsky EH, Goldstein MF, Dvarin DJ, Belecanech GA. Anaphylaxis to sublingual immunotherapy. *Allergy*. 2006; 61:1235
24. Antico A, Pagani M, Crema A. Anaphylaxis by latex immunotherapy. *Allergy*. 2006;61:1236–1237
25. Eifan AO, Keles S, Bahceciler NN, Barlan IB. Anaphylaxis to multiple pollen allergen sublingual immunotherapy. *Allergy*. 2007 May;62(5):567–8. Epub 2007 Feb 20.
26. Blazowski L. Anaphylactic shock because of sublingual immunotherapy overdose during third year of maintenance dose. *Allergy*. 2008 Mar;63(3):374. Epub 2007 Dec 8.
27. Pfeiffer GO. Sublingual diagnosis and treatment. *Trans Am Soc Ophthalmol Otolaryngol Allergy*. 1975; 15:109–113.
28. Grosclaude M, Bouillot P, Alt R et al. Safety of various dosage regimens during induction of sublingual immunotherapy. *Int Arch Allergy Immunol*. 2002;129:248–253
29. Samburgo R, Puccinelli P, Burastero SE, Di Rienzo V. The efficacy of sublingual immunotherapy for respiratory allergy is not affected by different dosage regimens in the induction phase. *Allergol Immunopathol*. 2003;31(6):329–337
30. Bagnasco M, Passalacqua G, Villa G, et al. Pharmacokinetics of an allergen and a monomeric allergoid for oromucosal immunotherapy is allergic volunteers. *Clin Exper All*. 2001; 31:54–60.
31. Passalacqua G, Villa G, Altrinetti V, et al. Sublingual swallow or spit? *Allergy*. 2001 Jun;56(6):578.
32. Allam JP, Bieber T, Novak N. Dendritic cells as potential targets for mucosal immunotherapy. *Curr Opin Allergy Clin Immunol*. 2009 Dec;9(6):554–557.
33. Cox LS, Linnemann DL, Nolte H et al. Sublingual immunotherapy: a comprehensive review. *J Allergy Clin Immunol*. 2006; 117:1021–1035
34. Wedi B. Status and indications for SLIT in comparison to SCIT. *Hautarzt*. 2008 Jul;59(7):537–43.
35. Khinchi MS, Poulsen LK, Carat F, André C, Hansen AB, Malling HJ. Clinical efficacy of sublingual and subcutaneous birch pollen allergen-specific immunotherapy: a randomized, placebo-controlled, double-blind, double-dummy study. *Allergy*. 2004 Jan;59(1):45–53.
36. Mauro M, Russello M, Incorvaia C, Gazzola GB, Di Cara G, Frati F. Comparison of efficacy, safety and immunologic effects of subcutaneous and sublingual immunotherapy in birch pollinosis: a randomized study. *Eur Ann Allergy Clin Immunol*. 2007 Apr;39(4):119–22.
37. Pokladnikova J, Krcmova I, Vlcek J. Economic evaluation of sublingual vs. subcutaneous allergen immunotherapy. *Ann Allergy Asthma Immunol*. 2008 May;100(5):482–489.
38. Antúnez C, Mayorga C, Corzo JL, Jurado A, Torres MJ. Two year follow-up of immunological response in mite-allergic children treated with sublingual immunotherapy. Comparison with subcutaneous administration. *Pediatr Allergy Immunol*. 2008 May;19(3):210–218.
39. Mungan D, Misirligil Z, Gürbüz L. Comparison of the efficacy of subcutaneous and sublingual immunotherapy in mite-sensitive patients with rhinitis and asthma – a placebo controlled study. *Ann Allergy Asthma Immunol*. 1999 May;82(5):485–490.
40. Saporta D, McDaniel AB. Efficacy comparison of multiple-antigen subcutaneous immunotherapy with multiple-antigen sublingual immunotherapy. *Ear Nose Throat J*. 2007; 86(8):493–497
41. Saporta, D. Comparison of treatment results in patients with inhalant allergies with or without asthma, treated either with Subcutaneous Injection Immunotherapy (SCIT) or Sublingual Immunotherapy (SLIT) using multiple antigens. Presented at the 68th AAOA Annual meeting, October 3, 2009. San Diego, CA.
42. Li, JT, Lockey RF, Bernstein L et al. Allergen immunotherapy: a practice parameter. *Ann All Asthma Immunol*. 2003;90:1–40.
43. Pajno GB, Morabito L, Barberio G, et al. Clinical and immunologic effects of long-term sublingual immunotherapy in asthmatic children sensitized to mites: a double-blind, placebo controlled study. *Allergy*. 2000;55:842–849
44. Saporta D. SLIT and asthma. *Townsend Lett*. October 2010;327:44–48.
45. Allergy immunotherapy: a practice parameter. American Academy of Allergy Asthma and Immunology. *Ann Allergy Asthma Immunol*. 2003;90(1 suppl 1):1–40.
46. Heejjaoui A, Dhivert H, Michel FB, Bousquet J. Immunotherapy with a standardized Dermatophagoides pteronyssinus extract. IV. Systemic reactions according to the immunotherapy schedule. *J Allergy Clin Immunol*. 1990 Feb;85(2):473–479.
47. Malling H, Weeke B. Immunotherapy. Position paper of the European Academy of Allergy Asthma and Immunology. *Allergy*. 1993;48(suppl 14):9–35.
48. Agostinis F, Tellarini L, Canonica GW, et al. Safety of sublingual immunotherapy with a monomeric allergoid in very young children. *Allergy*. 2005;60:133.
49. Leatherman BD, Owen S, Parker M et al. Sublingual immunotherapy: past, present, paradigm for the future? A review of the literature. *Otolaryngol Head Neck Surg*. 2007;136:S1–S20.
50. Information presented at the AAOA 69th Annual Meeting. Boston, MA; September 23–25, 2010.
51. Bufe A, Eberle P, Franke-Beckmann E, et al. Safety and efficacy in children of an SQ-standardized grass allergen tablet for sublingual immunotherapy. *J Allergy Clin Immunol*. 2009 Jan;123(1):167–173.e7.
52. Linna O, Kokkonen J, Lukin M. A 10-year prognosis for childhood allergic rhinitis. *Act Paediatr*. 1992; 81:100–102.
53. Johnstone DE and Dutton A. The value of hyposensitization therapy for bronchial asthma in children – a 14-year study. *Pediatrics*. 1968;42(5):793–801.
54. Moller C, Dreborg S, Ferdousi HA, et al. Pollen immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis (the PAT-Study). *J Allergy Clin Immunol*. 2002;109:251–256.

◆

Dr. Saporta completed his training in 1990 at Columbia Presbyterian Hospital in New York City. He is board certified in otolaryngology and has been a Fellow of the American Academy of Otolaryngic Allergy (AAOA) since 2001. His private practice in Elizabeth, New Jersey, is heavily oriented to the management of allergic conditions. Interested in the use of oral vaccines since early in his practice, Dr. Saporta presented a protocol for sublingual immunotherapy at the 64th annual meeting of the AAOA that since then has been successfully used for the management of allergic rhinitis with or without asthma.