Epicutaneous Immunotherapy (EPIT) for Food Allergy: Hugh A Sampson, MD; Professor of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY USA

Although the concept of epicutaneous immunotherapy was first described about 1,000 years ago in India, the first report of EPIT for treating allergic disease was published in 1921.(1) Shortly thereafter there were a number of reports from Europe describing various forms of EPIT, primarily placing allergen on scarified skin, for the treatment of environmental allergies, but soon thereafter this approach largely disappeared until recently.(1;2) EPIT targets the outermost layer of the skin, the epidermis, which is characterized by three unique features: barrier function provided by keratinocytes; potent immune surveillance afforded by keratinocytes and Langerhans Cells (LCs); and absence of vascularization, markedly reducing the risk of systemic reactions.(3) Antigen is taken-up by local LCs in the epidermis and transported to local draining lymph nodes where induction of IgM, IgG and mucosal IgA responses occur.(4)

Recently, Dupont and co-workers published the results of a pilot study designed to test the clinical efficacy and safety of EPIT using a novel Viaskin® Epidermal Delivery System (EDS) in 16 children with cow's milk allergy.(5) Viaskin® EDS is a modified form of EPIT based on allergen delivery to intact skin using an occlusive patch chamber.(6;7) Moisture generated under the occlusive chamber dissolves the lyophilized allergen protein that is loaded on the Viaskin® EDS and hydrates the cornified layers of the stratum corneum, which enhances protein penetration. Children treated with Viaskin® EDS for 3 months showed a tendency towards an increased oral milk challenge tolerance threshold dose compared to baseline; milk-EPIT (n=9): 1.77 ml to 23.61 ml (p=0.18) and placebo (n=7): 4.36 ml to 5.44 ml; p=NS.(5) Treatment was well tolerated with no systemic allergic reactions, but an increase in local eczematous skin reactions was observed in some patients. More recently a double-blind placebo-controlled EPIT trial was conducted in 54 peanut-allergic children and adolescents, *Arachild* (Dupont et al; personal communication). Viaskin® EDS containing 100 ug of peanut protein or placebo was placed on the skin daily for 18 months. Compared to the initial peanut DBPCFC threshold dose, 40% of those treated with Viaskin® developed at least a 10-fold increase in initial cumulative reactive dose OR cumulative reactive dose (CRD) > 1000 mg of peanut protein (3.3 peanuts), significant increases in peanut-specific IgG4, and no severe adverse events related to therapy. Currently a double-blind, placebo-controlled trial of peanut Viaskin® EDS is underway in 220 peanut-allergic adults evaluating the efficacy and safety of 50 ug, 100 ug and 250 ug of peanut protein Viaskins compared to placebo. To date, there have been no safety concerns and no subjects have dropped-out due to adverse reactions.

Based on pre-clinical and early clinical trials, EPIT may provide a safe and effective form of immunotherapy to treat patients with food allergy. However, extensive studies are necessary to establish the degree of protection afforded by EPIT and its long-term safety.

Reference List

(1) Senti G, von Moos S, Kundig TM. Epicutaneous allergen administration: is this the future of allergen-specific immunotherapy? Allergy 2011; 66(6):798-809.

(2) Senti G, von Moos S, Tay F, Graf N, Sonderegger T, Johansen P et al. Epicutaneous allergen-specific immunotherapy ameliorates grass pollen-induced rhinoconjunctivitis: A double-blind, placebo-controlled dose escalation study. J Allergy Clin Immunol 2012; 129(1):128-135.

(3) Nestle FO, Di Meglio P, Qin JZ, Nickoloff BJ. Skin immune sentinels in health and disease. Nat Rev Immunol 2009; 9(10):679-691.

(4) Mitragotri S. Immunization without needles. Nat Rev Immunol 2005; 5(12):905-916.

(5) Dupont C, Kalach N, Soulaines P, Legoue-Morillon S, Piloquet H, Benhamou PH. Cow's milk epicutaneous immunotherapy in children: a pilot trial of safety, acceptability, and impact on allergic reactivity. J Allergy Clin Immunol 2010; 125(5):1165-1167.

(6) Mondoulet L, Dioszeghy V, Ligouis M, Dhelft V, Dupont C, Benhamou PH. Epicutaneous immunotherapy on intact skin using a new delivery system in a murine model of allergy. Clin Exp Allergy 2010; 40(4):659-667.

(7) Mondoulet L, Dioszeghy V, Vanoirbeek JA, Nemery B, Dupont C, Benhamou PH. Epicutaneous immunotherapy using a new epicutaneous delivery system in mice sensitized to peanuts. Int Arch Allergy Immunol 2011; 154(4):299-309.