140 Localized Seminal Plasma Hypersensitivity: Patients' Reactivity To Seminal Plasma Proteins And Immunological Responses To Desensitization

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RATIONALE: Women with localized seminal plasma hypersensitivity (LSPH) are sensitized to non-carbohydrate protein moieties of prostate specific antigen (PSA) and/or PSA fragments but other proteins are likely relevant. Seminal plasma protein (SPP) immunotherapy (IT) alleviates localized vaginal symptoms. We investigated whether IT for LSPH elicited a Th2 to a Th1 cytokine shift.

METHODS: Two LSPH women were evaluated and treated. SPPs were separated by FPLC. IgE specific Western blotting was performed to all SPP fractions (Fxs) using autologous sera. PBMCs from each patient before and 16 hours post-IT were analyzed by flow cytometry (Accuri 6) for intracellular cytokine expression (IFNg and IL-13).

RESULTS: Fxs IIa, III and IV contained PSA and PSA fragments. In both women, titration skin testing to all SPP Fxs was positive for Fx III or IV which corresponded to PSA fragments (MW-10-16kd) whereas IgE specific western blotting was positive to PSA (MW-33-36kd). Both women received IT to Fxs containing PSA and PSA fragments. For patient 1, remarkable up-regulation of CD4+ intracellular IFNg and down-regulation of IL-13 was observed post-IT corresponding to complete symptom resolution. For patient 2, significant upregulation of IFNg was observed without a decrease in IL-13 corresponding initially to a complete treatment response but a subsequent recurrence of symptoms after two weeks of unprotected intercourse.

CONCLUSIONS: SPP IT in women with LSPH induces a Th2 to Th1 cytokine shift. Patient 2's diminished clinical response may reflect an inadequate IT dosage. This patient is currently receiving booster injections and follow-up immunologic studies are anticipated.

141 Procedures To Improve Quality Of Allergenic Extracts: The French Experience

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RATIONALE: In 2004, a new Note for Guidance for the quality and the delivery of allergenic named patient products required for manufacturers to provide a list of allergens to the regulatory agency (Afssaps) with precise specifications. The aim was to establish a decision making procedure in order to define a list of aeroallergens following the requirements of the new Note.

METHODS: A group APSI was created with representatives of the French society of allergology, trade unions, association for continuous medical education, committee of support of allergology and manufacturers. At the Afssaps, 2 committees of experts (clinicians and pharmacists) evaluated the quality of the data provided by the manufacturers. 73 aeroallergens were clinically validated. The clinical validation of the 11 remaining allergens was performed with a questioner send to allergists. 3 groups of allergens were defined: Gp1: allergens not validated; Gp2: the allergens under inquiry; Gp3: validated allergens classified in 4 categories according on published data on desensitisation. (a) No published studies, (b) insufficient, (c) partial, (d) consistent data.

RESULTS: Allergens were categorized: Gp 1:i.e. cough grass, false oat; Gp 2: not evaluated because of the lack of answers and Gp3 divided in: Gp3a:37 allergens, (i.e. rats, Acarus siro); Gp3b: 8 allergens (i.e.: dog, horse) Gp3c: 9 allergens, (i.e., cat); Gp3d: 12 allergens (i.e.: timothy grass, Dpt, Df).

CONCLUSIONS: It's the first experience of clinical and pharmaceutical validation of allergens extracts based on a decision making procedure in which allergists, companies and Afssaps were involved. It clarified the list of available allergens. It's an ongoing process.

142 Successful Immunotherapy for Poison Ivy

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RATIONALE: Allergic contact dermatitis to urushiol is a common problem for which avoidance is often not practical. There is published documentation of successful immunotherapy (IT) in guinea pigs but not humans.

METHODS: Nine hundred grams of fresh poison ivy leaves were extracted with 95% ethanol and evaporated to a concentration of 1.13 mg urushiol/ml. Serial 10-fold dilutions of this concentrate were prepared in 95% ethanol. Four subjects with clinical poison ivy allergy were tested with increasing concentrations using a standardized patch test for which reduction of reactivity was previously accepted by the FDA as proof of the efficacy of a barrier product. Three requested IT under a protocol consisting of 3-fold increases in IM dose of the ethanol extract at 1-2 wk intervals beginning with 10x the quantity of urushiol giving a "grade 3" reaction on the standardized patch test, and ending with paired injections of 170 ug into each deltoid repeated once. Toxicity was monitored clinically and by CBC, Diff, multi-chem and UA performed before, during and following treatment.

RESULTS: Mildly allergic subject #1 (the author) demonstrated no loss of sensitivity after a cumulative IT dose of 49 ug but a 3-fold reduction in patch test reactivity after 840 ug. Highly allergic subject #2 showed a >10-fold reduction in patch test reactivity after 778 ug. Moderately allergic subject #3 had not reached target dose by abstract deadline. No adverse effects were observed.

CONCLUSIONS: Poison ivy allergy responds to adequate dose immunotherapy.

143 Fullerene C60 And Fullerene - Allergen Conjugates Influence Allergic Responses In A Mouse Model Of Asthma

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RATIONALE: Nanoparticles may influence immune responses, serving as adjuvants or response modifiers in allergen immunotherapy preparations. This investigation assesses the influence of C60 fullerenes on immune responses to allergens.

METHODS: Asthma was induced in mice by the inhalation of ovalbumen (OA) solution during 14 days, after which the mice were treated with intramuscular injections of fullerene C60 derivates. Group 1 was treated with fullerene C60 (Sigma, USA) and Group 2 was treated with a conjugate of OA with 1,2 - metanofullerene carboxylic acid for 10 days. After both treatments, an OA challenge was done and the mice were sacrificed with blood and lung tissue collected. Serum levels of OA-specific IgE and IgG were measured. For histological procedures paraffin sections were prepared and stained by hematoxilin-eosin and PAS.

RESULTS: Induction of allergic asthma in mice led to an increase in OA specific IgE levels and parallel pathologic changes in the lungs including eosinophilic infiltrates in the mucosa and glandular hypersecretion. Group 1 and Group 2 mice had reduced OA specific IgE levels and less pathological changes in the lungs after allergen including less goblet cell hyperplasia and eosinophilic infiltration compared with the OA sensitized untreated mice.

CONCLUSIONS: Fullerene derivatives may modulate immune responses including switching of allergen specific IgE to IgG responses and elimination of allergen induced airway pathologic changes due to OA challenge in a mouse model of asthma. Fullerene conjugates of allergens may be candidates for new allergen vaccines.