

Immunomodulation with
Immunotherapy—"1911-2014"
Change the course of the disease.

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Disclosures/COI

- Speakers Bureau/Consultant:
 - Astra Zeneca, Merck, Genentech/Novartis, Mylan, Teva, Boehringer Ingleheim, Baxter, Alcon, Sunovium
- Consultant-G3B pharma,
- Adjunct Clinical Prof Stanford/Lucille Packard Children's Hospital

History

- "102 yrs"— last 25 notable
- "allergy"- Australian Pedi Clemens Freiherr von Pirquet—altered immune reactivity
- 1911-Leonard Noonan/John Freeman –grass immunotherapy—>SLIT, SCIT and Nonspecific IT –Anti IgE.....
- Goal—Control Sx of AR and Asthma, dec new sensitization and dec progression of As Sx.

Immunology-change the course of the disease

- Desensitization of the FcεR1-bearing mast and baso-upreg of H2receptor w/ 6 hrs
- T Cell responses
- IgE and IgG4 responses
- Regulation of mast cells, basophils and eos

- Tolerance
- T and B cell responses

- Burks A.W. "Update on Allergy Immunotherapy: PRACTALL", JACI 2013;131:1288-96

Immunomodulation

- Immunological effects (lab)
- Clinical evaluation:
 - Patient selection: Sensitivity(mono, poly), age, Sx, disease severity
 - Antigen and route of delivery
 - Duration of therapy
 - Parameters evaluated– QOL, Sx control, PFTs, exacerbations---need a biomarker

Antigen

- Antigen– FDA, CBER
- W/V,PNU, Standardized

- Protein, modified allergens (Chemical/Molecular)
- Adjuvants (incorporate immunostimulant molecules or co-mix adjuvant with allergen extract, viral-Capsids), Peptides, SLIT constructs

- Mix or individualized therapy (SCIT)
- Single allergen in Polysensitized subjects (SLIT)

Antigen Delivery-Route

- Subcutaneous
- Sublingual

- Intralymphatic
- Epicutaneous-skin patches
- (Bronchial)
- (Nasal)
- (Oral)

Dose --SIT

- **Extract Target Range 2007 2011**
- Short Ragweed 6-12 AgE U(ug) 6-12 AgE U (ug)
- Cat 1-4,000BAU 1-4,000 BAU
- Dust Mite 500-2,000 AU 500-2,000 AU
- Pasture Grasses 1-4,000 BAU 1-4,000 BAU
- Bermuda Grass 300-1,500 BAU
- Pollen 1:100-1:200 w/v
- Fungi HTD
- Insect HTD
- Dog, AP 15ug Canf1

- Grier,T, "How's my dosing?" ,AnnAAI 108(2012)201-204

Immunotherapy Parameters

- Task Force allergy Parameters– AAAI, ACAAI, JCAAI
- Anaphylaxis, Immunotherapy, Insect Sensitivity, House Dust mite...

- Work group, Editorial team, Reviewers,
- Update q 3 yrs
- Document--Preamble
- Summary statements—"to do"
- References Graded
- Annals or JACI– pub, on line
- (Summary Cards)

- Allergyparameters.org

Dose SLIT

- FDA pending: Timothy
- 5grass mix: Timothy, Kentucky Blue, Perennial Rye, Orchard, Sweet Vernal
- Ragweed
- HDM

- MonoRx in Polysensitized pt

- Dose Variable– SLIT daily dose equal to Monthly SCIT dose

Duration

- SCIT: 3-6 yrs (85%/85%)—remission 12 +yrs
- Buildup and then maintenance phase
- (Pre seasonal / Intermittent -adjuvants)
- SLIT: 2 yrs?

- Compliance/Knowledge: (Studies vs Patient surveys)
- SLIT
- SCIT

Clinical Efficacy

- SIT in AR pts dec late phase responses to local allergen challenge in skin and nasal mucosa.
- In asthmatics, nonspecific airway hyperreactivity and bronchial responses to inhaled allergen challenge were dec .
- Skin reactivity dec with SCIT and SLIT

How does Rx Schedule affect efficacy?

- Rush– Bee, IFA...
- Cluster
- Standard

- ? Increase reactions/safety
- ? Efficacy

- Administer in a Medically supervised facility

- Cox,L—Immunotherapy Parameter

Safety

- SCIT---Life threatening reaction 1:2.4 Million shots (0.1% mild reactions)—3-4 deaths per yr possibly attributed to shots—less over time.
- SLIT--- oral mucosal Sx noted

- **Anaphylaxis**---Parameters—
- Epinephrine
 - Epi Pen, AuviQ, (Twinject),Generic
 - IM Lateral thigh
 - Teach Patient,Family/Caregivers (teachers)
- Antihistamines treat the hives not the SSx

- Lieberman, Anaphylaxis Parameter

Summary—3 Key issues

- 1)
- 2)
- 3)

Thank you

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