Procedure

Allergen immunotherapy is the administration of gradually increasing quantities of an allergen vaccine to an allergic subject, reaching a dose which is effective in ameliorating the symptoms associated with subsequent exposure to the causative allergen.

Indications for immunotherapy

- **Hymenoptera venom immunotherapy** is the only effective preventive treatment for insect sting-induced anaphylaxis.
- **Inhalant allergen immunotherapy** reduces symptoms and/or medication needs for patients with allergic asthma and/or rhinoconjunctivitis.
- Others eg drugs are within specialist domain
- Immunotherapy for foods is a research tool currently
- Immunotherapy for eczema is a specialist procedure
For allergen immunotherapy, products may be either unmodified vaccines or vaccines modified chemically and/or by absorption onto different carriers:

- Aqueous vaccines
- Depot and modified vaccines
- Mixtures of allergen vaccines
- Sublingual immunotherapy
- Intranasal injections

Long-term advantages of immunotherapy

- Symptom improvement and/or reduction of the need for symptomatic drugs in allergic rhinitis and asthma.
- Long-lasting effect once discontinued.
- Prevention of the onset of new skin sensitizations.
- Prevention of the onset of asthma (?) - pre-emptive immunotherapy

Long-term benefits of immunotherapy
Pre-emptive immunotherapy

205 children with rhinitis
age: 6-14 yrs
grass or birch allergy
3 yrs immunotherapy

<table>
<thead>
<tr>
<th></th>
<th>SIT</th>
<th>CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No asthma</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>19</td>
<td>40-32</td>
</tr>
</tbody>
</table>

Contraindications to immunotherapy

- Serious immunopathologic diseases and immunodeficiencies.
- Malignancies.
- Severe psychological disorders.
- Treatment with beta blockers, even when administered topically.
- Other NSAIDS, ACE inhibitors
- Pregnancy (inhalet induction)

Contraindications to immunotherapy

- Poor compliance.
- Severe asthma, or uncontrolled by pharmacotherapy (FEV1< 70%).
- Significant cardiovascular diseases.
- Children under 5 years (relative contraindication).
Safety of immunotherapy

- Millions of subcutaneous immunotherapy injections are administered annually. The risk of a fatal or near-fatal systemic reaction is very small, but significant.
- Physicians prescribing or administering subcutaneous immunotherapy should be aware of these risks and institute appropriate procedures to minimize them.

Fatal reactions to immunotherapy

<table>
<thead>
<tr>
<th>Period</th>
<th>Fatalities</th>
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</thead>
<tbody>
<tr>
<td>1945-1984</td>
<td>46</td>
</tr>
<tr>
<td>1985-1989</td>
<td>17</td>
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</tbody>
</table>

Estimated risk for fatal reactions less than 1 per 2 million injections

Risk of reactions

- The safety of immunotherapy; a prospective study
- 2,989 patients
- Period 7 months
- Systemic reactions 25/2898 (0.8%)
- No fatalities
Risk factors for adverse reactions

- Uncontrolled asthma
- Severe asthma
- Use of beta blockers
- Rush immunotherapy
- Pregnancy?
- Build-up phase
- Aqueous preparations
- Use of new vials - reduce dose
- Technical errors eg wrong patient, iv injection

Higher risk during induction

<table>
<thead>
<tr>
<th></th>
<th>Induction</th>
<th>Maintenance</th>
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</thead>
<tbody>
<tr>
<td>Patients</td>
<td>1.887</td>
<td>2.691</td>
</tr>
<tr>
<td>Visits</td>
<td>38.287</td>
<td>113.550</td>
</tr>
<tr>
<td>Reactions</td>
<td>36</td>
<td>62</td>
</tr>
<tr>
<td>Rate/pts</td>
<td>1/32</td>
<td>1/47</td>
</tr>
<tr>
<td>Rate/visits</td>
<td>1/1063</td>
<td>1/1831</td>
</tr>
</tbody>
</table>

Practical aspect of immunotherapy

- Double check pt, allergen and dose
- Use post-lateral surface of arm
- Strong advice: do not share vials
- Document allergen number, dose, site given
- Pregnancy - notify immunologist
- Do not proceed unless a doctor is available
Practical aspect of immunotherapy

- Ensure sterile technique
- Gently shake vials for mixing
- Use 1ml insulin syringe
- Inject at 45° by deep subcutaneous route
- Check for blood and inject 15-30 secs
- Emla patches, ice for children
- Pre-treat with antihistamines

Desensitisation

Desensitisation to venoms

- Generally induction of desensitization for venoms will not be undertaken in GP.
- Patients may be referred to GP after the initial series of injections.
- Those receiving multiple venom injections should have a 30 minute gap.
- No vigorous activity for rest of the day
**Special authority for venoms**

- Will be done via immunologist
- Needs renewal every two years
- Usually done at time of FU by immunologist
- Only one SA for wasps - correct species!
- ACC form - may cover cost of adrenaline autoinjector

**Administration of venom injections**

- Lyophilised
- Usually will only need a single concentration for maintenance 100mcg/ml
- Antihistamines advised
- Stay for 45-60 mins post injection
- Pre/post injection vital signs incl BP, PEFR

**Inhalant immunotherapy**

- These come in three vials
- Already reconstituted
- Protocol in the pack
- Wait 15 mins between injections
- Wait at least 30 mins after each injection
- No vigorous activity or hot pools for rest of day
**Adverse effects of immunotherapy**

1. Non-specific reactions (likely non-IgE-mediated), discomfort, nausea, headache, arthralgia.

2. Mild systemic reactions; mild rhinitis/asthma (PEFR > 60%), responding to β₂-agonists/antihistamines. Pre-treatment with antihistamines helps.

**Large local reactions post treatment**

- Large local reactions > 5cm, may need dose reduction - suggest discussion with immunologist
- Extra antihistamines, cold packs

**Moderate/severe reactions**

3. Non-life-threatening systemic reactions; urticaria, angioedema, severe asthma (PEFR < 60%). Responding well to treatment.

4. Anaphylaxis; itching, urticaria, bronchospasm, with hypotension, requiring intensive care - *do not continue until specialist opinion sought*
Systemic reactions post treatment

- Hypotension or bronchospasm: initiate treatment for a systemic reaction
- Early administration of adrenaline deep IMI thigh 10mcg/kg to a maximum of 0.5mg
- Treat anaphylaxis based on organ involvement

Delay administration of injections

- URTI
- Asthma PEFR reduced by 20%
- Otherwise unwell

Gaps between injections

- < 10 days usual dose
- 11-20 days reduce by 25%
- 21-28 days decrease dose by 50%
- >28 days call immunologist
Other options for IT

- Oral immunotherapy (OIT): allergen immediately swallowed, as drops, tablets or capsules.
- Sublingual immunotherapy (SLIT): allergen kept under the tongue for 1-2 minutes, then swallowed (the sublingual-spit mode is no longer in use).

Adverse effects of SLIT

- In post-marketing studies, the overall rate of side effects (all grades) ranges between 3% and 8% of patients.
- The most frequently reported side effects are local (gastrointestinal); oral itching/swelling, nausea, stomach-ache.
- The side effects are usually mild and treatment discontinuation is rarely required.
- Recent reports of anaphylaxis

IT products in New Zealand

- Alustal (Stallergenes, EBOS)
- Phostal (Stallergenes, EBOS)
- Pangramin (ALK, NZMS)
- Alutard (NZMS)
Issues to consider

- Only Alustal is registered by MEDSAFE (but not combinations)
- Others imported under section 29
- Issue of ACC coverage
- Consent