



of allergy

Bee sting allergy and Immunotherapy

On the morning before her fifth birthday, Fiena is practicing her ballet steps on the stoep. A fairy party is planned. The anticipation is hard to bear. She performs a daring pirouette and feels a scorching stab on the side of her left foot. She emits a surprised and anguished squeal. Her mother rushes outside to find her sitting on the floor holding her bare foot and rocking in pain. A honeybee staggers sluggishly to the edge of the step and tumbles into the flowerbed.

The sting is removed. Ice is applied. Tears are wiped away and antihistamines are administered.

The following morning Fiena awakes barely able to contain her excitement. She ejects herself from under the bed covers and lands with an unexpectedly painful thud on the carpet. She looks down to find that her left lower leg and foot are enormously swollen and her toes look like shiny, plump, pink chipolata sausages.

The disappointment is fleeting. Following a substantial dose of anti-inflammatory medication and a second dose of antihistamine, Fiena immerses herself in the enviable task of being a Fairy Princess, albeit a sedentary one.

It takes at least three days for the swelling to subside.

The story of the bee sting around Fiena's 5th birthday fades in a growing collection of family memories.

The bee venom, however, generates another kind of memory, one that is firmly imprinted on Fiena's immune system. Her plasma cells continue to produce immunoglobulin E (Ig E) specific to bee venom.



Fiena turns five

It is 6 years later, when Fiena is participating in the junior interprovincial netball championships in Bloemfontein, that she receives another bee sting. She feels it under her T-shirt on her back as she lunges forwards to catch a low pass.

Within a few seconds she feels a sense of impending doom. Her skin becomes itchy and she develops a generalised urticarial rash. She feels short of breath and lies down on the grass because she feels light headed. She has developed anaphylaxis.

References:

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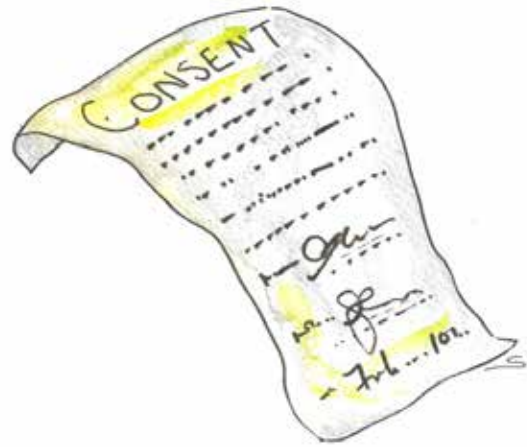
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The paramedics on duty at the event act quickly. Fiena receives intra-muscular adrenaline via auto-injector, oxygen and intravenous fluids, followed by oral antihistamines.

She is admitted to hospital for observation, and discharged after 24 hours in a stable condition, with the following:

- An adrenaline auto injector,
- An anaphylaxis action plan.
- Access to an emergency identification bracelet,
- And a referral to Dr Do-alot for immunotherapy.



A consent form must be signed prior to commencing immunotherapy.



A 'yellow topped' 'clotted' tube is required for Specific IgE testing

Specific IgE tests confirm Fiena's bee sting allergy.

Skin prick testing reveals that she is not sensitive to common inhalant allergens like grass pollens, house dust mite, moulds or animal dander.

She has no history of allergic rhinitis, eczema or asthma.

She has no chronic medical conditions and takes no daily medications.

In view of her history of a severe hypersensitivity reaction to a bee sting and a confirmatory Specific IgE test, Dr Do-alot recommends that Fiena receive injection immunotherapy for bee stings.

The necessary arrangements are made to order the allergen and appointments are scheduled.

Fiena's parents are counseled regarding the risks, benefits, costs, efficacy, duration and logistics of the treatment.

Consent and assent forms are signed.

Fiena is advised to carry her adrenaline auto-injector at all times. She receives education regarding anaphylaxis and how to recognise it, so that she is not afraid to use the injection should she need to.



Fiena carries an adrenalin auto-injector at all times as her risk of developing anaphylaxis to a bee sting is high.

About bees:

Bees, wasps, ants and sawflies are classified as Hymenoptera. The Ancient Greek words hymen (meaning 'membrane') and pteron (meaning 'wing') combine to describe the insects' translucent wings.

In countries with temperate climates, most adults will have been stung by a stinging insect at least once in their lives.

A Hymenoptera sting will usually produce a small local reaction in the skin. This is typically a painful, sometimes itchy, local wheal of about 2 cm in diameter with surrounding swelling of the subcutaneous tissue several centimetres in diameter.



Sketch of a Honey Bee (*Apis Mellifera*)

What is immunotherapy?

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

Allergen extracts are a preparation of an allergen obtained by extraction of the active constituents from animal or vegetable substances.

Allergen immunotherapy is the only treatment that can modify the immune response to allergens and alter the course of allergic diseases. Hymenoptera venom immunotherapy is the only effective preventive treatment for insect sting-induced anaphylaxis.

Who should receive Hymenoptera immunotherapy?

Only patients with a history of a systemic reaction to Hymenoptera stings who demonstrate Hymenoptera-specific immunoglobulin E (IgE) antibodies should receive immunotherapy. Most people will react to a bee sting. The reaction may be mild and local, or severe and systemic. The decision is obvious in those cases ... but what about the large local reaction or the mild systemic reaction?

The guidelines below are helpful when making a decision:

Severe systemic reactions stages 3 - 4	Yes
Mild systemic reactions stages 1-2	Adults (only if at risk) Children (<10 yr old) No
Local large reaction	No
Unusual reaction	No

When to start venom immunotherapy

Grading of systemic reactions:

1. Non-specific reactions (likely non IgE-mediated), discomfort, nausea, headache, arthralgia.
2. Mild systemic reactions; mild rhinitis/asthma (PEFR > 60%), responding to β_2 agonists/antihistamines.
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.

A large local reaction, therefore, is not an indication for venom immunotherapy.



How is immunotherapy given?

Immunotherapy is commenced by administering a minute dose of allergen. The dose is increased at weekly intervals, over about 3 months, until a maintenance dose is achieved. The patient then remains on this dose for three years or more. Immunological changes occur within a few weeks and include changes in immunoglobulin and T cell levels. The TH2 response is modified and TH1 cytokines are produced which results in a 'dampened' allergic response.



Increasing concentrations of immunotherapy allergen solution

The allergen is administered by deep subcutaneous injection, at 45 degrees, into the upper outer surface of the arm, using a sterile 1 ml graduated tuberculin syringe with an orange needle. Pre- and post-injection clinical status and observations must be checked including temperature, respiratory rate, blood pressure and peak expiratory flow rate (PEFR). Local or systemic reactions must be recorded. A patient with a PEFR of less than 70% of predicted should not be injected.



Deep subcutaneous injection into the upper outer arm

Immunotherapy should only be undertaken in a unit where full resuscitation facilities are available due to the potential risk of anaphylaxis. Storage, dilution and administration instructions must be firmly adhered to. Before administering an injection it is important to confirm that the correct antigen is being given, at the correct dose, to the correct patient. For at least 30 minutes after the injection is given, the patient must be observed for signs of a hypersensitivity reaction and treatment for anaphylaxis should be readily available and given without delay should a reaction occur. Patients should avoid heavy exercise or alcohol on the day of an injection, and should not have a hot bath soon after receiving one.

Contraindications to venom immunotherapy include the following:

- Serious immunopathologic diseases and immunodeficiencies
- Malignancies
- Severe psychological disorders
- Treatment with beta blockers
- Poor compliance
- Severe or uncontrolled asthma
- Significant cardiovascular diseases
- Children under 5 years, elderly and pregnancy (these are relative contraindications)

How successful is venom immunotherapy?

Venom immunotherapy has been shown to be protective in approximately 80% of bee and 95% of wasp venom-allergic patients.

The risk of systemic sting reactions when immunotherapy is stopped after 5 years reaches 15% in 5 to 10 years after stopping venom immunotherapy.

Following completion of venom immunotherapy it is advisable for patients to continue to carry their adrenaline auto-injectors as the possibility of anaphylaxis is not ruled out, however, when reactions to stings do occur following immunotherapy they typically tend to be mild.