

Allergen Immunotherapy

Introduction

This fact sheet is a summary of the various forms of immunotherapy. We focus primarily on food allergies and insect sting allergy (which are the core work of the Anaphylaxis Campaign) but also give some basic information on treatments for allergic rhinitis (hay fever). Some reference is made to treatments for eczema and asthma.

Throughout this Factsheet you will see brief medical references given in brackets. Full references are provided at the end.

What is allergen immunotherapy?

Allergy occurs when a person's immune system reacts in an inappropriate or exaggerated way to a food or substance that, in the majority of people, causes no symptoms. A food or substance that causes an allergic reaction is called an allergen.

Allergen immunotherapy, previously known as desensitisation, is a medical treatment for allergies. The idea is that the patient's immune system can be 'trained' to tolerate the allergen and therefore not cause allergic symptoms. Allergen immunotherapy for hay fever and asthma has been shown to have benefits for many years after stopping the treatment, where treatment has been ongoing for at least 3-5 years. This has not yet been shown for food allergy to date.

Research is also underway to assess whether immunotherapy can potentially reduce the risk of the development of asthma and new allergies. There is some evidence that pollen immunotherapy for hay fever reduces the subsequent risk of developing asthma and that therapy to treat one allergy reduces the subsequent risk of developing reactions to other allergens (Des Roches A, 1997; Purello D, 2001; Panjo GB, 2001).

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Allergen immunotherapy for hay fever

Immunotherapy is a proven effective treatment for allergic rhinitis (hay fever). Depending on what treatment is being given, it can be either through injection, drops or tablets under the tongue (sublingual).

Here, we focus on two treatments: subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), which have both been shown to give long-lasting benefit for some years after stopping treatment.

Subcutaneous immunotherapy (SCIT)

This treatment has been used since 1911 (Noon L, 1911; Freeman J, 1911). It involves injecting a small amount of the culprit allergen under the skin of the arm. The effectiveness of SCIT has been established in the treatment of allergic hay fever in numerous clinical trials (Cox et al, 2012). The injections of progressively increasing amounts of allergen are given regularly over a period of three to five years and are effective in treating reactions to many allergens, including trees, grass, weeds, mould, house dust and animal dander.

Not only does this therapy relieve symptoms, but also treats the allergy itself by targeting the underlying immunological causes.

The injections carry a small risk of triggering a severe allergic reaction shortly after treatment, so they must be given at a hospital allergy clinic.

Sublingual immunotherapy (SLIT)

This treatment involves the patient regularly placing an extract of the culprit allergen under the tongue for 1-2 minutes. The extract comes in one of two forms: drops or tablets. Generally, it has been shown that SLIT carries fewer risks than SCIT. Reactions, when they do occur, are mainly localised and non-life-threatening (Walker et al, 2011).

SLIT is more convenient than SCIT from the patient's perspective because only the first dosage needs administration under medical supervision. Afterwards the treatment can be done at home.

Several treatment programmes have been employed. It has been shown for grass pollen, for example, that SLIT is more effective if commenced daily a minimum of eight weeks before the onset of the grass pollen season. While SLIT doesn't involve any injections, it does require daily dosing and is thought to take longer to become effective compared to SCIT.

Allergen immunotherapy for atopic eczema

Immunotherapy to airborne allergens has been tried as a treatment in some people with atopic dermatitis (eczema).

However, a 2016 review concluded that the evidence for this was limited (Tam et al, Cochrane Review). The review group said: "Future studies should use high quality allergen formulations with a proven track record in other allergic conditions and should include participant-reported outcome measures."

Allergen immunotherapy for asthma

There is good evidence that immunotherapy for atopic asthma may be effective, although in general the risks of using SCIT, particularly for severe asthma, are considered too high due to the potential for causing an acute asthma attack.

Allergen immunotherapy for food allergies

Immunotherapy for food allergies was first attempted more than 100 years ago, but it is only in the last 5-10 years that this has become a potential treatment option. There are three main methods which are being assessed to deliver immunotherapy for food allergy:

1. Oral immunotherapy, where the doses are swallowed
2. Epicutaneous immunotherapy, where the food allergen is applied to the skin in a special patch or plaster
3. Sublingual immunotherapy

1. Oral immunotherapy (OIT)

In oral immunotherapy, small but increasing doses of the food allergen are given to affected individuals over a period of months, until the body is 'trained' not to react. A number of studies are underway or have been completed, both in the UK and abroad, demonstrating the effectiveness of this technique. However, up to 20% of patients do not tolerate the treatment, and others can experience frequent allergic reactions due to the doses, including anaphylaxis. Moreover, the effects are not generally long-lasting: if the doses are stopped, the allergy returns.

Several studies – both commercial and non-commercial – are currently taking place in the UK:

- i. **The Grown Up Peanut Immunotherapy Study (GUPI)** is being run at Guy's and St Thomas' NHS Foundation Trust, London, and is assessing the effectiveness and safety of Oral Immunotherapy in adults with peanut allergy. The study began in May 2018 and the estimated completion date is September 2021.
- ii. **Boiled Oral Peanut Immunotherapy (BOPI)** is a research programme based at Imperial College, London, which uses boiled peanut instead of roasted peanut to reduce clinical reactivity (Patel et al, 2019). Researchers propose showing that using boiled peanuts for OIT is better tolerated than conventional peanut-OIT, which uses roasted peanut flour. The study team are now studying this in a further clinical trial which began in mid 2019.

- iii. **Aimmune Therapeutics**, an international biopharmaceutical company with headquarters in the US, is currently sponsoring a number of studies in peanut-immunotherapy at multiple sites in the UK. Aimmune have submitted applications for marketing approval of their peanut-based product to the US and European Medicines regulators and are currently considering extending their studies to egg allergy. Further information is available at <https://www.aimmune.com>
- iv. **Camallergy** (Cambridge Allergy Ltd) is a spin-off company founded by researchers at Cambridge University Hospitals NHS Foundation Trust which is planning to launch a peanut-based oral immunotherapy treatment. In 2014, the team revealed results of their trials involving children with peanut allergy aged 7-16. The majority of participants were able to tolerate peanuts after the immunotherapy treatment, with further increasing levels of tolerance over time. There was no improvement in the control group (Anagnostou et al, 2014). A control group comprises participants who do not receive the treatment and are then used as a benchmark to measure the success of the treatment in those participants that did receive it. Camallergy is now preparing for the next phase of the studies to confirm the results in children and possibly adults. A private service for patients is now up and running. This typically includes seven visits to the allergy clinic and annual follow-up visits. Further information is available at www.camallergy.com

2. Epicutaneous immunotherapy (EPIT)

EPIT is a novel way of desensitising children with food allergy and is being developed by DBV Technologies, a global biopharmaceutical company with offices in the USA, France and Australia. Their product, Viaskin, is an electrostatic patch that activates the immune system through intact skin. The intention is that it will be self-administered, non-invasive and easy to use.

Studies are ongoing to assess Viaskin for milk and peanut allergy. The company says: "Viaskin safely provides allergenic information to the immune system without entering the bloodstream. Once applied to skin, Viaskin creates a condensation chamber that hydrates the skin and solubilizes the allergen allowing it to penetrate the epidermis." At the time of publishing this article, a study assessing EPIT in peanut-allergic children was currently recruiting in the UK. More information at www.dbv-technologies.com

3. Sublingual immunotherapy (SLIT) for food allergies

Sublingual immunotherapy is similar to oral immunotherapy, except the treatment (containing the food allergen) is held under the tongue rather than swallowed. A number of studies have been published investigating SLIT for food allergy including to milk and peanut. While SLIT appears to be much safer than oral immunotherapy, it is also less effective, although a recent study found some benefit after three years of treatment (Kim et al, 2019).

Researchers at Imperial College London are currently investigating whether using SLIT as a pre-treatment before OIT can improve the safety of conventional immunotherapy in cow's milk allergy. The study, known as SOCMA, began in July 2018 and is expected to finish at the end of 2020.

Other treatments under study

Many groups are investigating ways to improve outcomes in oral immunotherapy, predominantly for peanut allergy. Researchers in Melbourne are looking at whether combining peanut-OIT with probiotics improves treatment results, while a study led out of Sydney is assessing whether a dietary fibre supplement can have a similar effect. Finally, a group in Boston commenced a study in June 2019 to look at whether a medicine called VE416 (which contains inactive bacteria) in combination with vancomycin (an antibiotic) can improve outcomes in oral immunotherapy for peanut.

Final message

Immunotherapy treatment for food allergies must be conducted by medical experts in a clinical setting as the treatment is associated with a risk of reaction. It's a case of "don't try this at home".

Immunotherapy for people with insect venom allergy

In 2019 a drug called Alutard replaced Pharmedal in the UK as the immunotherapy treatment for people who are allergic to bee or wasp stings. Alutard, which has been widely used internationally for many years, received a UK licence in September 2019.

The basic principles underpinning insect venom immunotherapy apply to both drugs. An advantage to patients is that fewer visits to clinic are required for Alutard as doses are given every 6-8 weeks rather than every 4-6 weeks with Pharmedal.

People currently on Pharmedal can be switched over to Alutard once they have reached the maintenance phase of the treatment.

References

Anagnostou K, Islam S, King Y, Foley L, Pasea L, Bond S, Palmer C, Deighton J, Ewan P, Clark A, 2014. Assessing the efficacy of oral immunotherapy for the desensitisation of peanut allergy in children (STOP II): a phase 2 randomised controlled trial. *Lancet*, Volume 383, Issue 9925, P1297-1304, April 12, 2014.

Cox L, Calderon M, Pfaar O, 2012. Subcutaneous allergen immunotherapy for allergic disease: examining efficacy, safety and cost-effectiveness of current and novel formulations. *Immunotherapy* 2012 Jun;4(6):601-16. doi: 10.2217/imt.12.36.

Des Roches A, Paradis L, Menardo JL, Bouges S, Daures JP, Bousquet J (1997). Immunotherapy with a standardized Dermatophagoides pteronyssinus extract. VI. Specific immunotherapy prevents the onset of new sensitizations in children. *J Allergy Clin Immunol* 1997; 99:450–453

Freeman J (1911). Further observations on the treatment of hayfever. *Lancet* Sept 16, 1911; 2:814.

Kim HE, Yang L, Ye P, Guo R, Li Q, Kulis MD, Burks AW, 2019. Long-term sublingual immunotherapy for peanut allergy in children: Clinical and immunologic evidence of desensitization. *JACI*, <https://doi.org/10.1016/j.jaci.2019.07.030>

Noon L, (1911). Prophylactic inoculations against hayfever. *Lancet* June 10 1911; 1:1572.

Pajno GB, Barberio G, De Luca F, Morabito L, Parmiani S (2001). Prevention of new sensitizations in asthmatic children monosensitized to house dust mite by specific immunotherapy. A six-year follow-up study. *Clin Exp Allergy* 2001; 31:1392–139

Patel N, Vazquez-Ortiz M, Robb A, Shamji MH, Campbell DE, Turner PJ, 2019. Successful Desensitisation And Sustained Unresponsiveness Using Modified Peanut: Results From The BOPI Study.

Purello-D'Ambrosio F, Gangemi S, Merendino RA, Isola S, Puccinelli P, Parmiani S, Ricciardi L (2001). Prevention of new sensitizations in monosensitized subjects submitted to specific immunotherapy or not. A retrospective study. *Clin Exp Allergy* 2001; 31:1295–1302

Tam H, Calderon MA, Manikam L, Nankervis H, García Núñez I, Williams HC, Durham S, Boyle RJ, 2016. Specific allergy immunotherapy for the treatment of atopic eczema.

Walker SM, Durham SR, Till SJ, Roberts G, Corrigan CJ, Leech SC, Krishna MT, Rajakulasingham RK, Williams A, Chantrell J, Dixon L, Frew AJ and Nasser SM, 2011. Immunotherapy for allergic rhinitis. *Clinical & Experimental Allergy*, 41, 1177–1200. The Cochrane Collaboration.

Reviewers

This fact sheet has been peer reviewed by Dr Paul Turner, Clinician Scientist in Paediatric Allergy & Immunology at Imperial College London; and Prof John Warner, Professor of Paediatrics, Imperial College, London.

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Disclosures

Dr Turner is a Principle Investigator for the Aimmune and DBV studies and has received consulting fees from them.