Allergy Today

Allergy UK's publication for healthcare professionals

Winter 2020/2021

AllergyUK

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Dr Richard Weller, Clinical Academic Dermatologist at the University of Edinburgh



Professor Adam Fox, Professor of Paediatric Allergy

"Please keep up live webinars. Brilliant content"





Allergy UK is the operational name of the British Allergy Foundation. We are the leading charity for people living with allergic disease, providing support and advice about all kinds of allergic conditions. We act as the 'voice' of the millions of people who live with allergies, representing the concerns and healthcare needs of those affected by this multi-organ disease.

Our strategy for the next five years is centred on a new Mission:

"For everyone in the UK to take allergy seriously"

With our Vision that: "No-one should die from allergy"

The allergic community is at the heart of everything that we do and our work is focused on improving the lives of people who live with allergic disease.

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Foreword

Professor Adam Fox

Chair of the Allergy UK Health Advisory Board Consultant Paediatric Allergist, Evelina London Children's Hospital



Welcome to this edition of Allergy Today.

The arrival of a global pandemic this year has impacted on all our lives, and for many of us the impact has been life changing. As we look towards 2021, with a vaccine now available, we are all hoping for that 'light at the end of the tunnel' to get brighter, with the realisation that there is still some way to go before life returns to any kind of 'normal'.

At the spring peak of the pandemic, when we were still learning about the characteristics of this new virus, we were very aware of the particular anxieties and concerns of people living with allergic conditions. Many of those concerns were around the use of asthma medication, fears of increased vulnerability to the virus because of allergy and worries about access to medications and clinical support. For parents with children with food allergy there was a particular fear around the timely availability of emergency services if their child suffered anaphylaxis. Even hygiene precautions, such as regular hand washing, causes anxiety for someone with severe hand eczema, and someone with a latex allergy worries about the use of gloves to handle food in supermarkets. Whilst these are certainly extraordinary times, these do highlight many of the fears and anxieties that people with allergy, or with children with allergy, live with all the time – worries that have been heightened during this Covid-19 crisis.

Working collaboratively with the BSACI, Allergy UK has provided a range of information and support, through all its communication channels, to help support the allergic community and continues to do so.

While this has been a key focus, other work, including the collaboration of BSACI, Allergy UK, Anaphylaxis Campaign and other stakeholders to develop mandatory policy and training for schools, has continued. This remains high on our agenda for change and we will continue to pursue this with the Department for Education as an urgent priority.

Welcome

This is the time of year when we look back over the last year or so. Our Annual Report for 2019/20, which will soon be available on our website, is a powerful record of the work of our charity over that period, with a wide range of projects and campaigns to raise awareness and understanding of allergic conditions, including our work with key opinion leaders and decision makers.

Whilst the Covid-19 pandemic, which struck at the start of this financial year, has inevitably brought some challenges for the Allergy UK team we have continued to deliver the support services that our allergic community needs through our busy Helpline and other communication channels. These services have been needed more than ever as people with allergic conditions experience increased fear and anxiety about their condition and the virus, as well as concern about the cancellation of clinic appointments. Our team has worked tirelessly to serve our community during this time with the provision of up-to-date advice and information to help address their fears, and a voice at the end of the telephone to support them in these troubling times.

In this last month we have also been able to reinstate our very successful Masterclass programme with the launch of our first virtual Masterclass of three live streamed sessions. These have attracted a large audience of healthcare professionals and all three Masterclass sessions are available on our website, with CPD points available. This Masterclass topic was 'Understanding Food Allergy' and included sessions on Food Allergy in Childhood, Peanut Allergy, Cow's Milk Allergy, Atopic Dermatitis and Pollen Fruit Syndrome. Given the ongoing situation we have decided to focus on live streaming our Masterclasses in 2021 and more details of these will be available soon.

In this edition of Allergy Today we have articles on cat allergy, from both a clinician's and a vet's perspective, as well as on the microbiome and sublingual immunotherapy which we very much hope you will enjoy reading.



Carla Jones, CEO

Amena Warner, Head of Clinical Services

Allergy News

Check it. Don't chance it

During September and October Allergy UK and Anaphylaxis Campaign collaborated on a campaign to urge parents, teachers and school staff to check the expiry dates and the validity of life-saving Adrenaline Auto-Injectors (AAIs), review prevention measures and refresh staff training as pupils returned to schools after the Covid-19 lockdown. With around 5-8% of children in the UK having at least one food allergy, the campaign responded to parents' concerns that the lockdown may have meant that spare AAIs were out of date and that the required adrenaline dose for their child may have changed because of their child's current weight.



The campaign website included top tips for schools and links to a wide range of Allergy UK and Anaphylaxis Campaign resources to help schools manage the care of pupils with food allergy, including staff training resources and the SAAG (Schools Allergy Action Group) toolkit to help schools develop their own allergy management policy.

One Year to Go

Allergy UK is supporting the campaign by the Food Standards Agency (FSA) to raise awareness and understanding of the new food labelling requirements for PPDS (Pre-Packed for Direct Sale) foods which come into force on 1 October, 2021 in England, Wales and Northern Ireland. These will help protect food hypersensitive consumers by requiring more types of food to have potentially life-saving allergen information on the label.



On 1 October the campaign focused on a 'One Year to Go' message to encourage food businesses to check if the new labelling requirements affect them and find out what they need to do to comply.

Autumn Allergy Awareness Week



During the Covid-19 pandemic we are spending more time than ever indoors and in Allergy Awareness Week the focus was on the triggers of indoor allergies and ways to manage symptoms.

The Allergy House on the Allergy UK website, which identifies the 'hotspots' for indoor allergens has attracted over 30,000 visitors since its launch in 2019. www.allergyhouse.co.uk

NICE Guidelines

In September, The National Institute for Health and Care Excellence (NICE) published an update to their clinical guideline on anaphylaxis. (Guideline 134 - Assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode).

The 2020 update outlines that people should be prescribed two further adrenaline injectors before discharge after emergency treatment, and that they should be advised to carry these with them at all times.

<u>Click here</u> to read the full anaphylaxis guideline including the update.

World Atopic Eczema Day

September 14 marked World Atopic Eczema Day - a day when the patient community came together to raise awareness, understanding and standards of care for atopic eczema.

Atopic dermatitis or atopic eczema is the most common form of eczema. It is currently an incurable, chronic immune-mediated systemic disease with a debilitating effect on 2-10% of adults and 20% of children worldwide. The condition can affect personal relationships, decrease psychosocial functioning, bring sleep loss for family members and engender grief and a feeling of helplessness in dealing with a child's daily suffering. Atopic eczema may also result in work absence or decreased work productivity for parents.

Patient organisations around the world ran a coordinated awareness campaign to raise awareness of the condition and lobby for improved standards of care.

#FOODSENSITIVE Impact Study

This Study, launched in October, explores the impact of food allergy, food intolerance and coeliac disease on quality of life. The research is led by Dr Rebecca Knibb from Aston University, in collaboration with the Universities of Surrey, Manchester and Newcastle, Allergy Action, Guys and St Thomas and Birmingham University Hospitals NHS Trusts.

The online survey is open to people and parents with a child living with these conditions, with questionnaires about the ways in which they affect quality of life and the impact they have on day-to-day life. The research team is looking for adults, parents of children aged 0-17 years and young people aged 8-17 years to take part. The Study is funded by the Food Standards Agency.

Virtual Masterclass 2020

In November we launched our first virtual Masterclass with great success. The focus was on Understanding Food Allergy and we heard from specialists in the field of allergy, including Professor Adam Fox (Professor of Paediatric Allergy) and Dr Richard Weller (Clinical Academic Dermatologist at the University of Edinburgh), as well as members of Allergy UK's in house clinical team. We would like to thank everyone who was able to attend our event. For those who were unable to attend but are still interested, our sessions are now available to view online until 15 January 2021 www.allergyuk.org/health-professionals/events-and-masterclasses. CPD points are available to claim for each session you view.

To download past editions of **Allergy Today** please visit our website **www.allergyuk.org**



Cat Allergy

Chris Corrigan

Professor of Asthma, Allergy & Respiratory Science, King's College London Faculty of Life Sciences & Medicine

Chris Corrigan is Emeritus Professor of Asthma, Allergy & Respiratory Science in the King's College London Faculty of Life Sciences and Medicine, based at Guy's Hospital in South London and a Principal Investigator in the UK Medical research Council Centre for Allergic Mechanisms of Asthma based in London. He led in building the large adult allergy service, particularly the allergen immunotherapy service, and the severe asthma service based at Guy's Hospital, London.

Incidence of cat allergy

Cat allergy, like all "immediate hypersensitivity" or "allergic" reactions, arises as the result of inappropriate production of IgE antibody against one or more unique proteins ("allergens") manufactured by the plant or animal, which binds to the surface of mast cells, found in the "linings" of all organs that contact the exterior and basophils in the blood stream, causing the sudden release of histamine upon subsequent, further contact with the allergen. Like that of all "allergies", the incidence of cat allergy has been steadily increasing, as a result of increasing exposure to trigger factors arising largely from pollutants in the external environment, along with increasing exposure to cats. In certain individuals these triggers initiate inflammation in the skin and linings of the respiratory tract and bowels which may result in diseases such as eczema, asthma and food sensitivity. This inflammation also predisposes to the production of IgE-mediated

reactions to external, environmental proteins which may be inhaled (including "aeroallergens" such as grass and tree pollens, house dust mite, cat and dog dander), come into contact with the skin or be eaten in the diet'. Both pollution and exposure to allergens from domestic animals such as cats are more likely in overcrowded, "inner-city" environments and have resulted in the increased incidence of these diseases particularly in these environments, as studies confirm. There have been some suggestions that very early exposure to cats (in infancy and early childhood) protects against the development of IgE responses later in life, but this remains far from clear (1, 2). The prevalence of sensitisation to cat allergen, as shown by a skin prick test, is reported as 8-15% in studies across the world: this has approximately doubled in the past 30 years (1).

Allergens implicated in cat allergy

Although eight cat allergens have been characterised and could in theory contribute to symptoms of allergy, only three are of major clinical significance (1). Fel d1 (a secretoglobulin) is the dominant cat allergen to which essentially 100% of allergic individuals are sensitised (1). It is secreted predominantly by skin sebaceous glands, where it adheres to the skin and fur. Contrary to popular rumour, production is not related to fur length. It is secreted to a lesser extent by the salivary, lacrimal and anal glands. It can readily become airborne, where it is associated with particles of 4-9 μ M in diameter. The recombinant protein, which can be manufactured for immunotherapy, retains a structure similar to the natural protein. In addition, 30-60% of individuals sensitised to Fel d1 have been reported to be additionally

sensitised to the cat lipocalins *Fel d4* and *Fel d7*: these originate predominantly from the saliva. A minority (15%) of cat allergic subjects is sensitised to *Fel d2*, a determinant of cat albumin and so not secreted to any degree.

The characteristics of cat allergens and their impact on the home environment

Since they contaminate the skin, fur and saliva, cat allergens rapidly become dispersed throughout any dwelling in which a cat resides. The only way to prevent this is to exclude the animal completely from the house, but even then contamination may occur from clothing.

Although in some societies it is conventional to confine pets to outside dwellings, most cat owners would not accept denying their pets, which they regard as companions, access. Cat allergens are long lived and persistent: studies suggest that they remain detectable in houses for 6 months or more following the departure of the resident cat (3), and that confining the cat to "one room of the house" does not prevent permeation of cat allergen throughout the dwelling unless very strictly enforced. Finally, some studies suggest that, at least in some environments frequented by large numbers of people, including schools, cat allergen is in any



Symptomatology

Patients sensitised to cat allergens, like all "allergic" patients may suffer symptoms on exposure to the offending allergens. Release of histamine from mast cells within the respiratory tract may cause acute symptoms of allergic rhinoconjunctivitis ("hay fever"): itching, redness and running of the eyes and nose, with sneezing, coughing and nasal congestion and post-nasal drip, and may exacerbate existing asthma, causing wheezing and shortness of breath. Cat allergy has also been implicated in exacerbation of eczema and may in some individuals cause an urticarial rash ("hives") on skin contact with a cat following local histamine release from mast cells in the skin. As with all "allergic" diseases, the severity of symptoms varies markedly between individuals, ranging from mild but noticeable to extremely severe and disabling. Many patients who become sensitised (that is, develop a specific IgE response) to aeroallergens such as cat allergens develop no symptoms on exposure at all. The mechanism(s) of this wide variability in the severity of symptoms among sensitised individuals remains unexplained and cannot be predicted other than by actual challenge of the individual under controlled conditions.

Reduction of cat allergen exposure: the challenges

Apart from complete avoidance of contact with cats, various approaches have been scrutinised as a possible means of reducing symptoms in cat allergic individuals. Regular washing of the animals has been shown somewhat to reduce, but not abolish the airborne allergen content of the local environment (6), as has employing a microparticle room air filter in suitable environments (7), but it is less clear that these measures significantly reduce symptoms in cat allergy sufferers living in the same environment (even if the sufferer is not doing the washing). Furthermore, cats do not in general enjoy being immersed in water. Similarly, while vacuum cleaners with filters efficiently remove allergens from the filtered air, the act of vacuum cleaning itself, as well as emptying the waste bag afterwards may increase personal exposure (8, 9). There have been claims, not widely substantiated by their general availability, that, presumably through inbreeding, it is possible to produce cats expressing Fel d1 at reduced intensity; this would likely require an extensive inbreeding programme even if it were possible. At least one company has reported attempts to produce a "line" of cats in which the Fel d1 gene has been deleted using the same gene deletion/ silencing technology currently under investigation for

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management of serious, genetically-based diseases in humans. Again this would require an extensive inbreeding programme from gene-deleted male and female animals or possibly cloning of embryonic cells, and even if this were achieved it is not clear that such animals would be viable: the precise function and potential dispensability of the Fel d1 protein in normal cats is not clear. Finally, it would be a formidable challenge to demonstrate that any such measures are of therapeutic worth in blinded, controlled clinical trials, particularly since allergens other than Fel d1 may contribute to symptoms in cat allergic patients, and since many individuals sensitised to cat allergen may be sensitised to other perennial allergens as well (dog, house dust mite).



Treatment regimens

In terms of drug therapy, nasal and ocular symptoms of cat allergy will be alleviated to a variable extent by anti-histamine therapy, depending on their severity. Some patients may derive further benefit from additional anti-leukotriene therapy with drugs such as montelukast (leukotrienes are another product of mast cells which may contribute to symptoms). Conventional, non-sedating anti-histamines such as cetirizine, loratadine and fexofenadine are meant to be taken regularly once daily and, because of their long halflife (typically 16 hours) in the circulation, they do not attain optimal concentrations in the blood until after 3 days of commencing dosing: they are not, therefore, a "quick fix" for alleviating symptoms of accidental cat exposure, and ideally should be commenced at least a week in advance of any anticipated cat exposure by individuals known to be allergic. For those regularly exposed, regular daily treatment is mandatory. Faster acting, sedating anti-histamines such as

chlorphenamine afford faster relief from unexpected exposure but may cause poor concentration and drowsiness, and so are ideally taken only as an aid to sleep, and certainly not if contemplating driving or any other activity which requires full concentration. In addition to anti-histamines, the regular use of nasal corticosteroid sprays may further reduce symptoms of hay fever and the associated nasal congestion, while anti-histamine eye drops may augment the effects of anti-histamines taken by mouth (eye drops containing corticosteroids are liable to cause unwanted effects such as glaucoma and should be used only under expert medical supervision). Sufferers whose asthma is exacerbated by cat allergy will likely benefit most from regular inhaled therapy with a long-acting bronchodilator such as formoterol and a corticosteroid such as ciclesonide.

For those who suffer particularly severe symptoms despite full and regular dosages of these medicines, allergen immunotherapy is available. Because of the limited range of allergens responsible for the symptoms of cat allergy, this treatment is relatively well established and effective. It is usually performed with cat allergens modified so as not to activate an allergic reaction (nevertheless regular supervision in an allergy clinic, especially when commencing the treatment, is mandatory, and patients with very severe asthma may be advised to avoid it because of the very small but tangible risk of severe exacerbation of their symptoms). Treatment alters the body's immunological response to the allergen, damping down mast cell activation and acute release of histamine. It is not a cure, and rarely obviates the need to take antihistamines, but symptom control on cat exposure is typically markedly improved (by 50-80%: occasionally patients all but lose their symptoms, while occasionally others respond less well than anticipated). Cat allergen immunotherapy may be given either by a series of subcutaneous injections, or sublingually by placing dosages of the modified allergen in drops under the tongue. Treatment is typically given for a total of 3 years, and usually provides indefinite benefit. Because of the adage that allergen avoidance is always the best cure for allergies if feasible, many NHS Trusts have a policy not to offer immunotherapy to severely allergic patients simply to enable them to keep a cat, but will usually offer it to sufferers who have no option but to contact cats in the course of their occupations (such as veterinary surgeons or animal rescue and welfare staff). It is finally worthy of note that cat allergic

patients are frequently also allergic to other perennial allergens such as those from dogs and house dust mites (one study in the USA suggested that nearly 80% of individuals sensitised to cats were also sensitised to dogs (10)): this may potentially dilute the clinical impact of desensitisation to cat allergen alone.

Relinquishment of the cat – first or last resort?

Household pets make a wonderful contribution to the lives and physical and mental wellbeing of countless numbers of people, from young children to the elderly, the lonely and the infirm, and are well recognised to provide a wealth of emotional support and companionship. On the other hand, increasing pet

ownership, crowdedliving conditions and environmental changes are driving an increased prevalence of pet allergy, with symptoms which may range from mild but annoying to potentially life-threatening, and a considerable contribution to healthcare costs. Hopefully, continued study and further understanding of the mechanism of sensitisation to airborne allergens and how this is influenced by changes in environmental pollution, more advanced techniques to subvert IgE synthesis and refinement of allergen immunotherapy will enable us to divert or halt the course of allergic sensitisation in the future. This would be my first resort, and the abandonment of animals my last.

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Cat Allergy

Pete Wedderburn

Veterinary surgeon, radio/TV broadcaster, columnist and author

Pete Wedderburn (BVM&S CertVR MRCVS) qualified as a Veterinarian from Edinburgh, Scotland in 1985. He has worked in his own four veterinarian companion animal practice, Bray Vet, in Bray, County Wicklow, since 1991. Pete is well known as a media veterinarian in Ireland and the UK, who has presents

a regular breakfast television slot on Ireland AM on Virgin Media One for the past 15 years. Pete has also been working as a regular contributor to radio, both nationally and locally, for over 20 years, and is a prolific writer on animal topics.

Pete is currently an ambassador for Purina.

As a vet in practice, the main way that I encounter allergies is when they affect the animals I treat: just as allergies have become more common in the human world, so they have in the pet world. Dogs and cats commonly suffer from allergic skin disease, respiratory conditions and gastro-intestinal disorders. Vets are familiar with the broad ideas of treating allergies, including avoidance of allergen exposure and the use of both topical and systemic antiinflammatory medication.

However, as well as treating allergies in pets, vets are also very aware of the way that allergies can affect humans, and in particular, we are aware of the significance of human allergies to cats. There are three ways that this issue presents itself to us.

First, some vets and veterinary nurses suffer themselves from allergies to cats. Second, cat-owning families commonly describe the issues that human members of their family may have, caused by an allergy to cats. And third, people who do not keep pets, but have a yearning to do so, are frustrated by the fact that a family member is allergic to pet fur.

A) Veterinary staff who are allergic to cats

I know several colleagues who have been forced to stop seeing cats because of their intense allergic reaction. They have tried wearing gloves, masks and protective clothing, but even then, they are unable to be in a room with a cat for a sustained period. Their only answer has been to stop seeing cats, and to move to a different sector of the veterinary profession.

B) Family members who are allergic to cats

This is the scenario that vets have to deal with most commonly, with owners explaining the complicated household arrangements of living with a cat in a home where someone has an allergy to the animal. Typically, an owner may be a parent, who will explain that their cat has to be confined to certain parts of the house (e.g. the kitchen) because one of their children suffers from an allergy to the cat. In other cases, it may be the "other half" of a couple who live together. In both instances, the owner of the cat who brings the animal to the vet expresses disappointment that these restrictions are necessary. Most cat owners adore their pets, and they'd like to have their animals as a close part of their lives. There is a certain pleasure involved with having a cat sleep on the end of your bed: the reassuring, warm, weight of their body that you can feel near your feet, the pleasing sound of a relaxed cat purring, the

sense of companionship carried by their presence. I remember myself, as a teenager, feeling emotionally supported by my pet cat at times when the humans in my life were not as closely connected to me as they might have been. So, I can understand the sadness in people's eyes when they tell me that their cat cannot visit the bedroom areas of the house because one of the human members of their family would be likely to suffer an allergic reaction if they did so.

Sometimes this sadness goes even deeper, when people discover that confining the cat to designated areas of the house is not sufficient, and they are told that the only way that they can control the impact of the allergy on their family member is to relinquish their cat by rehoming. This can cause severe emotional distress, as pet cats are often seen as close members of the family, rather than simply animals sharing their home.

It's frustrating for me when people ask me for advice in such situations, as to date, I have not had many effective answers for them.

1. Restricting the areas that cats can access

My first step is generally to advise confinement of the cat to specific areas of the home, such as the kitchen area. This is often reasonably effective: such living areas are often largely free of soft furnishings, with non-porous floors and surfaces that can be easily cleaned. However, the practicality of confining a cat in this way varies from home to home: often, these days, houses are designed with open plan living. The kitchen is often seamlessly connected to the dining room and to the living area, allowing families to enjoy more spacious, open, homes. It can be surprisingly difficult to erect barriers to confine an agile, nimble and active small animal like a cat.

For people who cannot easily confine a cat to the kitchen area, the second answer can be to keep bedroom doors shut. This is not ideal either: if a cat is spending time on soft furnishings in the living area, the allergens from their saliva (and hence their coat and fur) are difficult to remove effectively. And bedroom doors are surprisingly difficult to keep closed all the time in a busy home with young people: the installation of door-closing springs is often needed.

In some cases, a cat may need to be excluded completely from the house, instead setting up an outdoor sleeping area for the animal. For most pet owners, this is not at all satisfactory: they feel that the cat cannot have

the life it deserves, as part of a human family, and they would prefer to completely relinquish the cat to a new home, despite their strong emotional attachment.

2. Removing cat allergens from the home environment



The second step is to take other steps to remove the allergens from the cat that have landed in the environment. Ideas include daily cleaning using a vacuum cleaner with a micro-filtration device (like a HEPA - high-efficiency particulate air - filter), then wiping surfaces down using spray furniture polish first (to limit Fel d 1 allergen particles from becoming airborne). Minimising porous surfaces in the home can help: replacing carpets with wooden or laminate floors, replacing curtains with blinds, and using hypoallergenic cushions and pillows instead of feather-stuffed ones. The use of air purifiers with HEPA filters may also be suggested, although the efficacy of these devices varies significantly.

3. Managing physical interactions with the cat

It's also important to pay close attention to the specific interactions between the allergic person and the cat. Ideally, they should avoid the cat at all times, but if they do have interactions, they need to wash their hands with soap and water immediately afterwards.

In many cases, attempts to exclude cats from specific zones of the home, to reduce the allergens in the environment, and to minimise contact between the cat and the allergic person, are not sufficient.

4. Reducing the allergen load carried by the cat.

Daily brushing and combing of the cat by a non-allergic member of the family may help to reduce the allergen load carried by the cat, given that the fur is the primary place that the Fel d 1 allergen will be carried on most fully-furred cats (after the allergen has been transferred to the cat's coat from the saliva by self-grooming).

In theory, regular bathing of a cat might remove Fel d 1 allergens from the cat's skin and coat, reducing

the shedding of the allergen in the environment. In practice, there is little evidence that this works: as soon as a cat grooms itself after bathing, a new load of allergen will be spread over their body. Furthermore, cats usually strongly dislike being bathed (I've heard it said that "cats are allergic to water" but that would be an inappropriate statement to use in a magazine about allergies). Suffice to say, it is not at all easy to give a cat a full body wash, and when this is not guaranteed to significantly help the issue, most owners are unlikely to be motivated enough to do this.



To date, there have been few other ways of reducing the allergen load on the cat, and in their absence, fictional theories have flourished. This is an area where the internet abounds with ideas, but the reality is far less helpful. Dr Google suggests the following possibilities, which sadly, are not backed up by science.

a. Hypoallergenic cats. Some breeds of cataremarketed as having lower level of allergens: in particular, hairless cat breeds like the Sphynx are sometimes rumoured to be less likely to be allergenic than other breeds. However, we now know that the active allergen that stimulates allergies in humans is largely Fel d 1, which is produced in the cat's saliva, spreading to the cat's skin and fur through grooming. And while this allergen is spread around the home on cat fur in most cases, it is also spread via skin dander, which is produced by hairless cats just as much (or perhaps even more) than by fully-furred felines. All breeds of cats produce Fel d 1, whether cross bred or pedigree, long haired, short haired or hairless.

Some years ago, genetically engineered hypoallergenic cats, marketed at high prices, seemed to offer a possible answer. In 2009, a company called Allerca received global media attention with specially created allergy-free cats, priced from \$4,000 to over \$7,000 each. However, doubts were soon cast on the reality of this claim: an ABC report in 2013 found that the

supposedly hypoallergenic cat that Allerca tried to sell to reporters was, in fact, an ordinary cat from a local pet breeder. There are still genuine scientific efforts being made to use the gene-editing tool CRISPR to remove the gene that makes Fel d 1 from cat cells, and then to breed cats that do not produce the allergen at all. However, this process is exceedingly complex: it is not just about editing the cat's genes in the laboratory. This would just be the first step, and it would then be necessary to work with cats' embryos, perhaps creating cloned cats with the new genetic code. And even if this could be done, there are fears that a cat that does not produce Fel d 1 may not be fully healthy. The precise physiological function of the allergen in the cat is not understood, and the possible consequences of its absence in an animal remain unknown.

- b. The surgical removal of cats' anal sacs. Cats and dogs have small glands on the inside of the anus that produce a scent-containing solution (a mini version of a skunk's scent producing apparatus). There is a persistent internet rumour about cats being less allergenic if these anal sacs are removed, but there is no evidence that this is successful. It seems that the anal sac secretion does contain feline antigens, which may contribute slightly to the overall allergenic challenge carried by the cat, but the removal of the sacs has not been shown to solve the problem. Indeed, it is possible that the dissemination of this idea may be linked to some confusion with a different issue: some animals that suffer themselves from allergy-related disease may have their anal sacs removed because their veterinarian believes that their peri-anal itchiness may be aggravated by chronic inflammation of the anal sacs.
- c. Daily dosing the cat with acepromazine, a sedative with anti-histamine properties, has been recommended by some websites, with the unproven claim that this "changes the composition of the cat's saliva". There is no evidence at all that this has any effect whatsoever on the cat's allergen load.
- d. Spraying the cat with products to reduce shedding of Fel d 1 may be suggested, but there is no evidence that this has any impact.

C) People who cannot keep cats because of an allergic person in the home

The third way that I hear about allergies to cats happens more often when I meet people away from my clinic. I am passionate about the benefits and pleasures of pet ownership, and so I often get into conversation with people about the animals in their lives. Sometimes people may explain that they don't keep pets because they are too busy, or because it "just isn't their thing"<mark>. But surprisingly commonly, I am</mark> told that the reason they cannot keep an animal is the fact that they or a family member suffer from allergies to pets. And allergies to cats seem to be far more common than allergies to dogs, rabbits or other pets. I am commonly asked "what pet do you recommend for children who are allergic to fur", and my answer is not enthusiastically received: a goldfish does not represent the type of human-pet relationship that parents want for their family members to enjoy.

The benefits of pet ownership have been clearly documented.

- Children who grow up with pets around them are more self-confident and socially adept than children whose families do not keep pets.
- Pets offer emotional support to children, showing what seems to be genuinely unconditional love (compared to the conditional love that parents and other family members often seem to show when children are going through challenging times like adolescence).
- Pets teach children valuable life lessons, including experiences like friendship, grief, responsibility, and many others.
- For older people, pets are often invaluable companions, with many health benefits, including reduced visits to the doctor, improved mental health, reduced incidence of certain diseases, better recovery after cardiac surgery and more self-reliance (one study found that the need for paid carer assistance was significantly lower when elderly people living on their own had a pet).

Cats are particularly appropriate as pets for our contemporary lifestyle: they are independent creatures who enjoy human company, but are able to be left on their own for longer periods than their canine cousins, who are more socially dependent.

To date, people who are severely allergic to cats have been deprived of the life-enhancing experience of sharing their lives with cats. The latest advances in helping manage allergies to cats may make a significant difference to the quality of life for these people, allowing them to engage in a popular and useful life activity from which they have, to date, been excluded.



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Human Microbiome and Allergy

Laura Phillips, Paediatric Allergy Dietitian

Laura qualified as a dietitian from the University of Surrey in 2003. She found a passion for working in paediatric allergy having gained a job at St Mary's Hospital, London in their tertiary MDT allergy clinic. For the last seven years she has worked at Colchester Hospital, Essex in MDT and dietetic led allergy clinics. Laura took up a Dietetic Clinical Advisory post at Allergy UK alongside this in September 2020.

The microbiome has become a trendy word in health over the last two decades but what does it really mean and how does this fit in with allergic disease? By 2025 it is expected that 50% of all Europeans will suffer from allergy. This staggering percentage will have undue impact on quality of life and cost to health services. The controversial 'hygiene hypothesis' was postulated many years ago with the theory, early exposure to certain microorganisms protects the immune system and prevents food allergy. Whilst we now find ourselves in an even more sterile world of a global pandemic, we need to seek ways to modulate our health to aid both our overall health and prevent or reduce allergic disease for the future. The microbiome leads on from the hygiene hypothesis and presents full of promise if we can unlock the answers; that in itself is proving to be challenging. This article will outline key areas within allergy.

What is the microbiome?

There is a complex balance of microorganisms including bacteria, viruses and fungi to make up the microbiota that are in many areas of the human body including but not exclusive to the gut, skin, lung, vagina and oral cavity. These microorganisms, their genes and how they interact





with the host is what makes up the microbiome. Within the human microbiome there is thought to be 100 trillion microorganisms that accounts for 3% of our mass, with 46 million bacterial genes, half being individual specific thought to be like a microbial fingerprint.

Key terms:

- **1. Microbiome** describes the microorganisms, their genes and the environment they are in
- Microbiota refers to microorganisms in a defined environment
- Probiotics are live bacteria when delivered in the correct amount deliver a positive health benefit to the host

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- 4. Prebiotics non-digestible foods are that promotes the growth of beneficial microorganisms in the intestines
- 5. Symbiosis is the relationships of organisms within a community
- 6. Dysbiosis is the disruption the microorganism balance

The genetic content varies greatly between the same microbes, so just understanding the microorganisms for different conditions is not enough and understanding how genes affect disease risk is just as important. The microbiota further communicates with the brain via the microbiota-gut-brain axis with suggested pathways via various routes including the immune system, nervous system and by involving microbial metabolites. External factors like stress and sleep may play a part in this relationship.

The focus of research is linked to the gut microbiome and specifically the large colon. The microbiota is divided into phyla, with the four main phyla being Firmicutes (including lactobacillus and clostridium strains). Bacteroidetes. Actinobacteria (including bidfidobacteria) and Proteobacteria. There appears to be a different optimum of these microbiota for different people and different conditions, this makes it challenging to make recommendations.

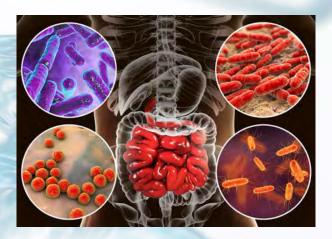
These microbial systems are influenced by many factors that can affect short and long-term health and disease. Dysbiosis is the upset of this balance and can occur in many conditions for example irritable bowel syndrome, inflammatory bowel disease, obesity and oncology but the focus of this article is how it plays a part in the development of allergic disease.

The richness of the microbiome is linked to the number of bacteria and the diversity is associated with how many species; these two aspects are key with what we are aiming for with in a healthy gut. The importance of the microbiome is that it is linked to digestion, vitamin boosting including folate, B2, B3, B12 and vitamin K, protection against disease, production of short chain fatty acids (SCFA) to reduce inflammation and immune regulation and protection against pathogen. Whilst the microbiome is not a visible it is viewed

as an additional organ as contributes to essential human health.

What disrupts the microbiome?

The aim is for the correct blend of microbiota for each individual's health but dysbiosis can easily occur. The relationship between the microbe and host can become disrupted by many factors for including age, genetics, birth mode, lower breastfeeding rates, antibiotics, limited diet, pets, siblings and illness.



Pregnancy and early life

Maternal diet can influence the infants microbiome. It has been proposed modulating the maternal microbiome pregnancy results in transmission of mediators (such as regulatory cytokines, antibodies and growth factors) through the placenta for foetal immune system development.

As highlighted mode of delivery, early feeding choices and antibiotic use in the neonatal period can affect the microbiota but also increase the risk of allergic disease. Infants who have a vaginal delivery are exposed to many different microbiota. If breast fed then human breast milk is rich in human milk oligosaccharides that helps to encourage the diverse gut bacteria including Bifidobacterium in the gut. This aids the production of short chain fatty acids to regulate the immune system.

Breastfeeding has been shown to have a influence on microbiome development, regardless of whether it was exclusive or together with formula milk and/or solids. Breastfeeding is recommended for the first 6 months of life as a minimum. In the UK as highlighted by the infant feeding study we

know the levels have dropped to 1% by 6 months old; we should continue to actively encourage. By introducing solid food, the infant's microbiome increases in Bacteroidetes and firmicutes and over the first three years of life starts to represent a microbiome more similar to an adult.

Food allergy

The British society of Allergy and Clinical immunology reports food allergy affects 4% of adults and 6-8% of children. Initial exposure of allergens occur via the skin or gut, but some infants become sensitised and potentially allergic to these allergens whilst others do not. Microbiota is necessary for the function of T cells to maintain host immune homeostasis, dysbiosis may trigger inflammatory responses through the immune system and imbalance of T cells leading to an increased risk of food allergy . It has been found that a low gut microbiota richness in early infancy is associated with subsequent food sensitization .

Eczema

An increasing number of both infants and adults have eczema. With a lifetime prevalence of 15-30% in children and 2-10% in adults, the incidence of atopic eczema has continue to increase. An increased susceptibility to eczema through genetics, infections and itching over time leads to the skin barrier becomes altered. Staph aureus on the skin is a common concern on the skin and can colonise, this can lead to increased inflammation, disease severity and the diversity of the skin microbiome will be affected negatively. The skin microbiome is important for the skin barrier and important to maintain. An increased microbial diversity of the skin can improve the integrity and homeostasis. Furthermore, integrity of the skin prevents the passage of food antigens causing sensitisation to proteins in foods and potentially resulting food allergy.

Asthma

The studies regarding asthma and the microbiome are very much more limited, one small study with only 47 infants showed children developing asthma had a lower diversity of the total microbiota than non-asthmatic children. It is also suggested that the composition and function of upper airway microbiota could influence asthma pathogenesis.

Probiotics

Probiotics are live bacteria when delivered in the correct amount deliver a positive health benefit to the host. The strains used are often based on Bifidobacterium and Lactobacillus species. Probiotics can be bought in drops, powders or supplemented in a food item.

The dose of probiotics are described in colony forming units (CFU) where each living bacteria is one colony forming unit. The amount required from research suggests 10⁷ - 10⁹ CFU are required but dependent on the strain. The exact type of bacterial species for different conditions is still emerging.

Lactobacillus strains have been explored for the prevention of eczema, it appears early intervention is key in pregnancy or early postnatal days. The World Allergy Organization suggested a likely benefit to using probiotics in preventing eczema in children with a family history of allergic disease, but the evidence is very low. With regards to specific strains a recent review presented a discussion that there is insufficient evidence for specific prebiotic or probiotic strains during pregnancy, lactation and early life to prevent the development of allergic disease in children. A Cochrane meta-analysis of the role of currently available probiotics for existing eczema also supports there is no evidence base for the role in improving eczema severity or quality of life. Ongoing research will continue for eczema prevention and cure, there is likely to be ongoing emerging evidence.

The research for probiotics in allergy has mainly been focused in eczema, food allergy and prevention. Studies have looked at other areas including prevention of asthma, dust mite allergy and allergic rhinitis but the evidence is limited and insufficient information to recommend. Despite a wealth of evidence for probiotics it still appears key that more long-term research studies are needed to more answers for the food allergic population. Many patients choose to still use a probiotic and if choosing a probiotic consider the following guidance: take the correct dose recommended, considerastrain linked to specific health conditions or multistrain, ensure it has been stored correctly

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(do not heat or will destroy it), remember safety; probiotics are not recommended for people who are immunocompromised and carefully check for allergens.



Prebiotics and dietary recommendations

Prebiotics are are non-digestible foods that promotes the growth of beneficial microorganisms in the intestines. Fermentation of these complex carbohydrates and fibres can produce short chain fatty acids (SCFA) for example acetate, propionate and butyrate. These SCFA are thought to be the link between the microbiota and host tissues. They help to improve the function and the integrity of the gut which then impacts on the inflammatory response and decreases toxic molecules.

To help increase these SCFA increasing these complex carbohydrates include encouraging a high-fibre diet (aiming for >30g/day for adults) which contains fruits and vegetables (1-2 g fibre per portion), wholegrains including cereals (5-8g per portion), beans and pulses (2-4g per portion) and nuts and seeds (1-3g per portion) is recommended by the UK government.

Diets high in plant based proteins and lower in saturated fat consistently helps to restore the microbiome diversity with long term habits being key.

TAKE HOME MESSAGES:

- The microbiome is a complex individual fingerprint that needs to be explored to fully understand recommendations for individuals.
- The picture of the microbiome in all areas of allergy is still emerging with the most evidence in eczema.
- There is limited evidence for probiotics but to support patients to make safe choices.
- In babies, encourage breastfeeding where possible and a wide range of foods in the first year of life especially homemade both for allergy tolerance and to diversify the microbiota.
- For adults encourage a healthy eating diet low in fat and meeting high fibre UK recommendations (30g/day).

House Dust Mite and Immunotherapy

Margaret Kelman, Specialist Allergy Nurse



Margaret recently joined Allergy UK as a specialist allergy nurse, living and working in Scotland with experience in providing care to children, young people and adults with both dermatological and allergic conditions, with a special interest in young people and food allergy, eczema and urticaria. She is currently involved in a unique project with the University of Edinburgh, funded by Allergy UK, to integrate research and development into everyday practice, through the development of novel nurse led allergy clinics within primary care. For this work Margaret was very fortunate to be awarded the Barry Kay award for excellence in allergy care and research in primary care at the BSACI conference this year.

What is a house dust mite?

The house dust mite is a tiny creature, only visible under the microscope, from the arachnid family related to the spider and acarina or tick families. House dust mites do not live on humans but feed primarily on the dead skin cells they shed. They are hygroscopic and prefer warm and humid conditions thriving in soft furnishings in the home eg mattresses, bedding, carpets upholstered furniture and curtains, Unfortunately no matter how clean your home it is impossible to eradicate house dust mites in the UK.

The main species of house dust mite within the UK are: Dermatophagoides farinae and Dermatophagoides pteronyssinus.

Why does the HDM cause allergy symptoms?

House dust mites cause symptoms in individuals allergic to dust mite, it is often not the mite itself but proteins in their droppings which cause the allergy. Each mite produces about 20 of these waste droppings every day and the droppings continue to cause allergic symptoms even after the mite has died (Allergy UK).

Common symptom of house dust mite allergy

House dust mites are a common cause of allergy in atopic individuals and the main cause of perennial allergic rhinitis type symptoms in the UK, however house dust mite is also a common cause exacerbation of asthma, and eczema symptoms.



The most common symptoms of house dust mite allergy include; sneezing, runny nose, stuffy nose, itchy nose, throat or mouth, postnasal drip, cough, red or watery eyes, itchy skin.

Allergic rhinitis is a common condition affecting round 40% of the population and is associated with asthma, has a high symptom burden and impaired health-related quality of life, sleep, adversely affecting school, work and social life. Patients with HDM allergy typically present with symptoms of moderate-to-severe rhinitis which is difficult to control with pharmacotherapy. (Demoly et al 2016).

Allergy testing

Allergy testing such as skin prick testing (SPT) and specific IgE blood testing are helpful to confirm a diagnosis of house dust mite allergy, but an individual may be sensitised to many allergens and it is often difficult to be certain that HDM is the allergen that is the main cause of symptoms. It is worth noting that around 90% of allergic rhinitis patients and 80% of eczema patients will test positive to HDM on skin prick test (yang, Zhu 2017). Component diagnostic testing for house dust mite is more expensive but is useful to compliment SPT/ IgE testing, and the correct interpretation of results is very important in order to distinguish between true polysensitization to multiple allergens and false-positive results resulting from cross-reactivity (Calderon 2015).

Recommended first line treatment includes house dust mite reduction this should include washing bedding etc at temperatures above 60 degrees centigrade

Treatment options

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It is widely accepted that it is impossible to eradicate house dust mite but effective reduction measures can reduce the 'allergen load' of symptomatic threshold in some people and is recommended as part of a holistic approach to treatment alongside pharmacotherapy to reduce symptoms. Medications to reduce symptoms include oral antihistamines, intra nasal antihistamine the preparations. with addition of corticosteroids or combined inhaled corticosteroids and antihistamine preparations. Leukotriene receptor agonists can be a useful addition to help with symptom relief. Immunotherapy should be considered as a third line treatment if symptomatic relief is not effective using pharmacotherapy, there is a considerable effect on a patients quality of life or the individual is unable to tolerate pharmacotherapy (Calderon 2015), (Walker 2011).

How does allergen immunotherapy work?

'Allergen immunotherapy involves the repeated administration of allergen extracts with the aim of reducing symptoms on subsequent allergen exposure, improving quality of life and inducing long term tolerance' (Walker et al 2011).

Allergen immunotherapy works by inducing immunological tolerance through a gradual reduction in IgE-mediated responses [Ellis 2019). In the allergic response the body activates a TH2 immune response to trigger an immunological process involving activation of lymphocytes IL-13 and IL-4, T cell and B cell production to trigger the mast cell to degranulate and release histamine causing vasodilation and vascular permeability and development of allergic symptoms including increase in mucus production and constriction of the airways.

Immunotherapy works by increasing allergen specific lymphocytes such as T regulatory cells and IL-10 which modulates the production of IL-4 and inhibits the production of IgE mast cell activation, alos inducing a immunological deviation from TH2 response to TH1 by increase IFN-y and suppression of IL-5 and eosinophil production and thereby inhibiting the allergic response, these changes to the immune system contribute to lasting tolerance (Yang, Zhu 2017).

There are two methods for administration of immunotherapy SLIT – Sublingual immunotherapy given as drops or tablet form and SCIT – Sub cutaneous immunotherapy given via injection by a trained clinician, the timing of this injectable method varies depending on where they are in administration schedule ie up dosing or maintenance.

For HDM immunotherapy the SLIT sublingual route is the preferred route used, this has a good safety profile with a much reduced risk of adverse side effects than SCIT, reported side effects have included itchiness and swelling in the mouth after taking the medication. One of the advantages of SLIT is home administration and can be given as drops or a tablet three times a week over the period of three years. The treatment needs to be given regularly in order to activate the immune system and build up tolerance and it may be a few months before any effect on symptom reduction is noted. Compliance with treatment is essential, therefore regular follows up are essential to trouble shoot any issues and ensure that the patient is continuing with daily administration of the therapy to ensure efficacy of the treatment. Careful risk assessment must be given those with uncontrolled or unstable asthma and contraindications for HDM immunotherapy include patients with active autoimmune disorders, AIDS, malignancy, and pregnancy (Pitsios 2015).

SLIT is safe for use with both children over 2 years and adults and studies have shown HDM SLIT to be a very effective in disease management with efficacy lasting after treatment ends with significant reductions in symptoms and reduced need for continued pharmacotherapy after SLIT therapy. This reduces the need for sustained medical pharmacotherapy and issues with adherence and side effects from long term use (Ellis 2019) (Demoly 2016) (Proctor 2020).

There is some evidence to show that Immunotherapy may also prevent new sensitisation and in children with allergic rhinitis may prevent the development of asthma symptoms (Ellis 2019) and therefore should be considered a routine treatment if pharmacotherapy is not giving effective relief from the symptoms of house dust mite.

The following guidelines are available to aid decision making when considering immunotherapy for house dust mite for both allergic rhinitis and asthma;

Aria https://www.euforea.eu/sites/default/files/2018-08/2008-ARIA-Report.pdf

BSACI https://www.bsaci.org/wp-content/uploads/2020/01/ImmunotherapyAllergicRhinitis2011.pdf

GINA https://ginasthma.org/wp-content/uploads/2019/04/GINA-2019-main-Pocket-Guide-wms.pdf

EAACI https://onlinelibrary.wiley.com/doi/epdf/10.1111/all.13749

And <u>NICE</u> is proposing development of guidelines for HDM immunotherapy. https://www.nice.org.uk/guidance/gid-ta10279/documents/draft-scope-pre-referral

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Allergy UK House Dust Mite information sheet https://www.allergyuk.org/information-and-advice/conditions-and-symptoms/12-asthma-and-respiratory-allergy#download_access

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