Standing Committee on Health, Aged Care and Sport

Inquiry into allergies and anaphylaxis

SANOFI

Foreward

As a clinical dermatologist and medical researcher, I welcome the establishment of this Inquiry. Allergy and allergic diseases are increasingly important and frequent conditions in the Australian setting. Therefore, this Inquiry brings this into focus and provides a significant opportunity for patients, families and healthcare providers to look towards a better future and better public health policy around allergic diseases.

There are six specific allergic diseases which often have some degree of overlap in an individual patient. These are: rhinitis (hay fever); asthma; atopic dermatitis (also known as atopic eczema); food allergy; urticaria; and anaphylaxis. A further condition, allergic contact dermatitis, needs to be also considered in the dermatology setting. The clinical overlap of these conditions is not a causative relationship but rather a 'diathesis' of genetic predisposition. This atopic diathesis is an interaction between environment, psychosocial and genetic factors that leads to the complex clinical presentation in each patient.

Currently there is a significant unmet need in the community around the understanding of allergic disease and in particular of atopic dermatitis. I am hopeful that the Inquiry will address the current high unmet need of those living with severe atopic dermatitis as well as the other allergic diseases which have severe impacts on patients' and their family's quality of life.

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Contents

Introduction

On September 12, 2019 The House of Representatives Standing Committee on Health, Aged Care and Sport commenced an inquiry into allergies and anaphylaxis in Australia. The inquiry follows a referral (August 27, 2019) from the Minister for Health.

Sanofi's submission will focus on the following terms of reference:

1. The adequacy and consistency of professional education, training, management/treatment standards and patient record systems for allergy and anaphylaxis.
2. Access to and cost of services, including diagnosis, testing, management, treatment and support.
3. Developments in research into allergy and anaphylaxis including prevention, causes, treatment and emerging treatments (such as oral immunotherapy).

A focus of this submission is the lack of community understanding of allergic disease and in particular of atopic dermatitis. It will also address the current high unmet need for effective treatment options for those living with severe atopic dermatitis and the impact this has on their quality of life.

As a global healthcare company Sanofi is dedicated to supporting people with healthcare challenges and transforming scientific innovation into healthcare solutions. A critical part of this is advocating for improved patient access to innovative treatment.

Sanofi welcomes the establishment of this Inquiry, and recognises it as a significant opportunity for patients, families and healthcare providers.

Allergy and allergic disease in Australia

WHAT IS ALLERGY?

Allergy occurs when an immune response is triggered by common substances (called antigens) in the environment that are otherwise harmless.[1] From a biological perspective, type 2 immune responses are the key drivers behind allergic disease.[2]

Following exposure to an allergen, the body responds by producing T-helper cells. Depending on the kind of foreign substance, different types of T-helper cells determine what happens to regulate the immune response.[3] The type 2 inflammatory pathway is prominently activated in response to allergic diseases, including asthma and atopic dermatitis, leading to the release of inflammatory cytokines, especially interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-9 (IL-9) and interleukin-13 (IL-13).[4]

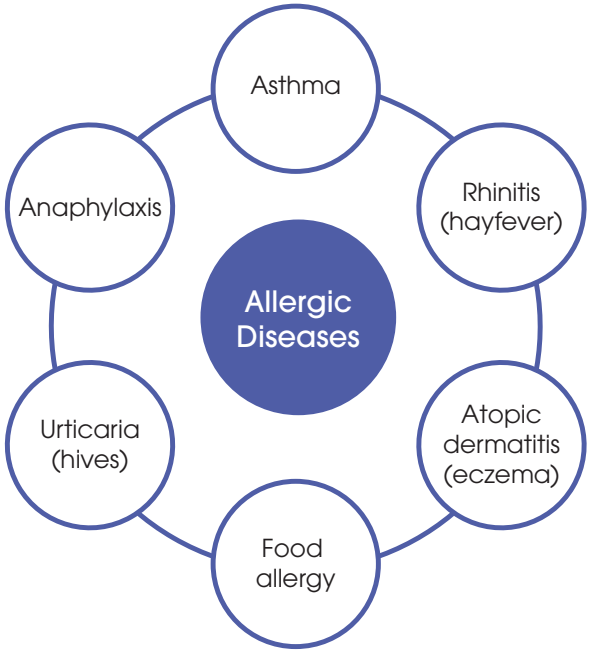
Allergies are a major public health problem and a significant cause of morbidity on a global scale.[5] Australia has one of the highest rates of allergic diseases world-wide, with rates continuing to rise, and these disorders are accompanied by a significant burden on both patients and health systems.[6]

"Allergic diseases are one of the fastest growing chronic health conditions in Australia, affecting approximately 1 in 5 Australians.[7]"

WHAT ARE ALLERGIC DISEASES?

Allergic diseases are one of the most common disease types globally. A recent review published by the European Union-funded project MeDALL (Mechanisms of the Development of ALLergy) classifies allergic diseases into **six different disease types**:

- rhinitis (hay fever),
- asthma,
- atopic dermatitis (commonly referred to as atopic eczema),
- food allergy,
- urticaria, and
- anaphylaxis.[8]



Understanding the differences between disease types and their unique characteristics is important because it can impact choice of diagnostic tests and responsiveness to therapeutic strategies.[8]

ALLERGIC DISEASES ARE COMPLEX

Allergic disease is not simple. For example, more than a decade ago, it was recognised that asthma is not a single disease but rather an umbrella term for a series of complex, overlapping individual diseases, each defined by its unique interaction between genetic and environmental factors.[9] The same is also true for other allergic diseases. To manage this, the optimal approach involves accurate diagnosis and primary prevention (allergen avoidance) combined with the appropriate use of medical therapies.[2]

Allergic diseases can manifest in the same individual as multi-morbidity, where one person can have more than one disease at the same time, or else follow a progression, often referred to as the 'atopic march'.[2] Atopic dermatitis has been highlighted as one of the first steps in the atopic march.[10]

For example, atopic dermatitis often appears first, with studies showing that approximately half of these patients will develop asthma, particularly if they have severe atopic dermatitis, and two thirds will develop

allergic rhinitis.[11] However, this does not mean that children will grow out of one allergic disease and into another; more often than not multiple allergic diseases persist.[12]

GROWING PREVALENCE OF ALLERGIC DISEASES IN AUSTRALIA

Allergic diseases are common in Australia; their prevalence is highest in young children but it is also becoming common in adolescents and young adults.[13]

- Around 10% of infants in Australia are affected by food allergy by the time they are 12 months old.[13]
- According to statistics from the 2017–18 Australian Bureau of Statistics National Health Survey:[14]
  - 1 in 9 Australians have asthma, and of these 3-10% have severe asthma, and
  - 1 in 5 Australians have allergic rhinitis.
- An estimated 25% of the population will suffer from urticaria at some point in their lives, and up to 3% will have chronic urticaria.[15]
- Anaphylaxis (a serious and rapid-onset allergic reaction) is reported to occur in 0.2% of children[16] and 3% of adults,[17] but an increase in incidence has been reported over time.[18]
- An estimated 32% of Australia's population will have atopic dermatitis at some point in their life.[19]

Amongst the six disease types under the allergic diseases umbrella, atopic dermatitis is the most common inflammatory skin condition in adults and children.[20]

ATOPIC DERMATITIS: BURDEN IN PERSPECTIVE

Affects children and adults

Reports suggest that atopic dermatitis can affect up to 25% of children and 7% of adults.[20] While primarily thought of as a disease that begins in childhood, in about half of paediatric patients atopic dermatitis persists into adulthood and becomes a chronic, lifelong condition.[21] Additionally, while most adults with atopic dermatitis have a history of childhood disease, onset in adulthood is recognised and may occur more commonly than previously thought.[22]

The symptoms are invasive

Despite 48.2% of moderate to severe atopic dermatitis patients using systemic therapies (corticosteroids or cyclosporin) in the past year, itch severity was on average 6.5 out of 10 on a numeric rating scale, with important implications for patients:[23]

- 85% had problems with itch frequency,
- 41.5% had problems with itch duration (itching ≥18 hours per day),
- 55% reported sleep disturbances on 5 or more days of the week,
- 21.8% had clinically relevant anxiety or depression.

Negatively impacts quality of life and overall well-being

There is a common misperception that atopic dermatitis is just a 'skin condition' that people can deal with themselves. In reality it has a huge impact on patients' lives and the lives of their families.

Atopic dermatitis has the highest burden of all skin conditions throughout life.[24] It has a considerable negative impact on the quality of life of patients and their families.[20] This negative impact extends beyond dealing with the physical symptoms (rashes accompanied by intense itching, skin dryness, cracking, redness, crusting and oozing) to mood, sleep, work productivity, relationships and everyday activities.[22]

In a recent survey of 100 Australian patients with atopic dermatitis:[25]

- Over half (54%) described that they understood that atopic dermatitis was a lifelong condition and did not expect it to get better.
- Close to half (43%) noted that atopic dermatitis caused a significant impact in relation to their self-esteem and confidence. Participants also spoke about this leading to social isolation.
- Almost one-third (32%) said their atopic dermatitis had an impact on relationships with family and friends.
- Three out of ten (28%) said that their condition impacted their ability to work, while for one-quarter (24%) it also impacted their day-to-day activities.

Increased risk of medical and mental health issues

A reciprocal relationship between the skin, and in particular pruritus (itch), and the psyche is well-documented,[26] and the possibility of a "psychiatric march" wherein common atopic dermatitis symptoms (itch and sleep disturbance) may lead to anxiety, depression and suicide has been suggested.[27]

Depression, anxiety, and suicidal ideation are more common among individuals with atopic dermatitis than those without.[28,29] Observational data from 13 European countries report that amongst patients with atopic dermatitis:[30]

- 10.1% also have diagnosed clinical depression,
- 17.6% also have diagnosed clinical anxiety, and
- 15.0% report having thoughts of suicidal ideation.

The occurrence of these comorbidities is severity-dependent, with data supporting a higher prevalence of depression and anxiety in patients with severe atopic dermatitis than those with milder disease.[29,31] As a result, patients with atopic dermatitis also have a high level

use of psychiatric healthcare treatments and services, including the use of antidepressant and anti-anxiety medications.[27]

Costs of care

The financial burden of atopic dermatitis is substantial. The out-of-pocket costs related to atopic dermatitis have recently been estimated to be as high as €927 (roughly AU$1500) per patient per year in Europe. These costs are higher than in other chronic diseases and pose a substantial burden on affected individuals.[32]

In Australia, in many cases patients must pay for over-the-counter and supportive medicines. The chronic nature of atopic dermatitis is such that these are ongoing requirements – emollients for example are the cornerstone of care and require daily application.

Regardless of severity, in all cases further indirect costs include the loss of income from time taken off work, travel and the cessation of employment.[33] Recently it was estimated that the annual out-of-pocket costs to patients with atopic dermatitis can be as high as AU$2000 per year.[34]

Hidden costs of atopic dermatitis

The hidden costs involved in managing atopic dermatitis are also significant. Sleep deprivation leads to tiredness, mood changes and impaired psychosocial functioning of the patient and their family, particularly at school and work.[35] The patient's lifestyle is often limited, particularly in respect to clothing, holidays, staying with friends, owning pets, swimming or the ability to play or do sports.[35]

Furthermore, the restriction on normal family life, for example increased work in caring for a child with atopic dermatitis, can lead to parental exhaustion and feelings of hopelessness, guilt, anger and depression.[35]

Adequacy and consistency of professional education, training, management/treatment standards and patient record systems for allergy and anaphylaxis

Recent research recognises that there are knowledge gaps, particularly amongst Australian General Practitioners and the treatment advice they provide to patients with atopic dermatitis.[36]

General Practitioners often receive very little dermatological training. This can result in inappropriate treatment, delayed referral to specialist care and a lack of recognition of the importance of atopic dermatitis in healthcare provision.[34] The ongoing training and education of healthcare providers remains a cornerstone of ensuring appropriate use of all available therapeutic options and resources to optimise patient care.

The Sanofi-sponsored ADvent initiative has been established at both a global and local level to address medical educational needs for healthcare professionals to extend beyond looking at atopic dermatitis as "just a skin disease" to a systemic type 2 immune disease. Its aim is to improve knowledge around a variety of related topics to help reduce disease burden and provide improved patient care. Topics include pathophysiology and immunology, the role of type 2 disease mechanisms, assessment of disease severity and burden, management of atopic dermatitis, and the role of emerging treatments.

To further help educate the medical community, several international updates and consensus 'best practice' recommendations for the management of atopic dermatitis have been published.[37,38] However, until recently, there were no local consensus recommendations for the management of adults with atopic dermatitis in Australia to establish treatment goals, and measurements upon which they can be based, which are of relevance in Australian clinical practice. In recognition of this need, expert consensus recommendations providing practical guidance of clinical relevance to specialists and primary care physicians in Australia were published in 2019.[22]

A key aspect of these educative initiatives is to emphasise the chronic nature of atopic dermatitis and highlight the need to take a holistic view of the patient. Physicians should be provided with education, support and resources to better enable them to develop long-term management strategies for patients, rather than simply prescribing treatment reactively. Such plans should focus on the need for consistency of therapy, the ongoing need for use of basic skincare treatments such as emollients and access to a range of other health services and supports to help with wider issues (e.g. sleep, mental health, stigmatism, social isolation) that contribute to the high burden of this disease.

Despite these many advances and important initiatives, data remain limited. There is no current true picture of the scale of the atopic dermatitis disease burden at either a national or global level. Strong and credible impact of disease data are needed. Prevalence data, alongside research into the economic costs of the disease (such as the cost of absences from work through illness) are also needed in order to develop a rigorous evidence base for policy development. It is approaches like this that will help support the case that investment in better care will be cost-effective.[34] One way in which this could be furnished is via the establishment of ongoing national clinical registries, which would enable data collection over time.

Access to and cost of services, including diagnosis, testing, management, treatment and support

Major milestones in atopic dermatitis include the development of diagnostic criteria, severity scores and identification of biomarkers for diagnostics, correlation with severity and prediction of therapeutic response.[2]

LACK OF HEALTHCARE PROFESSIONAL UNDERSTANDING ADDS TO THE BURDEN OF ATOPIC DERMATITIS

Recent Australian survey data highlights that, from the patients' perspective, there was poor understanding of their condition and its burden amongst healthcare professionals:[25]

- Close to half of all participants (48%) said that, in general, they felt health professionals dismissed their atopic dermatitis.
- Of the information given by healthcare professionals, psychological support was the least given information at only 2.86%.

Participants were asked what their message to people who make decisions about their condition would be. Over half of the cohort (56%) wanted to convey the message that their condition should be taken seriously – it can be debilitating, and it is life-long – and that there is a need for compassion and to actively listen to patients' needs.

Of direct relevance to Australia, the recent consensus recommendations provide clear definitions for atopic dermatitis, including diagnostic criteria and allocation of severity based on patient-related measurements and a direct measurement of sleep impact.[22] They offer different recommendations for Dermatologists and General Practitioners who often have significant time-constraint on patient consultations.

LACK OF RESOURCES NEGATIVELY IMPACTS PATIENT CARE

Atopic dermatitis is currently not included in any government health strategy. A lack of attention and resources can have impacts on the quality of care for patients, including:

- a limited number of treatment options for doctors to offer, and
- a lack of time that doctors are available to spend with their patients.

Compounding this further, patients with atopic dermatitis can have difficulty navigating their care system and often are not able to see a specialist in a timely manner, delaying treatment and optimised outcomes.[34] Lack of capacity and/or inadequate referral pathways create a significant impact in Australia where the burden of atopic disease is high.

Treatment access plays a significant role in management considerations, particularly if there is no financial reimbursement or inadequate coverage for medication for patients. Factors contributing to poor treatment outcomes include complexity of treatment regimens, lack of knowledge, and frequency of follow-up.[39] Suggested strategies to overcome these issues include the use of written action plans for patients, patient education, early and frequent follow up and providing support services to help improve quality of life.

Developments in research into allergy and anaphylaxis including prevention, causes, treatment and emerging treatments

Over the past decade significant advances have been made into understanding the mechanisms, and immune involvement in, the development of allergic diseases such as asthma and atopic dermatitis.[2] Current research is focused on new treatments that target specific aspects of the immune system that are involved in allergic diseases.[40]

The concept of "type 2 inflammatory disease" is based on the understanding that in atopic dermatitis, special immune cells (called T-helper 2 cells) are activated and result in the release of key type-2 cytokines (IL-4, IL-5 and IL-13), which then drive the underlying inflammatory processes. They trigger the inflammatory cascade via a positive feedback loop in the immune system. Biologic treatments for atopic dermatitis target the type 2 inflammatory pathway.

Whilst atopic dermatitis guidelines recommend a step-wise approach to treatment, many of the options available for patients with moderate-to-severe disease are of limited effectiveness and have serious long-term side effects.[2] The side effects of some treatments (e.g. immunosuppressants, corticosteroids) can, for some patients, be more detrimental than living with the symptoms alone. Due of the lack of treatment options, patients may drop out of the healthcare system and suffer in silence.

Identifying specific and effective biologic treatments continues to be an area of unmet need for patients. A number of research strategies have been investigated, but the most major breakthrough in treating atopic dermatitis has been achieved by modifying type 2 immune dysregulation.[2]

Conclusion

This parliamentary inquiry comes as a timely reminder of the high burden of unmet need in diagnosing and managing allergic diseases, and the significant impact these diseases have on Australian patients and their families.

Allergic disease has psychological effects, interferes with social interactions, and creates an economic burden not only for the patient, but for the family and for society at large.[5]

Several gaps have been identified in the adequacy and consistency of professional education, training, management/treatment standards and patient record systems for allergic diseases. Local consensus guidelines and educational initiatives have been implemented to help better facilitate holistic patient management approaches.

Given there are far-reaching impacts on quality of life, beyond the disease state itself, further resources and support to widen the scope of patient management to incorporate a multi-disciplinary care team approach are warranted. A key priority is the need for the generation of credible evidence on prevalence, economic costs and impact of disease to drive policy development.

Access to services including diagnosis, testing, management, treatment and support for allergic disease needs to be elevated in priority by health policy makers and funders to optimise best possible care outcomes for patients without impacting on already substantial out of pocket costs.

Research into allergic diseases has progressed at a rapid pace and has entered a new paradigm of targeted therapeutic approaches. Equitable access to such treatments requires urgent attention and will become increasingly common as healthcare moves closer towards more tailored diagnostic and treatment solutions.

It is only through the increased prioritisation of, and investment in, allergic diseases that the many Australians impacted will be able to fully contribute to the community and the economy to their full potential.

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