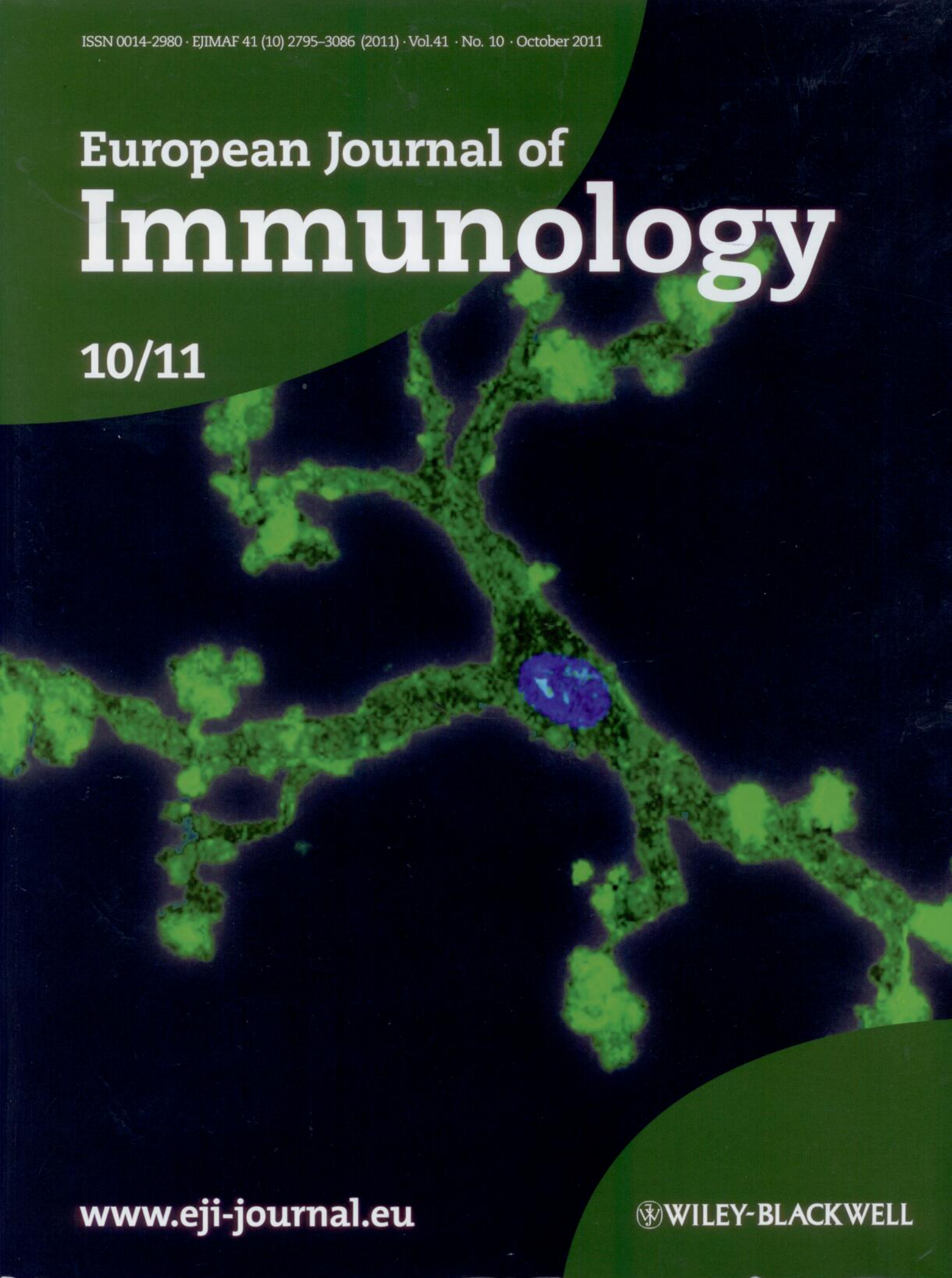


European Journal of **Immunology**

10/11



Fighting allergies beyond symptoms: The European Declaration on Immunotherapy

It is now well established that allergic diseases have an extremely high prevalence in developed societies, and are increasing in emerging countries. In fact, allergy is probably the most prevalent immunological disease. It is currently estimated that up to 30% of Europeans suffer from allergic rhinitis or conjunctivitis, while up to 20% suffer from asthma and 15% from allergic skin conditions [1]. The worldwide numbers are equally worrying. Almost half a billion suffer from rhinitis [2, 3] and approximately 300 million from asthma [4]. Compared with other chronic diseases, allergic diseases are more common than Parkinson's, Alzheimer's, stroke, coronary heart disease, cancer or diabetes. Food allergies are also becoming more frequent and severe. Occupational allergies, drug allergies and allergies to stings (occasionally fatal) add further complexity and concerns. Finally, new types of allergic diseases and allergies against previously non-allergenic substances are increasingly being reported; however, the fact that more patients are affected and that allergic conditions are nowadays more severe and complicated are not the only issues which make these diseases a matter of concern – the actual burden for patients and for society as a whole is very high.

The quality of life is severely affected in allergic patients. Although some allergic conditions are considered non-severe, others such as asthma or anaphylaxis can be life threatening. Allergic patients have increased disadvantages affecting their personal development, career progression and lifestyle choices. Allergic children demonstrate difficulty in coping at school and they develop associated learning difficulties and sleeping problems. As a result, it has been observed that sleepiness and mood swings frequently lead children to be isolated and even bullied by their peers. Allergic rhinitis in students increases by 40%, the chance of dropping a

grade in summer examinations, while taking a sedating drug may further increase this to 70% [5]. Young adult patients also face a significantly higher amount of problems in their work place due to increased numbers of sick days and a reduction in productivity. Many allergic patients report problems in their personal relationships. Finally, several studies have shown that allergic individuals have a higher risk of developing depression [6]. The impact of allergies on the quality of life can be as high, or higher, than diseases that are considered more 'serious' (i.e. diabetes).

The impact of allergy on health economics and macroeconomics is equally high. The associated reduction in productivity and the rising number of sick days taken by patients represent some of the biggest negative outputs recorded impacting national, business and health economies in Europe. Allergy incidents and their increase have an adverse effect on the European economy due to both direct costs (e.g. for asthma alone, the pharmaceutical cost stands at €3.6 billion per year and the cost of health care services at €4.3 billion per year) [7] and, perhaps to an even greater degree, indirect costs. In total, 15% of the population receiving long-term treatment in Europe is due to allergies and asthma, making them the most common reasons for treatment among the young age group [8]. Among the direct medical costs, diagnostic tests, consultations and medication represent the primary components, while a major cost item is hospitalisation, usually associated with severe exacerbations of asthma or severe anaphylactic reactions.

Moreover, performance deficits, loss of productivity and absenteeism are closely linked to allergy suffering and have a major effect on macro-economics. Asthma and rhinitis are estimated to result in more than a 100 million lost workdays and missed school days each year in



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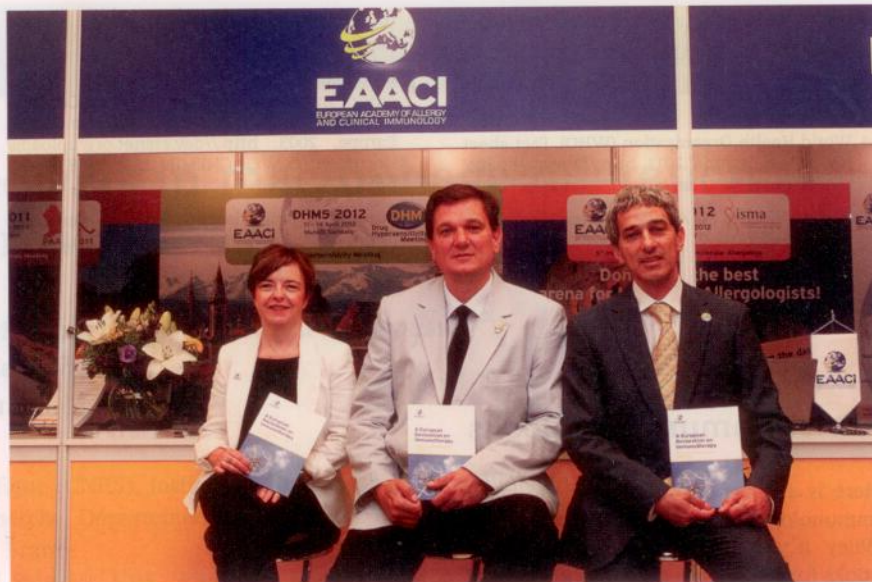
Europe (not only are children absent from school on any given day, but parents are also absent from work or have reduced productivity) [9]. Recently, it became apparent that, in addition to absenteeism, hundreds of millions of Euros are also lost by presenteeism, a condition in which people go to work, but are unable to perform to their capacity. The total cost of asthma alone is estimated at more than €25 billion annually [7]. The cost of rhinitis is probably higher but, unfortunately, large scale socioeconomic studies in Europe are lacking. Unpublished investigations by the Global Allergy and Asthma European Network (GA²LEN) calculate the current loss due to untreated allergic rhinitis-related presenteeism to be approximately €100 billion annually to employers. This is based on employment figures from European statistics but does not measure the loss to society due to presenteeism at schools or universities.

Understanding and monitoring the costs of allergic diseases should be a priority. Health care systems that are not taking into account the rapid increase in prevalence, increase in severity and cost of allergies are in danger of collapsing from these conditions alone.

Drug therapy to control symptoms elicited by allergic diseases is very effective nowadays; however, these treatments are only directed at diminishing the inflammation or blocking the symptoms of the disease. This is, of course, a necessary strategy but acting on the cause of diseases, whenever it is possible, is the objective of all medical professionals. Nowadays, allergen immunotherapy is the only treatment which is directed at the cause of allergies, combating allergies beyond the symptoms. Allergen immunotherapy has been shown to be able to change the course of the disease, improving symptoms and decreasing the need for medication. In some studies, its effects have been shown to persist even after the actual treatment is interrupted. Therefore, it is considered a disease-modifying therapy.

Allergen immunotherapy was initially developed 100 years ago in parallel with anti-infectious vaccines, when the causal substances and underlying mechanisms were not known. After empirically observing that these “desensitising” vaccines were clinically effective, the underlying mechanisms of action were discovered. Nowadays it seems clear that allergen immunotherapy acts by increasing specific tolerance to the allergen by inducing a very specific type of cell, known as regulatory T cell, which prevents the development of allergic reactions against that allergen [10]. This results in a progressive decrease in symptoms upon exposure to the allergen and, subsequently, in an improvement of the patient [11]. Allergen immunotherapy has not received adequate attention from the European research funding bodies; however, this could be one of the most rewarding fields in terms of return, translational value and European integration. It is also a field in which Europe is recognised as a leader worldwide.

Research in the field of allergen immunotherapy is extremely difficult, basically because the effects of the treatment are measurable only after a relatively long period of time, usually after one year, achieving an optimal effect after three to five years. This fact hampers the possibility of undertaking large independent trials, which need a substantial economic



Victòria Cardona, Cezmi Akdis and Nikos Papadopoulos presenting the European Declaration on Immunotherapy at the recent EAACI Congress 2011 in Istanbul.

investment. Until now, most of these trials have been conducted by allergen manufacturers. In this regard, the European Academy of Allergy and Clinical Immunology (EAACI) is actively working to increase the knowledge of this situation among relevant stakeholders in order to promote policies to support the knowledge and use of allergen immunotherapy and to prioritise funding of research in the field.

One of the initiatives that have been undertaken is the development of the European Declaration on Immunotherapy. This document, signed by EAACI, GA²LEN and the European Federation of Allergy and Airway Diseases Patients Association (EFA), and with the support of most of the National Allergy Societies, was published in June 2011 and is available at www.eaaci.net. The aim of this document is to illustrate the current status of the allergic epidemic in Europe, to highlight the impact of such diseases on patients' health and overall quality of life, to provide data regarding the socioeconomic impact for society and to raise the question of awareness among the relevant governing bodies and the need to undertake proactive initiatives to fight allergies. The European Declaration on Immunotherapy has been forwarded to members of the European Parliament, and also to politicians at a national level, in order to synergise actions in the field. Along these

lines, EAACI, together with GA²LEN and EFA, would like to call upon Europe's policy-makers to coordinate actions and improve individual and public health in allergy by:

- (i) Promoting immunotherapy awareness
- (ii) Updating national healthcare policies to support allergen immunotherapy
- (iii) Prioritising funding for immunotherapy research
- (iv) Monitoring the macroeconomic and health economic parameters of allergy
- (v) Streamlining medical disciplines and specialties

We believe that this European Declaration on Allergy Immunotherapy is one of the first steps to achieving these aims.

Cezmi Akdis
EAACI President
e-mail: akdisac@siaf.uzh.ch

Nikos Papadopoulos
EAACI Secretary General
e-mail: ngp@allergy.gr

Victòria Cardona
EAACI Vice-President
Communications and Membership
e-mail: vcardona@comb.cat