

REVIEW ARTICLE

Towards a European registry of severe allergic reactions: current status of national registries and future needs

M. Worm¹, F. Timmermans², A. Moneret-Vautrin³, A. Muraro⁴, I. I. Malmheden Yman⁵, M. Lövik⁶, S. Hattersley⁷ & R. Crevel⁸

¹Department for Dermatology and Allergy, Allergy-Center-Charité, Charité Campus Mitte, Medical University Berlin, Germany; ²Nederlands Anafylaxis Netwerk – European Anaphylaxis Taskforce, Dordrecht, the Netherlands; ³Department of Internal Medicine – Clinical Immunology and Allergy, University Hospital, Nancy, France; ⁴Referral Centre for Food Allergy Veneto Region Department of Paediatrics – University of Padua, Italy; ⁵National Food Administration, Uppsala, Sweden; ⁶Department of Environmental Immunology – Norwegian Institute of Public Health, Oslo, and Department of Cancer Research and Molecular Medicine – Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway; ⁷Food Standard Agency, Food Allergy Branch, London, UK; ⁸Unilever Safety & Environmental Assurance Centre, Bedford, UK

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Correspondence

ILSI Europe a.i.s.b.l., Avenue E. Mounier 83,
Box 6, B – 1200 Brussels – Belgium.
Tel.: +32 2 771 00 14
Fax: +32 2 762 00 44
E-mail: publications@ilsieurope.be

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Abstract

The incidence of severe allergic reactions is largely unknown and information about triggering allergens, aggravating factors, demography of patients and medical care is lacking. A European wide registry could provide a powerful tool to improve the management of severe allergic reactions from both a medical and a public health perspective. Analysis of existing registries regarding the type and quality of data being collected was used to develop a plan for a pan-European registry, including the type of system to be used and the range of data to be entered. Surveillance will provide evidence for the efficacy of risk management measures and may identify the emergence of new allergenic foods, and aid monitoring of novel foods, ingredients and technologies. Patients need a clear indication of factors that may increase their risk of having an adverse reaction, which such a registry can help compile. Based on the collected data, food businesses will be able to develop educational programmes for allergen risk assessment and allergen risk communication. Finally, and most importantly preventive measures can be developed and government agencies receive population based data which may be relevant for legislative purposes.

Allergies are among the most common diseases and food allergy as a common cause of severe allergic reactions is estimated to affect between 2% and 4% of the population of industrialized countries, with a prevalence of up to 8% in children. The burden on those directly affected, as well as on their families, is being increasingly recognized (1). Ongoing research is likely to provide accurate and reliable information on the size of the population at risk, as well as the importance of different allergenic foods. Research is also generating information about the distribution of minimum eliciting doses within the allergic population for the more common allergenic foods.

The present lack of data impairs estimation of the public health impact of allergic reactions in general and in particular reactions to foods. The effectiveness of allergen control measures and educational efforts for prevention are difficult to evaluate and prioritise. Absence of such information also

affects the clinical management of allergic reactions, as experience with regard to treatment, circumstances and etiological agents is not collected systematically and effectively. The present article examines the systems that have been put in place in several European countries for recording severe allergic reactions. It then considers the type of information that such registries should hold to meet the needs of different stakeholders (clinical, public health, regulatory, industrial) and outlines a proposal for a pan-European registry of severe allergic reactions.

Severe allergic reactions – a public health problem in Europe

Anaphylaxis is the most severe manifestation of an allergic reaction (2). It may occur following exposure to allergens from a variety of sources including foods, insect venom, drugs and others. An international symposium acknowledged

that a well-accepted definition of anaphylaxis was lacking, contributing to a wide variation in diagnosis and management and they proposed one of the following criteria to be present: first, the acute onset (minutes to hours) with involvement of skin/mucosa and compromised airways or reduced BP or hypotonia/syncope or second, two or more of the following: history of severe allergic reaction, symptoms of skin/mucosal tissue/compromised airways, reduced BP or associated symptoms or in suspected food allergy: gastrointestinal effects after exposure to known allergen (minutes to hours) and third hypotension after exposure to a known allergen for that patient (minutes to hours) (3).

Anaphylaxis is characterised by the sudden onset and rapid progression of *multiple* signs and by the simultaneous involvement of more than one organ system. The presence of mucocutaneous signs is a key to differentiate anaphylaxis from similar clinical syndromes of different aetiology (e.g. myocardial infarction, syncope, septic shock). Other reactions that may be life threatening, such as, severe asthma or angioedema are therefore included in the term 'severe allergic reactions'.

Foods are involved in a significant number and often a majority of published anaphylactic cases (4–7). In earlier published hospital-based series of patients with anaphylaxis, foods accounted for 25–60% of all anaphylactic reactions in which the cause had been established with reasonable certainty (8–10). Table 1 shows this trend continuing to the present day in more systematic epidemiological analyses.

Among foods, peanuts and tree nuts account for a high proportion of the more severe reactions (11, 12) and deaths (4, 13, 14), but other foods also feature depending on age and demographics (15).

Severe reactions to food allergens generate fear and anxiety (16). This is one of the principal reasons why many people with food allergy experience a severely reduced quality of life (17). Studies considering the occurrence of severe allergic reactions, including anaphylaxis, indicate a risk in public places like kindergarten or schools and point to the need for public legislation to deal with such cases (18). The common use of 'May contain –' and similar warning labels on prepacked foods constitute an important public health issue. On one hand, they may mislead and unnecessarily worry patients, who are at low risk of experiencing a severe reaction, which leads to reduction of the allergic consumer's choice. On the other hand, they may be ignored by the allergic consumer because of their wide use, increasing the risk of reactions among those consumers.

A pan-European registry for severe allergic reactions could considerably improve the management of such reactions in Europe, as well as provide a means of evaluating and prioritising risk management measures, and introduce a surveillance system which would identify potential novel allergenic foods.

Materials and methods

The types and kinds of registries that already exist in Europe and the quality of information they are producing has been reviewed and compared. Initial discussions about the available registries indicated the need to develop criteria for the acquisition of data at a European level, based on the needs of different stakeholders. An expert group was established and coordinated by the ILSI-Europe Food Allergy Task Force for this purpose, and included people working in the field of allergy, with particular focus on severe allergic reactions. The group was multidisciplinary and representatives from ongoing registries from different countries were invited to participate.

Description of current registries in Europe

Currently, there is no pan-European registry for severe allergic reactions. However, national or regional registries exist in some countries in the European Community and associated states (Fig. 1). The structure, content, inclusion criteria and modes of operation of these registries are presented later, followed by a discussion of their advantages and disadvantages.

Sweden

Since 1993, all physicians in Sweden have been asked to report life-threatening and fatal allergic reactions caused by food as they occur (19). Suspected food samples are collected by doctors and dieticians, sufferers and their families, food control authorities and food manufacturers and are analysed by the National Food Administration. Data regarding the severity of the reaction, the estimated amount of food consumed and the age and gender of the sufferer are also collected. In some of the fatal cases, gastric contents have also been analysed.

Since its creation over 15 years ago until the end of 2008, the registry has investigated 215 allergic reactions, implicating milk (60 cases), tree nuts (35 cases), peanuts (35 cases) and eggs (27 cases). Legume products together accounted for 63 cases, one-third of the total. The most severe reactions

Table 1 Food is a frequent cause of anaphylaxis. Proportion of cases involving food as reported in the literature (12, 32–34)

Study	Location	Total number of cases	Number of cases involving food	Proportion of cases involving food (%)
Pumphrey & Stanworth (1996)	Northern England	172	103	60
Decker et al. (2008)	USA	211	70	33
de Silva et al. (2008)	Australia	123	104	85
Makinen-Kiljunen and Haahtela (2008)	Finland	530	279	53

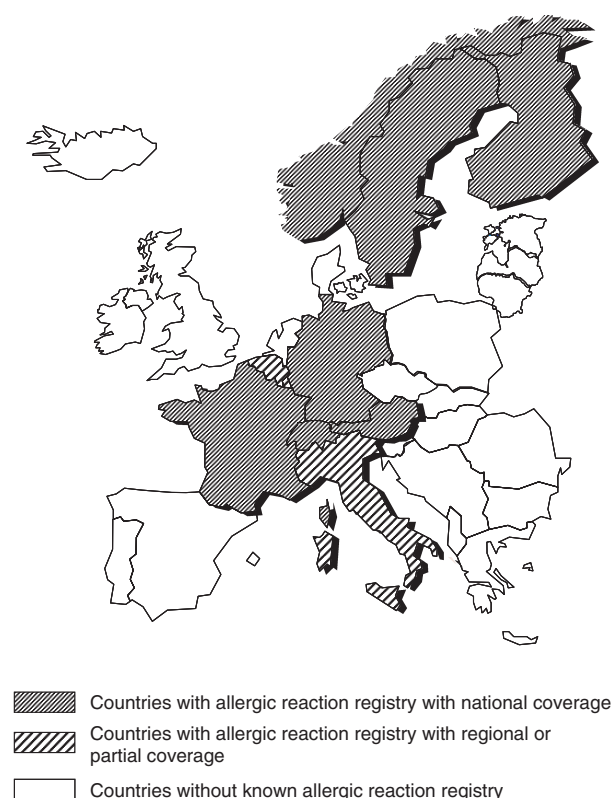


Figure 1 Allergic reactions registries in Europe (2009).

(84 cases) were caused by peanuts (25 cases), tree nuts (18 cases), milk (13 cases), soy (11 cases) and pea protein/lupine (5 cases).

Thirteen of the reactions to food featured fatal anaphylaxis, eight of which have been described in detail (19). The causative foods were peanuts (four deaths), soy (four deaths), hazelnut (two deaths) and milk (two deaths) with one unknown cause (20). The majority of those who died in anaphylactic shock were children and youngsters, between 6 and 22 years of age. Many of them suffered from mild to moderate asthma, two cases were classified as severe. Combination with exercise or intake of cold beverages were probably aggravating factors in some of the cases. In many of the cases reported, the National Food Administration has been able not only to detect the causative food (protein) but also to estimate the dose causing the allergic reaction.

Norway

The Norwegian National Reporting System and Register of Severe Allergic Reactions to Food ('Matallergiregisteret' – 'The Food Allergy Register') (21) was started in July 2000. The Register is a collaborative venture between the Norwegian Institute of Public Health and the Norwegian Food Safety Agency. Food allergen analyses are performed by the Norwegian Veterinary Institute. Food allergen surveillance is an important purpose of the Register.

The basic idea is that as a public health-focused register, information should be collected at the interface where the patient first meets the health care system, before patients have been filtered through a referral system to specialists. The reporting system therefore focuses on first-line health care providers: emergency wards and family practices, but does not exclude other clinicians, while remaining voluntary. The register collects three categories of information: information about the patient, the reaction and its circumstances, serological data and analytical data on the implicated food allergens. A one-page reporting form containing patient-related information must be completed in all cases. The form contains questions structured to collect the patient's national identification number which is a unique identifier, contact data for the physicians involved and the patient's regular doctor, a brief medical history with regard to asthma and allergy and a more detailed description of the incident that triggered the report. As a practical definition, a serious reaction is defined as an event that triggered an unscheduled visit to a doctor within 24 h.

Blood specimens are submitted with about 80% of the reports. Sera are analysed for specific IgE by ImmunoCap® (Phadia AB, Uppsala, Sweden) and further screened for specific IgE against a dot-blot array of 170 allergens. Serum specimens are stored in a registered diagnostic (not research) bio bank, and can only be used for purposes that have diagnostic value for the patient. Food specimens are sent in with about 10% of the reports.

A comprehensive report of the case and general information about relevant food allergies is sent back to the reporting doctor. When relevant, results from the food allergen analyses are given to the Norwegian Food Safety Agency, for possible regulatory action. The register has helped to identify several cases of mislabelling or allergen contamination (22). Emerging allergens have also been identified such as lupine (23) and fenugreek (24). The most common allergens causing severe reactions in Norway have been found to be peanut, hazelnut and shrimp, whereas cases of fish allergy are infrequent (21).

The Norwegian Register data indicate that severe food allergic reactions among young adults may represent an underestimated problem (21). Because of the incomplete reporting of cases, the data collected by the Register represent only the minimum incidence of severe food allergic reactions in Norway. However, the qualitative information and food allergen surveillance data are found to be very valuable.

France

The Allergy Vigilance Network was created by CICBAA in 2001 (Circle of Clinical and Biological Investigations in Food Allergy). It is a nonprofit organization partially subsidized by the National Food Safety Agency (AFSSA). Private practice allergists and hospital allergists can participate in the network on a voluntary basis and free of charge. The Network currently has 456 members in French-speaking countries, as well as in Belgium (29), UK (4), Luxemburg (3), Algeria (5), Italy (5), Morocco (4) and some others. The majority of members are full time allergy practitioners (231) but also other disciplines like paediatricians (59), pneumologists (61), internists (14), dermatologists (15), biologists (16),

Table 2 Summary of the comparative analysis between the analysed registries

Findings	Norway	Sweden	Germany	France	Italy
Initiator	NIPH (Government)	NFA (Government)	Charity (nongovernment) (Clinicians)	CICBAA (nongovernment) (Clinicians)	Referral Centre for Food Allergy – Veneto Region, Padua General University Hospital (Government-Clinicians)
Year established	2000	1990	2006	2001	2007
Funding	Gov.	Gov.	Nonprofit	EU-ending 2008	Gov.
Medium for Collecting data	Paper	Paper	Internet-based questionnaire forms	Paper/e-mail preformatted form	Web-based program
Source of data	GP	Paediatricians Emergency Department Clinicians	Allergy centres	Allergist	Emergency Department
	Emergency Department				Paediatric Units
Kind of data					Allergist
Data recovery	Food related cause Nonstructured	Food-related cause Nonstructured	All causes Structured	All causes Structured	All causes Structured
Cases reported	700 (since start)	Only cases where the suspected food (allergen) has been confirmed are included in the 178 (since start)	462 (2007)	604 (2007)	500 (since start in January 2008)
Reporting	Voluntary	Voluntary	Voluntary	Voluntary	Voluntary
Ask to report/ frequency	No	No	Every 6 months	Every 15 days/by e-mail	No
Feedback/ report to	Submitting clinicians	Scientific community (publications) Health authorities Health care system	Scientific community (publications) Patient education	Medical community (publications) Members of AVN Health authorities	Scientific community (publications) Health authorities Health care system Info to general public
	Health authorities Health care system	Health care system			
	Info for general public	Info to general public			
	Professionals	Info to food producers			
	Regulatory use	Regulatory use			
	If possible and when applicable; analysis is possible for food and serum	Yes, analysis is possible for food and serum	Not centrally, if done results are reported	Not centrally, analyses are performed, results are reported	Not centrally, if done results are reported
Material collection					

anaesthetists (2) and other specialists (15). The purposes of the Allergy Vigilance Network are to report cases of lethal or severe anaphylaxis, to provide AFSSA and the medical community with information on the prevalence and cost of severe food allergies and of sensitisations to food in the population on a large scale (2, 25, 26). Furthermore, the risk assessment of new foods and of new industrial food products is another purpose of the Allergy Vigilance Network (27).

Data are collected via a standardized form that is sent out to the network by e-mail every 15 days. This form requests details concerning sex, age, clinical symptoms, medical and therapeutic conduct at the time of emergency, as well as results of any allergy tests (size of skin prick tests and level of specific IgEs) performed subsequently. Associated factors are also considered. Any allergen is registered. The notification of idiopathic anaphylaxis including the list of all investigations that have been carried out is encouraged. Cases are included if there is a diagnosis of anaphylaxis according to criteria published previously (3). Acute reactions involving only skin symptoms are excluded. The quality control criteria are the standard requirements for allergy testing. The primary and secondary analysis of the data is performed by clinical research assistants. The network has a scientific board that can be consulted and which implements any suggested improvement. The data collected are reported in French and English by e-mail to all the members and the notification is forwarded to AFSSA and to DGCCRF (Ministry Department for Surveillance of Consumption and Suppression of Fraud). The data are published on an annual basis and are available for scrutiny on <http://www.cicbaa.org>. Of 738 cases of food anaphylaxis reported from 2002 to 2008, 80.5% were referred to an emergency room. Hospitalization after initial care occurred in 59.3%, and the use of adrenalin was 44.5%, and severity was underestimated in 5.6%. Anaphylactic shock accounted for 36.6% of cases, while 47.7% were serious systemic reactions without cardiovascular collapse. A diagnosis of laryngeal angioedema was made in 12.2% of cases and serious acute asthma in 3.5%. Mortality was estimated at 1.68%. Of 108 allergenic foods, the most frequently encountered were tree nuts, peanuts, crustaceans, latex-group foods, snails, celery, lupine flour and cows' milk. During the same period, 278 cases of drug anaphylaxis were recorded (4).

The strength of the Allergen Vigilance Network is a high total number of members ensuring the documentation of anaphylaxis within a large area of Europe. The networking relies on enthusiastic allergists who agree with the scientific supervision of university coordinators. However, the functioning depends largely on the personal commitment of the allergy internists at the university hospital and also requires manpower for daily communications. Not all members who are interested in being within the network are active.

Germany/Austria/Switzerland

The register of anaphylaxis (Network for Online Registration of Anaphylaxis, NORA e.V.) in German-speaking countries started in 2005 with a questionnaire to doctors in Berlin and Brandenburg on the need for such a register. Responses

revealed that many different specialists take care of patients with anaphylaxis. Responses also revealed that drugs, food and venom were the most frequent causes of severe allergic reactions (28). Over 70% of the doctors agreed there was a need for an anaphylaxis register and agreed to participate. Doctors suggested that participation could be improved by continuing medical education (CME) credits, feedback of the results and the option to participate in educational programmes. A register, based on the survey findings, was developed. Data are collected through a validated online questionnaire on age, gender, symptoms, location where the reaction took place, diagnosis, eliciting factors, cofactors, treatment and preventive measures for patients who experienced severe allergic reactions (Table 3).

Currently, 74 specialised allergy centres throughout Germany, Austria and Switzerland are participating. The centres cover different disciplines practising allergology in German-speaking countries including dermatologist, paediatricians, ENT and internal medicine doctors. The data are acquired through the online questionnaire and are secured by an individual password for each centre. The inclusion criterion to input a severe allergic reaction into the registry is the onset of pulmonary and/or cardiovascular symptoms independently of the onset of other symptoms. However, the complete symptom panel of each patient is assessed. The anaphylaxis registry is embedded into the network of online registration of anaphylaxis (NORA e.V.) a nonprofit organisation that is the umbrella for the anaphylaxis network. Data safety issues and ethical approval within the network are addressed.

Up to January 2009, 1163 anaphylactic reactions have been reported, (203 cases in children and 960 in adults). The most frequent causes in children were peanuts and tree nuts, followed by milk and hen's egg, while insect stings were the most frequent in adults (> 50%), followed by drugs and food allergens.

One task of the anaphylaxis registry is to obtain information about the medical care of affected patients. This indicates that adrenalin is only used in a minority of patients.

The advantage of an online registry is the direct data entry by the reporting doctor. This enables a continuous evaluation of the data and by using tick boxes and certain data entry restrictions; only fully completed cases can be finished, which ensures data of high quality. At present, only allergy centres enter their data, which ensures a high quality of diagnostic data, but at the expense of missing some data as not all individuals are referred to and/or seen by an allergy-centre. So far, the online registration system has been well received and used, although attempts to involve more centres continue.

Italy

At present, the Italian health system does not provide a registering system for anaphylaxis at a national level. However, in 2006, the Veneto Region Government established a Reference Centre for Food Allergy, whose mission is to provide evidence-based guidelines for allergic diseases, and to implement them across the Region. A surveillance system

Table 3 Suggested data collection (web based). Example of a data sheet for an allergic reaction relational database management system (35). (Additional information by form)

Personal data
Health status (prior to allergic reaction)
Incident data
Circumstances
Reaction data
First time reaction (Yes; No)
Fatal reaction (Yes; No)
Symptoms
Skin [tick box, nonexclusive (except the first item)]
Gastrointestinal [tick box, nonexclusive (except the first item)]
Respiratory [tick box, nonexclusive (except the first item)]
Circulation [tick box, nonexclusive (except the first item)]
Eliciting factors
Not known (Yes; No)
Food [tick box, and nonexclusive selection possibility]
Drugs
Insects
Latex
Specific immunotherapy
Other eliciting factors
Cofactors contributing to the reaction
Treatment
Emergency treatment?
First professional medical treatment
Which drugs were applied for the treatment?
(Tick box, and nonexclusive selection possibility)
Which clinical diagnostic tests were performed?
(Tick box, and nonexclusive selection possibility, except the first two items)
Follow up of the Patient
After treatment at the Emergency department, is the patient taken in the hospital for observation? (Yes; No)
At discharge from hospital
Is the patient referred to an allergist? (Yes; No)
Has the patient been prescribed emergency drugs? (Yes, No)
Reference to allergist
Counselling about prevention allergic reaction (Yes, No)
Counselling about the trigger (Yes, No)
Counselling about what to do after allergic reaction. (Yes, No)
Information given about patient support groups (Yes, No)
Counselling/advice about immunotherapy (Yes, No)
Other

for anaphylaxis was thus designed and an area-based regional Registry for anaphylaxis was established in north-eastern Italy. The Registry fully monitors a population of 4.5 million inhabitants, 700 000 of whom are under the age of 15.

The aim of the Veneto Region Registry for Anaphylaxis (VRRRA) is the real-time registration of cases of anaphylaxis occurring within the whole region and requiring an ER visit and/or hospitalization. The project plans to involve emer-

gency departments, paediatric departments and units, the local allergist network and the GPs network.

The planning phase consisted of (i) sharing the operational case definition in order to define the cases eligible for registration, (ii) defining the information to be collected on each case, (iii) defining and planning for a dedicated training programme for professionals involved and (iv) planning/building a technological platform to support the registry.

Currently, all the 38 Emergency Departments for adults, two Paediatric Emergency Departments and 22 Paediatric Units in the Region are enrolled in the project and currently are registering the cases that occur.

The system is a web-based user-friendly database, collecting a selected set of data that are useful for clinical decisions both in the acute and in the chronic phase with a stepwise approach. The information is available in real-time for the users connected to the network. This technical choice allows clinicians to share the information within the whole area under surveillance and, with the patient's consent, visualize the patient case record in real-time to other clinicians in the network, thereby circulating useful information including the patient's history, previous episodes and causal agents which will help to reach a more timely diagnosis.

Comparative analysis

Consideration of the different existing registries indicates a number of common features, but also significant differences, particularly in the type and manner in which data are collected. Although in some countries allergic reactions registries have existed for a number of years, little is known about the epidemiology of allergic reactions in the general population. While the existing registries document allergic reactions, and in some countries are analysed to provide data on causative allergens, data are not collated at a European level to inform management strategies for patients or to educate health care professionals and reporting doctors.

Data collection

The oldest registry initiated by the Swedish government together with paediatricians also collects data from an asthma study. Data are collected on a voluntary basis mainly from paediatricians but also from hospital emergency rooms. More than 200 confirmed cases have been collected to date and the causative food identified. In many of the cases also the dose of the food (protein) causing the reaction was established. The Norwegian system started in 2000 and by the end of 2008 this article form-based system with open questions grouped around certain themes has collected about 700 severe food allergy cases. The sources for reporting are broader than the Swedish system, as they include General Practitioners, Emergency Departments and, in principle, all clinicians. The newer registries use electronic communication media. The French system, which started in 2001, uses paper forms and electronic mail form to collect data. The French system is a structured interactive system, where participants are asked every 2 weeks whether there are any cases to report. The data on allergic reactions from all causes come

from members of the Allergy Vigilance Network, who are clinicians, mainly allergy specialists and some Emergency Health Clinicians. The system from German-speaking countries uses Internet-based questionnaire forms, with a structured and input-guided format for registering allergic reactions from all causes. The predefined choice input fields ensure the structured collection of the data and prevent non-logical erroneous inputting of data, leading to a validated reporting mechanism. Data are sourced from associate allergy centres in Germany, Austria and Switzerland. The latest system set up in Europe is the Italian system. This registry is implemented in the Veneto clinical area, which comprises several hospitals and emergency departments. It is also an Internet (intranet)-based system, but has a two stage collecting process. The first stage is also used to guide the clinician in making a diagnosis and a particular advantage is that it can thus be used as a triage system for emergency and hospital departments, facilitating the difficult task in diagnosing food induced anaphylaxis. The second stage is collection of the follow-up data for completion of the registered incident.

An overview of the data collected by the various registries, by which means, and from whom is summarised in Table 2.

Data assessment and distribution

All the systems are used for giving feedback to the scientific and clinical community on causes of allergic reactions. Reports are also generated to inform Health Authorities and for regulatory use. Although some of the data are used to influence national policy on prevention of (severe) allergic reactions, this is by no means common practice. Country-specific data are only exchanged by publications in peer-reviewed allergy journals and thus only available to a restricted public. This comparison of the registries that have been established in a number of European countries has highlighted that existing national injury and food adverse reaction information systems are not able to record allergic or anaphylactic reactions as a specific category. The use of the existing registries is thus limited to governmental and medical health care professionals. Societal use of the registries (by industry and or patient organisations) is restricted and therefore use of the data for practical and educational use is only possible indirectly.

Advantages of a pan-European registry

The incidence of severe food allergic reactions is largely unknown and there is a general lack of information about triggering allergens and/or triggering factors such as the route of exposure, the location, situation or conditions where the exposure occurred, exercise, alcohol, medication etc. Knowledge about age and gender distribution as well as health care system handling of the cases is also scarce. Registries provide the medical community with important information and increased knowledge about a defined disease. In a European register of severe allergic reactions, data such as demographical data and circumstances, causes and treatment can be collected in a standardised fashion thereby increasing awareness, interest and knowledge among health care personnel

and food providers (industrial, restaurant and catering). The register can also provide knowledge about the differences or similarities among different European countries inasmuch as there are various food habits that may change the scope of food allergy. An important advantage of a pan-European registry, in contrast to National ones, would be the added statistical power that comes with a larger input of standardised and uniform data. Even registries in smaller countries, such as Norway, have been able to flag emerging allergens; a European-wide registry should be able to achieve the same goal faster and for less prominent allergens. Besides it might offer the opportunity to compare declarations from emergency specialists and allergists as the frequency of causes depends on the reporting group.

Whenever a registry is established several issues need consideration. The first concerns data quality, both in terms of diagnosis, but also in terms of comprehensive coverage: if severe allergic reactions are documented it is very important to consider who is providing the data. Besides emergency departments such data must also be obtained from other clinicians treating allergic patients. The second aspect concerns the purpose for which the data are collected; stakeholders need to be identified and consulted on what they expect to get from the data, and it may be difficult to reconcile all their requirements.

For public authorities such a register could assist food allergen surveillance and compliance activities in detecting unexpected allergens in commercial food products because of incorrect labelling or caused by missing or inaccurate information or (cross-) contamination. It will also provide valuable information about the public health significance of undeclared allergens. Surveillance can also give early information to authorities about whether introduction of new foods and/or newly developed food processing technologies might pose a risk for allergic consumers. It could also examine the proportion of adverse reactions attributable to food that is sold unpackaged, and which is therefore not legally required to have an ingredient label. Legal authorities can provide information to stakeholders such as suppliers, producers etc. based on data from the registry. The food producers can use information generated by the registry to ensure allergen awareness for staff education and training, as well as for safe production of products.

Technical aspects

It is suggested that the configuration of the registry could be a centralized European Register, which should be securely connected to EU Member State Allergic Reaction Registries. An Internet-based system would need to be flexible, reliable, possible to support and maintain. A multi-language and multi-operating system is preferable. Security would need to be established by a two layer encrypted password controlled access, with data input via a two stage process. The first stage would be the initial data collection in which the operator is guided through the input process and supported in establishing the correct diagnosis. The second stage would be the follow-up after the patient is secured, treated and referred to an allergist or allergy spe-

cialist, and preferably should be as soon as possible after the occasion/reaction.

When the completed case is submitted to the National register, a copy would simultaneously be sent to the centralized European Register. This would provide a system for National reporting activities, a back up of the National register and an EU overview. The system would use state of the art information technology already available, but the innovative part would be the pan-European Registry. The Registry would require the commitment and co-operation of health care professionals, governmental bodies, food businesses all over Europe and setting up this cross disciplinary co-operation will be a huge innovative challenge.

Data aspects

In a system that would generate data and information to be used for informing policy makers, food manufacturers, health care professionals, patients and all those who take care of allergic individuals at risk of severe allergic reactions, it is critical that the appropriate information is collected.

Patient-specific data related to the disease should be collected by health care professionals in order to get the appropriate information that can be used by other doctors to optimise treatment of anaphylaxis as well as to give advice and guidance to the patient. Information can also be used to prevent future incidents, e.g. determining a causative allergen, the dose causing the reaction and how the food was processed and how the food product involved was sold, i.e. pre-packaged and labelled or sold loose. Further information gained could be used to prevent future incidents by determining whether it was a deliberate ingredient that was not correctly identified via food labelling, other information or a possible cross-contaminant. Reactions may also occur because the allergic individual does not recognise the food as a threat or because information is not provided in situations where food is sold loose. An overview of data to be collected can be found in Table 3. A high quality of data maximises the value of the registry.

Discussion

One of the primary strengths of a pan-European register would be the ability to obtain an estimate of the incidence of severe allergic reactions (including anaphylaxis) over time. Whilst a mandatory pan-European register might be the ideal, we need to build on the existing national registries which are all voluntary. The incidence of other allergic conditions such as asthma has been found to be increasing over time. Whether this is the case also with anaphylaxis is not known, but studies in UK and Australia show there has been an increase in hospitalization for anaphylaxis (29, 30). A pan-European register could also provide information on such trends. Data from National registers of severe reactions (Norway; Finland) show that among adults, women are more frequently represented than men. The contrary is true for children. National registers further reveal that severe reactions have two age peaks, one peak between 0–5 years, and another peak at 20/25–35 years.

Studies of severe allergic reactions to foods point to poorly controlled asthma being a significant risk factor for severe reactions, as is severe wheeze among children. Intake of cold beverages and exercise are other factors linked to the severe outcome of a reaction, but little is known so far about the contributing effect of alcohol and drugs. The influence of such cofactors could rapidly become apparent from a pan-European register because of the data will offer scope for analyses of high potential statistical power.

To advise food allergic patients effectively, the allergens of concern need to be known including the characteristics of the allergen, the amounts needed to elicit reactions and preferably the risk behaviour. To effectively treat reactions, knowledge of what treatment protocols lead to optimal outcomes is needed. The registry could also have a medical educational dimension. As severe reactions are fairly rare, few doctors acquire medical experience of such reactions. The information kept and updated in a pan-European register could thus be a valuable tool for clinicians. The information from such a registry could also be used to provide information about the effects of different amounts of allergen. More significantly, it could provide feedback on the efficacy of allergen management protocols in industry by identifying trends in incidence and relating them to aspects of allergen exposure. It could also validate estimates of the risk of a reaction from a given level of exposure to a particular allergen derived from statistical modelling techniques. Based on these estimates, it would be possible to develop food safety standards to assure the safety of allergic consumers. Studies in Sweden have shown that a reduction in fatal cases from 1.75 per year to 0.86 per year was probably largely because of better management of high-risk people. Establishing a pan-European registry for severe allergic reactions could thus also play a major role in food allergen risk management.

Proposal for a registry

Herewith we analysed the current situation on reporting of severe allergic reactions in Europe. Several systems which have been in place for different lengths of time and which follow different data acquisition protocols have been identified. The comparative analysis of the different existing registries revealed clearly the advantages and disadvantages of different data collection systems and demonstrated the need of a unified data collection system in order to set a basis to answer the following possible questions.

- The occurrence (number) and circumstances of (severe) allergic reactions.
- The reasons why the presence of the allergen was not apparent to the individual.
- The characteristics of the allergens in relation to the severity of the allergic reactions i.e. data for prioritising high-risk allergens.
- The current practices in the emergency health care system for treating allergic reactions and the expertise/training needed by the staff involved.

Such a pan-European registry should be ideally based on an online electronic system, which should consider different items regarding demographic data, symptoms, eliciting factors, co factors and treatment modalities (Table 3). Such prospective data would be acquired by clinicians seeing allergic patients (e.g. allergists, paediatricians, emergency physicians, dermatologists, GP's, etc.). It would not only help to identify persons who are at risk and high-risk situations but would also give new insights into open questions like the definition and development of a method of diagnosis for anaphylaxis or the identification of novel eliciting factors for anaphylaxis. The data on the treatment measures will help to identify the current therapeutical situation and will be the basis for improvement of insights into the medical treatment of affected patients. Recent data from the anaphylaxis registry of German speaking countries clearly revealed that adrenaline is only rarely used even in severe allergic reactions. At the moment emergency plans for the acute treatment of severe allergic reactions have been developed at a European level (GAIN campaign) and will be disseminated throughout Europe. Such activities will help not only to improve but also unify the medical treatment of patients at risk of anaphylaxis.

The European Anaphylaxis Taskforce suggested in 2007, that a Europe-wide network of stakeholders (allergists [clinicians and researchers], health and food authorities, regulators and politicians, food and pharmaceutical industry and patient organisations) could work together to develop a variety of tools to ensure the safest possible environment for allergic individuals at risk of severe allergic reactions (31). A pan-European registry of such reactions would make a valuable contribution towards this aim.

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