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OPINION ARTICLE

Epidemiology of Contact Allergy in Europe: Current Situation and Outlook for the Future

La epidemiología de la alergia de contacto en Europa. Situación actual y perspectivas

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Contact allergies, and indeed contact dermatitis in general, are currently a major health problem. While their clinical manifestations are not usually very severe, they inevitably affect patients' quality of life, interfering with both social relations and work activities and generating significant economic costs. It is crucial, therefore, to gather, analyze, and interpret all information that can help us to better understand the epidemiology of contact allergies in the general population and, subsequently, to propose preventive measures. The classic epidemiological approach is to obtain a representative sample of the population, study it (for example, by collecting demographic data, information on possible exposure to allergens, and previous episodes of contact dermatitis), and finally to perform diagnostic patch testing of individuals in that sample. This approach is rarely used, however, because it presents several drawbacks, some of which are summarized in the conclusions of the Glostrup studies.^{1,2} Among them are the following: a) high costs; b) practical difficulties, such as

studying only a limited number of allergens; c) the need to recruit a large number of patients, usually several thousand, in order to make relatively accurate estimates, even with less common allergens; and d) limited agreement to participation, leading to the possibility of selection bias, which can undermine the main advantage of such population studies.

In view of these design difficulties, the epidemiological study of contact allergies relies greatly on the analysis of data from the practices of several skin allergy units or dermatology departments. This approach also presents certain advantages, such as lower costs, the possibility of ongoing epidemiological surveillance, and the high positive predictive value of performing patch tests in individuals with suspected disease. Contact allergy research groups in several countries have in fact recognized the potential value of such multicenter cooperative efforts.

Benefits of Clinical-Epidemiological Surveillance Networks

Unlike the results obtained from a single department or from sporadic special studies, the continuous collection

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and subsequent analysis of demographic and clinical data from several centers offer the following advantages:

1. Quality control: comparison of the results of a given dermatology department with the mean results for all departments in order to identify any divergence. This is both a consequence of and a prerequisite for further studies.
2. Subgroup analysis: only on the basis of a large enough sample can a higher risk of contact allergy in small, well-defined subgroups be identified.
3. Epidemiological surveillance: on the basis of sufficiently reliable data it is possible to evaluate time trends as well as regional differences in the prevalence of sensitization to certain allergens.

Quality Control

Each department takes responsibility for its own clinical practice, trying to follow the appropriate guidelines for all procedures, including patch testing.³⁻⁵ Confidence in the group's method and results, however, can only be built by comparing them either with a standardized reference (obtained, for example, by using a "round robin" procedure to review entries) or with the results of the other departments. With regard to patch testing, both British and central European groups have successfully implemented quality control and standardization procedures.^{6,7} In European countries with centrally managed health care, the participation of contact allergy units in setting standards of care should facilitate dermatologists' efforts to provide good medical care.

Subgroup Studies

Certain contact allergies are only important in small subgroups of the population, such as those working in certain occupations. From the statistical point of view, such subgroups can only be identified if they are part of a database (usually from multicenter projects) that is large enough to make it possible to detect characteristic patterns of contact allergy. Sample size is also important if certain statistical biases (sex, age, etc) are to be corrected for and scientifically valid conclusions reached.⁸ We have recently seen an example of this in the German Information Network of Departments of Dermatology (IVDK) with regard to the preservative methylchloroisothiazolinone-methylisothiazolinone (MCI-MI): we detected an abnormally high prevalence (around 10%) of sensitivity in a subgroup of patients whose common characteristic was nonoccupational exposure to paint. This finding served to alert the authorities to the high concentrations of this substance in water-based paints, subsequently confirmed by chemical analysis. As a result, limits on the use of MCI-MI in water-based paints were established. It was later confirmed that the levels of sensitization to the substance returned to normal in the subgroup of users.⁹ Clearly, this type of analysis is only possible with a) continuous data collection, b) ongoing analysis of the data, and c) sufficiently large databases.

Epidemiological Surveillance

Unlike quality control (which may be seen by some as a necessary evil), epidemiological surveillance is an exciting possibility offered by networks, as seen in the previous example. Surveillance involves the continuous collection and analysis of data; this makes it possible to identify both time trends and regional differences that can lead to further research or directly to preventive actions. Surveillance data need not be complete or totally accurate, and therefore a commitment to surveillance requires no more than the usual quality measures applied in clinical practice.

Increased frequency of sensitization to a substance is obviously an indication of an emerging problem that will alert researchers and, hopefully, the regulatory authorities. This has recently been seen in the case of some preservatives used in cosmetics.¹⁰ The most recent example was the case of methyldibromo glutaronitrile. The German IVDK published two studies (one using data collected nationwide in 1996¹¹ and one with international data in 2000¹²) in which increases in the number of positive patch tests to this substance were demonstrated. These findings were later confirmed in a study by the European group.¹³ The use of methyldibromo glutaronitrile in cosmetics is currently banned in the European Union.

A high frequency of sensitization to specific substances maintained over time is indicative of a persistent problem. An example of this has been (and, in fact, still is for most countries) the high prevalence of sensitization to chromium, resulting mainly from exposure to cement or leather. In Denmark the addition of ferrous sulphate to cement was shown to prevent sensitization in workers exposed to chromium.¹⁴ With the surveillance networks already in place it will be possible to study the consequences of introducing this measure in the European Union. All that is needed will be to analyze the data from routine patch testing in the subgroup of construction workers with suspected contact allergy.

Finally, a decrease in the frequency of sensitization to a substance is an indication of the effectiveness of preventive measures. For example, in Germany in the 1990s, glyceryl monothioglycolate was the most important allergen in hairdressers, half of whom were found to be sensitized.¹⁵ This contrasted with the lower prevalence of sensitization seen in other European countries.¹⁶ The considerable health burden these data revealed led the industry to withdraw the compound from their products. With this step the prevalence of allergy to this substance fell, as was soon demonstrated by the fact that the subgroup of young hairdressers who began working after the compound had been withdrawn and who had presumably never been exposed to the allergen had sensitization rates as low as 0%.¹⁷

Another example is the downward trend in nickel sensitization observed in those countries that have implemented laws regulating the release of nickel from metal objects. This is the case in the Nordic countries¹⁸ and, more recently, in Germany since the adoption of the relevant European Community regulation.¹⁹ However, in Germany even the youngest patient subgroups (in whom the effects of the measures to reduce exposure should be

most noticeable) do not reach prevalence rates close to 0%. Since 2000, the rates have remained stable at around 10% to 20% in women under 17 years of age and at about 1% to 9% in men in the same age group.²⁰ In this case as well, data from the epidemiological surveillance networks were necessary to confirm that the problem persists despite regulatory efforts to reduce exposure. This information, together with the findings of recent studies on the excessive release of nickel from consumer goods^{21,22} should provide sufficient evidence for the European Union and the various national authorities to adopt urgent measures.

Prospects

Despite some similarities, the result of a common European market, exposure to contact allergens may vary greatly from one European country to another, reflecting differences in industrial profile, regulations, and consumer habits. The discrepancies between the data obtained from skin allergy units from different countries^{23,24,25} can guide us to a better understanding of the different routes of exposure (although there may be methodological differences despite adherence to international guidelines).

In 1996 a European surveillance network was created to analyze routinely collected data in various contact allergy units in several European countries (European Surveillance System on Contact Allergies [ESSCA]; www.essca-dc.org). ESSCA has been fully operational since 2001, with several surveillance networks currently participating, among them the British Contact Dermatitis Group; the IVDK in Germany, Switzerland, and Austria; the Northeast Italian Contact Dermatitis Group; and, more recently, the 5 hospital dermatology departments affiliated with the Spanish Group for Research Into Contact Dermatitis and Skin Allergy/ Spanish Surveillance System on Contact Allergies (see the article by García-Gavin et al in this issue). The role of ESSCA is to provide ongoing feedback to its members concerning data collected and results obtained, and then, provided that the quality of these is adequate, to proceed to analyze the data, initially for surveillance purposes and subsequently for subgroup analysis as the data sample grows.

The ultimate goal is for ESSCA to act as a network of networks, unifying the data collected by national surveillance networks through their centrally coordinated efforts. As an alternative to the publication of data on an individual basis, the national surveillance networks, as well as the hospitals themselves (as is the case of St John's in London and the Hospital Gentofte in Copenhagen), may contribute to European surveillance by either providing their data or publishing them following ESSCA guidelines (for example, after correcting for age and sex).⁸ Only by coordinating and standardizing the publication of results and by following established epidemiological and clinical procedures will researchers interested in contact allergy achieve the greatest impact on public health in this area in Europe.

Conflict of Interest

The author declares that he has no conflict of interest.

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