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REVIEW

Klaus E. Andersen

Occupational issues of allergic contact dermatitis

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Abstract Occupational contact dermatitis is often of multifactorial origin, and it is difficult to determine the relative significance of the various contributing factors. Contact allergies are relevant in 20–50% of recognised occupational contact dermatitis cases. The reported frequency in different studies varies, depending on differences in how occupational diseases are notified and recognised, in types of occupation in a geographical area, and the ''quality'' of the dermatological examination, including the accuracy of the diagnostic patch-test investigation. However, the clinical relevance of the reported contact allergies is often uncertain. Many occupational contact dermatitis patients with documented contact allergies develop chronic eczema, in spite of work changes and attempted allergen avoidance. Recognition/non-recognition of a notified case may be based on circumstantial evidence, because of difficulties in the establishing of a firm proof of work exposure and subsequent development of skin disease. Reliable quantitative exposure measuring techniques are needed. Methods are developed for the measurement of exposure to allergens such as nickel and acrylates, which makes it possible for exposure–effect relationships to be established with increased certainty. For prevention of allergic contact dermatitis it was a major step forward, with mandatory ingredient labelling of cosmetic products. However, improved labelling of the presence of contact allergens in household and industrial products is needed. For the identification of hazardous contact allergenic compounds, guinea pig or mice assays are still required. The local lymph node assay (LLNA), which is an objective and sensitive mouse assay has now been internationally validated and accepted.

Keywords Allergic contact dermatitis · Contact allergy · Occupational skin disease · Skin · Diagnostic tests · Patch tests · Epidemiology · Dermatotoxicology · Local lymph node assay

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K. E. Andersen
Department of Dermatology,
Odense University Hospital,
5000 Odense, Denmark
E-mail: kea@dou.dk
Tel.: +45-6541-2700
Fax: +45-6612-3819

Introduction

Approximately 80–90% of occupational contact dermatitis is located on the hands, either alone or together with other sites. However, the multifactorial background of hand eczema and the difficulties in establishing the diagnosis of occupational contact dermatitis raise a lot of questions in daily practice when individual patients with suspected work-related eczema are being assessed. Firstly, it is difficult for one to define the word ''occupational''. Bruze (2000) gave a pragmatic solution by suggesting that the diagnosis of occupational hand eczema requires (1) identification of an exposure hazard at the workplace, (2) exposure to this factor, and (3) demonstration of a relationship between the exposure and the dermatitis under investigation, with regard to type, localisation and course. Secondly, the multifactorial background of hand eczema makes it difficult for one to determine the relative importance of endogenous factors and hazardous exposure at both work and home, and the balance may change over time in the same patient. This background must be taken into consideration when the importance of contact allergy for occupational dermatitis is discussed.

Epidemiological data

Meding (1990a) found in her large population-based study in Gothenburg that the 1-year period prevalence

Table 1 Dominating occupational causes of dermatitis, in per cent

Recognised occupational contact dermatitis	Women $n=281$	Men $n=150$	Total $n=431$
Allergic contact dermatitis	29	32	30
Allergic contact dermatitis + irritant dermatitis	10	6	9
Nickel contact allergy	9	2	7
Irritant dermatitis	40	46	42
Atopic dermatitis	12	14	12

of hand eczema was 11% and the most common types of hand eczema were irritant dermatitis (35%), atopic hand eczema (22%) and allergic contact dermatitis (19%). Looking at the occupational cases of hand eczema, she found significant differences in the 1-year period prevalence of hand eczema that depended on type of occupation, with cleaners having the highest period prevalence of 21.3% (Meding 1990b). However, data on the prevalence of occupational irritant and allergic contact dermatitis vary from clinic to clinic and from country to country due to lack of standardisation of case definitions and methods (Diepgen and Coenraads, 2000).

Recently, The Danish National Board of Industrial Injuries (2000) published the causes of a consecutive series of 431 recognised cases of occupational contact dermatitis for the first half of 1999. It showed a surprisingly high frequency of contact allergies as the dominant cause of recognised occupational eczema (Table 1). An allergic contact dermatitis was judged to be the main or significantly contributing factor for the development of eczema in 48% of the cases for women and in 40% for the men. The most common contact allergens were, for women: rubber chemicals (7.8%), rubber latex (6.4%) and nickel (6.0%); for men: nickel (7.3%), chromate (7.3%), and epoxy resin (6.0%). Wet work was, for women, the most frequent cause of recognised irritant dermatitis; for men it was exposure to cutting fluids and solvents.

The reported frequencies of allergic contact dermatitis are difficult to compare with results from other publications, because they depend on a number of variables, which include types of industry in the geographical area, specific exposures, the notification system, national regulations, and variation in judgment between the professionals involved (Andersen 1998).

Diagnosis of allergic contact dermatitis

The diagnosis of allergic contact dermatitis depends on patient history, dermatitis pattern, exposure history, and proper diagnostic patch testing that includes a choice of patch test materials. The European standard series is not sufficient. Testing with additional allergens depending on exposure and specific occupations gives a substantial number of extra contact sensitivities (Menné et al. 1992). In many occupational cases a stepwise approach in patch testing is necessary. Initial testing may include the standard series, working materials and products, followed by subsequent aimed testing with ingredients that are selected on the basis of the outcome of the first test. Thus, the diagnosis of allergic contact dermatitis is based on a number of criteria that require quite an effort from the dermatologist, while the same is not the case for the diagnosis of irritant contact dermatitis, which is often a diagnosis of exclusion because there is no diagnostic test available to confirm the diagnosis. Up-to-date textbooks review all possibilities and pitfalls (Adams 1999; Kanerva et al. 2000b; Rycroft et al. 2001).

Two points that are related to diagnostic patch testing will be raised here: the quality of the patch test material and the determination of relevance. All efforts to improve the complicated bioassay, diagnostic patch testing, lose momentum if just one factor is deficient. The patch test material that is used should be of the highest possible quality. Today, only the TRUE test patch system provides a selected group of 24 standard patch test allergens of pharmaceutical standard with documented purity, dose, stability and bioavailability. Most other contact allergens are dissolved or suspended in petrolatum and this may result in an uneven distribution in the vehicle, which gives rise to variation in patch test dose—possibly amplified by the variation in amount of petrolatum applied to the test chamber (Fisher and Maibach 1984; Antoine and Lachapelle 1988; Andersen et al. 1996; Kanerva et al. 2000a). This uncertainty is added to all the other sources of variation when diagnostic patch testing is performed, such as status of the patient's skin, other technical details, and readings. It would be a major step forward if the top 100 common occupational allergens became available in pharmaceutical quality for diagnostic patch testing.

The determination of relevance of a patch test response is another controversial point. Lachapelle (1997) proposed a detailed relevance scoring system using ranking scales for current and past relevance. In some cases determination of relevance is obvious, but for a number of common contact allergens, such as nickel, cobalt and colophony it may be difficult. A set of guidelines, prepared for individual allergens, on how one could determine the relevance of a positive patch test to the substance in question, might be helpful. The dermatologist should, perhaps, spend more time with the patient after reading the patch tests, to determine the relevance. It is a demanding task, but can help the dermatologist to improve the prognosis of allergic

contact dermatitis to formaldehyde, and, perhaps, also to other environmental allergens (Agner et al. 1999).

Exposure assessment

Assessment of exposure is a significant part of the evaluation of a case of possible occupational allergic contact dermatitis. It is a two-step procedure: Firstly, a qualitative exposure assessment is made, which shows in the patient's environment the presence or absence of the allergen in question. This is based on product information and chemical analysis (Fregert 1988). Secondly, a quantitative exposure assessment is made, which is problematic because the techniques for sampling and analysis have not yet been developed for standard use. The methods vary in complexity and include:

1. Removal techniques, such as skin washing and wiping.
2. Surrogate skin techniques, where a chemical collection medium is placed on the skin.
3. Fluorescent tracer techniques, where a fluorescent compound is added to the product in question, and contamination of exposed workers is quantified by measurement of the fluorescence from the skin after work, by video imaging techniques.
4. Biological monitoring, when detailed pharmacokinetic analysis of the chemical involved for quantification has been performed (Van Hemmen and Brouwer 1995).

The choice of method depends on the chemical in question, as well as practical and economical factors. All methods should be regarded as providing only estimates of dermal exposure until proper validation studies have been concluded. Recent studies have developed methods for determination of nickel exposure that use atomic absorption spectrometry of samples from fingernails and stripped stratum corneum (Kristiansen et al. 2000). The relative intermediate precision was in the range of 6–12%, with a limit of detection of 0.2 μg nickel per g nail and 1 ng nickel per skin sample. Another group has developed a tape-stripping method which uses Fixomull tape combined with gas chromatography, to assess occupational exposure to the multifunctional acrylates that are used in surface coating of wood furniture (Surakka et al. 1999). The removal efficiency of tripropylene glycol diacrylate (TPGDA) was approximately 80% at various skin sites, and doses as small as1 μl were measurable after 30 min of exposure to the skin. It is important research, because it increases the possibility for the establishment of a more scientifically based proof of occupational exposure, instead of just circumstantial evidence. A whole-body exposure chamber has also been developed, which makes it possible for airborne contact dermatitis to be studied in realistic and controlled experiments (Lidén et al. 1998).

Dose–response relationship

Nobody doubts that increased allergen exposure leads to aggravation of allergic contact dermatitis in a sensitised individual. However, in the occupational setting multiple exposures and individual factors are the rule, therefore it may be difficult for the results of carefully designed experiments to be extrapolated to the occupational situation. Nickel allergy is an example. Nickel-allergic subjects who work in banks and shops and have prolonged contact with nickel-containing coins, even with sweaty palms and fingers, rarely develop hand eczema or aggravation of pre-existing hand eczema. In clinical exposure studies with the detergent sodium lauryl sulphate (SLS) in nickel-allergic individuals it was found that the effect of the detergent on the nickel response depended heavily on the mode and time relationship between the two exposures. For example, there was no effect on the nickel reactivity when SLS was administered simultaneously with the allergen by an open application procedure on normal forearm skin (Menné and Calvin 1993). However, the nickel reactivity was decreased when contact dermatitis was provoked by SLS 1 month prior to a nickel closed-challenge patch test on the compromised skin area on the back (Hindsén et al. 1997). In contrast, the nickel reactivity was increased on forearm skin if SLS dermatitis was provoked by immersion in SLS solution a few hours prior to the nickel challenge (Allenby and Basketter 1993).

These studies gave important information and have led to the development of a more realistic model, where nickel exposure is administered directly to the skin of the hands and fingers. In a double-blind, placebo-controlled study that used volunteer nickel-allergic individuals with hand eczema and controls, daily immersion for 10 min for 2 weeks in solutions containing 10 or 100 ppm nickel caused significant increase in local vesicle formation and local blood flow, compared with controls (Nielsen et al. 1999).

Preventive measures

Prevention of occupational allergic contact dermatitis is complicated and includes individual, technical, economical and legislative aspects (Wahlberg 2000). It was a major step forward in the efforts to prevent allergic contact dermatitis when ingredient labelling of cosmetic products became mandatory. However, we need improved labelling of the presence of contact allergens in household and industrial products. The 1% (10,000 ppm) limit in the European Union for declaration of contact allergenic ingredients in household and industrial products is not sufficient as a preventive measure, because many important environmental contact allergens, e.g. preservatives and fragrance chemicals, provoke allergic contact dermatitis in sensitised individuals at much lower concentrations. With regard to

the identification of new occupational allergens, the World Health Organisation (WHO) took the initiative a few years ago to promote criteria for classification of skin-sensitising and airway-sensitising substances based on human evidence and predictive animal tests (Flyvholm et al. 1997). Predictive animal assays described in OECD and national guidelines have served well through the past 30 years to identify hazardous contact allergenic substances. Guinea pigs have been the laboratory animals of choice for these tests. However, a mouse assay, the local lymph node assay (LLNA), has now been developed and validated and will be used more in the future (Dean et al. 1999). The sensitivity and specificity of the LLNA is comparable to the best guinea-pig assays, and it has the advantages that is more objective, requires less space in the animal house, less test substance and is less stressful for the animals.

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