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Epidemiology of Contact Dermatitis

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1. Introduction

Substances that are responsible of contact dermatitis can be irritant, as chemical or physical agents that causes irritant contact dermatitis (ICD), or sensitizers, when causes a tissue inflammation damage with allergic mechanism (allergic contact dermatitis or ACD). ICD results from contacts with irritant substances, while ACD is a delayed-type immunological reaction in response to contact with an allergen in sensitized individuals. Primary lesions of occupational contact dermatitis (OCD) are usually found at the site of contact with the irritant or allergen; in the case of ACD, secondary lesions may occur subsequently on other sites of the body that have never been in contact with the allergens (Meneghini & Angelini, 1984).

Contact dermatitis is a common inflammatory skin disease in industrialized countries, with a great socioeconomic impact. It is one of the most common occupational diseases (Coenreaads & Goncalo, 2007; Saint-Mezard et al 2004). Epidemiology is also used to analyse whether it is more common in specific groups, and which factors are associated with the occurrence of contact dermatitis (or its subtypes) in specific populations or subgroups.

2. Factors contributing to contact dermatitis

Studies have been investigated a possible association between different factors and contact sensitization.

2.1 Gender and age

Women are usually more frequently patch-tested, and have more positivity results than men (García-Gavín et al, 2011). Gender differences may be attributed to social and environmental factors; females are more likely to have nickel sensitivity because of increased wearing of jewellery, and males are more likely to have chromate sensitivity from occupational exposure (Ruff & Besilto, 2006).

Rui et al estimate the prevalence of nickel, cobalt and chromate allergy in a population of consecutive patients and investigate the possible association with individual and occupational risk factors (Rui et al, 2010). This study showed interesting associations between some occupations and nickel, chromate and cobalt allergy.

ACD in children, until recently, was considered rare (Hammonds et al, 2009). One of the largest population-based patch test studies of unselected pediatric patients, which also provides specific relevance information, found the prevalence of past or current relevant reactions to be 7%, with a higher risk seen in females (Mortz et al, 2002). This is considerably lower than the prevalence in selected pediatric populations (symptomatic patients). Nickel is the most common sensitizer in almost all studies pertaining to pediatric contact dermatitis. Thus, the real prevalence of ACD (defined as a positive patch test with clinical correlation with the dermatitis experienced by a symptomatic individual) ranges from 14% to 77% among children referred for patch testing due to clinical suspicion of contact dermatitis (Bruckner et al, 2000; Fernández Vozmediano & Armario Hita, 2005; Seidenari et al, 2005; Lewis et al, 2004).

Eczema in adults usually exists for years, compromising quality of life and occupational choices. The flexural areas, shoulders, head-and-neck, and hands are typically affected in 5-15% of cases (Katsarou et al, 2001). The relationship between atopy and contact allergy remains unclear. Atopic dermatitis is a risk factor for allergic contact sensitization (Dotterud & Smith-Sivertsen, 2007). ACD increases with age in atopics (Lammintausta et al, 1992).

Contact dermatitis is a significant health problem affecting the elderly people. Impaired epidermal barrier function and delayed cutaneous recovery after injury enhances susceptibility to both irritants and allergens. Exposure to more numerous potential sensitizers and for greater durations influences the rate of allergic contact dermatitis in this population. Medical co-morbidities, including stasis dermatitis and venous ulcerations, further exacerbate this clinical picture (Prakash & Davis, 2010). Aging is correlated with the rate and type of contact sensitization, but only a few studies have evaluated patch test reactivity in elderly individuals with an adequately large population (Nedorost & Stevens, 2001; Balato et al, 2011).

2.2 Race

Black people may be less susceptible to sensitisation by weaker allergens and have a lower incidence of ICD because of greater compaction of the lipid component of the stratum corneum, conferring improved barrier function (Robinson, 1999; Astner et al, 2006). Ethnicity is a possible endogenous factor implicated in ICD. While there is a clinical consensus that blacks are less reactive and Asians are more reactive than Caucasians, the data supporting this hypothesis rarely reaches statistical significance. Modjtahedi SP et al conclude that race could be a factor in ICD, which has practical consequences regarding topical product testing requirements, an ever-expanding global market, occupational risk assessment, and the clinical thinking about ICD (Modjtahedi & Maibach, 2002).

2.3 Exposure to irritants and allergens

The most important risk factor for OCD is the exposure to irritants. Well-known irritants are water (wet work), detergents and cleansing agents, hand cleaners, chemicals, cutting fluids,

and abrasives. ACD is a common skin condition that can be difficult to diagnose without the aid of a specific diagnostic tool called patch testing. Patch testing performed with a relevant panel of contact allergens is the ultimate confirmatory test of ACD (see Chapter titled "Allergens (patch test studies) from the European Baseline Series" on this book). Correctly identifying the inciting allergen permits appropriate personal avoidance.

2.4 Personal history of atopic dermatitis

General population studies have repeatedly found that atopic dermatitis is the most important risk factor for hand eczema (Meding & Swanbeck, 1990; Dotterud & Falk, 1995; Yngveson M et al, 2000; Mortz et al, 2001; Meding & Jarvholm, 2002; Bryld et al, 2003; Josefson et al, 2006). Thus, the effect of atopic dermatitis seemed to level off with increasing age. Whether association between hand eczema on the one hand and atopic dermatitis or atopy on the other hand is explained by null mutations in the filaggrin gene (de Jongh et al, 2008; Carlsen et al, 2011), by an altered immune response (Davis et al, 2010; McFadden et al, 2011), or by their combination is currently unknown. Future studies should aim to investigate the distribution of these risk factors.

2.5 Other possible association

Studies have re-investigated a possible association between these lifestyle factors (alcohol drinking and tobacco smoking) and contact sensitization (Thyssen et al, 2010).

2.6 Analyzed literature

A substantial number of studies have also investigated the prevalence of contact allergy in the general population and in unselected subgroups of the general population (Thyssen et al, 2007). These studies have demonstrated variations in the prevalence of contact allergy depending on the selected study population and year of investigation. These studies are of high value as they tend to be less biased than studies using clinical populations and as they are important for health care decision makers when they allocate resources. Literature was examined using Pubmed-Medline, Biosis, Science Citation Index, and dermatology text books. Search terms included hand eczema, hand dermatitis, general population, unselected, healthy, prevalence, incidence, risk factor, and epidemiology. In observational studies on contact dermatitis, the ascertainment of cases varied from intensive efforts by a medical examination of the complete study population to the relatively easy-to-apply method of self-administered questionnaires; or by a combination of both. However, a diagnosis of contact dermatitis based on a self-administered questionnaire is significantly less valid than the diagnosis based on examination by a dermatologist (McCurdy et al, 1989).

3. Hand eczema in the general population

Information on the prevalence of hand eczema, contact sensitivity and contact dermatitis in the general population can be obtained from cross-sectional studies that were performed recently (Thyssen et al, 2009; Nielsen et al, 2001a, 2001b; Mortz et al, 2001;

Sosted et al, 2005; Lerbaek et al, 2007). Several studies have investigated the incidence of hand eczema in the general population (Bo et al, 2008; Hald et al, 2008; Moberg et al, 2009; Lind et al, 2007).

Hand eczema is the most frequent occupational skin disease. In many jobs the skin on the hands is subjected to damage caused by contact with skin irritants and contact allergens. Several studies have investigated the incidence and prevalence of hand eczema in the general population.

3.1 Usefulness of patch testing

Patch testing remains the gold standard for the diagnosis of ACD (Devos & Van Der Valk, 2002; Uter W et al, 2009). Quality control of patch testing is both a prerequisite for, and an objective of, clinical epidemiology of contact dermatitis. Continuous development of test standards concerning the composition of test series, test concentration, and vehicle and standardization of test readings is provided by the national and international research groups on contact dermatitis.

Many studies in contact dermatitis are based on populations that have been patch tested; usually this means that the participants visited a clinic or a hospital for being evaluated on having contact dermatitis. There are a variety of types of irritant reactions - some can look identical to allergic reactions. The recognised convention for recording patch test reactions is as follows:

+/- doubtful: faint erythema only

+ weak: erythema, maybe papules

++ strong: vesicles, infiltration

+++ extreme: bullous IR: irritant

3.2 Measures of disease frequency (incidence and prevalence)

The epidemiologist deals with necessity of data on defined populations. The most basic setting giving rise to epidemiological data is the evaluation of the occurrence of a disease in the presence of an exposure. The exposure may be present or absent and the disease may be present or absent.

Measures of disease frequencies include *prevalence*, which is the amount of disease that is already present in a population; *incidence*, which refers to the number of new cases of contact dermatitis during a defined period in a specified population; and "incidence rate" (IR), which is the number of non-diseased persons who become diseased within a certain period of time, divided by the number of person-years in the population. All measures of disease frequency consist of the number of cases as the numerator, and the size of the population under study as the denominator. Sensitivity and specificity of the diagnostic instruments used are important. In epidemiological studies, an overestimation of prevalence can result from low sensitivity/specificity.

The three most important types of observational study in the epidemiology of contact dermatitis are follow up studies, case-control studies and cross-sectional studies. In follow-

up studies, selection of subjects is based upon exposure to the factor of interest. Instead of exposure, the presence or absence of a risk factor (e.g. nickel allergy, or atopy) can also be chosen as basis for comparison. In case-control studies, the subjects are selected according to their disease status. Information on the past exposure of the persons with contact dermatitis (cases) and the non-diseased persons (controls) is collected. In cross-sectional studies, a study population is selected regardless of exposure status or disease status (in contrast to case-control and follow-up studies).

Data on the incidence and prevalence of occupational dermatoses are scarce. The most important sources of data are occupational disease registries, case series of patients visiting dermatology clinics, and a limited number of cross-sectional studies in one or more occupational groups.

3.3 Incidence and prevalence of contact dermatitis and contact sensitisation

Incidence of hand eczema: Several studies have investigated the incidence of hand eczema in the general population (Lantinga et al, 1984; Yngveson M, 2000; Meding & Jarvholm, 2004; Brisman J et al, 1998; Meding et al, 2006; Lind, 2007; Lerbaek et al, 2007). The median incidence rate was 5.5 cases/1000 person-years (range 3.3–8.8). Stratified by sex, the median incidence rate of hand eczema was 9.6 cases/1000 person-years (range 4.6–11.4) among women and 4.0 cases/1000 person-years (range 1.4–7.4) among men (Thyssen et al, 2010).

Prevalence of hand eczema: Few studies showed that the 1-year median prevalence of hand eczema in the general population was 9.7% (11.4% among women and 5.4% among men) and that the 1-year weighted average prevalence was 9.1% (10.5% among women and 6.4% among men) (Lantinga et al, 1984; Agrup, 1969; Peltonen, 1979; Menné et al, 1982; Kavli & Forde, 1984; Meding, 1990; Meding & Swanbeck, 1987; Meding & Jarvholm, 2002; Ortengren, 1999; Meding et al, 2001; Brisman J et al, 1998; Montnemery et al, 2005; Bo et al, 2008; Fowler et al, 2006; Hald et al, 2008; Svedman et al, 2007; Lind et al, 2007).

Population studies may give valuable information on the magnitude of the disease problem. Different data was found when compared the frequencies of positive path-tests reactions in the general population and in eczema patients at a dermatological clinic in the same area (Menné & Knudsen 1997) (Table 1). Publications based on data of patients visiting dermatology clinics and/or patch testing units can not be used to directly derive population related incidence or prevalence estimates. Data from incidence studies may support and direct strategies for the prevention of contact allergy and ACD, supporting conclusions derived from clinical surveillance data.

Nickel sulphate is the most common allergen in the standard series and the most common cause of allergic contact dermatitis, particularly in women. This gender difference is traditionally explained by increased exposure in women, due to direct skin contact with nickel-releasing metal, such as in jewellery, wristwatches, and clothing accessories. A possible association between nickel allergy and hand eczema in women has been addressed and supported by several population-based studies, whereas an association has been questioned in men (Nielsen et al, 2002; Peltonen, 1979; Meijer et al, 1995) (Tables 2 and 3).

Test substances	General population % positive of tested			Dermatological clinic % positive of tested		
	Men n=279	Women n=288	Total n=567	Men n= 262	Women n= 416	Total n= 672
Potassium dichromate	0.7	0.3	0.5	1.9	2.7	2.4
Neomycin sulfate	0.0	0.0	0.0	3.4	3.7	3.6
Thiuram mix	0.7	0.3	0.5	4.6	2.7	3.4
p-phenylenediamine	0.0	0.0	0.0	1.9	2.7	2.4
Cobalt chloride	0.7	1.4	1.1	2.3	2.7	2.5
Benzocaine	-	-	NT	0.4	0.7	0.6
Caine mix	0.0	0.0	0.0	-	-	NT
Formaldehyde	-	-	NT	1.9	2.2	2.1
Colophony (colophonium)	0.4	1.0	0.7	4.6	5.4	5.1
Quinoline mix	0.4	0.3	0.4	1.9	0.5	1.0
Balsam of Peru (<i>Myroxylon pereirae</i>)	0.7	1.4	1.1	3.4	5.4	4.6
N-isopropyl-N-phenyl-para-phenylenediamine (IPPD)	0.4	0.0	0.2	1.2	0.0	0.5
Wool alcohols (lanolin alcohol)	0.4	0.0	0.2	1.2	1.7	1.5
Mercapto mix	0.7	0.0	0.4	1.2	0.2	0.6
Epoxy resin	0.4	0.7	0.5	0.8	0.2	0.5
Paraben mix	0.4	0.3	0.4	0.8	0.2	0.5
para-Tertiary-butylphenol-formaldehyde resin (PTBP resin)	1.1	1.0	1.1	0.4	1.2	0.9
Fragrance mix	1.1	1.0	1.1	6.1	7.1	6.7
Ethyenediamine dihydrochloride	0.4	0.0	0.2	0.8	0.2	0.7
Quaternium-15	0.4	0.0	0.2	0.0	0.0	0.7
Nickel sulfate	2.2	11.1	6.7	4.2	16.1	11.0
Cl+Me-isothiazolinonec	0.4	1.0	0.7	0.4	0.7	0.6
Mercaptobenzothiazole	0.4	0.0	0.2	1.2	0.2	0.6
Primin	-	-	NT	0.4	1.5	1.0
Thiomersal	3.6	3.1	3.4	-	-	NT
Carba mix	0.7	0.0	0.4	-	-	NT

Table 1. Comparison of frequencies of positive patch-test reactions in the general population and in eczema at a dermatological clinic in the same area of greater Copenhagen in 1990 (Menné & Knudsen 1997).

Study	N	Allergens used for	Positive	Three most common
		patch testing	reaction to	allergens
			nickel; total (%)	
Nielsen et al, 1992	567	TRUE-tests	6.7	Nickel, thimerosal,
				cobalt/Balsam of Peru
Nielsen et al, 1998	469	TRUE-tests	10.8	Nickel, fragance mix,
				and thimerosal
Schäfer et al, 2001	1141	Standard series	9.9	Nickel, fragance mix,
				and thimerosal
Akasya-	542	Standard series	19.1	Nickel, potassium
Hillenbrand, 2002				dichromate, and
	5			palladium chloride
Lazarov, 2006	2156	TRUE-tests	13.9	Nickel, fragrance mix,
				and potassium
				dichromate
Dotterud &	1236	TRUE-tests	17.6	Nickel, cobalt, and
Smith-Sivertsen,				thimerosal
2007				
García-Gavín et	1161	Spanish standard	25.8	Nickel, potassium
al, 2011		series		dichromate, and cobalt
				chloride

Table 2. Studies on contact dermatitis in the general population (list is not extensive).

Study	п	Allergens used for Positive		Three most common
		patch testing	reaction to	allergens
			nickel; total (%)	
Röckl et al, 1966	357	Not given; MCl/MI and PPD	2.5	Chromium, HgCl ₂ , and formaldehyde
Weston et al, 1986	314	Standard series	7.6	Neomycin, nickel, and chromium
Barros et al, 1991	562	Standard series	0.9	Neomycin, thimerosal, p-tertiary-butylphenol- formaldehide
Dotterud & Falk, 1994	424	Epiquick test	14.9	Nickel, cobalt, and MCl/MI
Mortz et al, 2001	1146	TRUE-tests	8.6	Nickel, fragance mix, and thimerosal/colophony /cobalt

Table 3. Studies on contact dermatitis in children (general population) (list is not extensive).

3.4 Current view on the spectrum of contact allergy to important sensitizers across Spain

In 2005, the Spanish Society of Allergology and Clinical Immunology (Sociedad Española de Alergología e Inmunología Clínica (SEAIC) in collaboration with the Allergy and

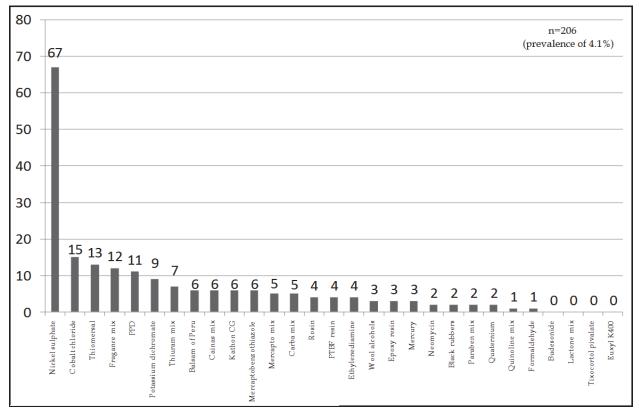


Fig. 1. Etiologic agents for contact dermatitis in Alergológica-2005.

Immunology Laboratory Abelló undertook the "Alergológica 2005" study with the aim of obtaining epidemiologic, clinical and socioeconomic information on allergic patients seen and treated by Allergology specialists in Spain.

In the particular case of contact dermatitis, the results from epicutaneous tests from the standard Spanish series for contact dermatitis were recorded by taking readings at 48 and 96 hours, and evaluating erythema-infiltration, papules and vesicles. Two hundred-six cases of contact dermatitis were diagnosed, which represents a prevalence of 4.1%. The mean age of the patients was 42.5 years and females clearly outnumbered men (2.5:1). In the etiology of contact dermatitis (Figure 1), the leading causes were metals, nickel and cobalt, together with chromium, with a total of 91 cases. Thiomersal is in third place with 13 cases, which represents 6.2% of all causes (Muñoz-Lejarazu, 2009).

3.5 Current view on the spectrum of contact allergy to important sensitizers across Europe

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 (Hospital del Mar, Barcelona; Hospital La Princesa, Madrid; University General Hospital, Alicante; Complexo Hospitalario Universitario, Santiago de Compostela; and University Hospital Puerto Real) (García-Gavín et al, 2011). Nickel sulphate remains the most common allergen with standardized prevalences ranging from 19.7% (central Europe) to 24.4% (southern Europe). While a number of allergens shows limited variation across the four regions, such as

- 1. Contact allergy was independent of enhanced IgE responsiveness.
- 2. The median prevalence of contact allergy was 20% (adults 15–69 years).
- 3. Contact allergy to a wide range of allergens as well as multiple contact allergy was observed in both children and adults.
- 4. Contact allergy was most commonly observed against nickel, fragrances, and thimerosal.
- 5. The proportion of nickel allergy out of contact allergy to at least 1 allergen has been increasing significantly over the past 4 decades.
- 6. The median prevalence of nickel allergy among women was 17.1%.
- 7. A median prevalence of 81.5% women, have pierced ears.
- 8. Pierced ears are a strong risk factor for nickel allergy.
- 9. Nickel contact allergy may be associated with hand eczema in women.
- 10. Heavy smoking may be a risk factor for nickel allergy.

Table 4. Main findings from epidemiological population-based studies (published between 1966 and 2007) investigating contact allergy in the general population or subgroups of the general population (Thyssen et al, 2007).

Myroxylon pereirae (5.3-6.8%), cobalt chloride (6.2-8.8%) or thiuram mix (1.7-2.4%), the differences observed with other allergens may hint on underlying differences in exposures, for example: dichromate 2.4% in the UK (west) versus 4.5-5.9% in the remaining EU regions, methylchloroisothiazolinone/methylisothiazolinone 4.1% in the South versus 2.1-2.7% in the remaining regions (Uter et al, 2009).

The continuous collection and analysis of data within multicenter clinical epidemiology offer practical findings. Thyssen et al (2007) described main findings from epidemiological population-based studies (Table 2) investigating contact allergy in the general population or subgroups of the general population.

4. Occupational contact dermatitis

Work-related dermatoses, in particular hand dermatitis, are still among the most prevalent occupational diseases. Understanding the epidemiology of OCD is essential to determine etiologic factors of the disease and to make recommendations for its prevention.

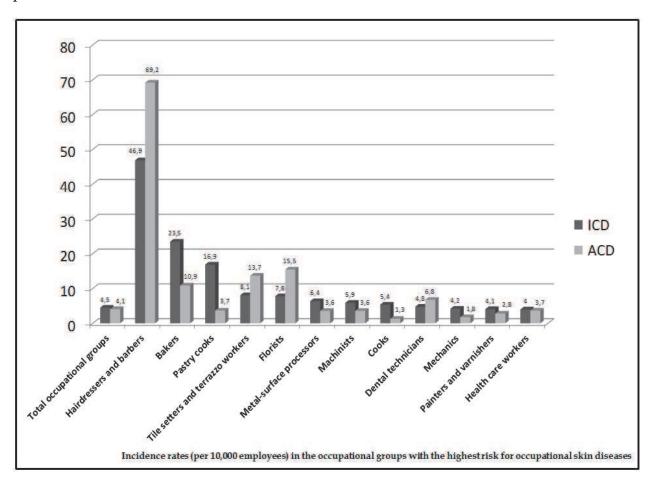


Fig. 2. Incidence rates of ICD and ACD in the occupational groups with the highest risk for occupational skin diseases (Diepgen & Coenraads PJ, 2000).

Different professions have differing risks for occupational skin disease. Those at the highest risk for a contact dermatitis are hairdressers (yearly rate 120/100,000), printers (rate

71/100,000), machine tool operatives (rate 56/100,000), chemical/petroleum plant operatives (rate 45/100,000), assemblers (rate 35/100,000), and machine tool setters (rate 34/100,000) (Cherry et al, 2000). Accurate estimates of the incidence of occupational skin disease are difficult to find but a recent report from the EPIDERM and OPRA occupational skin disease surveillance project suggests a rate of 13 per 100 000 per year 5 and a prevalence of 15 per 10,000 of those ever employed has been quoted (Cherry et al, 2000).

Occupational disease registries provide national incidence data based on the notification of occupational skin diseases and are available in many countries. Although the comparison of national data are hampered by differences across countries in reporting and the definition of occupational diseases, the average incidence rate of registered occupational contact dermatitis in some countries lies around 0.5-1.9 cases per 1,000 full-time workers per year (Dickel et al, 2002; Halkier-Sorensen, 1996). The highest incidence rates were seen in hairdressers (Diepgen et al, 2000). In Figure 2, the incidence rates of ICD and ACD of employees of the twelve groups with the highest risk for an occupational skin disease are presented.

4.1 OCD in different work forces

The majority of work-related dermatoses, in particular hand dermatitis, comprise contact dermatitis (90-95%); the rest are of other dermatoses such as contact urticaria, oil acne, chloracne, chemically-induced leucoderma, and infections. In this section, different "work-related OCD" are discussed.

Health care workers (especially nurses) are often affected by OCD, whose "occupational sensitization pattern" comprises thiuram (rubber compounds), thiomersal (vaccine preservative) and several biocides (glutaraldehyde, formaldehyde, glyoxal and benzalkonium chloride) (Schnuch A et al, 1998). Operating-room staff is a subset of health-care workers (preparation and clean up may involve exposure to cleaning and disinfecting agents, and some workers may also have exposure to sterilizing agents, such as glutaraldehyde, and some workers may use ethylene oxide).

The frequency of OCD **in dental personnel** (dentists, dental assistants, dental technicians and orthodontics) has steadily increased over the last decades and currently considered to be about 40% (Uveges et al, 1995).

Hand eczema is a well-known and potentially severe drawback to the **hairdressing profession**. Hair cosmetic producers provide the hairdresser with a great variety of chemicals to fulfil stylist and customer desires. Smit et al studied a cohort of apprentice hairdressers (n=74) and nurses (n=111) and found an average incidence rate of hand dermatitis of 32.8 cases/100 person-years for the hairdressers, compared with 14.5 cases/100 person-years for the nurses (Smit et al, 1994).

Construction workers (bricklayers, manufacturers of concrete elements...) are in contact with wet cement products in the form of mortar or concrete. ACD due to hexavalent chromium in cement is still the most important contact allergy. Also, other substances have been identified (e.g., cobalt, tuber additives, epoxy resin, hexamenthylendiamine and isophorondiamine) (Geier & Struppek, 1995).

Metal workers are exposed to numerous exogenous factors that play a substantial role in the development of ACD as well as ICD. Even though nickel is regarded as the most frequent source of all reported metal allergies, metal-work fluids are the most important cause of irritant hand dermatitis (also exposed to other chemical irritants, such as cleaning detergents, solvents and degreasers) (Itschner L et al, 1996). Metal polishers remove excess metal and surface defects from various items such as the accessory parts of cars. The most commonly polished metals are aluminium, brass, bronze and zinc (Adams 1999).

4.2 Social and economic impact of contact dermatitis

The total economic impact of OCD is high according to the following costs (Diepgen & Coenrads, 2000):

- Direct costs of medical care, workers compensation or disability payments.
- Indirect costs associated with lost workdays and loss of productivity.
- Costs of occupational retraining.
- Costs attributable to the effects on the quality of life.

5. Conclusion

Numerous studies have investigated the prevalence and risk factors of hand eczema in the general population. Contact sensitization has become a significant public health problem. In many parts of the world, more than 20% of the adult population is suffering from contact allergy. The profile of sensitizations may differ in each country. However, nickel sulphate is the most prevalent allergen practically everywhere. Patch testing remains the gold standard for the diagnosis of ACD. Quality control of patch testing is both a prerequisite for, and an objective of, clinical epidemiology of contact dermatitis. Publications based on data of patients visiting dermatology clinics and/or patch testing units cannot be used to directly derive population related incidence or prevalence estimates.

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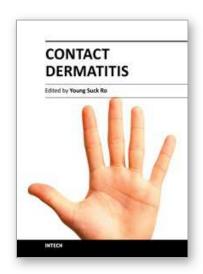
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