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Allergic Contact Dermatitis in Children

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1. Introduction

Contact allergy (CA), a pathologic response after (usually repeated) contact to environmental substances of low molecular weight occurring in a varying proportion of exposed persons, often results in clinical disease, allergic contact dermatitis (ACD), which can be disabling. CA is diagnosed by patch testing, a technique of controlled exposure of patients suspected to have ACD to a standardized set of substances frequently found to be the cause of ACD (Uter, 2004). ACD is an inflammatory reaction of the skin that follows percutaneous absorption of antigen from the skin surface and recruitment of previously sensitized, antigen-specific T lymphocytes into the skin (Rietschel & Fowler, 2001a). Although sensitivity to contact allergens occurs in 10-20% of the adult population, the exact incidence and prevalence of sensitization in children is unknown. ACD in children is not rare. The documented rates of ACD in children are on the increase (Militello et al., 2006; Goossens & Morren, 2006). Sensitization to contact allergens begins in infancy and continues to be more common in toddlers and young children. Infants, even neonates, may be sensitized (Fisher, 1994a; Bruckner et al., 2000). The rate of positive results may vary with referral patterns, selection criteria for patch testing, regional and social variations in allergens exposure and the allergen tested (Militello et al., 2006; Goossens & Morren, 2006; Wahlberg & Lindgerg, 2006).

2. Epidemiology (prevalence and incidence)

Previously, ACD was once wrongly considered uncommon in the pediatric population (Hjorth, 1981). It was thought that children had reduced exposure to contact allergens during childhood. The second reason was less susceptibility of the child immune system to contact allergens (Mortz & Andersen, 1999). However, during the last 10-20 years, several reports have described a considerable number of children with CA and ACD (Pevny et al., 1984a; Pevny et al., 1984b; Weston & Weston, 1984; Rademaker & Forsyth, 1989; Barros et al., 1991; Dotterund & Falk, 1995; Motolese et al., 1995; Katsarou et al., 1996; Rudzki & Rebandel, 1996; Stables et al., 1996; Manzini et al., 1998; Brasch & Geier, 1997), confirming that CA and ACD may be frequent in children and may cause significant problems. Prevalence of positive patch tests without clinical correlation (CA) in population-based studies is different from the prevalence of ACD (positive patch test with clinical correlation) in patients referred for patch testing.

2.1 Prevalence of contact allergy in a selected population

Patch test studies in series of selected children with suspected ACD have reported frequencies of positive reactions varying from 14% to 71% of patients. Of these, about 56-93% was of current relevance (Weston & Weston, 1984; Pevny et al., 1984b; Fisher, 1994a; Rudzki & Rebandel, 1996; Stables et al., 1996; Manzini et al., 1998; Bruckner et al., 2000; Machovcová et al., 2001; Wöhrl et al., 2003; Heine et al., 2004; Lewis et al., 2004; Jøhnke et al., 2004; Vozmediano & Hita, 2005; Wahlberg & Lindberg, 2006; Goossens & Morren, 2006; Jacob et al., 2008). Among the children with a positive patch test 3.2% to 54.4% had multiple contact allergies (Mortz & Andersen, 1999).

2.2 Prevalence of contact allergy in an unselected population

In the general pediatric population, the prevalence of ACD may be underestimated, which can be attributed to the low frequency of patch tests performed on children (compared to adults) and by the fact that in clinical practice, manifestations of ACD are often attributed to morphological look-alikes, such as atopic dermatitis (AD) or irritant dermatitis (Militello et al., 2006). The results from patch testing in children and adolescents in the general population revealed that 13-24.5% had positive patch tests to standard allergens. The prevalence of past or current relevant reactions was found to be 7%, with a higher risk seen in females (Dotterund & Falk, 1995; Bruckner et al., 2000; Mortz et al., 2001; Jacob et al., 2008). Few population-based studies have examined contact sensitization in asymptomatic healthy children. Barros et al. (Barros et al., 1991) patch tested 562 Portuguese school children (5-14 years old) with 25 allergens. Positive reactions were seen in 13.3%. Multiple sensitivities were seen in 2% of the children. Dotterud et Falk (Dotterund & Falk, 1995) patch tested 424 Norwegian school children (7-12 years old) with 20 allergens. One or more positive reactions were seen in 23.3%. Multiple sensitivities were seen in 8.5% of the children. Weston et al. (Weston et al., 1986) patch tested 314 otherwise healthy American children and adolescents under the age of 18 years with 20 allergens. He found at least one positive patch reaction in 20%. In Bruckner et al. (Bruckner et al., 2000) population-based study of 95 healthy asymptomatic children aged 6 to 67.5 months was showed that the prevalence of sensitization was 24.5% (≥ 1 positive reaction to an allergen). In our group of Czech schoolchildren, positive reactions were detected in 30.7%. Multiple sensitivities were seen in 8.7%. The relevance of reactions was 61% (Machovcová, 2006).

2.3 Prevalence related to sex

Sex may also play a role on the different prevalence in children. While some authors (Weston et al., 1986; Barros et al., 1991; Stables et al., 1996) detected similar prevalence in both boys and girls, other (Dotterund & Falk, 1995; Wantke et al., 1996; Goossens & Morren, 2006) reported a higher prevalence in girls. This is especially the case for nickel (Brasch & Geier, 1997; Wöhrl et al., 2003) and after the age of 12 (Rademaker & Forsyth, 1989; Rudzki & Rebandel, 1996; Katsarou et al., 1996; Goossens & Morren, 2006). Brasch & Geier (Brasch & Geier, 1997) found significantly more girls than boys reacted to nickel (25.0% vs. 4.5%). Hormonal factors may be a contributory factor here (Brasch & Geier, 1997; Goossens & Morren, 2006).

2.4 Prevalence related to age

Sensitization to contact allergens begins in infancy and continues to be more common in toddlers and young children (Seidenari et al., 1992; Giordano-Labadie et al., 1999; Vozmediano & Hita, 2005; Militello et al., 2006; Clayton et al., 2006; Garg et al., 2009; De Waard-van der Spek & Oranje, 2009), the age of sensitization can occur very early. In study of Bruckner et al. (Bruckner et al., 2000), 45% of patients with positive reactions were younger than 18 months. Even neonates may be sensitized (Fisher, 1994a; Bruckner et al., 2000). Fisher (Fisher, 1994a) reported a 1-week-old infant with strongly positive patch test reaction to epoxy resin, manifesting as band-like dermatitis above the wrist because of vinyl band that was made of an epoxy resin. A 7-month-old child has revealed ACD from nickel–plated snaps on the back (Fisher, 1994a). Motolese et al. (Motolese et al., 1995) studied 53 infants (3 months to 2 years) with dermatitis and patch tested them. Positive patch tests were seen in 32 (60%) and 20 out of the 32 sensitized infants had clinically relevant contact allergies. Hjorth (Hjorth, 1981) thought that patch test reactions in infants were predominantly irritant reactions, especially when testing with nickel sulfate. In a study of Jøhnke et al. (Jøhnke et al., 2004) it was confirmed that increasing numbers of infants positively patch tested to nickel sulfate but most reactions were transient and probably irritant or non-specific nature. Experimental CA to plants of the *Rhus* genus has also been induced in infants, showing that sensitization is possible (Epstein, 1961). Manzini et al. (Manzini et al., 1998) reported that the highest sensitization rate was noted in children aged up to 3 years. It is still unclear why some sensitivities, for example nickel, are prevalent in the young but less common in the old. Possible explanations include changing trends in exposure to nickel (i.e. increased use of imitation jewellery and different frequencies of ear piercing in different generations) or loss of clinical allergy because of avoidance, induction of tolerance, or inability to mount an immune response despite continuing exposure (Garg et al., 2009). Recall studies showed persistence of CA to nickel after 8 years in 79% and 60% to other allergens (Nielsen et al., 2001; Garg et al., 2009). Others found that lanolin, only 41% had persistent allergy at 5 years (Carmichael et al., 1991). The increase in fragrance allergy with age may be because of cumulative exposure to toiletries and increased use of medicaments (Garg et al., 2009).

3. Contact sensitisation and atopic dermatitis

The relationship between CA and atopy is frequently discussed and still not settled (Rystedt, 1985; Schnuch et al., 2006). Several studies have been performed in children with suspected CA or suffering from AD or chronic dermatitis. Patch testing in symptomatic children with dermatitis has revealed positive reactions in 15% to 52% of subjects (Rademaker & Forsyth, 1989; De Groot, 1990; Katsarou et al., 1996; Rudzki & Rebandel, 1996; Stables et al., 1996; Shah et al., 1997; Vozmediano & Hita, 2005; Goossens & Morren, 2006; Wahlberg & Lindgerg, 2006). Some authors have indicated that ACD is less prevalent in patients with AD (Uhr, 1960; Rystedt, 1985; De Groot, 1990; Katsarou et al., 1996; Stables et al., 1996; Brasch & Geier, 1997). Several authors were unable to detect differences between atopic and nonatopic subjects in this regard (Marghescu, 1985; Pambor et al., 1991; Goossens et al., 1995; Akhavan & Cohen, 2003; Beattie et al., 2007; Milingou et al., 2010). Against this others have even found a greater prevalence of ACD in patients with AD (De la Cuadra et al., 1990; Lammintausta et al., 1992; Dotterund & Falk, 1995; Lugovic & Lipozencic, 1997; Giordano-Labadie et al., 1999; Clayton et al., 2006). A higher prevalence of CA in AD could

be explained by the alterations of the epidermal barrier and the greater permeability of irritated skin in AD that favours sensitization to ACD (Dotterund & Falk, 1995; Vozmediano & Hita, 2005). Moreover, patients with AD are chronically exposed to potentially more sensitizers because of the topical medications used for their skin (Giordano-Labadie et al., 1999; Vozmediano & Hita, 2005; Clayton et al., 2006). Also there exists a higher probability of false positive results in the patch tests conducted in patients with AD (Lammintausta et al., 1992; Mortz et al., 2001). Seguraro Rodriguez et al. (Segurado Rodriguez et al., 2004) found that a family history of AD (85%), female sex (74%) and age 11-16 (63%) were predisposing risk factors to sensitization. On the other hand, Giordano-Labadie et al. (Giordano-Labadie et al., 1999) systematically evaluated contact sensitization in a series of atopic pediatric patients. It was observed that 43% of the 114 children who patch tested had positive reactions without association with AD. From Vozmediano's (Vozmediano & Hita, 2005) point of view, AD did not affect the sensitization to the different allergens, although a higher number of irritative responses or false positives were frequently observed. Onder and Adisen reported only 0.3% of the patients having AD and positive patch test reactions in their study in a pediatric population in Turkey (Onder & Adisen, 2008).

4. Clinical presentation

The clinical characteristics of ACD are the same in children as in adults (Militello et al., 2006; Goossens & Morren, 2006). The classical clinical presentation of ACD is pruritic eczematous dermatitis. The location can be important for identification of the causal allergen since contact dermatitis is generally restricted to the contact site. Textile allergens usually cause dermatitis in areas in which the garment continually rubs against the skin, such as sub-axillary and/or flexural areas of the extremities. Cosmetic allergens tend to produce facial, neck or periorbital dermatitis. Shoe allergens often present on the dorsum of the feet (Goossens, 2001; Militello et al., 2006; Goossens & Morren, 2006). Spreading of the dermatitis, often in the form of small papules, may occur far from the original contact site and may be generalized. This can be explained by hematogenous dissemination of the allergens (Goossens, 2001) or by contact with allergenic or allergen-contaminated surfaces, transfer of an allergen via the hands to the face or other sites, which gives rise to an 'ectopic' contact dermatitis. CA can be caused also by products that have come in contact with the parents or other persons in the environment of the children ('connubial' or 'consort' dermatitis). The 'ectopic' or 'connubial' reactions are commonly involved the skin of the eyelids or neck. Additionally, distant or widespread eruptions (commonly referred to as 'Id' reactions) can often be triggered by localized ACD to such chemicals as nickel and poison ivy (Goossens, 2001; Militello et al., 2006; Goossens & Morren, 2006). Untreated reactions from highly potent allergens, such a poison ivy, can be severe and last for several weeks (Militello et al., 2006). Continued exposure even to low levels of allergen can perpetuate these skin eruptions indefinitely. Recognizing potential pediatric patients with ACD either as the primary diagnosis or the confounding factor is crucial. Often the findings are difficult to distinguish, clinically and histopathologically, from AD or irritant dermatitis (Goossens, 2001; Militello et al., 2006; Goossens & Morren, 2006).

5. Diagnosis and patch testing in children

Diagnosis rests on taking a substantial clinical history. Essential is an extensive and standardized anamnesis that covers all possible etiological factors like hobbies, leisure time

activities, use of topical pharmaceutical products and cosmetics and contact with plants (Goossens, 2001). The children and their parents can themselves provide many indications but often need to be convinced that the allergenic product may not have been introduced only recently into their environment. Indeed, it can take several days before the clinical symptoms and signs appear after the contact. The delay in reaction by 24-48 hours after allergen exposure can make difficulties to establish (Goossens, 2001). Children and their parents are not typically aware of this delay in reaction and often search for immediate associations. A detailed history of events during the week preceding the onset of symptoms is vital (Militello et al., 2006).

The gold standard for definitive diagnosis of ACD is epicutaneous patch testing (Militello et al., 2006; Goossens & Morren, 2006). Most authors agree that the patch testing in children is safe (Weston et al., 1989; Rademaker & Forsyth, 1989; Fisher, 1994b; Goossens & Morren, 2006), the only problems being mainly technical due to small patch test surface (Rademaker & Forsyth, 1989; Goossens & Morren, 2006), hypermobility, particularly in smaller children (Shah et al., 1997; Goossens & Morren, 2006). Patch testing involves the placement of a small amount of potential allergens under occlusion on the patient's back. These patches are typically removed after 48 hours and an initial reading is performed. A delayed reading at 72 and/or at 96 hours is recommended. Positive reactions are evaluated according to the criteria of the International Contact Dermatitis Research Group as – (negative), +- (doubtful) and +, ++, +++ (weak, moderate and strong reaction, respectively) depending on the grade of erythema, induration or blistering that occurs at the site of allergen placement (Wahlberg & Lindgerg, 2006). The patch test concentrations have been discussed in detail in the literature (Goossens & Morren, 2006). Some authors have recommended lower concentrations (Hjorth, 1981; Pambor et al., 1991), particularly with regard to specific allergens such as nickel and formaldehyde (Fisher, 1991), mercurials (Fisher, 1994b), potassium dichromate and thiuram mix (Fisher, 1994b). The others use the same test concentrations as those used in adults (Pevny et al., 1984a; Pevny et al., 1984b; Stables et al., 1996; Seidenari et al., 1992; Motolese et al., 1995; Worm et al., 2007).

Children should be tested strictly based on the indication using a standard protocol. A negative patch test result does not exclude contact dermatitis. False-negative reactions have various causes, often 'missed' allergen, which may be picked up by detailed questioning (Goossens, 2001; Goossens & Morren, 2006). For the skin tests, the possible risks of overlooking a CA are thus centred on the allergen itself, the test method, the test concentration and vehicle used, the time of reading and, finally, the relevance (Goossens, 2001).

6. Clinical relevance

Contact sensitization, however, does not necessarily equate with clinical diseases. Clinical relevance of allergic reactions on patch testing was determined according to the clinical history, type of dermatitis and the allergen concerned. Relevance of allergens should be determined for all patients with one or more positive reactions. Clinical relevance was confirmed if the allergen was found to be present in the patient's environment, the dermatitis corresponded to point(s) of contact with the allergen and the dermatitis significantly improved upon isolation of the allergen, or recurred with re-challenge (positive use test) (Jacob et al., 2008). Reported clinical relevance in children has been varied between 20% and 93% (Pevny et al., 1984b; Rademaker & Forsyth, 1989; Pambor et al., 1991; Stables, 1996; Mortz & Andersen, 1999).

7. The common allergens in children

Nickel is always the most common allergen in children, followed by cobalt, mercurials (thimerosal and metallic mercury), rubber chemicals (thiuram mix, carba mix, mercapto mix and mercaptobenzothiazole, PPD) and fragrance mix. The most frequent sources are costume jewellery (nickel in earrings), medications, footwear, cosmetics and plants (Rademaker & Forsyth, 1989; Barros et al., 1991; Stables et al., 1996; Militello et al., 2006; Goossens & Morren, 2006).

7.1 Nickel

Nickel is by far the most common allergen in patients of all ages, including children. Nickel was the top allergen in children in 14 of the 17 studies of patch testing summarized by Mortz and Andersen (Mortz & Andersen, 1999). Even in younger children nickel allergy is not uncommon (Jøhnke et al., 2004). Published rates of nickel sensitization in children range between 10% and 24% (Wöhrl et al., 2003; Heine et al., 2004; Lewis et al., 2004; Seidenari et al., 2005; Vozmediano & Hita, 2005; Clayton et al., 2006; Militello et al., 2006; Goossens & Morren, 2006; Milingou et al., 2010). Ear piercing along with atopy is regarded as a major risk factor for the development of nickel sensitization, especially in girls (Militello et al., 2006; Goossens & Morren, 2006). Nickel sensitization sources in children are numerous: jewellery (earrings), jean studs, belt buckles, zippers or buttons (Clayton et al., 2006). Sensitization to nickel is not necessarily followed by ACD, but infants with a reproducible positive reaction to nickel sulfate could represent a group at risk of developing clinically manifest nickel dermatitis later in life (Magnusson & Moller, 1979). In agreement with earlier studies in older children and adults (Dotterund & Falk, 1995; Mortz et al., 2001; Uter et al., 2004; Jøhnke et al., 2004), a female predominance of positive reactions to nickel sulfate was found in infants (girls 13.1% and boys 4.0%). Despite a marked decrease in nickel allergy and nickel dermatitis in young women after nickel regulation came into force (Schnuch & Uter, 2003; Thyssen et al., 2009; 2011), the prevalence of nickel allergy remains very high, and seems to have stabilized at a high level (Schnuch et al., 2011). However, women who were ear-pierced after regulatory intervention in Denmark had a significantly lower prevalence of nickel allergy and dermatitis than women who were ear-pierced before (Thyssen et al., 2009; 2011). It is important to emphasize that nickel allergy remains very prevalent in some European countries. The proportion of positive patch test reactions to nickel sulfate has remained stable at 10%-20% among young female German dermatitis patients (< 18 years) since the beginning of the new millennium (Schnuch et al., 2011). The 2005-2006 clinical patch test data registered in 10 European countries and reported to the European Surveillance System on Contact Allergies revealed high prevalence of nickel allergy in western, southern, central and north-eastern Europe, being, respectively, 20.8%, 24.5%, 19.7% and 22.4% (Uter et al., 2009). There may be several explanations for this finding (Thyssen et al., 2011), but it is generally accepted that excessive nickel release from consumer items is one of the most important single factors (Schnuch & Uter, 2003).

7.2 Thiomersal and metallic mercury

Sensitization to thiomersal (an organic mercurial compound) is frequently observed in infants and children. The widespread use as a preservative in a variety of compounds, including vaccine and antitoxin preparations, ophthalmic drops and contact lens solutions,

may explain the high rate of positive patch test reactions (Katsarou et al., 1996; Militello et al., 2006; Goossens & Morren, 2006; Milingou et al., 2010). Low clinical relevance along with sensitization rates is probably related to its presence in vaccines (Novák et al., 1986; Osawa et al., 1991; Lee et al., 2009). Recently, percentages of sensitization in children have increased from 2.3% (Barros et al., 1991) to 10% (Möller, 1997) due to iatrogenic sources (antiseptics, topical medications, thermometers and vaccines) and footwear (Novák et al., 1986; Osawa et al., 1991; Militello et al., 2006; Goossens & Morren, 2006; Lee et al., 2009).

7.3 Topical antibiotics

Neomycin, bacitracin and gentamycin are topical antibiotics with high rates of allergic contact sensitization in children (Heine et al., 2004; Seidenari et al., 2005; Jacob et al. 2008). Neomycin sulfate has remained second place in the most common culprits in ACD for close to 25 years (Spann et al., 2003; Lee et al., 2009). It is a topical antibiotic with multiple clinical indications, including use for superficial wounds or burns and can be found in many over-the-counter products in the US or Europe. It is also formulated in combinations with other antibiotics, antifungals or corticosteroids (Lee et al., 2009). Menezes de Pádua et al. (Menezes de Pádua et al., 2005) found 2.5% positive reactions to neomycin, while in 1.1%, ACD was additionally diagnosed.

7.4 Cosmetics allergens

The market for cosmetic products specially formulated for children is expanding and usage of cosmetics being seen to increase in children. Consequently, one can expect cosmetics to become more important causes of ACD in children (Goossens et al., 2002). At least one cosmetic or cosmetic ingredient gave a positive reaction in 30% of the children investigated (Goossens et al., 2002; Goossens & Morren, 2006). Almost every ingredient may be responsible for cosmetic dermatitis (Goossens et al., 2002; Goossens & Morren, 2006). Fisher (Fisher, 1995) further stated that children often become allergic to cosmetics used by the mother or the person taking care of them. The localizations often involved seem to be the forehead and the cheeks, with perfume, lipstick, hairspray or nail lacquer as the responsible agents (Fisher 1995; Goossens et al., 2002; Buckley et al., 2003; Goossens & Morren, 2006). However, children often use cosmetic products themselves and this may not always be revealed immediately (Goossens et al., 2002; Goossens & Morren, 2006).

7.4.1 Fragrances

The use of cosmetic products in babies and young children can cause perfume allergy (Fisher 1995; Goossens et al., 2002; Buckley et al., 2003; Goossens & Morren, 2006). A large numbers of perfumed products are marketed especially for children (Rastogi et al., 1999; Kohl et al., 2002). Fragrance allergy is increasingly common and even young children are exposed (Rastogi et al., 1999). Exposure is usually due to perfumes or to other aromatic topical products such as moisturizers or deodorants. Typical sites of involvement include face, neck and axillae, in addition to full systemic contact dermatitis (Tomar et al., 2005; Garg et al., 2009; Lee et al., 2009). Fragrance allergy is usually detected by patch testing to three mixtures of scented compounds: Fragrance Mix I, Fragrance Mix II and *Myroxylon pereirae* tree extract *(*Balsam of Peru). The rate of sensitization to fragrance appears to increase with age (Buckley et al., 2003; Lee et al., 2009). The *Myroxylon pereirae* tree extract

(Balsam of Peru) is used as a screen for fragrance allergy, due to its wide usage and natural cross-reactivity with other frequently encountered fragrances (Tomar et al., 2005; Garg et al., 2009; Lee et al., 2009). These allergens (or chemically similar ones) are also used in soft drinks and flavouring such as cinnamon, cloves, curry and vanilla. Although dietary intervention remains controversial, there is evidence that it may help those with significant disease that is not resolving with more typical fragrance avoidance (Magnusson & Wilkinson, 1975; Salam & Fowler Jr., 2001; Tomar et al., 2005). Although guidelines for the maximum concentration of preservatives and fragrances in cosmetics have been provided (Goossens et al., 2004), it has been demonstrated that toys may contain much higher concentrations of fragrance (Rastogi et al., 1999). No extra safety requirements for toys intended for children are required (White, 2000).

7.4.2 Preservatives

Conti et al. (Conti et al., 1997) reviewed contact sensitization to 8 preservatives (imiadazolidinyl urea, diazolidinyl urea, parabens, formaldehyde, quaternium-15, Katon CG, Euxyl K400 and butylated hydroxyanizole) in the child population and found 7.3% of the children reacted positively. Almost 50% of preservative-sensitive children had AD. Baby toilet tissues have been occasionally reported to cause CA in babies and those who take care of them. The allergens considered most often are fragrances and preservatives. Methylchloroisothiazolinone and methylisothiazolinone (MCI/MI) is widely used as a preservative in many products (De Groot & Herxheimer, 1989). Tosti et al. (Tosti et al., 2003) found MCI/MI to be a frequent cause of ACD, i.e. in 7 of 95 children between 3 and 11 years old were positive to MCI/MI. The use of moist toilet papers (baby wipes) can be responsible for ACD, especially of perianal area (De Groot et al., 1991). MCI/MI was replaced from them by other preservatives, particularly with Euxyl K400 (methydibromoglutaronitrile and phenoxyethanol) (Senff et al., 1989) and 1,2-dibromo-2,4-dicyanobutane (Van Ginkel & Rutdervoort, 1995).

7.4.3 Sorbitan sesquioleate

De Waard-van der Spek and Oranje (De Waard-van der Spek & Oranje, 2009) found 3 children patch tested positive to sorbitan sesquioleate (SSO), all clinically relevant. Two children used emollient contained SSO as emulsifier. They also reported a child positive patch tested to Adaptic non-adhering dressing containing SSO. Castanedo-Tardan and Jacob (Castanedo-Tardan & Jacob, 2008) reported the case series of 6 pediatric patients with clinically relevant contact allergy to SSO. 5 children were atopics and suffered with recalcitrant dermatitis.

7.5 *Para*-Phenylenediamine and tattoos

An increased prevalence of *para*-Phenylenediamine (PPD) allergy has been noted in the pediatric population. Eczematous reactions are mostly seen at the site of the tattoo and they may be long-lasting (Lewis et al., 2004). Henna dye is a dark green powder, used for hair dyeing and body tattooing. Henna itself is relatively safe. However, PPD is added on an illegal basis in semi-permanent tattoos (black henna tattoos), in order to obtain a darker colour and a faster drying time than natural henna can provide. Although many parents and consumers believe these black henna tattoos to be temporary, adverse events to them

(scaring and sensitization) can be permanent. PPD is a very potent contact sensitizer included in the European baseline series for patch testing. PPD is also contained in permanent hair dyes and related compounds (Lee et al., 2009). The content of PPD in semi-permanent tattoo ink has been reported to vary between 0.4 and 15.7%, far exceeding the limit permissible for hair dyes (<6%) (Brancaccio et al., 2002; Avnstorp et al., 2002; Sosted et al., 2006; Lee et al., 2009). The long duration of skin contact, the high concentrations of sensitizing materials (diaminobenzenes or diaminotoluenes) and the lack of a neutralizing agent increase the risk of skin sensitization. Because of the worldwide vogue for skin painting, a greater number of patients sensitized to PPD and diaminobenzenes or diaminotoluenes can be expected (Le Coz et al., 2000; Onder et al., 2001; Neri et al., 2002; Jovanovic & Slavkovic-Jovanovic, 2009). The unusually severe reactions to PPD in young 12 to 15 year old adolescents have occurred after dyeing their hair having been previously sensitized to PPD in black henna tattoo at a younger age. In some cases, the children developed severe angioedema-like reactions necessitating admission to hospital and intensive care treatment (Sosted et al., 2006). Severe allergic reactions were reported in 1.4% of women and 1.3% of men after dying their hair (Sosted et al., 2005). Sensitization to PPD is potential for lifelong sensitization and systemic contact dermatitis can be evoked with exposure to cross-reactors such as benzocaine, diuretics (hydrochlorothiazide) and sulfonamide medications (Sosted et al., 2006; Lee et al., 2009). Notably, 25% of those allergic to PPD can also be reactive to semi-permanent dyes found in synthetic clothing. PPD base, being a part of the European baseline series, is regarded as a screening agent for contact allergy to *para* and azo compounds in hair dyes, but not for textile and leather dye allergy (Koopmans & Bruynzeel, 2003).

7.6 Rubber compounds

Rubber additives are typically present in many rubber products (e.g. elastic waistbands, socks, swimwear, shoes, toys, cosmetic applicators and adhesives) and could be main allergens from them. Thiurams, mercapto chemicals and less commonly carbamates are the responsible allergens in rubber allergy in children; thiourea derivates in neoprene may also be the cause of dermatitis (Goossens & Morren, 2006; Lee et al., 2009). Roul et al. (Roul et al., 1998) reported a particular type of diaper dermatitis called 'Lucky Luke' dermatitis. The rubber parts used for a new anti-leaking system in these diapers provoked the reaction. Mercaptobenzothiazole and thiuram derivates are also present in certain types of glues (Roul et al., 1996; Cockayne et al., 1998). Type I allergic reactions may also occur (contact urticaria syndrome), sometimes associated with a type IV reaction. It is typical for children who had undergone multiple surgical operations (for example children suffering from spina bifida). Moreover, these children are particularly susceptible to natural rubber latex proteins in this regard (Goossens & Morren, 2006).

7.7 Toxicodendron dermatitis (Poison Ivy, Poison Oak, Poison Sumac)

Toxicodendron (Poison Ivy) dermatitis can occur at any age, although infants are apparently not as easily sensitized as adults. After the age of 3, children become highly susceptible and by 12 years of age nearly all have become sensitized to poison ivy (Kligman 1974). Plants belonging to the Rhus family are the ones most often involved in ACD among children living in the United States (Goossens & Morren, 2006). The oleoresin (urushiol) of the sap of the *Toxicodendron* plants contains catechols, which are very strong sensitizing chemicals. The

eruption produced by poison ivy is characterized by redness, papules, vesicles and bullae plus linear streaking. Occasionally, urticaria and eruptions, resembling erythema multiforme, measles or scarlatina, occur from systemic absorption of the poison ivy antigen (Rietschel & Fowler Jr., 2008b). Exposure can be direct or indirect, such as transfers of the allergen via animals, tools, clothing, golf clubs, etc. (Goossens & Morren, 2006; Rietschel & Fowler Jr., 2008b), which is more difficult to diagnose (Epstein 1971). A few cases of phytophotodermatitis from *Toxicodendron* in children were also reported (Goossens & Morren, 2006).

8. Treatment

The cornerstone of treatment of ACD is proper allergen avoidance. Once an allergen is identified, patients must be educated on potential exposures, cross-reacting chemicals, preventive measures, as well as offered suggestions for avoidance. This may be especially difficult in households with small children affected, as the products that are used by the patents and sibling may also need to be considered as sources for allergen exposures.

Emollients can be added after a bath in an effort to retain hydration and restore the barrier function of the skin. Barrier repair also decreases pruritus and reduces visible scaling and dryness. Physical barrier creams may be useful in cases in which the allergen exposure cannot be avoided. Patients should apply the creams before and during the exposure in an effort to decrease absorption (Lee et al., 2009).

Topical corticosteroids are the first-line treatment modality for mild cases of ACD but they are not without risk and can cause multiple cutaneous side effects with extensive and long term use (Militello et al., 2006; Goossens & Morren, 2006; Jacob & Castanedo-Tardan, 2007; Lee et al., 2009). When selecting a topical corticosteroid for treatment, it is important to choose one that the patient is not allergic to in terms of the active ingredient (the steroid component) and inactive ingredients in the vehicle (Lee et al., 2009). As with any topical steroid, the risk of atrophy, teleangiectasias, tachyphylaxis and systemic absorption should be kept in mind, especially in areas of increased sensitivity such as face, groin and flexural area (Militello et al., 2006).

Topical calcineurin inhibitors (TCIs) are another therapeutic option and should be considered when steroid-sparing agents are required. These agents can be used for certain areas, such as the face, axilla and groin, which are more susceptible to steroid-induced atrophy (Lee et al., 2009).

In cases of widespread and severe reactions, Militello et al. (Militello et al., 2006) recommended at least 3 weeks of oral prednisone in combination with topical therapy. Shorter courses often lead to rebound flares of the dermatitis. Systemic corticosteroids are generally started at 1 mg/kg per day (Brasch, 2009). Oral H1-antihistamines are widely used as an adjuvant nonspecific treatment for pruritus in infants and children. They also cause drowsiness that may help with sleeping disturbances from pruritus (Militello et al., 2006; Lee et al., 2009).

9. Conclusions

ACD in infancy is more frequent than was initially suggested, although its true prevalence and incidence continue to be unknown. Age and sex influence its development, but the

principal factor associated with ACD is the pattern of exposure to the various allergens (Vozmediano & Hita, 2005). In the unselected population, the prevalence of CA is about 20% (Mortz & Andersen, 1999; Weston & Weston, 1984; Barros et al., 1991), while in the selected population, the prevalence of ACD is found to be variable, with a mean of 40% (Mortz & Andersen, 1999; Wöhrl et al., 2003; Heine et al., 2004; Lewis et al., 2004; Seidenari et al., 2005; Vozmediano & Hita, 2005; Militello et al., 2006; Goossens & Morren, 2006; Jacob et al., 2008). The susceptibility to contact sensitization increases with the age. The most important allergens observed in this population are metals, mercury, pharmaceutical products and cosmetics (Vozmediano & Hita, 2005; Militello et al., 2006; Goossens & Morren, 2006; Jacob et al., 2008). ACD in childhood may also affect decisions regarding future occupations in adulthood. Therefore, it is very important that any CA in a child is recognized and dealt with in time. The impact of CA must not be underestimated, both on a complex individual scale of quality of life and socio-economically, for example, due to job options (Uter et al., 2004). Patch testing is both well tolerated and diagnostically essential in the evaluation of pediatric patients with potential ACD. Once allergen is documented, treatment relies on symptomatic use of topical or oral corticosteroids and meticulous allergen avoidance (Militello et al., 2006). Good information on preventing the development of ACD in children is useful for the caregivers.

10. Acknowledgment

Many thanks to Mrs. Susan Harley and Mr. Christopher J. Garlick for their linguistic assistance.

The project was supported by grants MZOFNM 2005/6904

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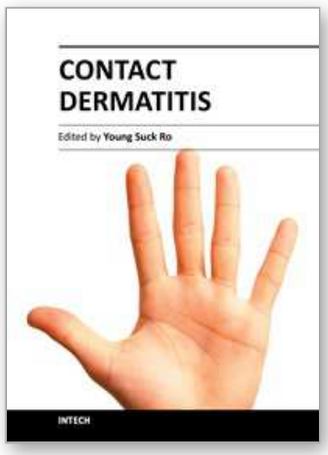

Contact Dermatitis

Edited by Dr. Young Suck Ro

ISBN 978-953-307-577-8
Hard cover, 180 pages
Publisher InTech
Published online 16, December, 2011
Published in print edition December, 2011

This book centralizes on the subject of contact dermatitis. It aims to provide the dermatologist with a sound base of clinical wisdom and key scientific findings to make an accurate diagnosis and management plan. SPECIAL FEATURES: - Describes numerous possible allergens that cause contact dermatitis. - Provides details of research in the basic sciences to help our readers understand more about contact dermatitis. - Provides a comprehensive description of recently developed methods that have evolved for the diagnosis of contact dermatitis. - Provides a concise, clinically focused, user-friendly format, which can rapidly improve your knowledge of the disease. The past decade has seen significant changes in contact dermatitis. Our understanding of the pathophysiology, our diagnostic approaches, and management of the disease has evolved. In this volume, some of the world's most highly regarded experts discuss areas that have seen significant improvement, as well as areas for future development.

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