XXII World Allergy Congress

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Contact dermatitis in Children New Contact Allergens

Luz Fonacier, MD

Section Head of Allergy

Training Program Director in Allergy & Immunology

Winthrop University Hospital

Professor of Clinical Medicine

SUNY at Stony Brook

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Objectives:

1. Recognize important contact allergens in children
2. Recognize emerging contact allergens in children

WINTHROP University Hospital
Long Island, New York

Genetics of Nickel Contact Dermatitis

- **Two filaggrin mutations were screened in a European cross-sectional population that underwent PT with a standard panel of 25 allergens**
- **Results suggest that the filaggrin loss of function mutations represent a risk factor for contact sensitization to nickel, especially in combination with a history of adverse reactions to jewelry**
- **No association with sensitization to other common allergens was seen**

Novak N, Baurecht H, Schafer T, et al. Loss-of-function mutations in the filaggrin gene and allergic contact sensitization to nickel. J Invest Dermatol 2008;128(6): 1430–5.

Contact Dermatitis & Patch Testing in Children

- 53 children (3 mos-2 years) with eczematous dermatitis
- 60% had a (+)patch test
  - Relevant allergens in children are similar to adults
- Increasing rate of sensitization might be due to new trends
  - Body piercing
  - Tattooing
  - Cosmetic products
- Adolescents constitute a significant portion of the population allergic to nickel
  - Kutting et al recommend that ear piercing be delayed until after10 years of age
- Face, hands and feet were the most common sites involved in ACD in children at AIIMS, New Delhi.**

Fonacier L, Dreskin S, Leung DL. “Allergic Skin Diseases”. 2010 Primer on Allergic and Immunologic Diseases , 6th Edition. The Journal of Allergy and Clinical Immunology. Volume 125, Issue 2, Supplement 2 (February 2010) S 138-149

Motolese et al.Patch testing in infants. AJCD; 6:3 153-159, 1995

Sharma V, AsatinD. Pediatric contact dermatitis. Sy mposium Pediatric Dermatoses 2010. Vol 76 : 514-520.

Kutting B, Brehler R, Traupe H. Allergic contact dermatitis in children: strategies of prevention and risk management. Eur J Dermatol 2004;14:80-5.

Contact Dermatitis in Children

- **Poison ivy, oak, sumac**
- Nickel: Most common allergen along with other metals
- Thimerosal probably due to immunizations
- Fragrance
  - Balsam of Peru
- Rubber chemicals
  - Mercaptobenzothiazole
- Preservatives

Veien et al. Contact Dermatitis in Children. Contact Dermatitis 1982;8:373
Motolese et al.Patch testing in infants. AJCD; 6:3 153-159, 1995

Role of Atopy in Contact Dermatitis

- **Atopic dermatitis is associated with a higher rate of irritant contact allergy due to disturbed barrier function**
- **However, the rate of (+) PT in atopics & non-atopics was similar or even lower than that in non-atopics**
- **Atopic eczema may be an important risk factor for the development of ACD in children rather than in adults**
  - **In the study by the NACDG, of those with a (+) PT, children (34.0%) were more likely than adults (11.2%) to have a final diagnosis that included atopic eczema**
- **ACD to nickel and Kathon CG was more frequent in atopic children***

Seidenari S,Giusti F, Pepe P, Mantovani L. Contact sensitization in 1094 children undergoing patch testing over a 7-year period. Pediatr Dermatol 2005;22:1-5.

COMMON AREAS OF INVOLVEMENT IN CD AND AD

- **Eyelid**
  - **ACD (55%–63.5%)**
  - **AD accounts for less than 10%,**
- **Lips**
  - **NACDG with allergic cheilitis, 37% had at least 1 of the atopic triad**
- **Hands**
  - **The prevalence of hand eczema is two- to tenfold higher in patients with AD**
- **Flexural areas of the neck**
- **Dermatitis with Scattered Generalized Distribution**

Correlation of sites of dermatitis and sensitizers in children

- **Nickel remains most frequent cause at any regional site**
- **Facial dermatitis: propolis * Nickel , fragrance mix ****
- **Neck : Kathon CG***
- **Feet : potassium dichromate ***
- **Flexural areas of the limbs: nickel, Kathon CG ***
- **Hands: nickel, cobalt, potassium dichromate, thiuram mix, PPD, vehicles ****
- **Feet: mercapto mix, mercaptobenzothiazole (MBT), PPD ****
- **Eyelids: nickel, fragrance mix, amerchol, sorbitan sesquioleate, balsam of Peru**
- **Hands & feet: nickel, chromate, cobalt*****

*Seidenari S,Giusti F, Pepe P, Mantovani L. Contact sensitization in 1094 children undergoing patch testing over a 7-year period. Pediatr Dermatol 2005;22:1-5.
**Beattie PE, Green C, Lowe G, Lewis-Jones MS. Which children should we patch test? Clin Exp Dermatol 2006;32:6-11.
SYMPOSIUM –
*** Unpublished data

SPECIFIC CONTACT ALLERGENS IN AD

- **Medicinal-induced ACD in subjects with AD***
  - **Emollients (most common)**
  - **Topical Antibiotics/Antiseptics**
  - **Topical Corticosteroids**
  - **Related risk factors were the severe disease, an early onset (at an age of <6 months), presence of IgE-mediated sensitization**
- **Compositae***
  - **Herbal medicaments and cosmetics**
  - **Higher prevalence of (+) PT to compositae in children, therefore CD to compositae should be suspected in patients with a personal or family history of atopy, & dermatitis exacerbated in summer with plant exposure**

* Mailhol C, Lauwers-Cances V, Rancé F, Paul C, Giordano-Labadie F. Prevalence and risk factors for allergic contact dermatitis to topical treatment in atopic dermatitis: a study in 641 children. Allergy. 2009;64:801–6. doi: 10.1111/j.1398-9995.2008.01890.x

****Paulsen E, Otkjaer A, Andersen KE. Sesquiterpene lactone dermatitis in the young: is atopy a risk factor? Contact Dermatitis 2008;59(1):1–6.**

Nappy Rash

- **Most common form of ICD in early infancy**
  - **Predisposing Factors**
    - **Dampness and maceration of the covered area**
    - **Prolonged contact with organic liquids**
    - **Increased microorganisms**
      - Ammonia from bacteria , *Candida albicans*
- **Allergic Contact Dermatitis**
  - **Deodorants, preservatives in diapers**
  - **Creams and oils applied many times a day**
  - **"Lucky Luke dermatitis" due to the use of derivates of the rubber (mercaptobenzothiazole) and glues (*p*-terbutylphenolformaldehyde resin) used in the manufacture of some types of nappies**

Roul S, Ducombs G, Leaute-Labreze C, Taïeb A. 'Lucky Luke' contact dermatitis due to rubber components of diapers. Contact Dermatitis. 1998;38:363–4. doi: 10.1111/j.1600-0536.1998.tb05796.x

Nickel

Why is nickel the allergen of 2008

- **Rising incidence of nickel allergy in the US**
  - **NACDG 1985-1990: 10.5%**

    2003-2004: 18%
- **High nickel sensitization documented in children**
- **Resurgent issue of biomedical device complications due to metal (specially nickel)**

Kornik R and Zug K. Dermatitis 2008;19(1):3-8

"Does sensitization begin in infancy?"

- In asymptomatic children, nickel was the most common (+) allergen
  - 12.9% of children aged 6.0 - 67.5 months were (+) to nickel
- Children < 16 months accounted for 7 of 11 (+) results to nickel (? Irritant vs allergic)

Where does this well-documented epidemiology of nickel sensitization lead us?

Kütting et al recommend that ear piercing be delayed until after 10 years of age (presumably to allow for the development of immune tolerance)

Bruckner AL, Weston WL, Morelli JG. Does sensitization to contact allergens begin in infancy? Pediatrics 2000;105:e3
Kütting B, Brehler R, Traupe H. Allergic contact dermatitis in children: strategies of prevention and risk management Eur J Dermatol 2004;14:80–5 Kütting B, Brehler R, Traupe H. Allergic contact dermatitis in children: strategies of prevention and risk management Eur J Dermatol 2004;14:80–5

METAL IMPLANT "ALLERGY"
Often suspected but rarely documented

Orthodontics

- 10% of population are nickel allergic
- Pre orthodontic testing for metal allergy is not routine
- In patients with contact allergy to orthodontics, nickel is the most common allergen
- Flexible titanium-nickel arch wires are thought to release increased amounts of nickel compared to stainless steel
  - one article recommends avoiding them in nickel sensitive patients

Kornik R and Zug K. Dermatitis2008;19(1):3-8
Rahilly G, Price N. Nickel allergy and orthodontics J Orthod 2003;30:171–4

Hair Products
P-phenylenediamine (PPD)
Contact Allergen of 2006

Body painting & temporary tattooing (lasts until stratum corneum is shed)

Cosmetics

- Facial cosmetic dermatitis
  - Bilateral
  - Patchy
- Eyelid
- Neck
  - “run-off” pattern
  - Cosmtics applied to face, scalp or hair often initially affect the neck
  - Most afftected site of ACVD from nail varnish is the neck
- Lips

Consort/Connubial Dermatitis: primarily fragrance

Dermatitis of the Eyelid

- Allergic contact dermatitis: 55-63.5%
  (*as high as 72% if eyelid alone)
- Irritant contact dermatitis: 15%
- Atopic dermatitis: < 10%
- Seborrheic dermatitis: 4%

Fonacier L, Dreskin S, Leung DL. “Allergic Skin Diseases”. 2010 Primer on Allergic and Immunologic Diseases , 6th Edition. The Journal of Allergy and Clinical Immunology. Volume 125, Issue 2, Supplement 2 (February 2010) S 138-149

Reitschel RL et al. Common contact allergens associated with Eyelid dermatitis: data from the NACDG 2003-2004 study period. Dermatitis 2007; 18:78-81

*Valsecchi et al. Eyelid Dermatitis: an evaluation of 150 patients. Contact Dermatitis.1992;27:143-7

Lip dermatitis (Cheilitis)

- **Most common differential diagnoses**
  - **Atopic dermatitis**
  - **ACD**
    - **Most relevant allergens**
      - Fragrance mix
      - Myroxilon pereirae
      - Nickel
  - **Irritant Cheilitis**
    - **May occur concomitantly with atopic dermatitis**
    - **Lip Licking**
    - **During dentition as a result of excessive saliva production**

Lip dermatitis (Cheilitis)

- Not uncommon to have more than one factor contributing to cheilitis (atopy & allergy, or ACD & ICD)
  - >1/3 of patients with ACC had another contributing condition
- Cheilitis history should include a review of atopy, lip licking, cosmetics (especially lipsticks, balms, glosses), moisturizers, sunscreens, jewelry, recent dental procedures, dental appliances, amalgams, oral hygiene products (such as toothpastes, mouthwashes, and gums), musical instruments, foods, spices
- Identification of clinically relevant positive allergens is higher in the overall patch-tested population (50.7%, n = 5,096) than in lip-only subgroup
- PT with a broader selection of supplementary allergens, including the patients' own products (especially lip products) and food and oral hygiene products, is critical to identifying relevant allergens

Emergent and Unusual Allergens in Cosmetics

- **Nail lacquer**
  - Ectopic dermatitis of the eyelids, face, or neck
    - other areas: trunk and genitals
  - Most common allergen: tosylamide formaldehyde resin
    - Resin emits allergenic water-soluble monomers & dimers even when polymerized and solid
  - Additional allergens:
    - Formaldehyde, ethylene dichloride, phthalates, guanine, methyl methacrylate, epoxy resin, nitrocellulose, polyester resin, amyl acetate, butyl acetate
- **Lipstick**
  - Various D&C dyes & inorganic pigments (titanium dioxide, D&C yellow 11 and D&C red 7 (allergic cheilitis) & Eosin
  - Oily base: Castor oil (ricinus oil): suspends pigment
  - Additives (ie. emollients), antioxidants (ie gallates), sunscreens
- **Shellac** (lacca or gomme-laque)
  - pump or aerosol hair sprays, shampoos, eyeliners, mascaras, nail lacquers, lipsticks
  - In most cases, reaction persisted for some time after the withdrawal of the offending agent

Pascoe D et al. Dermatitis 2010 Vol 21 No 3:127-137

Emergent and Unusual Allergens in Cosmetics

Lipstick

- Composition:
  - wax: hold the shape of the lipstick and ease of application
    - beeswax, carnauba wax, or candelilla wax
  - Various D&C dyes & inorganic pigments
    - Titanium dioxide
    - D&C yellow 11 and D&C red 7 (allergic cheilitis)
    - Eosin: notorious allergen, now rarely used
  - Oily base: suspend the pigment.
    - Castor oil (ricinus oil): important base in lipstick production.
  - Additives (ie. emollients), antioxidants (ie gallates), sunscreens

Pascoe D et al. Emergent and Unusual Allergens in Cosmetics **Dermatitis Vol 21 No 3 2010 127-137**

Emergent and Unusual Allergens in Cosmetics

Shellac (lacca or gomme-laque)

- Secreted by female insect Laccifer (Tachardia) lacca
- Viscous gummy resin hardens to form a substance called lac used as protective shell for the insect's larvae
- For human uses, lac is crushed, washed, dried, chemically refined, then drawn into thick sheets called shellac
- Found in pump or aerosol hair sprays, shampoos, eyeliners, mascaras, nail lacquers, and lipsticks
- Recommended patch-test concentration: 20% in ethyl alcohol
- In most cases, reaction persisted for some time after the withdrawal of the offending agent

Pascoe D et al. Emergent and Unusual Allergens in Cosmetics **Dermatitis Vol 21 No 3 2010 127-137**

Emergent and Unusual Allergens in Cosmetics

Octocrylene

- Chemical sunscreens have ironically become the most frequent photoallergens and contact allergens
- Children tend to develop acute ACD, whereas adults are more prone to Photocontact Dermatitis
- Most common allergens:
  - benzophenone-3 (oxybenzone), isopropyl methoxy dibenzoylmethane, and butyl methoxy dibenzoylmethane (avobenzone).
- Octocrylene (2-ethylhexyl-2- cyano-3,3-diphenylacrylate) is an ultraviolet B–filtering cinnamate increasingly used the past 10 years

Pascoe D et al. Emergent and Unusual Allergens in Cosmetics **Dermatitis Vol 21 No 3 2010 127-137**

Emergent and Unusual Allergens in Cosmetics

Conclusion

- Allergic contact dermatitis from cosmetics is a common problem, and the formulation of cosmetic products is constantly changing
- Several classes of allergens (in nail lacquers, lipsticks, and other products) that we suspect will continue to increase in importance in the coming years
- Constant vigilance and continued cooperation from the cosmetic industry are necessary to respond to these and future allergens as they emerge.

Pascoe D et al. Emergent and Unusual Allergens in Cosmetics **Dermatitis Vol 21 No 3 2010 127-137**

Lanolin

- Rate of lanolin allergy has significantly declined over the last two decades, from 3.7% in 1994 to 1996 to 1.8% in 2005 to 2006 ($p < .0001$)
- Cosmetics & topical medications were the most common sources
- Male sex, atopic dermatitis, and co-reactivity to other allergens were statistically higher in lanolin-positive patients than in allergic, but lanolin-negative, patients
- Current clinical relevance was high (83.4%) whereas occupational relevance was very low (2.5%).

Erin M. Warshaw et al. Positive Patch Test Reactions to Lanolin: Cross-Sectional Data from the North American Contact Dermatitis Group, 1994 to 2006. Dermatitis. April 2009. 20;2:79-88

Lanolin Exposure

- Personal care products & toiletries clothing, and industrial sources. moisturizers, lipsticks, shampoos, and soaps
- Ointment bases for topical medicaments such as antibiotics, corticosteroids, and analgesics
- In fact, few makeup products contain lanolin, whereas it is a relatively common component of moisturizers and creams

Erin M. Warshaw et al. Positive Patch Test Reactions to Lanolin: Cross-Sectional Data from the North American Contact Dermatitis Group, 1994 to 2006. Dermatitis. April 2009. 20;2:79-88

Cigarettes

- **Underreported & under recognized cause of ACD**
  - **~46 million smokers in the US**
  - **Nearly 3000 teens take up the habit of smoking cigarettes every day in the U.S. alone**
- **Patch Testing is recommended in smokers with dermatitis involving hands, face, & neck**

Zoey R. et al. Allergic Contact Dermatitis from Cigarettes. Dermatitis. 2009;20:6–13
Jones K, Garfitt SJ, Calverley A, Channa K. Identification of a possible biomarker for colophony exposure. Occup Med 2001;51: 507–9.
Watsky KL. Airborne allergic contact dermatitis from pine dust. Am J Contact Dermat 1997;8:118–20. Kato A, Shoji A, Aoki N. Contact sensitivity to cigarettes. Contact Dermatitis 2005;53:52–3
Sasaya N, Oiso N, Shigeru K, Kawada A. Airborne contact dermatitis from cigarettes. Contact Dermatitis 2007;56:173–4
Dawn G, Fleming CJ, Forsyth A. Contact sensitivity to cigarettes and matches. Contact Dermatitis 1999;40:236–8

WINTHROP University Hospital
Long Island, New York

Cigarettes

- **Potential source of allergens from cigarettes :**
  - **Filters**
  - **Paper**
  - **Tobacco**
  - **Flavoring**
- **Allergens:**
  - **Cocoa**
  - **Menthol**
  - **Licorice**
  - **Colophony: heat activated allergen released from cigarette paper & filters**
    - **associated with airborne ACD**
    - **can cause asthma**
  - **Formaldehyde**

Cigarettes

- Non-occupational ACD from cigarettes
  - dermatitis on 2nd & 3rd digits of hand
  - erythema, edema, and scaling on lips
  - vesicular dermatitis on his first, second, and third digits as well as on his lower lip

Zoey R. et al. Allergic Contact Dermatitis from Cigarettes. Dermatitis. 2009;20:6–13
Rycroft RJG. Tobacco dermatitis. Br J Dermatol 1980;103:225–8.

Formaldehyde in Cigarette Smoke

- Formaldehyde in vapor phase in cigarette smoke in a concentration of 2.5 to 11 mg per puff and 70 to 100 mg in mainstream smoke (the smoke exhaled from an individual's mouth)
- Amount is thought to be ciliatoxic and most likely carcinogenic
- Consistent contact with formaldehyde in cigarette smoke could potentiate the development of contact dermatitis from formaldehyde

Hoffman D, Hoffman I. Chemistry and toxicology. In: Burns DM, editor. Smoking and tobacco control monograph no. 9. Silver Spring: KMB Group, Inc ; 1998. p. 55–104.
Ezughah FI, Murdoch SR, Finch TM. Occupational airborne allergic contact dermatitis from medium-density fibreboard containing phenol-formaldehyde resin-2 (PFR-2). Contact Dermatitis 2001;45: 242.
Finch TM, Prais L, Foulds IS. Allergic contact dermatitis to medium-density fibreboard containing melamine-formaldehyde resin. Contact Dermatitis 1999;41:291.

Patch-Testing with Cigarettes

- Vary with brand
- Smoked or unsmoked
- individual components (i.e., unsmoked tobacco, smoked tobacco, filters, and paper)
- Kato and colleagues:
  - (as is): unsmoked tobacco, smoked tobacco, unsmoked filter, smoked filter, unsmoked paper, birch tar, pine tar and coal tar (all tars were prepared in 3% petroleum), nicotine (prepared in 4% purified water and petroleum), cosmetics used by the patient, chocolate, cinnamon, the Japanese standard series, and the fragrance series.6
- Sasaya and colleagues: six brands of cigarettes the patient smoked
  - (i.e., with the unsmoked tobacco, unsmoked filters, and unsmoked papers), nicotine (in 4% purified water), purified water, and petroleum.7
- Dawn and colleagues: ‘‘smokers’ series’’
  - made up of phosphorous sesquisulfide (a component of matches that allows them to ignite from friction) 1% pet and (as is): ‘‘strike-anywhere’’ match heads, unsmoked filters, cigarette paper, smoked tobacco (i.e., ‘‘partially combustible remnants of tobacco from filter end of cigarette’’), cigarette ash (burned remnants of the cigarette no longer connected to the filter end), unsmoked tobacco, and smoked filters.2

Kato A, Shoji A, Aoki N. Contact sensitivity to cigarettes. Contact Dermatitis 2005;53:52–3.
Sasaya N, Oiso N, Shigeru K, Kawada A. Airborne contact dermatitis from cigarettes. Contact Dermatitis 2007;56:173–4.

What's New with Contact Dermatitis in Children?

- Unlike Europe, there appears to be an increasing incidence of allergic sensitization to nickel in North America
  - Old sources such as metal buttons on jeans
  - New sources of nickel ACD such as cell phones
- New insight was offered into the possible genetics of nickel contact allergy
- Shellac has been reported in North America as being a possible cause of ACD to mascara
- Cigarettes are not only ciliatoxic and carcinogenic but can cause ACD
- Old allergens learn new tricks while new allergens emerge to challenge our quest for a definitive diagnosis.

In conclusion

- **Contact dermatitis is underestimated in children**
- **Patch testing even in children can help identify allergens and may lead to early resolution of ACD**
- **The collaboration between pediatrician, allergist and dermatologist is strongly needed not only for diagnosis but also for monitoring new environmental substances that, with increasing frequency, are used in the childhood**

Thank You

WINTHROP
University Hospital
Long Island, New York