

## **Contact Dermatitis Updates**

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#### Disclosures

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Consultant and Speaker for National Eczema Association



## Learning Objectives

- 1. Discuss updates from the North American Contact Dermatitis Group
- 2. Patch testing on novel atopic dermatitis biologics?
- 3. Highlight the 5 most recent allergens of the year and how they may be relevant to your patients



## Part 1

# Updates from the North American Contact Dermatitis Group

## North American Contact Dermatitis Group (NACDG) Data

#### TABLE 3. Strength of Reactions/Clinical Relev

Substance	N	% Positive
Nickel sulfate hexahydrate 2.5% pet.	4107	18.2
Methylisothiazolinone 0.2% aq. (2000 ppm)	4112	13.8
Fragrance mix I 8.0% pet.	4113	12.8
Hydroperoxides of linalool 1% pet.	4087	11.1
Benzisothiazolinone 0.1% pet.	4113	10.4
Methylchloroisothiazolinone/ methylisothiazolinone 0.02% aq.	4113	9.0
Propolis 10.0% pet.	4112	8.6
Myroxylon pereirae resin (balsam of Peru) 25.0% pet.	4113	7.4
Cobalt (II) chloride hexahydrate 1.0% pet.	4118	7.3
Formaldehyde 2.0% aq.	4111	6.8

4121 patients were tested between 2019-2020 at 13 centers

- Tested to 80 standardized allergens
- 51.2% of patients with final diagnosis of ACD

#### Allergic Contact Dermatitis in Children

2001-2018 NACDG patch tested 1,871 children compared to 41,699 adults

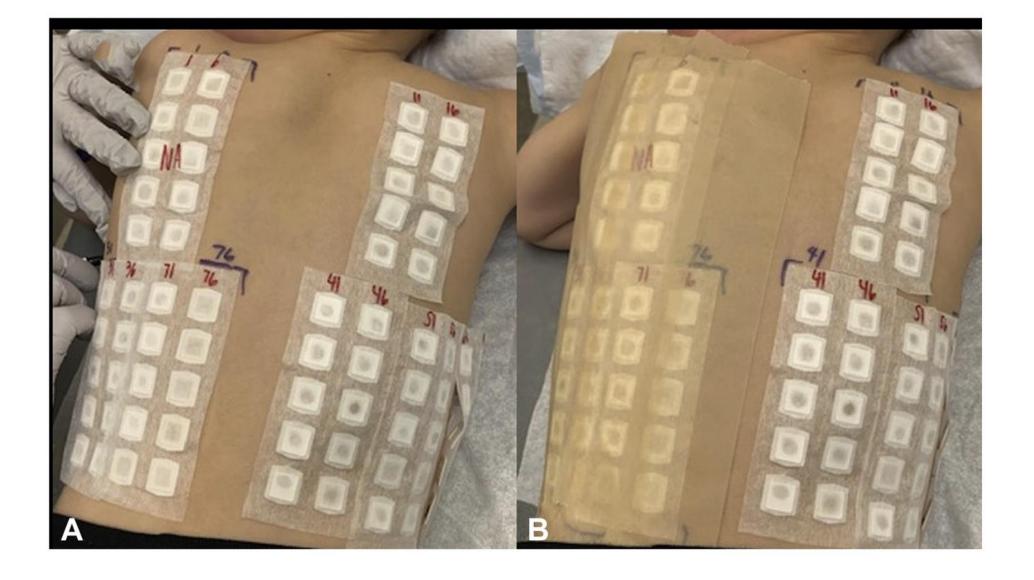
• Average age = 12.4 years

Compared to adults, children were more likely to:

- Have history of atopic dermatitis (52.6% vs 23.5%)
- Have history of asthma (22.9% vs 15.1%)

Similar rates of ACD diagnosis (55.2% vs 57.3%) and positive patch testing rate (49.2% vs 52.2%) between children and adults

Nickel sulfate hexahydrate, 2.5% pet.  Thimerosal 0.1% pet.  Cobalt (ii) chloride hexahydrate, 1.0% pet.  Sodium gold thiosulfate, 0.5% pet.  Hydroperoxides of linalool  Methylisothiazolinone, 0.2% aq. (2000 ppm)  Neomycin sulfate, 20.0% pet.  Fragrance mix I, 8.0% pet.  Formaldehyde, 2.0% aq.	Children (0-17 years) n, (%) N=1110
Cobalt (ii) chloride hexahydrate, 1.0% pet.  Sodium gold thiosulfate, 0.5% pet.  Hydroperoxides of linalool  Methylisothiazolinone, 0.2% aq. (2000 ppm)  Neomycin sulfate, 20.0% pet.  Fragrance mix I, 8.0% pet.	432 (23.3%)
Sodium gold thiosulfate, 0.5% pet.  Hydroperoxides of linalool  Methylisothiazolinone, 0.2% aq. (2000 ppm)  Neomycin sulfate, 20.0% pet.  Fragrance mix I, 8.0% pet.	29 (16.9%)
Hydroperoxides of linalool  Methylisothiazolinone, 0.2% aq. (2000 ppm)  Neomycin sulfate, 20.0% pet.  Fragrance mix I, 8.0% pet.	220 (11.8%)
Methylisothiazolinone, 0.2% aq. (2000 ppm)  Neomycin sulfate, 20.0% pet.  Fragrance mix I, 8.0% pet.	28 (8.2%)
Neomycin sulfate, 20.0% pet. Fragrance mix I, 8.0% pet.	15 (6.6%)
Fragrance mix I, 8.0% pet.	47 (6.4%)
	118 (6.3%)
Formaldehyde, 2.0% aq.	87 (4.7%)
	22 (4.5%)
Carmine, 2.5% pet.	9 (4.3%)





## Even Smaller Kids....





#### **ARTICLE IN PRESS**

#### **ORIGINAL ARTICLE**

# Prevalence of allergic contact dermatitis in children with and without atopic dermatitis: A multicenter retrospective case-control study

Hadley Johnson, BS,<sup>a,b</sup> Marcella R. Aquino, MD,<sup>c,d</sup> Alan Snyder, MD, MSCR,<sup>e</sup> Reid W. Collis, MD,<sup>f</sup> Katlein Franca, MS, MSc, PhD,<sup>g</sup> Alina Goldenberg, MD, MAS,<sup>h,i</sup> Jennifer Y. Sui, BA,<sup>j,k</sup> Dawn Z. Eichenfield, MD, PhD,<sup>j,k</sup> Brittany J. Kozy, MS, RN, CPNP,<sup>1</sup> Jennifer K. Chen, MD,<sup>m</sup> Chelsea Shope, MD MSCR,<sup>e</sup> Ari M. Goldminz, MD,<sup>n</sup> and JiaDe Yu, MD, MS<sup>b</sup>

#### 912 children with and without AD referred for patch testing

#### Children with AD

- have longer duration of dermatitis (4.1 vs 1.6 years)
- more likely to have generalized dermatitis
- seen more providers
- more likely to have multiple positive patch tests

**Bacitracin, cocamidopropyl betaine, and carba mix** were significantly more prevalent in children with AD

#### **Atopic Dermatitis**



**Allergic Contact Dermatitis** 





13 year old female with long standing history of atopic dermatitis

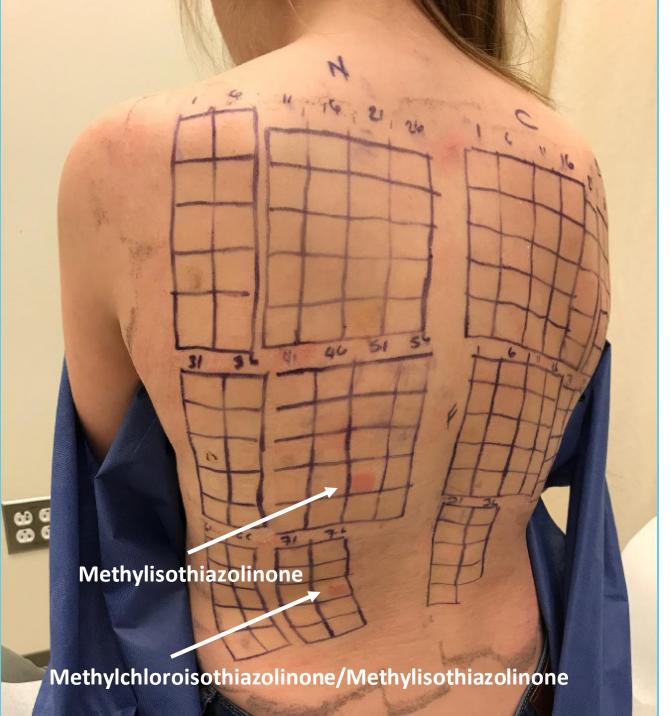
Over the last 2 years has worsening hand dermatitis

Thought it was due to basketball and stopped playing but has not had improvement

Topical steroids are somewhat beneficial







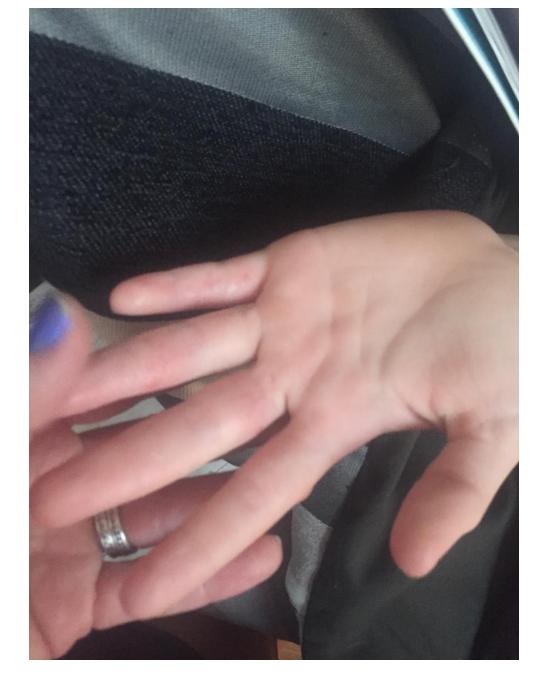


#### Slime

Homemade with ingredients such as glue, dish detergent, laundry detergent, borax, etc

Many ingredients contain MI (glue, detergent) or are very irritating (borax)







## Allergic Contact Dermatitis in Older Adults

	OA			
Allergen	Positive (%)	Relevant (%)		
Fragrance mix I 8.0% pet	848/5366 (15.8)	718/5366 (13.4)		
MI 0.2% aq	519/3739 (13.9)	451/3739 (12.1)		
Hydroperoxides of linalool 1.0% pet	221/1659 (13.3)	190/1659 (11.5)		
Benzisothiazolinone 0.1% pet	221/1659 (13.3)	101/1659 (6.1)		
Myroxylon pereirae resin (balsam of Peru) 25.0% pet	577/5366 (10.8)	504/5366 (9.4)		
MCI/MI 0.02% ag	164/1659 (9.9)	144/1659 (8.7)		
Nickel sulfate hexahydrate 2.5% pet	501/5366 (9.3)	277/5366 (5.2)		
Formaldehyde 2.0% aq	348/3739 (9.3)	281/3739 (7.5)		
Neomycin sulfate 20.0% pet	498/5366 (9.3)	133/5366 (2.5)		
Bacitracin 20.0% pet	424/5366 (7.9)	165/5366 (3.1)		

From 2009-2020, **5399 older adults** > 65 years of age were patch tested

More likely to have ACD

More likely to involve scalp, trunk, and anogenital

More likely to react to fragrances, formaldehyde, benzisothiazolinone, and iodopropynyl butyl carmabate

Older adults **LESS likely to react to nickel** 

85 year old female with a 1.5 year history of rash on the entire body. She does not have a history of atopic dermatitis.

She notes that since the inception of the rash, her daughter has given her various essential oil concoctions to "calm the skin."

She has seen 3 previous dermatologists and report minimal benefit from topical steroids.

Biopsy demonstrated hypersensitivity reaction

She was referred to me for patch testing





#### TOO MUCH RASH!

Started on 40mg of prednisone x 1 week, 20mg of prednisone x 1 week, 10mg of prednisone x 2 weeks

Patch testing was done on the 2<sup>nd</sup> week of prednisone 10mg



## Patch testing photos



Positive for Fragrance Mix 1 and avoidance led to significant improvement in her dermatitis (but not clearance)



## Supplemental allergen testing is important

19.5% of patients in one series have negative patch testing on a core series (NACDG 80 or ACDS 90) but had positive *relevant* reaction to a supplemental series

58.8% of supplemental series allergens with positive reactions > 1% are not on the core series

Gallates, cinnamic alcohol, phenyl salicylate, Grotan BK, and abitol are most common allergens missed with routine testing

## Long Term Changes in Allergen Prevalence

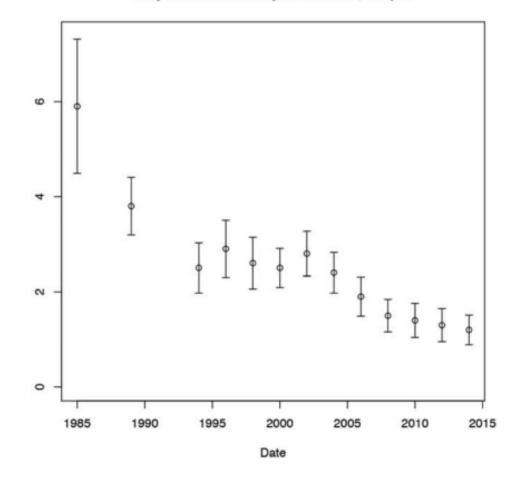
Analysis of trends of allergens between 1984-2016

47 allergens had sufficient data to analyze

23 had decreasing rates of positive reactions

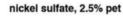
4 had increasing rates of reactions

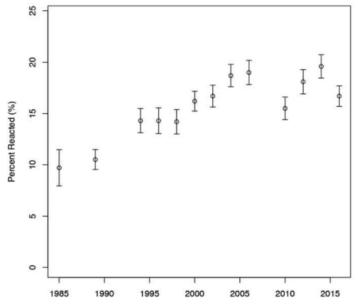
#### ethylenediamine dihydrochloride, 1% pet



#### TABLE 2. Significant Increase Overall

	Patch Test	No. Evaluable	Positive Reactivity Total No. Change in Proportion Data Period						
Туре	Preparation	Records	Patch Tests	Proportion (SD*)	Initial	Final	Start Date	End Date	Adjusted P
Botanical	Compositae mix, 6% pet	9	42,827	0.9% (0.23)	1%	1.9%	2001	2016	<0.001
Metal	Nickel sulfate, 2.5% pet	13	54,352	7% (1)	9.7%	17%	1984	2016	<0.001
Preservative	MCI/MI, 0.01% aq	12	50,507	6.3% (0.44)	0.5%	6.8%	1984	2016	<0.001
Preservative	Thimerosal, 0.1% pet	7	26,420	4% (0.84)	6.2%	10%	1984	2002	0.004





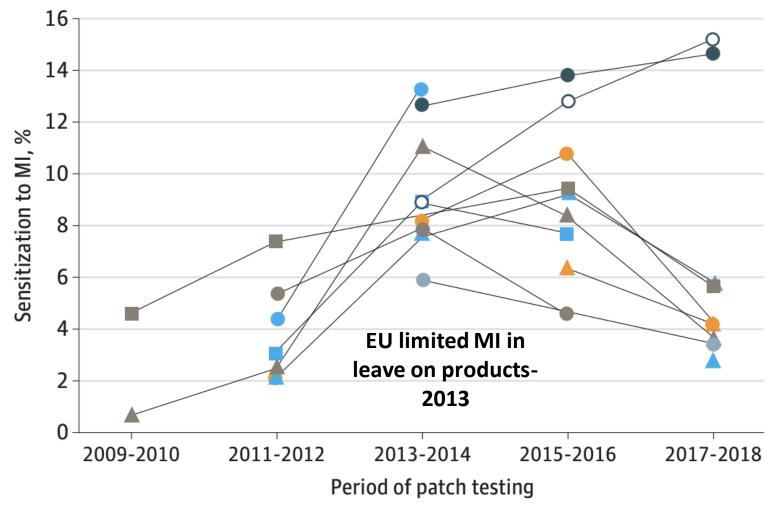


#### **TABLE 3.** Significant Decrease Overall

				Change in	Positive Reactivity Proportion		Data Period		
	Patch Test	No. Evaluable		Proportion			Start		
Туре	Preparation	Records	Patch Tests	(SD*)	Initial	Final	Date	Date	Adjusted P
Adhesive	<i>p</i> -Tertiary-butylphenol formaldehyde resin, 1% pet	13	53,138	0.2% (0.31)	0.8%	1%	1984	2016	<0.001
Anesthetic	Benzocaine, 5% pet	15	63,888	-2.1% (0.57)	3.5%	1.4%	1984	2016	<0.001
Antimicrobial	Neomycin sulfate, 20% pet	13	54,439	-0.5% (0.8)	6.6%	6.1%	1984	2016	<0.001
Antimicrobial	Bacitracin, 20% pet	13	59,324	-1.2% (0.56)	7.8%	6.6%	1992	2016	<0.001
Fragrance	Fragrance mix I, 8% pet	12	54,999	-1.1% (0.67)	11%	10%	1992	2016	<0.001
Fragrance	Balsam of Peru, 25% pet	13	54,449	2.7% (0.62)	3.3%	6%	1984	2016	<0.001
Hair chemical	Glyceryl thioglycolate, 1% pet	8	35,958	-0.3% (0.31)	2.1%	1.8%	1992	2008	<0.001
Metal	Potassium dichromate, 0.25% pet	12	53,322	-0.8% (0.3)	2.4%	1.6%	1985	2016	<0.001
Metal	Cobalt chloride, 1% pet	13	59,331	-0.8% (0.53)	6.8%	6%	1992	2016	<0.001
Preservative	Diazolidinyl urea, 1% aq	9	34545	-0.2% (0.57)	1.9%	1.7%	1984	2008	0.012
Preservative	DMDM hydantoin, 1% aq	9	36,606	-0.4% (0.5)	1.5%	1.1%	1984	2008	0.015
Preservative	2-Bromo-2-nitropropane-1,3-diol (bronopol), 0.5% pet	13	54,348	-0.6% (0.65)	2.6%	2%	1984	2014	<0.001
Preservative	Paraben mix, 12% pet	7	29,231	-0.6% (0.42)	1.1%	0.5%	1984	2014	0.006
Preservative	lmidazolidinyl urea, 2% pet	12	53,185	-0.7% (0.29)	2.1%	1.4%	1985	2014	<0.001
Preservative	Formaldehyde, 1% aq	13	58,385	-1% (0.51)	6.8%	5.8%	1985	2016	<0.001
Preservative	Chloroxylenol (4-chloro-3,5-xylenol), 1% pet	10	40,021	-1.2% (0.52)	1.7%	0.5%	1984	2016	<0.001
Preservative	Glutaraldehyde, 1% pet	10	45,042	-2.5% (0.33)	3.3%	0.8%	1992	2014	<0.001
Preservative	Quaternium-15, 2% pet	13	54,472	-3.3% (0.78)	6.7%	3.4%	1984	2016	<0.001
Preservative	lmidazolidinyl urea, 2% aq	9	37,532	0% (0.4)	1.5%	1.5%	1984	2008	0.009
Preservative	DMDM hydantoin, 1% pet	13	54,369	0% (0.37)	0.8%	0.8%	1984	2014	<0.001
Preservative	Diazolidinyl urea, 1% pet	15	63,592	0.1% (0.93)	1.3%	1.4%	1984	2014	<0.001
Rubber chemical	Black rubber mix, 0.6% pet	9	35,490	-0.4% (0.38)	1.4%	1%	1984	2014	<0.001
Rubber chemical	Mercapto mix, 1% pet	10	39,055	-2.3% (0.49)	2.7%	0.4%	1984	2016	<0.001
Rubber chemical	Thiuram mix, 1% pet	10	44,275	-2.3% (0.43)	5.5%	3.2%	1985	2016	<0.001
- Rubber chemical	Mercaptobenzothiazole, 1% pet	12	48,846	-2.4% (0.51)	2.9%	0.5%	1984	2016	<0.001
Solvent	Propylene glycol, 30% aq	9	43,369	-1.6% (0.36)	3.8%	2.2%	1996	2016	<0.001
Stabilizer	Ethylenediamine dihydrochloride, 1% pet	13	53,974	-4.7% (0.72)	5.9%	1.2%	1984	2014	<0.001
Surfactant	Cocamidopropyl betaine, 1% aq	9	42,833	-1.7% (0.27)	2.8%	1.1%	2001	2016	<0.001



#### Methylisothiazolinone- A Tale of Two Continents



- NACDG, US, 0.2%
- ESSCA, Eastern EU, 0.02%
- ESSCA, Eastern EU, 0.2%
- ESSCA, Southern EU, 0.02%
- ▲ ESSCA, Southern EU, 0.2%
- ESSCA, Southern EU, 0.05%
- ESSCA, Western EU, 0.2%
- ▲ ESSCA, Western EU, 0.02%
- ESSCA, Western EU, 0.05%
- IVDK, Central EU, 0.05%
- O NACDG, Canada, 0.2%



Reeder MJ, Warshaw E, Aravamuthan S, Belsito DV, Geier J, Wilkinson M, Atwater AR, White IR, Silverberg JI, Taylor JS, Fowler JF Jr, Maibach HI, DeKoven JG, Buhl T, Botto N, Giménez-Arnau AM, Gallo R, Mowad C, Lang CCV, DeLeo VA, Johnston G, Pratt MD, Brockow K, Adler BL, Houle MC, Dickel H, Schuttela ar MLA, Yu J, Spiewak R, Dunnick C, Filon FL, Valiukeviciene S, Uter W. Trends in the Prevalence of Methylchloroisothiazolinone/Methylisothiazolinone Contact Allergy in North America and Europe. JAMA Dermatol. 2023 Mar 1;159(3):267-274. doi: 10.1001/jamadermatol.2022.5991. PMID: 36652228; PMCID: PMC9857829.

## Part 2

# Patch Testing on Novel Immunosuppressants



#### North American Contact Dermatitis Group Expert Opinion-2012

Topical steroids on the patch testing site should be avoided for 3-7 days prior to patch testing

Prednisone < 10mg OK but best if discontinued

IM Triamcinolone at least 4 weeks prior to patch testing

TNFa, methotrexate, and ustekinumab OK

Azathioprine, cyclosporine, mycophenolate mofetil, and tacrolimus has dose dependent effect (lower = better)

#### But...

Newer biologics not available

JAKi not available

Newer information needed

NACDG Update in the works!



## **Dupilumab Probably Negative Effect**

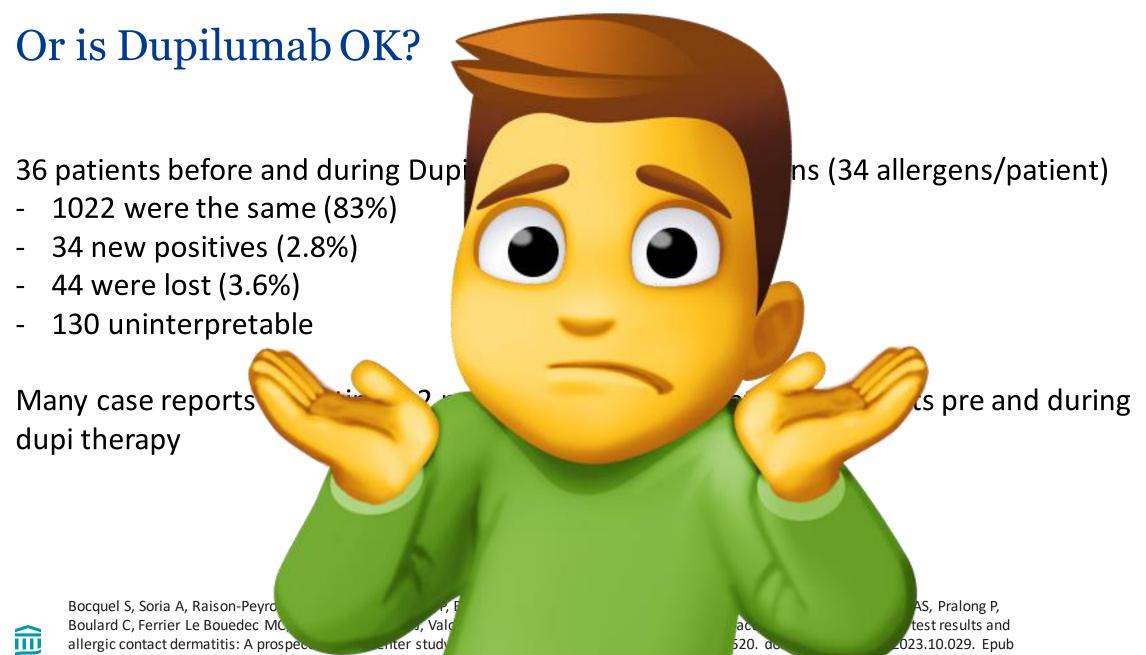
Results are mixed

Jo et al. 144 allergen pairs tested prior to, during or after dupilumab

- 17 were lost
- 8 were new
- 71 were persistent
- 48 unknown

Raffi et al. 23 patients tested pre and post dupilumab

- 7/23 patients became negative post dupilumab
- 13 reactions were lost out of 125 positive reactions



2023 Oct 21. PMID: 37871801.

## If you can patch test without, do it...but usually need it

explored either. We confirm that PTs are often positive and relevant for DUPI-treated AD patients. PT reproducibility during DUPI therapy seems to have been preserved within the limits of this study. Our results also suggest that DUPI does not always effectively treat ACD. Therefore, we conclude that it is important to perform PTs on all DUPI-treated patients with partial responses or worsening eczema during treatment to look for ACD, especially on head and neck, eyelids, and hands.



#### JAKi NOT OK

**TABLE 1** Patch test results at 96 h.

Hapten	Patch testing under dupilumab	Patch testing under upadacitinib
Fusidic acid sodium salt 2.0 pet	2+	2+
Amerchol L 101 (lanolin) 50.0 pet	3+	3+
Thiuram mix	1+	-
4-tert-butylphenol formaldehyde resin 1.0 pet	1+	-
<ul> <li>Corticosteroid Mix 2.1 pet</li> <li>Hydrocortisone-17-butyrate 1.0 pet</li> <li>Tixocortol-21-pivalate 1.0 pet</li> <li>Budesonide 0.1 pet</li> </ul>	1+	-
Budesonide 0.01 pet	1+	-
Betamethasone-17-valerate 1.0 pet	1+	-
Clobetasol-17-propionate 1.0 pet	1+	-
Dexamethasone-21-phosphate disodium salt 1.0 pet	1+	-
Desoximethasone 1.0 pet	1+	-
Betamethasone 17,21-dipropionate 1.0 pet	2+	-
Methylprednisolone aceponate 1.0 pet	1+	-
n a natient treated with duniluman then with unadacitinih: Differences in		



#### Or is it?

29 year old male with a long history of AD failing dupilumab and currently well controlled on upadactinib 15mg daily. Presents to clinic with residual dermatitis of the forehead, back of the ears, and posterior neck.





#### Positive for decyl glucoside and coco-glucoside

#### Ingredients:

Water, Lauryl Glucoside, Coco-Glucoside, Acrylates Copolymer, Sodium Cocoyl Glutamate, Scocoate, Panthenol, Pentylene Glycol, 1,2-Hexanediol, Disodium Edta, Caprylyl Glycol, Sodium

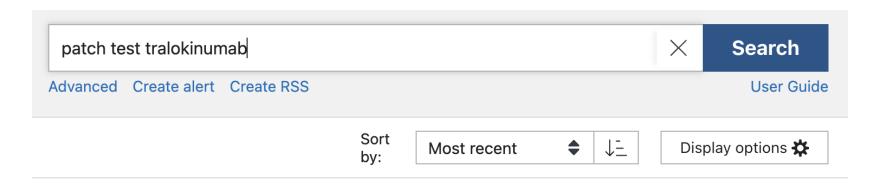




mate\*, Glycerin, Sucrose is Ingredient



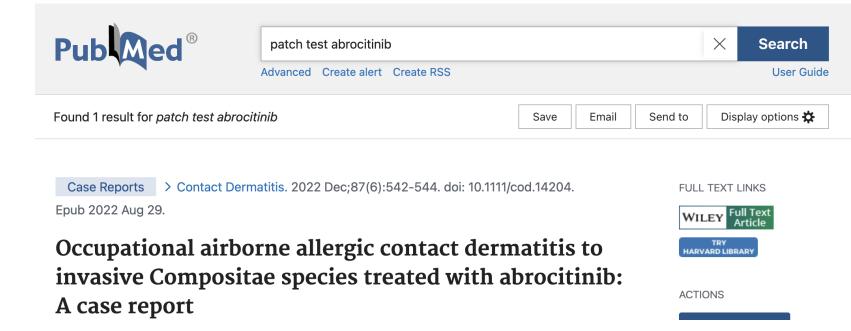




No results were found.



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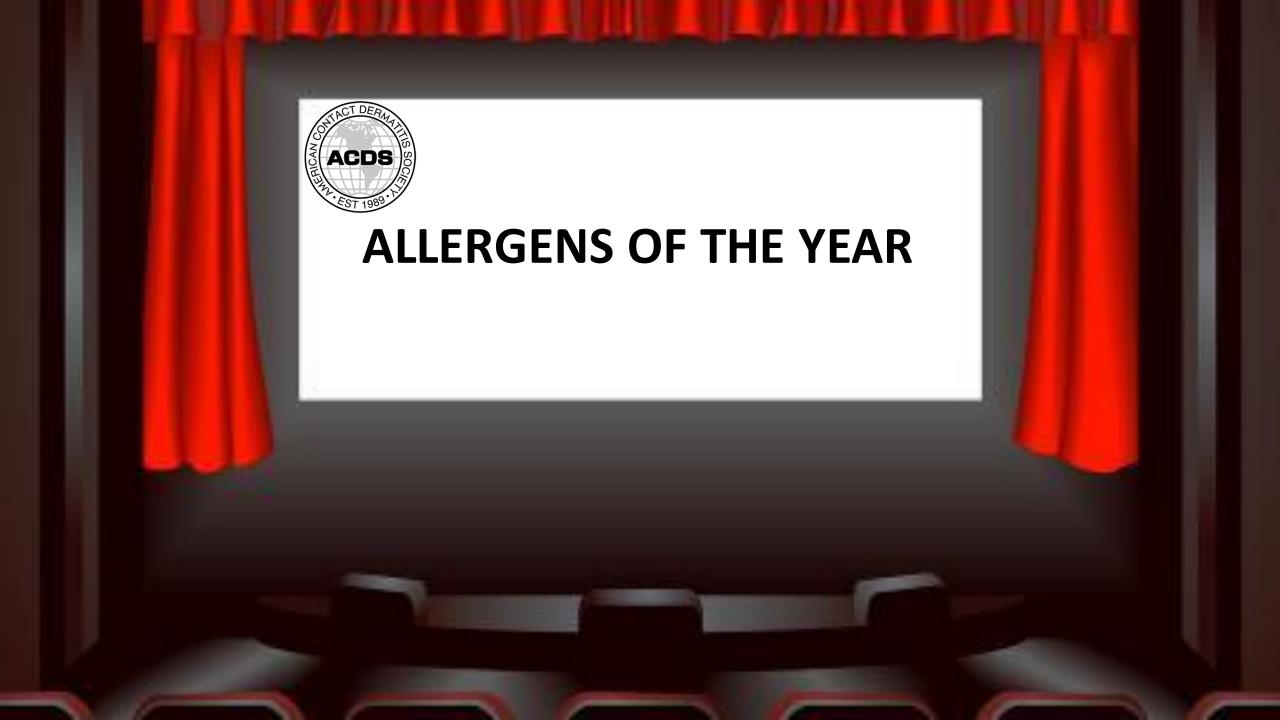




## Part 3

# 5 Most Recent Allergens of the Year





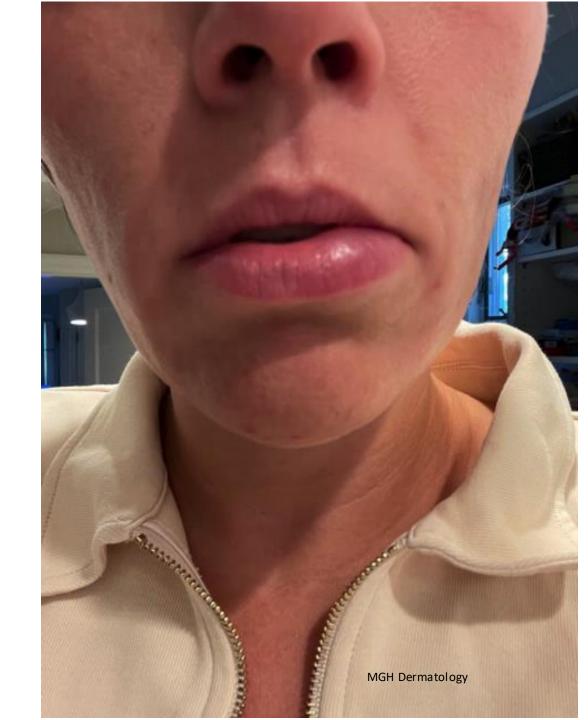
#### Case #1

42 year old otherwise healthy female with 9 month history of intermittent lower lip predominant swelling without urticaria or other systemic rashes/symptoms

Lip swelling lasts < 12 hours on average and she notes correlation with drinking > 2 glasses of wine at a sitting and swelling would appear 24-48 hours later

Workup for HAE and prick testing was negative





Patch testing was weakly positive (1+) to sodium metabisulfite

Avoidance of all wines x 2 months led to complete resolution

Went to a retirement party and had > 2 alcoholic beverages and had mild lip swelling within 2 days



## 2024 AoY Sodium Metabisulfite aka "Sulfites"

Antioxidant and preservative in personal care products, foods, beverages, and medications

#### **NOT** "sulfates" = sodium laurel sulfate

Occur naturally in some foods and beverages and may be added to others

In wines, acts as an anti-oxidant to prevent secondary fermentation

Also found in local anesthetics (systemic contact dermatitis), catheters, cosmetics, etc

## Sulfites Prevalence

Current prevalence in North American ~3.3% of patch tested patients

28.8% of dermatitis occurs on the face followed by 20.5% on the hands

Can also cause Type 1 hypersensitivity symptoms including asthma and death has been reported

FDA bans use of sulfites on raw fruits and vegetables



#### TABLE 5. Sulfite Content of Food and Beverages

High (>100 ppm)	Moderate to High (50-99.9 ppm)	Low to Moderate (10.1–49.9 ppm)	Low (<10 ppm)
<ul> <li>Dried fruit (excluding dark raisins and prunes)</li> <li>Bottled lemon juice (nonfrozen)</li> <li>Wine</li> <li>Molasses</li> <li>Sauerkraut juice</li> <li>Grape juice (white, white sparkling, pink sparkling, and red sparkling)</li> <li>Pickled cocktail onions</li> </ul>	<ul> <li>Dried potatoes</li> <li>Wine vinegars</li> <li>Gravies/sauces</li> <li>Fruit toppings</li> <li>Maraschino cherries</li> </ul>	<ul> <li>Pectin</li> <li>Shrimp (fresh)</li> <li>Corn syrup</li> <li>Sauerkraut (without juice)</li> <li>Pickled peppers</li> <li>Pickles/relishes</li> <li>Corn starch</li> <li>Hominy</li> <li>Frozen potatoes</li> <li>Maple syrup</li> <li>Imported jam/jelly</li> <li>Fresh mushrooms</li> <li>Imported sausage/meat</li> <li>Cordial alcohols</li> <li>Dehydrated vegetables</li> <li>Corn bread/muffin mix</li> <li>Canned/jarred clams</li> <li>Clam chowder</li> <li>Avocado dip/guacamole</li> <li>Imported fruit juices</li> <li>Imported soft drinks</li> <li>Cider</li> <li>Cider vinegar</li> </ul>	<ul> <li>Crackers</li> <li>Malt vinegar</li> <li>Sugar (especially beet sugar)</li> <li>Gelatin</li> <li>Canned potatoes</li> <li>Coconut</li> <li>Fresh fruit salad</li> <li>Dry soup mix</li> <li>Pizza dough (frozen)</li> <li>Pie dough (frozen)</li> <li>Grapes</li> <li>Domestic jams/jellies</li> <li>Soft drinks</li> <li>Instant tea</li> <li>Beer cookies</li> </ul>

#### TABLE 6. Consumer Marketed Sulfite Removing Devices

		Studies on Sulfite		
Device	Cost	Instructions	Reduction	Product Claims
PureWine <sup>®</sup> The Phoenix <sup>®</sup>	\$69.99 for 1 pouring device and 3 BioPod <sup>TM</sup> wine purifying cartridges.	Insert BioPod™ cartridge into The Phoenix Base, insert The Phoenix firmly into wine bottle and twist. Tilt bottle vertically to pour. Wait 3–5 seconds for pour.	None found	Removes histamines and sulfites from wine.
PureWine The Wave®	\$14.99 for 1 The Wave that treats a 750 mL bottle of wine.	Whole-bottle wine purification.  Place The Wave on the mouth of the wine bottle. Wine is filtered as poured through the filter housing.	None found	Removes histamines and sulfites from wine.
PureWine The Wand TM	\$24.99 for 8 single use wands, each treats 1 glass of wine.	Place wand in a 6 oz glass of wine for at least 1 minute with intermittent gentle stirring.	None found	Removes histamines and sulfites from wine. After 8 minutes, up to 95% of the histamines and sulfites may be removed.
Drop It <sup>®</sup> Original Wine Drops	\$13.99 for 1 bottle of drops which will treat up to 55 glasses or 9 bottles of wine.	Add up to 4 drops per 5-6 oz glass of wine, swirl for 20 seconds.	None found	Reduces tannins and sulfites in wine.
Üllo Original wine purifier	\$79.99 for wine purifier and 4 Selective Sulfite <sup>TM</sup> full bottle filters. \$24.99 for 6 replacement Selective Sulfite <sup>TM</sup> full bottle filters.	Insert filter into wine purifier reservoir. Place wine purifier over glass. Pour wine slowly into purifier reservoir. Whole bottle requires 2-4 minutes to filter.	None found	30-85% reduction in free sulfites in wine.

#### Case #2

13 year old girl with a life long history of flexural atopic dermatitis that is well controlled with topical steroids and topical emollients

Developed a new facial rash 3 months ago that has been difficult to treat

Topical steroids and calcineurin inhibitors led to some improvement but would re-flare







Patch testing was positive for Amerchol L101 aka Lanolin Alcohol

Upon further questioning, she has been using Aquaphor as a moisturizer on the lower face daily as recommended by another dermatologist

Avoidance led to complete improvement



## What is Lanolin?

Contact allergen of the year in 2023

Wool WAX derived from sheep wool

Free fatty alcohol component of lanolin is the allergenic portion

Best test is Amerchol L101 50% or Lanolin alcohol 30%



Jenkins BA, Belsito DV. Lanolin. Dermatitis. 2023 Jan-Feb;34(1):4-12. doi: 10.1089/derm.2022.0002. PMID: 36917502.



## Lanolin Paradox

Overall a weak sensitizer

Lanolin applied to "damaged" skin more likely to be allergenic compared to lanolin applied to "normal" skin

Atopic dermatitis, stasis dermatitis, leg ulcers, wounds, etc all more likely to react to lanolin

Jenkins BA, Belsito DV. Lanolin. Dermatitis. 2023 Jan-Feb;34(1):4-12. doi: 10.1089/derm.2022.0002. PMID: 36917502



## Case #3

3 year old with a 7 month history of waxing and waning nodule on left thigh with localized itching

There was also ipsilateral lymphadenopathy

MRI showed nodular foci in the subcutaneous fat in the left thigh





Patch testing demonstrated a strong positive (2+) reaction to aluminumchloride hexahydrate

What is the potential cause?



# Vaccine granuloma due to aluminum allergy!

Aluminum is contact allergen of the year in 2022

It is present in various vaccines especially childhood vaccines such as D-Tap-HepB-IPV which this child had received at 4 and 6 months

Vaccine granulomas can occur months to years later (0.35-1.18% prevalence)

Localized itching is common and may take years to resolve



Gordon SC, Bartenstein DW, Tajmir SH, Song JS, Hawryluk EB. Delayed-type hypersensitivity to vaccine a luminum adjuvant causing subcutane ous leg mass and urticaria in a child. Pediatr Dermatol. 2018 Mar;35(2):234-236. doi: 10.1111/pde.13390. Epub 2018 Jan 4. PMID: 29314223.

TABLE 1 Immunizations containing aluminum<sup>8</sup>

TABLE 1 IIIIIIIIIIIII COITAIIIIII aluiiiiiiii				
Vaccine	Aluminum product			
Adenovirus	FD&C Yellow #6 aluminum lake dye			
Anthrax (Biothrax)	Aluminum hydroxide			
DT (Sanofi)	Aluminum phosphate			
DTaP (Daptacel)	Aluminum phosphate			
DTaP (Infanrix)	Aluminum hydroxide			
DTaP-IPV (Kinrix)	Aluminum hydroxide			
DTaP-IPV (Quadracel)	aluminum phosphate			
DTaP-HepB-IPV (Pediarix)	Aluminum hydroxide, aluminum phosphate, aluminum salts			
DTaP-IPV/HiB (Pentacel)	Aluminum phosphate			
Hib (PedvaxHIB)	Aluminum hydroxyphosphate sulfate			
Hep A (Havrix)	Aluminum hydroxide			
Hep A (Vaqta)	Amorphous aluminum hydroxyphosphate sulfate			
Hep B (Engerix-B)	Aluminum hydroxide			
Hep B (Recombivax)	Aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate			
Hep A/Hep B (Twinrix)	Aluminum phosphate, aluminum hydroxide			
Human Papillomavirus (HPV) (Gardasil)	Amorphous aluminum hydroxyphosphate sulfate			
Human Papillomavirus (HPV) (Gardasil 9)	Amorphous alumium_hydroxyphosphate sulfate			
Japanese Encephalitis (Ixiaro)	Aluminum hydroxide			
Meningococcal (MenB - Bexsero)	Aluminum hydroxide			
Pneumococcal (PCV13 - Prevnar 13)	Aluminum phosphate			
Td (Tenivac)	Aluminum phosphate			
Td (Mass Biologics)	Aluminum phosphate			
Tdap (Adacel)	MGHinRatingates/state			
Tdap (Boostrix)	Aluminum hydroxide			

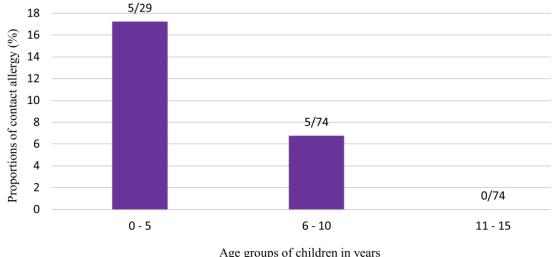
## **Aluminum Contact Dermatitis**

#### Also found in:

 Antiperspirants, sunscreens, immunotherapy, cans, dental work

Aluminum allergy wanes with age

Test to 10% Aluminum chloride hexahydrate





## Case #4

14 year old girl with history of arm and leg rash x 2 years

Worse when playing hockey (plays 11/12 months)

Tried numerous interventions including wearing socks under pads and wearing tights to prevent direct contact with the skin

Prednisone helps as does betamethasone and triamcinolone ointment











## Potential Allergens in Shin Guards



**Front Plate:** Plastic and/or fiber

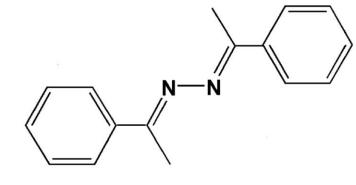
- Not usually problematic

**Inner padding:** Foam rubber, polyurethane foam, textile, or EVA (ethyl vinyl acetate)

- Potential source of allergens!
- Rubber accelerators, p-tert butyl formaldehyde resin (rubber glue), textile dyes have all been previously reported

However, many cases were reportedly negative and thought to be irritant contact dermatitis only until....

## ACDS Allergen of the Year 2021



**Acetophenone Azine-** Generated during the production of ethyl vinyl acetate (EVA) foam

"Potent" allergen found in 14% of footwear in one study

Also seen in flip-flops, ski boots, swimming goggles, bike saddle

## **Preventative Methods**

Double layer of moisture wicking socks (white) or cotton pad between the shin guard and sock

Powder the shin guard with corn starch to absorb sweat

Glue a canvas inlay onto the foam portion of the guards

Switch shin guards to ones that do not have EVA foam or rubber coating. Polyurethane can be a safe choice.

## Testing for Acetophenone Azine

Not yet commercially available

Buy from Sigma-Aldrich and make 1% or 0.1% in petrolatum or acetone

Contact hockey supplier to see if they make pads without EVA (they do)



## Case #5

26 year old male with history of T1DM who has been using a continuous glucose monitoring system x 10 years. Developed rash a few years into using these

Previously tried Freestyle Libre which gave him a rash 2-3 days into a 2 weeks cycle which forces him to move it prematurely to the other arm (should be 2 weeks)

Currently using Omnipod insulin pump as well which also gives him a rash but more tolerable



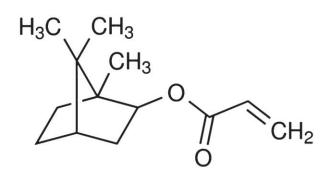






## Contact dermatitis to ANY ADHESIVE MEDICAL DEVICE Allergic contact dermatitis Irritant contact dermatitis Isobornyl acrylate **OCCLUSION** 2,2'-methylenebis(6-tert-butyl-4-methylphenol) monoacrylate ALLERGENS Dipropylene glycol diacrylate IRRITANT N,N-dimethylacrylamide **FRICTION ACRYLATES** Cyanoacrylates **Epoxy resin INCREASED** Colophonium **HUMIDITY**

## Positive Testing to Isobornyl Acrylate



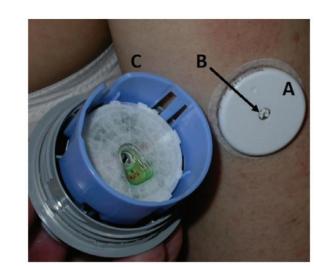
**Isobornyl Acrylate (IBOA)-** acrylate monomer used in plasticizers, UV-cured glue, and casings

Allergen of the year in 2020

Found in the sensor of Freestyle Libre and Omnipod

Other acrylates were mostly negative in 15 patients tested

Test at 0.1% pet (now available at Dormer)



## Allergy to Continuous Glucose Monitoring and Insulin Pump







## ACD to Glucose Sensors and Insulin Infusion

More than 1/3 of patients report dermatitis from the sensors

Lag time of months-years before rash develops

Common culprits: acrylates, colophonium, ethyl cyanoacrylates, epoxy resin, etc.

Difficult to know the exact allergen in some cases due to manufacturer not willing to share raw materials

#### Common in Children

14/264 children with T1DM had reactions to glucose sensors (5.3%)

FreeStyle Libre was the most common cause of ACD in these children (11/19 reactions)

IBOA caused majority of the reactions 7/19

**TABLE 3** The allergens identified in the different medical devices

Glucose sensor				
Manufacturer	Product	Part of medical device		Allergen
Abbott	Freestyle libre	Housing	*	Isobornyl acrylate <sup>6a</sup>
				N,N-dimethylacrylamide <sup>16</sup>
Dexcom	G4 <sup>b</sup>	Housing		Ethyl cyanoacrylate <sup>8a</sup>
	G5 <sup>b</sup>			
Medtronic	Enlite	Таре		Abitol <sup>a</sup>
				Abietic acid <sup>a</sup>
				butyl acrylate <sup>a</sup>
				Colophonium <sup>20a</sup>
		Housing		Isobornyl acrylate <sup>15</sup>
				N,N-dimethylacrylamide <sup>15</sup>
Insulin pump				
Insulet corporation	Omnipod	Tape	2	Colophonium <sup>20</sup>
		Hous	sing	★ Isobornyl acrylate <sup>5</sup>
Medtronic	Paradigm Minimed quick-set	Hous	sing	Isobornyl acrylate <sup>15</sup>



## **TABLE 1.** Allergens Contained in Diabetes Medical Devices

Medical Device	Allergen(s) Identified
Cliniset	Phenoxypoly(ethylenoxy) ethylacrylate <sup>6</sup>
Disetronic	Isobornyl acrylate <sup>6</sup>
Actrapid insulin pump	Epoxy resin <sup>7</sup>
Omnipod	Isobornyl acrylate, colophonium,
	dipropylene glycol diacrylate <sup>8-12</sup>
Paradigm MiniMed Quick-set	Isobornyl acrylate <sup>13</sup>
FreeStyle Libre	Isobornyl acrylate, sesquiterpene lactones, N,N-dimethylacrylamide 14-19
Enlite sensor	Colophonium, abitol, abietic acid, butyl acrylate, isobornyl acrylate <sup>8,13,20</sup>
Dexcom G4	2-Ethyl cyanoacrylate <sup>21-23</sup>
Dexcom G5	Ethyl cyanoacrylate <sup>20</sup>
Dexcom G6	2,2'-Methylenebis(6- <i>tert</i> -butyl-4-methylphenol) monoacrylate <sup>24,25</sup>



## So What's an Alternative?

Free Style Libre 2 and Dexcom does NOT have isobornyl acrylate

No alternatives for insulin infusions but can use barrier protection between the device and skin

- Hansaplast Blister Plaster
- Tegaderm, Mepilex, or Duoderm thin can also work as long as they are thin enough for the needle to penetrate the skin



#### **Take Home Points**

All populations, regardless of age, can get ACD and patch testing is important to consider

Allergen prevalence changes over time with old players (formaldehyde releasers) not as relevant today as new players (methylisothiazolinone)

Patch testing on novel AD biologics not ideal but dupilumab not as bad as JAKi

ACDS Contact Allergens of the Year are great papers to review every January to look for potential relevance to your practice!



# Lebrikizumab Phase 3 Randomized Controlled Clinical Trial

6 months – 18 years of age

Failed standard treatments of atopic dermatitis

Injectable every 4 weeks

16 weeks with 52 week extension study afterwards



A Study of Lebrikizumab (LY3650150) in Participants 6 Months to <18 Years of Age With Moderate-to-Severe Atopic Dermatitis (ADorable-1)

J2T-MC-KGBI - ClinicalTrials.gov - NCT05559359

The main purpose of this study is to measure the effect, safety and how well the body absorbs Lebrikizumab in pediatric participants 6 months to <18 years of age with moderate-to-severe atopic dermatitis (AD).

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