



MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

Allergic Contact Dermatitis

Mari Paz Castanedo Tardan, MD

Assistant Professor of Dermatology

maripaz@med.umich.edu

Disclosure

- I have no conflicts of interest to disclose.

Objectives

Describe

- What is Allergic Contact Dermatitis?
- Pathogenesis

Review

- Epidemiology
- Clinical presentation
- Diagnosis

Discuss

- Common and relevant contact allergens

What is it?

When the skin comes in contact with external agents, many adverse events can occur including contact dermatitis which can be either irritant or allergic

- **Irritant** contact dermatitis (ICD) accounts for ~ **80%**
- **Allergic** contact dermatitis (ACD) accounts for ~ **20%**

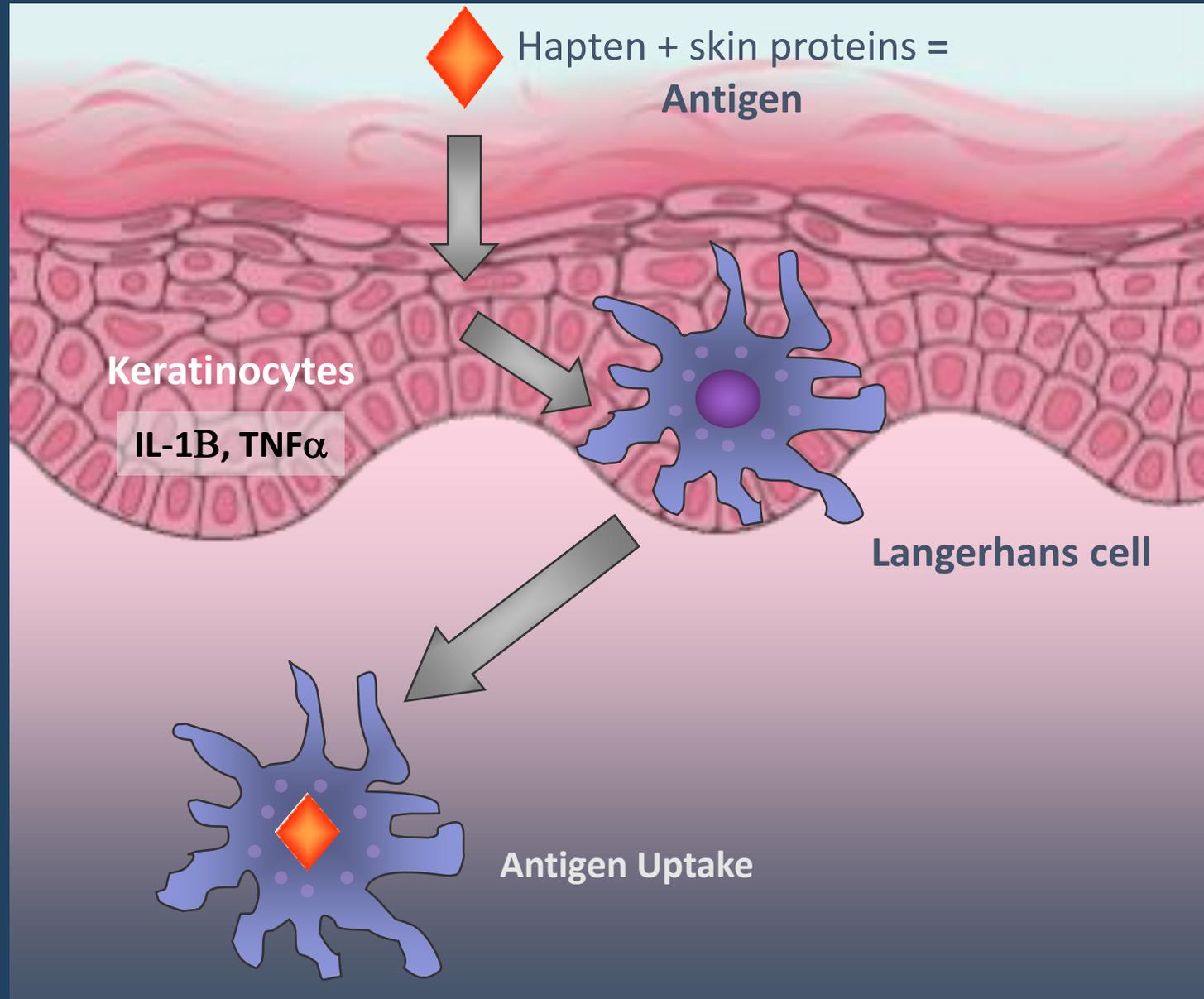


Pathogenesis

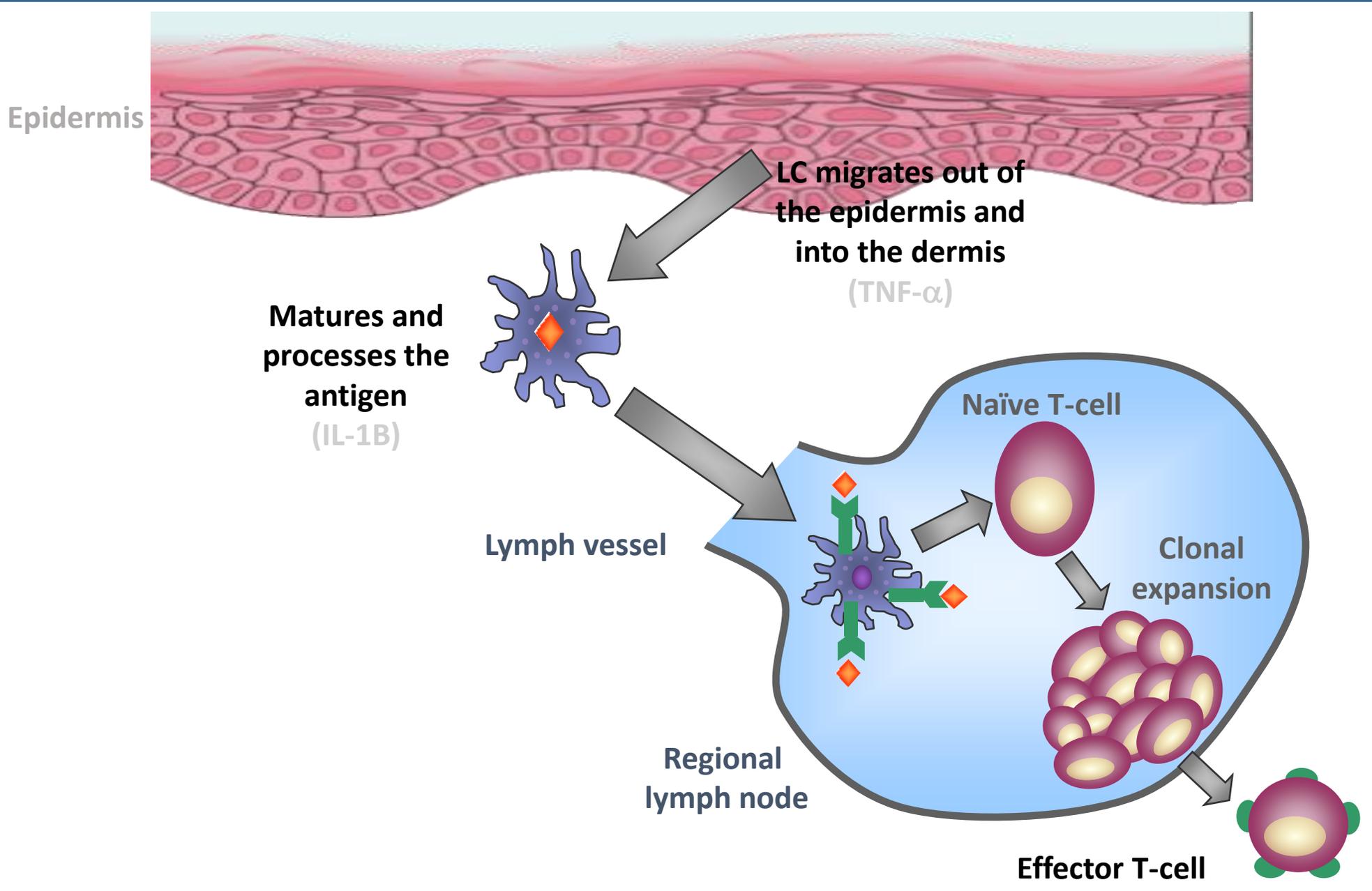
ACD is a **delayed, type IV, T-cell mediated** hypersensitivity reaction within the skin that results from contact between the skin and an allergenic external agent

- Previous exposure and sensitization to a specific chemical **IS required**
- 2 distinct phases:
 - **Sensitization phase** (when the individual first comes in contact with the allergenic chemical)
 - **Elicitation phase**

Sensitization Phase



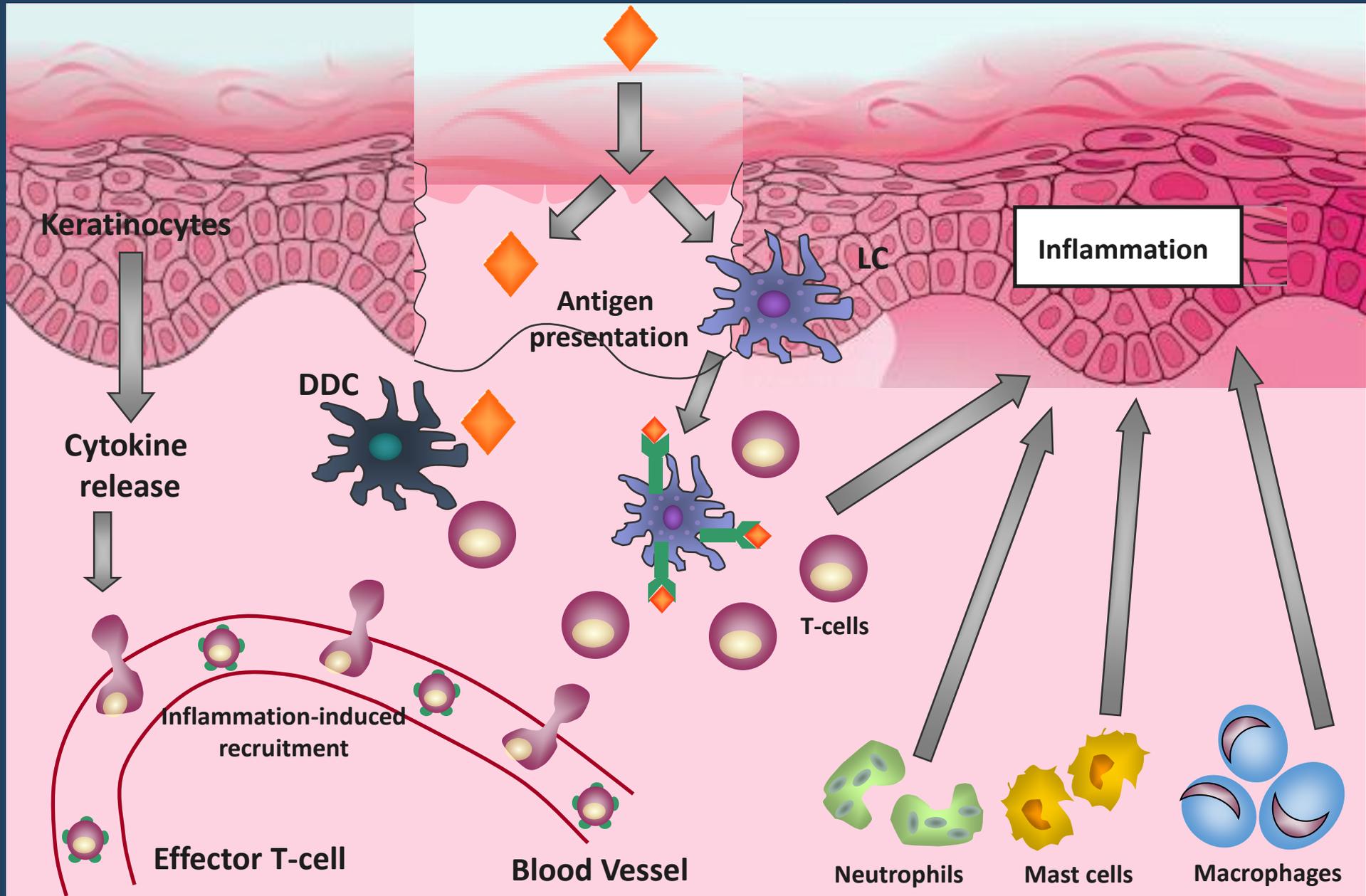
Sensitization Phase



Elicitation Phase

- If immunologic memory develops, when a sensitized individual is subsequently re-exposed to an antigen, the effector/memory T-cells recognize the antigen, proliferate and call in other inflammatory cells.
- **Once sensitized**, all that is needed to **elicit** a reaction is contact with a low concentration of the causative chemical.

Elicitation Phase



Epidemiology

- In an analysis of 2013 claims data from private and governmental insurance providers, nearly 85 millions Americans saw a physician for some form of skin disorder (exceeding current annual estimates for CV disease and DM)
- According to this report, **contact dermatitis was the 5th most prevalent skin disease in the US** with a total population medical cost of US \$1.529 billions
- The economic burden of this disease is high not only from medical expenditures, but also in terms of school absences and work time loss (estimated economic cost of \$3 billion per year)
- More than 13 million Americans have sought some type of treatment for this chronic condition **each year**
- ACD can affect individuals in all walks of life / can occur at any age
- 1-10% lifetime prevalence in industrialized societies
- Most common cause of occupational skin disease in industrialized countries

Some Occupations at Risk for Contact Dermatitis

Hairdressers



Food handlers



Florists



Construction workers



Healthcare workers



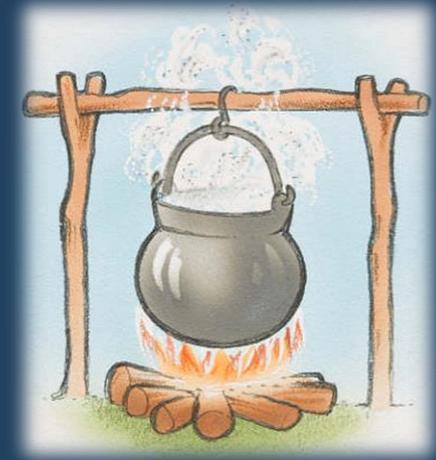
Maintenance/housekeeping personnel



Clinical presentation

- ACD manifests as a **eczematous dermatitis**

- Eczematous → from the Greek “*to boil over*”
- Dermatitis → inflammation that usually manifests as **erythematous, edematous, pruritic skin**



- It may co-exist with other eczematous dermatoses such as ICD and atopic dermatitis which can complicate the diagnosis.

Eczematous Dermatitis

Acute

Erythematous, edematous, with vesiculation (oozing)



Subacute

Erythematous and scaly



Chronic

Erythematous and lichenified



Fourth Edition
Dermatology

JEAN L. BOLOGNIA
JULIE V. SCHAFFER
LORENZO CERRONI



SECTION EDITORS

Jeffrey P. Callen
Edward W. Cowen
George J. Hruza
Joseph L. Jorizzo

Harvey Lui
Luis Requena
Thomas Schwarz
Antonio Torrelo

It is all about location!



Clinical presentation

- The **distribution of the dermatitis** is usually the **single most important clue to the diagnosis of ACD**
- Acute ACD (and many cases of subacute and chronic ACD) are well demarcated and **localized to the site of contact with the allergen**
- **Topography:**
 - peri/infraumbilical area → suggests metal snaps in jeans and belt buckles
 - facial, eyelid, lip, and neck patterns of dermatitis → cosmetic-related contact allergy
- However, ACD can also have a “patchy” (commonly) or even diffuse distribution depending on the allergen involved and/or the development of autoeczematization
 - Secondary eczematous lesions appear distant from the primary site of exposure

Misconceptions

False	Truth
Contact allergy always occurs <i>only</i> at site of exposure to the offending agent	Typically, the area of greatest dermatitis is the area of greatest contact with the offending allergen(s), but because allergens may be carried to other sites , dermatitis may appear in other locations and/or be more widespread ; also because body sites differ in responsiveness to allergens, on occasions, the most severe dermatitis may occur at a site distant from the primary exposure site (e.g. hair dye and eyelid, neck, ear dermatitis)
ACD is always bilateral	ACD is not always bilateral even when the antigen exposure is bilateral (i.e. shoe or glove allergy)
If an allergen is applied to a whole body area, the whole surface area is involved equally	Even when exposure is uniform (i.e. contact allergy to ingredient of a cream that is applied to the whole face), eczematous manifestations are very often patchy .
Allergy develops only to new substances	Allergy usually develops after months or years of contact .

Example of allergen carried to other site



Example of dermatitis occurring at site “distant” of primary exposure site



Allergic Contact
Dermatitis to
hair dye

© Waikato District Health Board 2018



Diagnosis

- **Patch Testing** -where allergic reactions are reproduced on the patient's back over several days- is the **gold standard for the diagnosis of ACD**

Patch testing = In vivo “elicitation test”

- Caveat: Sensitization does not necessarily equate with clinical disease (contact sensitivity/allergy to “X” is not the same as allergic contact dermatitis to/secondary to “X”)

Patch Testing and Prick Testing are NOT the same

- **Prick Testing** test for immediate, type I, IgE-mediated hypersensitivity reactions such as:
 - Allergic rhinitis
 - Allergic conjunctivitis
 - Allergy-induced asthma
 - Urticaria
 - Food allergy
- Some of the allergens tested via **Prick Testing** include:
 - Food
 - Pets
 - Dust mites
 - Pollens
 - Grasses, etc...
- In the U.S., Prick Testing is performed by an Allergist.
- Prick Testing is not usually useful in patients with eczematous dermatitis.



Patch Testing

- A screening series of allergens is used:

- **T.R.U.E. TEST[®] (Thin-Layer Rapid Use Epicutaneous Patch Test)**

- Approved by the FDA, consists of 3 panels of pre-impregnated allergens
- Currently screens for **36** substances
 - 35 allergens
 - 1 negative control

- **American Contact Dermatitis Society (ACDS) Core Allergen Series**

- Currently screens for **80** allergens
- What we currently perform at UofM

- **North American Contact Dermatitis Group (NACDG) screening series**

- Currently screens for **70** allergens



The Medical Necessity of Comprehensive Patch Testing

Tian Hao Zhu, MD,* Raagini Suresh, BS,† Erin Warshaw, MD,‡§ Pamela Scheinman, MD,||
Christen Mowad, MD,¶|| Nina Botto, MD,** Bruce Brod, MD,†† James S. Taylor, MD,‡‡
Amber Reck Atwater, MD,§§ Kalman Watsky, MD,|||| Peter C. Schalock, MD,¶¶|| Brian C. Machler, MD,***
Stephen Helms, MD,††† Sharon E. Jacob, MD,‡‡‡ and Jenny E. Murase, MD**§§§

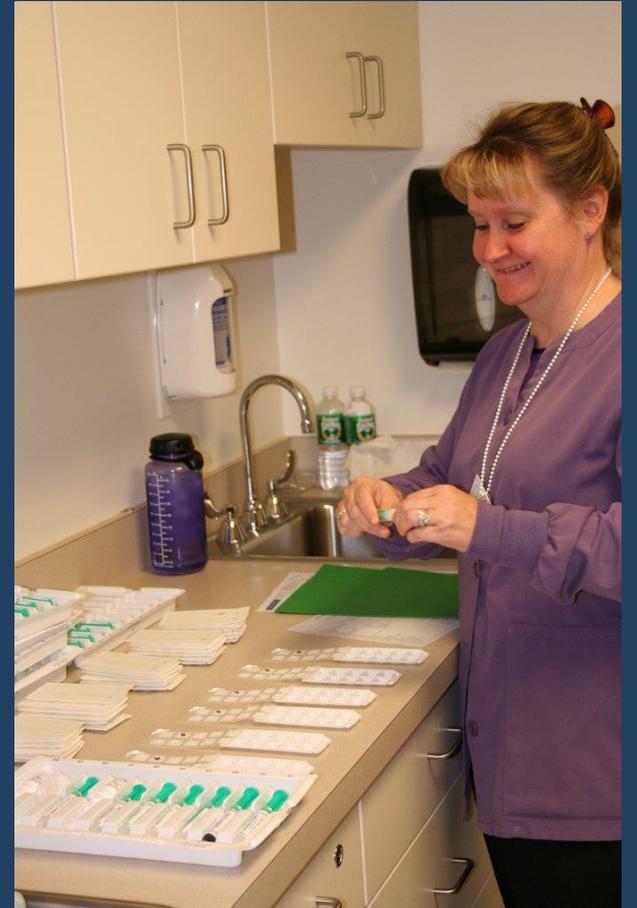
- **The “cure of ACD” is avoidance**, therefore in order to properly manage ACD, it is paramount to accurately identify the causative allergen(s) so they can be avoided.
- Studies have shown that medical history alone is inadequate to diagnose ACD in most cases.
- The commercially available T.R.U.E. test (35 allergens and 1 control) at most detects 66% of the clinically relevant reactions identified by the NACDG screening series of 70 allergens. Notably, up to 50% of allergens causing occupational dermatitis are missed.

Patch Testing

- Time consuming and labor-intensive
- **Requires 3 clinic visits the same week (Monday, Wednesday, Friday)**
- Significant investment of personal time by the patient and considerable clinic time by the physician

Patch Testing

- **1st step:** Our nurse prepares the test allergens (chemicals in proper concentration and vehicle)
- At UofM Dermatology → ACDS Core Allergen Series



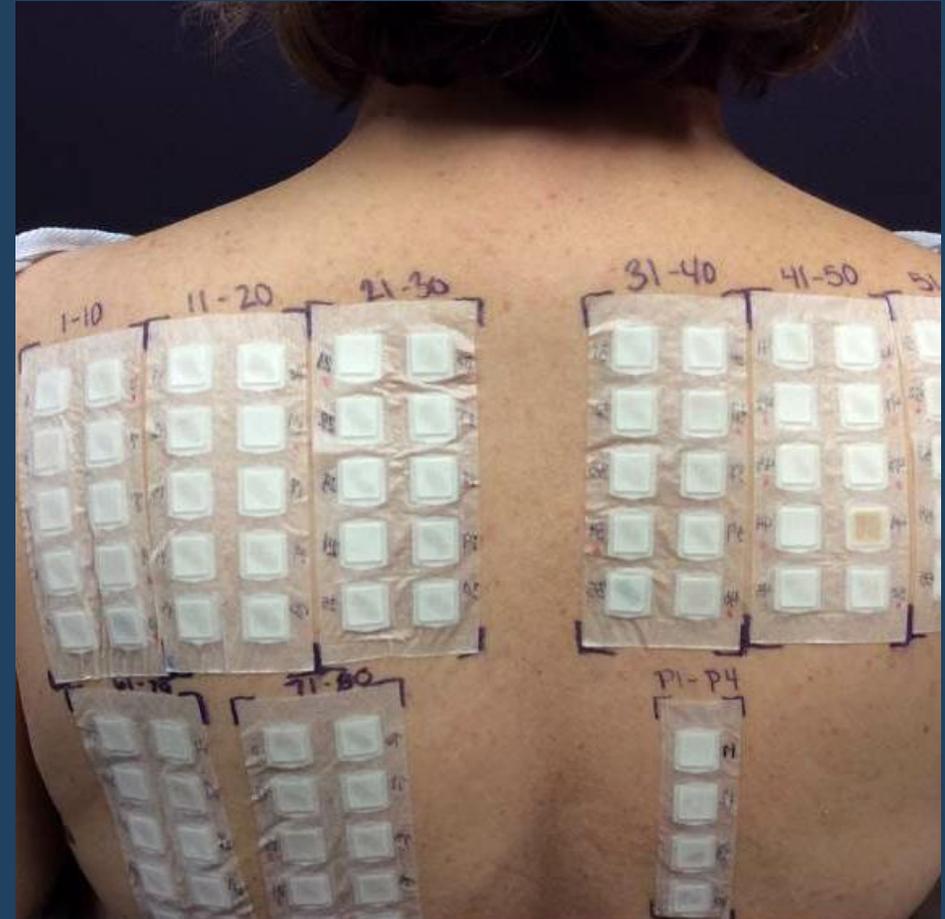
Major groups of allergens routinely tested include:

- Ingredients in personal care products such as:
 - Fragrances
 - Preservatives
 - Sunscreens
- Topical medications:
 - Antibiotics
 - Steroids
- Rubber and adhesive related chemicals
- Metals
- Etc...



Day 1 (first visit): Monday

- Test materials = patches, are applied usually to the upper back then covered with a hypoallergenic tape and left in place until next visit (Wednesday).



Day 3 (second visit): Wednesday

Patch removal, skin marking, preliminary interpretation of result



Day 5 (third visit): Friday

- Final interpretation

- Each site where an individual allergen was placed is assessed for erythema, edema, infiltration, scaling and blisters and the reaction is graded
- Based on these variables the patient is determined to have contact sensitization, an irritant reaction, or no (negative) reaction to each allergen

1+	=	<i>Weak / Mild</i>		1+ reaction
2+	=	<i>Strong</i>		2+ reaction
3+	=	<i>Extreme</i>		3+ reaction
IR	=	<i>Irritant reaction</i>		Pustular/ Irritant reaction
?	=	<i>Doubtful reaction</i>		
(-)	=	<i>Negative reaction</i>		

Day 5 (third visit): Friday

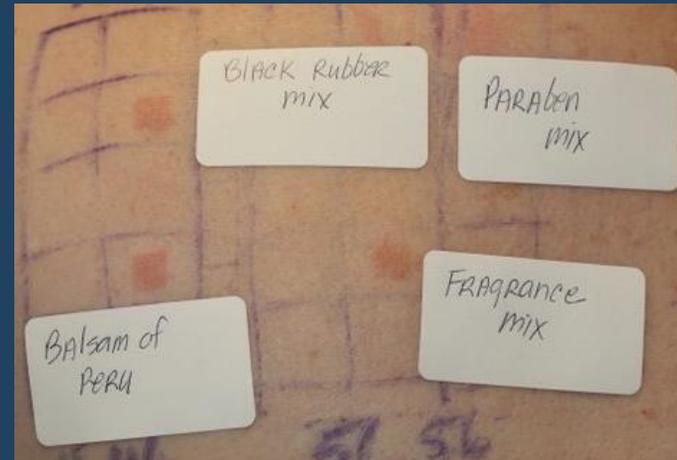
2+ reaction



3+ reaction



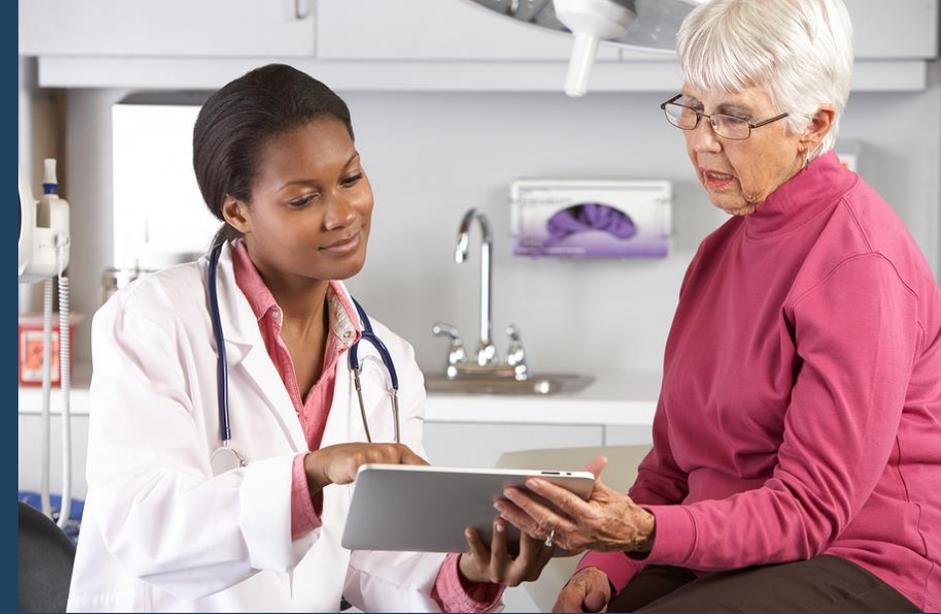
Day 5 (third visit): Friday



- The patch tester must now integrate the results of patch testing with the patient's history, exposures, and physical examination to **determine whether the positive allergic reaction is clinically relevant** for the patient's dermatitis

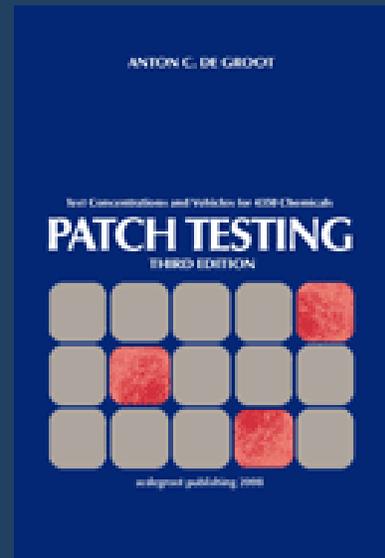
Day 5 (third visit): Friday

- **Patient education** regarding:
 - Their allergen(s)
 - Where could this allergen(s) be found
- **Avoidance strategies**
- **List of safe products / safe alternatives free of their contact allergen(s) – American Contact Dermatitis Society (ACDS), Contact Allergen Management Program (CAMP)**
- Patient education is critical for successful treatment and long-term prevention of recurrence



A world with many contact allergens!

The Third Edition of Anton de Groot's *Patch Testing: Test Concentrations and Vehicles for 4350 Chemicals*



Culprits

- The common allergens that cause ACD may be found in:



Common & Relevant Contact Allergens



North American Contact Dermatitis Group Patch Test Results: 2013–2014

Joel G. DeKoven, MD, MHSc,* Erin M. Warshaw, MD, MS,†‡ Donald V. Belsito, MD,§ Denis Sasseville, MD,||
Howard I. Maibach, MD,¶ James S. Taylor, MD,# James G. Marks, MD,** Joseph F. Fowler, Jr, MD,††
C.G. Toby Mathias, MD,‡‡ Vince A. DeLeo, MD,§§ Melanie D. Pratt, MD,|||| Matthew J. Zirwas, MD,¶¶
and Kathryn A. Zug, MD###

Dermatitis. January/February 2017

4871 pts were patch tested to a series of 70 allergens, 3255 pts (66.8%) had at least 1 positive reaction, 2412 pts (49.5%) were ultimately determined to have a primary diagnosis of ACD.

TABLE 5. Strength of Reactions/Clinical Relevance

	Substance	n	Positive Reactions
1	Nickel sulfate hexahydrate, 2.5% pet	4850	975
2	Fragrance mix I, 8.0% pet	4858	576
3	MI, 0.2% aq	4857	527
4	Neomycin sulfate, 20.0% pet	4857	409
5	Cobalt (II) chloride hexahydrate, 1.0% pet	4859	361
6	Bacitracin, 20.0% pet	4858	360
7	<i>Myroxylon perei</i> resin (balsam of Peru), 25.0% pet	4859	348
8	4-Phenylenediamine base, 1.0% pet	4853	342
9	Formaldehyde, 2.0% aq	4858	339
10	MCI/MI, 0.01% aq	4856	309
	Fragrance mix II, 14.0% pet	4859	277
	Formaldehyde, 1.0% aq	4858	274
	Lanolin alcohol (Amerchol L 101), 50% pet	4859	260
	Quaternium-15, 2.0% pet	4856	235
	Carba mix, 3.0% pet	4859	234
	Iodopropynyl butylcarbamate, 0.5% pet	4859	229
	Cinnamal (cinnamic aldehyde), 1.0% pet	4858	203
	Diphenylguanidine, 1.0% pet	4859	185
	Methyldibromo glutaronitrile/phenoxyethanol (Euxyl K 400), 2.0% pet	4855	179
	OPDMA, 0.1% aq	4859	172
	Thiuram mix, 1.0% pet	4859	153
	Propylene glycol, 100.0% aq	4859	137
	2-HEMA, 2.0% pet	4859	128
	Propylene glycol, 30.0% aq	4859	106
	Potassium dichromate, 0.25% pet	4859	105
	Tixocortol-21-pivalate, 1.0% pet	4859	102
	2-Bromo-2-nitropropane-1,3-diol (Bronopol), 0.5% pet	4859	101
	Benzophenone-4, 10.0% pet	4857	100

Contact Allergens of the Year (CAoY)

- 2018 – Propylene glycol
- 2017 – Alkyl Glucosides
- 2016 – **Cobalt**
- 2015 – **Formaldehyde**
- 2014 – Benzophenones
- 2013 – **Methylisothiazolinone**
- 2012 – Acrylates
- 2011 – Dimethyl Fumarate
- 2010 – **Neomycin**
- 2009 – Mixed dialkyl thioureas
- 2008 – **Nickel**
- 2007 – **Fragrance**
- 2006 – **p-Phenylenediamine**
- 2005 – Corticosteroids
- 2004 – Cocamidopropyl betaine
- 2003 – **Bacitracin**
- 2002 – Thimerosal
- 2001 – Gold
- 2000 – Disperse Blue

ones in **RED** = among **top 10**



Nickel

- #1 identified (testable) cause of ACD
- CAY 2008
- Strong, silver-color metal
- ACDS to nickel particularly affects females
- Jewelry (costume), zippers, buttons, snaps, belt buckles, hair pins, eyeglass frames, razor blades, bra underwire, orthopedic implants, keys, coins, tools, utensils, as well as many other metal-containing objects

The high rate of nickel sensitivity can be attributed in large to ear piercing



Traditionally, the prevalence of nickel sensitivity has been **higher in women**

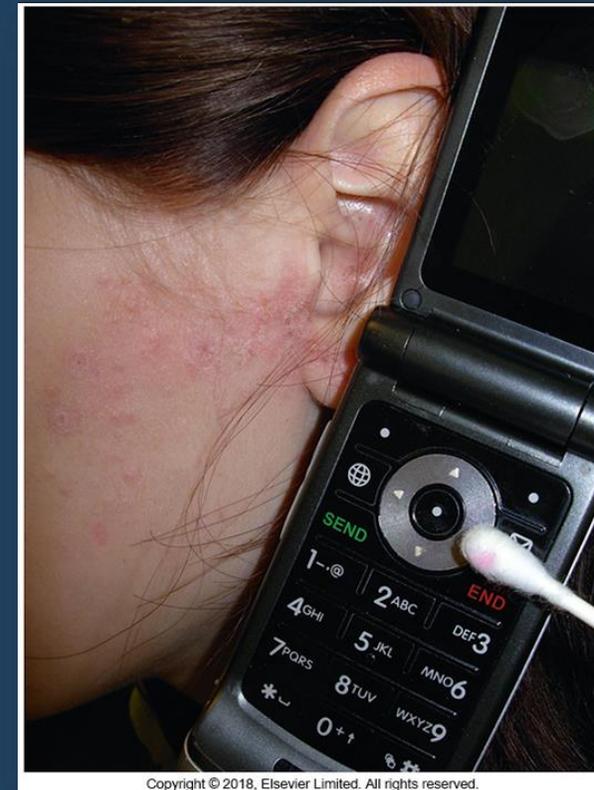
Nickel

- Allergy on the rise in the US (based on NACDG data):
 - 1985: 10.5% of patch tested patients
 - 2006: 19%
 - 2013-2014: 20.1%
- In Europe, there has been a significant reduction in nickel allergy as a result of legislation limiting nickel release from items in contact with the skin



ACD to Nickel

- Most commonly occurs at sites of contact with earrings, necklaces, back of watches, belt buckles or metal snaps
- Eyelid dermatitis from metal eyelash curlers or eyeglasses can also be seen
- Facial dermatitis due to ACD to nickel within **cellular phones** is well described



The presence of nickel is demonstrated by a positive dimethylglyoxime test (pink indicator)

Fragrances



- **2nd most common contact allergen** in North America with a rate of 11.9%
- CAY 2007
- Ubiquitous in our environment. They are used to provide a pleasant odor and have been used extensively for centuries

- **Natural or synthetic**

- 1% of population is sensitive

- Women > men



- ACD to fragrance is diagnosed by patch testing patients to three mixes: fragrance mix I (n 8) , fragrance mix II (n 6) and Balsam of Peru (complex mixture)

Fragrances - cha

- Fragrances can also be *fragrances*
- The above often occur



sant odor = *masking*

“unscented”

Unscented is not the same as fragrance-free

More cha

- Also, there are other purposes i.e. they can be used for other purposes
- E.g. benzyl alcohol as fragrance- rather than fragrance
- The product is fragrance-free as long as it contains benzyl alcohol



other purposes
fragrance

as fragrance-
rather than fragrance

Index Case

- 67 y/o female
 - April 2010, while vacationing in the Dominican Republic, developed severe photo-distributed dermatitis
 - Feb 2011, while on a cruise in the Caribbean, developed facial dermatitis with marked swelling



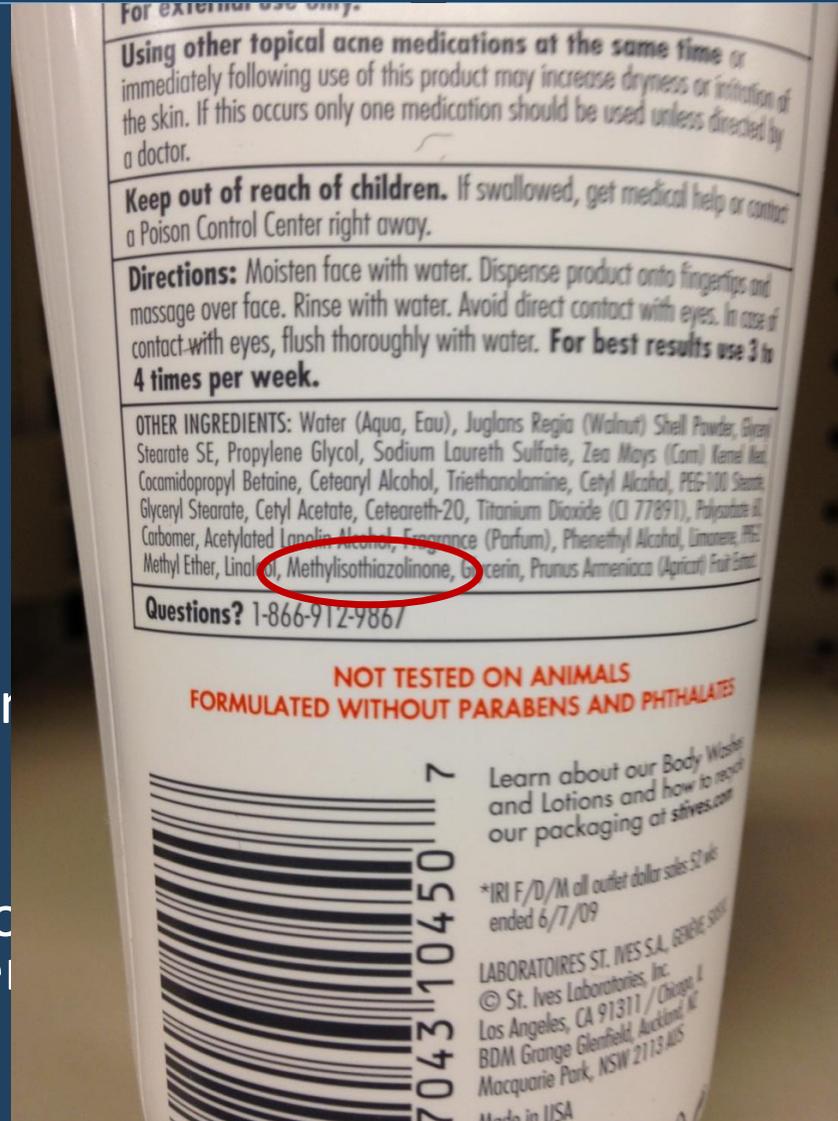
Index Case

- Given her h/o photodistributed and photoinduced dermatitis when traveling to places with intense sunlight, she was patch tested and photo-patch tested to sunscreen ingredients only, on June 2011
- Also tested to **patient's own sunscreen products (x 7)**

48 hrs

96 hrs

- 3+ Neutrogena ultra sheer sunblock
- 3+ Neutrogena pure sunblock
- 3+ Neutrogena sensitive sunblock SPF 30
- 1+ Neutrogena sensitive sunblock SPF 60
- 1+ Aveeno daily moisturizer with SPF
- 1+ **Oxybenzone** (Benzophenone-3)
- 1+ Benzophenone-8
- No photo aggravation
- **Oxybenzone** was in majority of the sunscreens
- Suspect possible additional added NACDG + Supplement



- 3+ Neutrogena ultra sheer sunblock
- 3+ Neutrogena pure sunblock
- 3+ Neutrogena sensitive sunblock SPF 30
- 1+ Neutrogena sensitive sunblock SPF 60
- 1+ Aveeno daily moisturizer with SPF
- 1+ **Oxybenzone** (Benzophenone-3)

aggravation

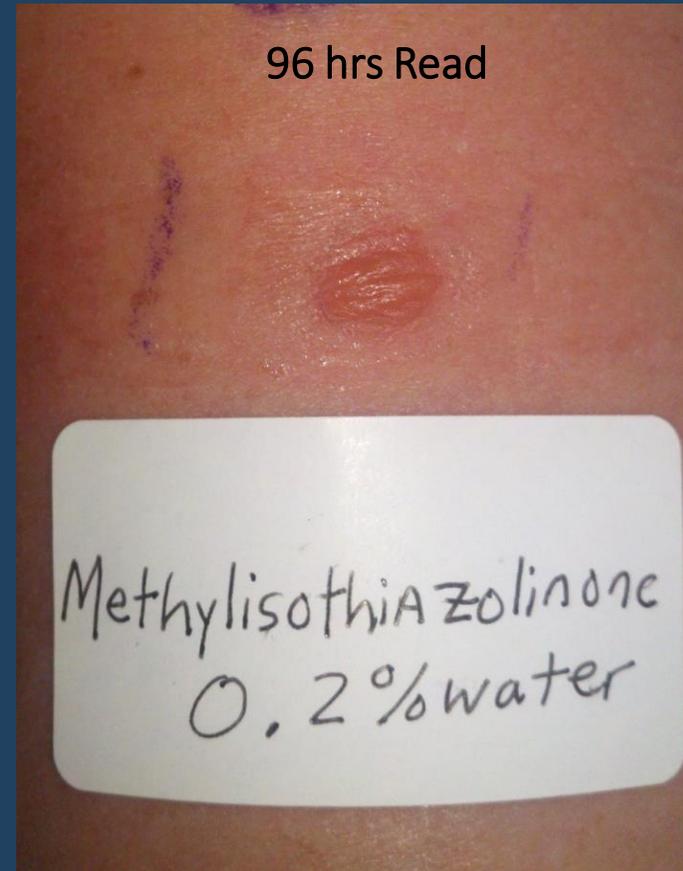
Notes: Questionable (?) reaction to Methylisothiazolinone/Methylisothiazolinone

Results of all 3+ products pooled: Methylisothiazolinone **ALONE** (MI) was a common irritant in all products

They wanted to add a patch of MI alone, but we did not have it available

Follow-up

- Patient returned for a solitary patch to Methylisothiazolinone
- MI 0.2% in water applied



Background

- Methylchloroisothiazolinone (MCI) with Methylisothiazolinone (MI) in a 3:1 combination = MCI/MI (trade names: Kathon CG, Euxyl K 400) used in industrial and consumer products since the early 1980s
- MCI more potent sensitizer of the mix
- MCI/MI one of the most frequently used preservatives in toiletries
- MCI/MI one of the most common causes of preservative contact allergy → 10th most common contact allergen in North America

Background - MCI/MI

- Until recently, the maximum concentration for all personal care products in the European Union was: 15 ppm (11.25 ppm MCI and 3.75 ppm MI)
- Maximum concentration in the U.S.:
 - 15 ppm for rinse-off products
 - 7.5 ppm for leave-on products (5.62 ppm MCI and 1.87 ppm MI)

Background - MI (alone)

- Due to the believe that MI was a weaker sensitizer when compared to MCI...
- In 2005, **MI alone** began to be used as a separate preservative in all personal care products at a concentration of **100 ppm**
- The introduction of MI alone has lead to a more than **25-times increase** in the permitted concentration of MI in cosmetics:
 - From 3.75 ppm (one quarter of 15 ppm MCI/MI) to 100 ppm

Background - MI (alone)

- Parallel to the increased presence of MI in personal care products, cases of allergic contact dermatitis to MI began to be published all around the world
- Similarly, there has been an increase in the frequency of sensitization to MCI/MI
 - In part due to increasing exposure to MI alone in personal care products

The Problem



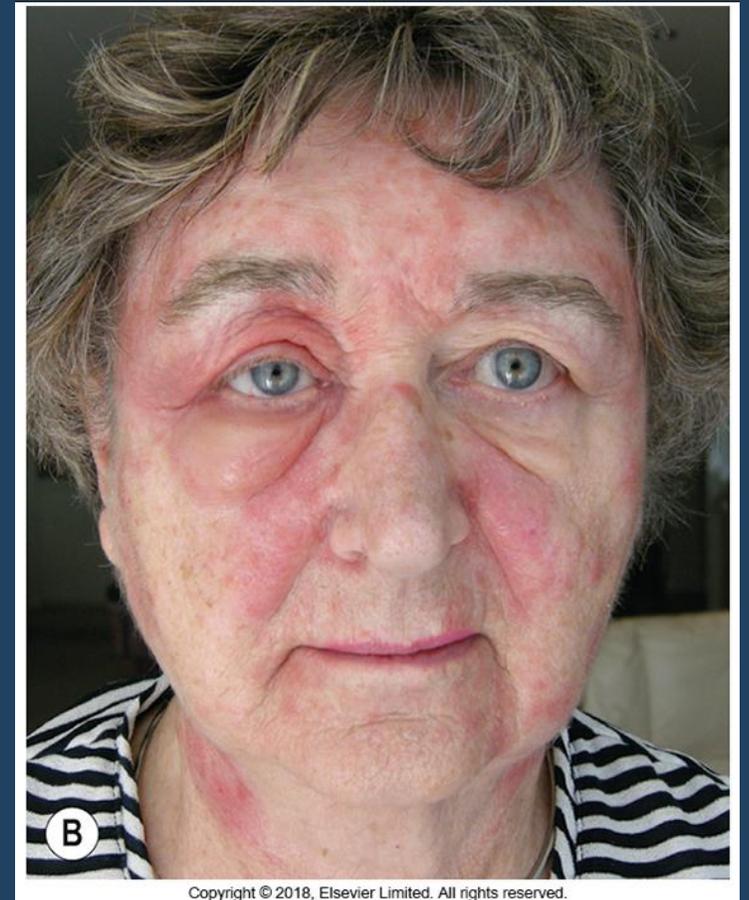
- Patch testing to MCI/MI (75ppm/25ppm) but not MI alone, can miss MI allergy
 - Due to low concentration of MI in the patch test substance.

Contact Allergy to MI alone

- 1st occupational cases:
 - 2004 - Isaksson et al → wall-paper glue
 - 2006 - Thyssen et al → **paint**
- Airborne contact dermatitis after exposure to MI from carpet glue and wall paint

Contact Allergy to MI alone

- 2010, Garcia-Gavin et al: 7 non-occupational cases related to cosmetics/toiletries:
 - 6/7 - perianal dermatitis from **moist toilet paper**
 - 1/7 – eyelid dermatitis from **make-up remover**
- Allergic contact dermatitis to methylisothiazolinone in a wet wipe used to remove make-up.



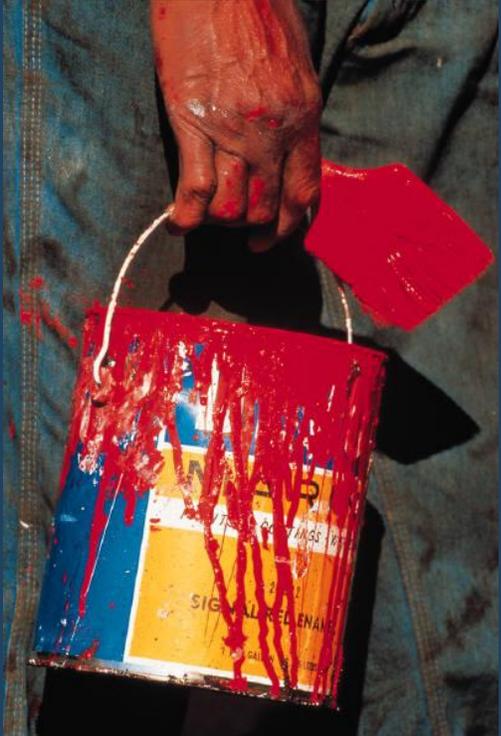
Wet Wipes

- The use of wipes for intimate hygiene is an important sensitization source for MI (also MCI/MI).



The use of such products in non-keratinized and occluded areas could be responsible for this.

Sources of Exposure



Contact Allergy to MI

- Allergic reactions to MI are increasing at dramatic rates in both the EU and the US → **epidemic of contact allergy to MI**
- **3rd most common** contact allergen in North America
 - Due to increasing exposure to MCI/MI in cosmetic products
 - Increasing exposure to MI in industrial applications (paints)
 - Exposure to MI alone in cosmetics







Leave-on product



House-hold products



TRADER JOE'S
**LIQUID
DISH SOAP**
LAVENDER TEA TREE SCENT

PLANT BASED FORMULA
BIODEGRADABLE
HYPOALLERGENIC
CUTS THROUGH GREASE

NET 25 FL OZ (1.6 PT) 739ml.



LIQUID DISH SOAP

LAVENDER TEA TREE SCENT

Trader Joe's Lavender Tea Tree Scent Liquid Dish Soap for handwashing dishes uses a biodegradable and biobased formula that works to safely remove tough grease and grime. Rinses sparkling clean. Gentle on skin.

INGREDIENTS: WATER, SODIUM COCO SULFATE (COCONUT AND PALM KERNEL OIL), LAURAMINE OXIDE, CAPRYLYL/MYRISTYL/GLUCOSIDE, COCO BETAINE, UREA, ALCOHOL DENATURED, PHENOXYETHANOL, GLYCERIN, LAVANDULA ANGUSTIFOLIA (LAVENDER) OIL, METHYLISOTHIAZOLINONE, MELALEUCA ALTERNIFOLIA (TEA TREE) LEAF OIL

DIST. & SOLD EXCLUSIVELY BY:
TRADER JOE'S, MONROVIA, CA 91016

DIRECTIONS FOR USE: Dispense into sink or directly on sponge. Wash dishes and rinse thoroughly.

NOT FOR USE IN AUTOMATIC DISHWASHERS

NO ANIMAL TESTING | NO PHOSPHATES

SKU# 58328



How to use: Squeeze body wash onto a wet pouf or washcloth and work into a rich, creamy lather.

+ contains neutralizing fragrance agents
Dove and NutriumMoisture are registered trademarks.

INGREDIENTS: WATER (AQUA), COCAMIDOPROPYL BETAINE, SODIUM HYDROXYPROPYL STARCH PHOSPHATE, LAURIC ACID, SODIUM LAUROYL GLYCINATE, SODIUM LAUROYL ISETHIONATE, HYDROGENATED SOYBEAN OIL, GLYCINE SOJA (SOYBEAN) OIL OR HELIANTHUS ANNUUS (SUNFLOWER) SEED OIL, SODIUM CHLORIDE, GLYCERIN, GUAR HYDROXYPROPYLTRIMONIUM CHLORIDE, BMDM HYDANTOIN, STEARIC ACID, FRAGRANCE (PARFUM), CITRIC ACID, BHT, TETRASODIUM EDTA, METHYLISOTHIAZOLINONE, IODOPROPYNYL BUTYLCARBAMATE



1-800-761-DOVE
1-800-761-3683
www.dove.com
83273753



© UNILEVER,
Trumbull, CT 06611
Made in U.S.A.

Welcome to Dove > Body Wash and Beauty Bars > Body Wash > Sensitive Skin Body Wash



Sensitive Skin Body Wash

Dove Sensitive Skin Body Wash is hypoallergenic: it's our best body wash for sensitive skin.

Screen shots from CURRENT webpage

Ingredients



Water (Aqua), Cocamidopropyl Betaine, Sodium Hydroxypropyl Starch Phosphate, Lauric Acid, Sodium Lauroyl Glycinate, Sodium Lauroyl Isethionate, Hydrogenated Soybean Oil, Glycine Soja (Soybean) Oil, Sodium Chloride, Glycerin, Phenoxyethanol, Guar Hydroxypropyltrimonium Chloride, Stearic Acid, Citric Acid, **Fragrance (Parfum)**, Sodium Isethionate, BHT, Tetrasodium EDTA, Iodopropynyl Butylcarbamate.

Ingredients correct at time of publishing. Always check product packaging.



Neomycin



- CAY 2010
- Most common sensitizing topical antibiotic
 - **4th most common allergen** in North America!
- Cross reacts with other aminoglycosides
- Co-reacts but not cross-reacts with Bacitracin

Your allergy to Neomycin means you could react to certain closely related antibiotics. You could develop a rash all over your body if you are given one of these by mouth or injection. **DO NOT USE:**

Tobramycin	Spectinomycin
Gentamicin	Streptomycin
Butirosin	Dihydrostreptomycin
Paromomycin	Netilmicin
Framycetin	Sisomicin
Kanamycin	Ribostamycin
Amikacin	

Cobalt

- **5th most common allergen** in North America
- CAY 2016
- Common false positive due to irritation
- **Co-reacts** with nickel (NOT the same thing as cross-react)
- Found in costume jewelry; metal objects (buckle, zipper, coin, key, tools); metal implants (orthopedic **prosthesis**, dental), blue dye for enamel, glass, ceramic, porcelain, crayons, blue paints; hair dyes (light brown) Vitamin B-12 (cyano-cobalamine), etc...
- **Practically speaking, best way to avoid cobalt is to avoid nickel**

Cobalt spot test = **disodium-1-nitroso-2-naphthol-3,6-disulfonate**

OTC Neosporin not only contains Neomycin!



Bacitracin

- 6th most common contact allergen in North America!
- CAY 2003
- In addition to causing a type IV (delayed, T-cell-mediated) hypersensitivity reaction, it can also cause a type I (immediate, IgE-mediated) hypersensitivity reaction



Balsam of Peru



- 7th most common contact allergen in North America
- *Myroxylon pereirae* also known as Balsam of Peru, is a substance derived from *Myroxolon balsamum*, a tree that is native to El Salvador
- **Marker for fragrance allergy**
 - Because its main components (cinnamic acid, cinnamyl cinnamate, benzyl benzoate, benzoic acid, benzyl alcohol, and esterified polymers of coniferyl alcohol) are naturally derived, they have a significant number of natural cross-reactors
 - Certain foods, such as tomatoes and tomato-containing products, citrus fruit peel/zest, chocolate, ice cream, wine, beer, vermouth, dark colored sodas, and spices such as cinnamon, cloves, curry, and vanilla, have chemical ingredients related to Balsam of Peru
- Consumption of these foods may result in a systemic reactivation of ACD in some patients allergic to Balsam of Peru

Para-phenylenediamine (PPD)

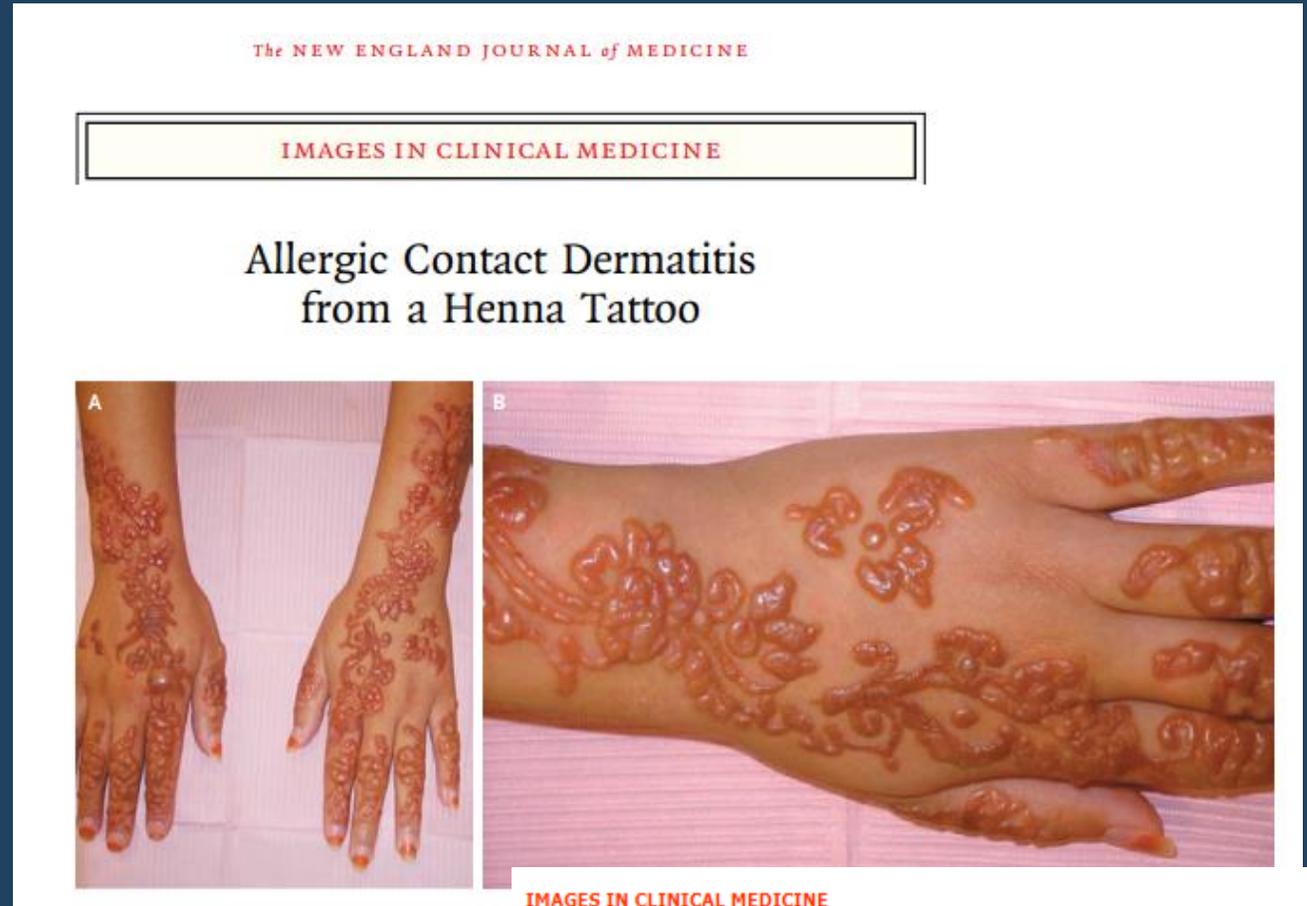
- 8th most common contact allergen in North America
- CAY 2006
- Dark dye used in almost all permanent **hair dyes** and some semi-permanent hair coloring
- Potent contact allergen which triggers severe acute contact dermatitis in sensitized individuals
- Also in “**black**” **henna tattoos** (contaminant = adulterated henna)



Clinical examples of ACD to PPD



ACD to PPD in hair dye



IMAGES IN CLINICAL MEDICINE

Allergic Contact Dermatitis from a Henna Tattoo

Colby C. Evans, M.D., and John D. Fleming, M.B., B.S.

N Engl J Med 2008; 359:627 | August 7, 2008 | DOI: 10.1056/NEJMicm062327

Para-phenylenediamine (PPD)



Young girl left with horrific burns and permanent scarring after receiving henna tattoo on holiday



Nick Reilly

Yahoo News UK 17 August 2017

[Follow](#)

Para-phenylenediamine

- Cross reactivity with:

- PABA plus **PASSTE**:

- PABA
- Para-aminosalicylic acid
- Azo and aniline dyes
- Sulfonamides
- Sulfonylureas
- Thiazides
- Ester anesthetics (they only have 1 "i") - procaine, benzocaine, cocaine, tetracaine

Formaldehyde

- 9th most common contact allergen in North America
- CAY 2015
- Found in:
 - Embalming fluid, formalin
 - Personal care products AND topical medications = **formaldehyde releasing preservatives**
 - permanent press or “wrinkle-free” textiles (**melamine and urea formaldehyde resins**)
 - cleaning products, disinfectants
 - Paper
- Occupational: metal working, cutting oils, paints, inks, lacquers, cleaning products
- **Notable irritant** (careful when interpreting patch test results)
- Pts w/ formaldehyde allergy commonly present with hand and/or generalized dermatitis (slow recovery)

Formaldehyde Releasing Preservatives

- Formaldehyde is released by these common preservatives:
 - quaternium-15
 - DMDM hydantoin
 - diazolidinyl urea (Germall II)
 - imidazolidinyl urea (Germall, imidurea)
 - 2-bromo-2-nitropropane-1,3-diol (Bronopol)
- and in industry tris nitromethane (Tris Nitro)



Imidazolidinyl urea
(formaldehyde-releasing
Preservative)

Methylchloroisothiazolinone/
Methylisothiazolinone (MCI/MI)

Fragrance

DMDM hydantoin
(formaldehyde-releasing
Preservative)



**Ketoconazole Shampoo, 2%
For Topical Application Only**

Dosage:
One application of the shampoo should be sufficient and then intermittently as needed.

Directions for Use
Apply the shampoo to the damp skin of the affected area and a wide margin surrounding this area. Lather, leave in place for 5 minutes, and then rinse off with water.

Active ingredient: ketoconazole
Inactive ingredients: coconut fatty acid diethanolamide, disodium laureth sulfosuccinate, FD & C Red No. 40, hydrochloric acid, imidurea, laurdimonium hydroxypropyl hydrolyzed collagen, PEG-120 methyl glucose dioleate, purified water, sodium chloride, sodium hydroxide, and sodium lauryl ether sulfate.

Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature]. Protect from light.

Made in Israel
Manufactured By Perrigo, Yeruham 80500, Israel
Distributed By

Perrigo®

Allegan, MI 49010
www.perrigo.com

: 4L926 RC B4

Rev 04-13



Conclusion

TABLE 5. Strength of Reactions/Clinical Relevance

	Substance	n	Positive Reactions
1	Nickel sulfate hexahydrate, 2.5% pet	4850	975
2	Fragrance mix I, 8.0% pet	4858	576
3	MI, 0.2% aq	4857	527
4	Neomycin sulfate, 20.0% pet	4857	409
5	Cobalt (II) chloride hexahydrate, 1.0% pet	4859	361
6	Bacitracin, 20.0% pet	4858	360
7	<i>Myroxylon pereirae</i> resin (balsam of Peru), 25.0% pet	4859	348
8	4-Phenylenediamine base, 1.0% pet	4853	342
9	Formaldehyde, 2.0% aq	4858	339
10	MCI/MI, 0.01% aq	4856	309

Most common culprits of ACD in North America:

- 2 metals
- 2 fragrances
- 3 preservatives
- 2 topical antibiotics
- 1 hair dye ingredient

Reasons why I LOVE this field

- Play detective
- Learn about what people do
- In-vivo process: “experiment”
- Potential to cure the rash
- Team work
- Public health

