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California Society of Allergy, Asthma and Immunology
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Contact Dermatitis for the Allergist

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LEARNING OBJECTIVES

- Discuss various presentations of contact dermatitis
- Discuss the role of patch testing and practical aspects of emerging and important allergens

The Diagnosis of Contact Dermatitis is based on

Location,

Location,

Location,

TABLE 2. Sites of Dermatitis and Final Diagnoses

Characteristic	Primary site, n (%)	Any of Up to 3 Sites, n (%)*
Dermatitis site†	n = 4928‡	n = 4928‡
Hand	1063 (21.6)	1316 (26.7)
Scattered generalized	896 (18.2)	1187 (24.1)
Face	788 (16.0)	1117 (22.7)
Eyelids	557 (11.3)	690 (14.0)
Lips	251 (5.1)	354 (7.2)
Trunk	217 (4.4)	538 (10.9)
Scalp	191 (3.9)	331 (6.7)
Arm	177 (3.6)	579 (11.7)
Anal/genital	108 (2.2)	165 (3.3)
Other	93 (1.9)	124 (2.5)
Neck	83 (1.7)	443 (9.0)
Most exposed areas	76 (1.5)	96 (1.9)
Ears	71 (1.4)	136 (2.8)
Only under clothing	34 (0.7)	38 (0.8)
Eyes	22 (0.5)	48 (1.0)
Erythroderma	4 (0.1)	6 (0.1)
Nose	1 (0.0)	10 (0.2)

DeKoven et al. NACDG Patch Test Results:2017–2018 March 2021.DERMATITIS

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Hands

Irritant Contact



- Lesions often localized in webs of the fingers
- Extends onto dorsal & ventral surfaces (“apron” pattern), palms & ball of the thumb
- Less responsive to topical CS
- May precede ACD
- Diagnosis of exclusion

Allergic Contact



- Vesicles
- Favors fingertips, nail folds & dorsum of hands
- Less commonly involve palms (thicker skin)
- Relevant allergens PT:
  - Nickel, Potassium Dichromate, rubber components, PPD, cobalt

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Face

	Dermatitis Distribution	Likely Products
	Lateral face: including the preauricular area, jaw line and lateral aspect of the neck	Shampoo and/or conditioners rinsed down over these areas
	Unilateral face	May be due to transfer of allergens such as nail cosmetics, connubial or consort dermatitis related to hair dye, fragrances of topical medication from the partner
	Central face: involving the cheek, nose, chin and forehead	Moisturizers, wrinkle creams, topical medications, make up or gold (contamination of make-up foundation after being released from jewelry)
	Full face	Airborne contactants, facial cleansers, make up foundation

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Eyelid alone

	Dermatitis Distribution	Likely Products
	Eyelid involving the upper and/or lower eyelid extending beyond the orbit	Shampoos and conditioners
	Upper Eyelid alone	May be Irritant

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Eyelid Plus

	Dermatitis Distribution	Likely Products
	Eyelid plus the face	Facial cleansers
	Eyelid plus scalp or forehead	Hair products such as dyes, bleaching agents, setting lotions, sprays, gels, and mousses
	Some combination of eyelids, face and neck	Ectopic dermatitis from nail polish and acrylic nail dermatitis

Lips

	Dermatitis Distribution	Likely Products
	Both top and bottom lips and both sides are equally affected	Lanolin, propolis, propyl gallate, fragrance mix (FM), Balsam of Peru (BOP), and flavorings commonly found in lip balm and lip cosmetics
	Lower lip is involved more than the upper lip or if one side is involved more than the other	Toothpaste containing the allergens CAPB, propylene glycol, spearmint and menthol is likely the cause

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Scattered / Generalized

Textile Dyes

- Primary sensitization: occupational exposure to cross-reacting chemicals
  - PPD in hair dressers
- Disperse dyes accounts 2/3 of textiles ACD
  - TT™: only Disperse blue 106
- High false (-) to PT to pieces of clothing (usage conditions may not be replicated)




Formaldehyde Resin

- Primary sensitization: occupational exposure to formaldehyde in HCW, embalmers, cabinetmakers
- Common in highly finished garments (wrinkle free, permanent press, reduce shrinking, increase strength)
  - Uniforms, water-resistant laboratory coats, zip-up greens of machinists, military wool garments, furniture cotton upholstery
- Sub-acute and chronic dermatitis
- Slow resolution of dermatitis even with careful avoidance
  - As much as 50% still had constant dermatitis *



Dermatitis: 2007. Vol 18 (1) 40-44

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PPD (Paraphenylenediamine)

- Highly sensitizing allergen
- Hair dye: most common route of sensitization
- Growing risk of sensitization from black henna tattoos, especially in children

Dermatitis: 2007. Vol 18 (1) 40-44 doi: 10.2310/6620.2007.05003

THE GREATEST ABUSE OF PATCH TESTING IS

FAILURE TO USE THE TEST

Colman, 1982

- **The diagnosis of ACD made solely by history is under suspected, under diagnosed or misdiagnosed when compared with those patch tested**
(Sherbets EF. Controversies in contact dermatitis. Am J Contact Dermat 1994;5:130-135)

- **Relief of symptoms average 143 days sooner on patch tested vs. non patch tested patients** (RajagopalanR et al. Cutis 1996;57:360-364)

Selecting Allergens

Screening Patch Test
T.R.U.E. Test® (35 allergens, currently the only FDA approved PT for ≥ 6 y.o.)

Expanded Patch Test
North American Standard Series (~70 allergens)
ACDS Core Allergen Series (80 allergens)

Allergens grouped for specific exposure
(hairdresser, shoes, plants, vehicles, metals, antibiotics, corticosteroids, photoallergens, etc)

Patient Products

Allergens from cosmetic & other industry

allergEAZE®:(www.smartpractice.com)
SmartPractice
3400 E. McDowell Road Phoenix, AZ 85008-7899
Ph: 800.522.0800
info@smartpractice.com

Dormer laboratories®:
(http://www.dormer.com)
91 Kelfield Street #5
5040 Toronto, ON M9W CANADA
Ph: 866 976 7637

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T.R.U.E.® vs Finn loaded Allergens

Hypothetical detection rate of TT® vs. NACDG: 57.9-70.4%

	T.R.U.E. ®	NACDG
Antigen Components	Thimerosal, gold, quinoline mix	None of these
Individual vs. “mixes”	caine mix	benzocaine & dibucaine
	parthenolide	sesquiterpene lactone mix & compositae mix
Different sensitivities for some allergens tested	T.R.U.E. Test ® Misses: 50% Fragrance 62% Balsam of Peru 56% Thiuram	Finn Misses: 25% nickel 21 % neomycin 28% MCI/MI
	T.R.U.E. Test ® better for Nickel	Finn better for Formaldehyde

TABLE 3. Strength of Reactions/Clinical Relevance

Substance	n	% Positive	Positive Reactions
Nickel sulfate hexahydrate, 2.5% pet	4937	16.2	803
MI, 0.2% aq (2000 ppm)	4938	15.3	756
MCI/MI, 0.02% aq (200 ppm)	4940	11.0	543
Fragrance mix I, 8.0% pet	4944	9.2	456
Hydroperoxides of linalool, 1% pet	4934	8.9	439
Formaldehyde, 2.0% aq	4928	7.4	367
BIT, 0.1 % pet	4946	7.3	359
Myroxylon pereirae resin (balsam of Peru), 25.0% pet	4940	7.1	350
Cobalt (ii) chloride hexahydrate, 1.0% pet	4946	6.7	331
4-Phenylenediamine, 1.0% pet	4926	5.6	279
Bacitracin, 20.0% pet	4937	5.5	274
Neomycin sulfate, 20.0% pet	4938	5.4	269
Formaldehyde, 1.0% aq	4938	5.4	267
Propolis, 10.0% pet	4939	4.7	234
Fragrance mix II, 14.0% pet	4944	4.4	219

Not in the True Test ®

The top 15 most frequently positive allergens

- 2 metals
  - nickel & cobalt
- 2 antibiotics
  - neomycin & bacitracin
- 4 fragrances
  - FM I, FM II, M. pereirae (BOP), hydroperoxides of linalool
- 4 preservatives
  - MI*, MCI/MI*, BIT*, formaldehyde [1% & 2%]
- p-phenylenediamine
- propolis

*Isothiazolinone family

DeKoven et al. NACDG Patch Test Results:2017–2018 March 2021.DERMATITIS

Patch Test Recommendations for Children 6-12 y.o.

Primary Allergens				Secondary Allergens	
1	Bacitracin	11	Fragrance mix 1	1	black rubber mix
2	Budesonide	12	Fragrance mix 2	2	dialkyl thioureas
3	Carba mix	13	Lanolin alcohol	3	mercaptobenzothiazole
4	Cobalt chloride	14	MCI/MI	4	para-phenylenediamine
5	Cocamidopropyl betaine	15	Myroxylon pereirae (Balsam of Peru)	5	p-tert butyl phenol formaldehyde resin
6	Colophonium	16	Neomycin sulfate		
7	Compositae mix/ dandelion extract	17	Nickel sulfate		
8	Disperse blue	18	Potassium dichromate		
9	Ethylenediamine	19	Quaternium 15		
10	Formaldehyde	20	Tixocortol-1-pivalate		

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Jacob SE, Brod B, Crawford GH. Clinically relevant patch test reactions in children—a United States based study. Pediatr Dermatol. 2008 Sep-Oct;25(5):520-7*

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The “Right Time to Read”

Most true allergic reactions occur between 72-96 hours.

Allergens that may peak early

- thiuram mix
- carba mix
- balsam of Peru

Allergens that Disappear after 5 Days

- Balsam of Peru
- Benzoic Acid
- Disperse Blue #124
- Fragrance mix
- Mercury
- Methylydibromogluteronitrile/ phenoxyethanol
- Octyl gallate

Delayed Patch Test Reactions after 5 days

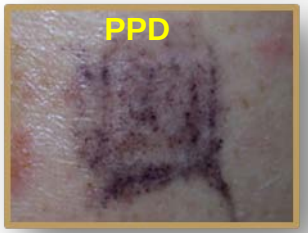
- Metals
  - Gold
  - Potassium Dichromate
  - Nickel
  - Cobalt
- Topical Antibiotics
  - Neomycin
  - Bacitracin
- Topical Corticosteroids
- PPD

Davis M et al. Delayed Patch Test reading after 5 days : the Mayo Clinic Experience. JAAD Aug 2008; 59 (2):225-233
Higgins et al. The relevance of 7-day patch test reading. Dermatitis. 24(5):237-240, 2013.

Characterize Reactions

Irritant Morphology
Pustules, Dry Skin, Scaling,
Petechiae, Shiny Skin,
Cigarette Paper Appearance

Expected Discoloration
Dye retention

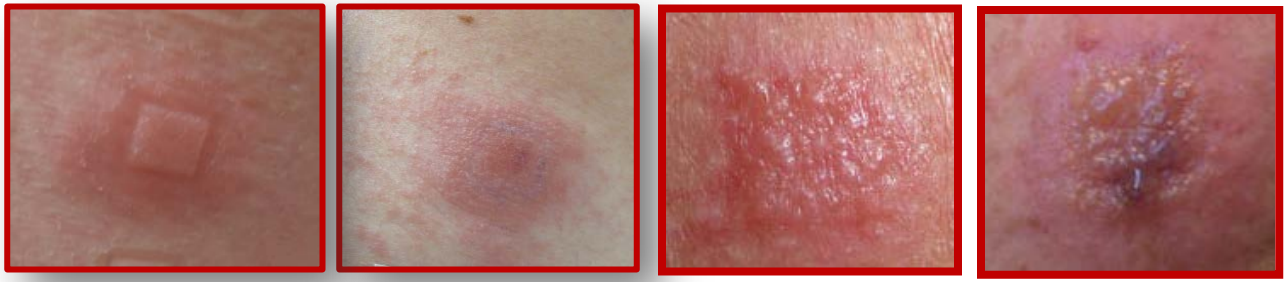


Unique Appearance

Characterize Reactions

Allergic Morphology

- **Erythema, infiltration & edema filling application site**
- **Papules**
- **Vesicles, Bullae**



Determining Relevance

Current Relevance

- ***Definite***
  - (+) “use test” with suspected item or
  - (+) PT with the object or product
- ***Probable***
  - Suspected allergen is verified in known skin contactants with a consistent clinical presentation
- ***Possible***
  - If patient’s skin is in contact with materials that likely contain the suspected allergen
- ***Past***
  - Patient no longer has exposure to the (+) allergen

CAUSES OF FALSE POSITIVE REACTIONS

Use of irritant substances

- Sharply demarcated
- Confined to disc area
- Shiny, often w/ blister
- Burning or painful

Pressure reaction

Edge effect

- **Angry Back Syndrome**
  marked 2+ to 3+ surrounded by (+/-) or (+) responses to contiguous site
- **Excited Skin Syndrome**

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Methylisothiazolinone

- **Preservative in cosmetics and toiletries**
  MI (singly or MCI/MI) was used in 1125 cosmetic products in the US*
  - **24% (n = 275) in shampoos**
  - **18% (n = 206) in conditioners**
  - **10% (n = 117) in baby soaps & detergents**
- **Household products: dishwashing liquid, soaps, laundry detergents, stain removers, fabric softeners,**
- **MCI/MI mix** (Trade name: Kathon CG) at 3:1

Mix misses ~ 40% of allergy to MI (low concentration in mix)

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*US FDA Voluntary Cosmetic Ingredient Registration
Castanedo-Tardana & Zug. Contact Allergen of the Year 2013 Dermatitis, 24 (1)
Lundov MD, Thyssen JP, Zachariae C, et al. Prevalence and cause of methylisothiazolinone contact allergy. Contact Dermatitis 2010;63:164-167

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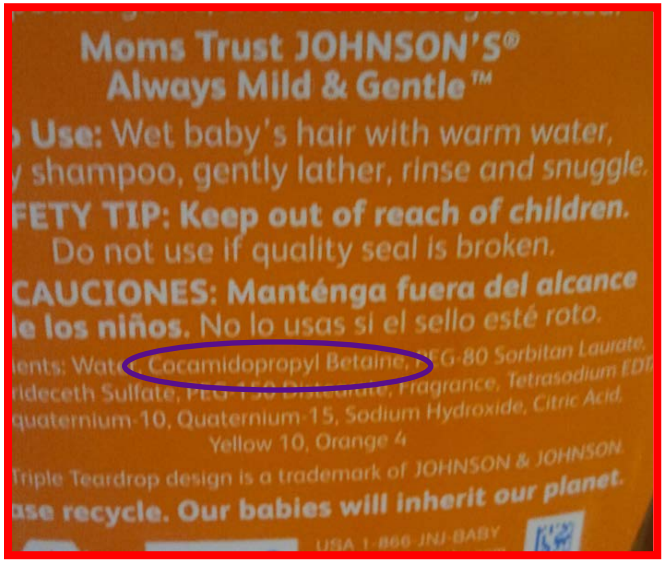

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Cocoamidopropyl betaine

- Amphoteric surfactant in shampoos, bath products, eye & facial cleaners, liquid detergents, surface cleaners, deodorants, pet products
- Second most common allergen in shampoo
- Areas of Involvement
  - Face: 30.2%
  - Neck: 14.3%
  - Hands: 12.7%
  - Eyelids: 9.5%
  - Scalp: 4.8%
  - Scattered: 23.8%
- Positive reactions to this allergen are often clinically relevant

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Fragrance

Fragrance Mix I	Balsam of Peru *(Myroxylon pereirae)*	Fragrance Mix II
Cinnamic alcohol 1%	Cinnamic acid	Coumarin 2.5%
Cinnamic aldehyde 1%	Benzoyl Cinnamate	Hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyral) 2.5%
a-Amyl cinnamaldehyde (amyl cinnamal) 1%	Benzoyl Benzoate	Citronellol 0.5%
Hydroxycitronellal 1%	Benzoic acid	Farnesol 2.5%
Geraniol 1%	Vanillin	Citral 1.0%
Isoeugenol 1%	Nerodilol	a Hexyl cinnamic aldehyde 5.0%
Eugenol 1%		
Oak moss 1%		

Other fragrance sensitizers: Lyral, jasmine, lavender, sandalwood, tea tree oil, ylang ylang oil, lemongrass oil, jasmine, Narcissus

Fragrance mix I & Balsam of Peru (in TT) pick up 60-70% of all ACD to fragrances at best

Fragrance Mix

- Patch Test Low specificity
  - Mild Irritant, caution with weak (+) reactions
- Increased probability of a relevant FM patch-test
  - Increased strength of test reaction
  - Repeated (+) reaction on retest
  - (+) to one of its ingredients

48 hours

96 hours

Fragrance Mix I

Devos SA et al. Relevance of Positive Patch-Test Reactions to Fragrance Mix. Dermatitis, Vol 19, No 1, 2008: 43–47

TOPICAL CORTICOSTEROID (TCS) HYPERSENSITIVITY

- Overall, between 0.2% - 5% of all dermatitis patients have TCS allergy
  - 85% of these patients have multiple TCS allergies

Suspect allergy (active molecule or vehicle)
- all patients who don't respond to TCS
- those who get worse with TCS
- those who improve initially, then flare

↓

In this population TCS allergy is seen in:
- 19% - 22% of these adults
- 25% of these children

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Brown F, Wilkinson SM. Effective prescribing in steroid allergy: Controversies and cross-reactions. Clin Derm 2011 29:287-94.
Baeck M, Marot L, Nicolas JF, et al. Allergic hypersensitivity to topical and systemic corticosteroids: a review. Allergy 2009 64:978-994

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Steroid Classifications

Potency

Potency & side effects are related to saturation of the GCRs in different cell types

- Class 1 → Class 7
- Super-, high-, moderate-, low-potency

Allergenicity

Cross reactivity based on 2 immune recognition sites- C 6/9 & C16/17 substitutions

- Reaction to more than one screening agent, reasonable to use a class C steroid

Steroid	Group A	Group B	Group C	Group D1	Group D2
Prevalence	2.7%	1.5%	<0.2%	0.8%	0.8%
Examples	Hydrocortisone acetate	Triamcinolone	Desoximetasone	Betamethasone dipropionate	Hydrocortisone butyrate
	Prednisone	Desonide	Clocortolone	Betamethasone valerate	Hydrocortisone valerate
	Tixocortol (marker Group A)	Fluocinonide	Dexamethasone	Clobetasol propionate	Prednicarbate
	Methylprednisolone acetate	Budesonide	Betamethasone sodium phosphate	Mometasone	Hydrocortisone aceponate
	Cloprednol	Amcinonide	Fluocortolone	Fluticasone	Methylprednisolone aceponate
	Fludrocortisone	Halcinonide		Aclomethasone	
	Prednisolone	Fluocinolone			

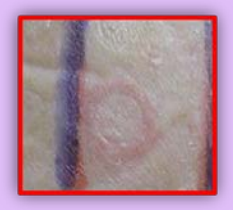
Warner MR, Camisa C. Topical Corticosteroids. In: Wolverton SE, ed. Comprehensive Dermatologic Drug Therapy, 2nd ed. Saunders, 2007. p 595-624.
Berth-Jones J. Topical Therapy. In: Burns T, Breathnach S, Cox N, Griffiths C, eds. Rook's Textbook of Dermatology, 8th ed. Wiley-Blackwell. Ch. 75.

Issues to patch testing with steroids

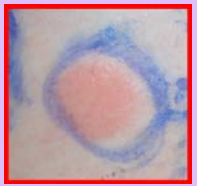
Corticosteroid concentration
Too high - pharmacologic effect suppresses the allergic reaction
Too low - not enough steroid to elicit reaction

Vehicle
petrolatum base
penetrates less

- Late reactions
  - Additional reading Day 6-7
  - ~30% of TCS allergy would be missed without late reading*



Budesonide 0.1% in Petrolatum
72 hours



Product: 7 days

- Rim reactions:
  True positives

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*Issaksson M et al. Patch testing with corticosteroid mixes in Europe. Contact Dermatitis 2000;42:27-35

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Systemic Contact Dermatitis

intravenous

orally

inhalation

intramuscular

Contact sensitized individual

transcutaneous

per rectum

intravesical

Generalized (or localized) dermatitis

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Systemic Contact Dermatitis

- usually appears within hours to 2 days after systemic exposure to allergen
- rarely associated with systemic symptoms
- patch tests should be (+) as cutaneous sensitization has occurred as part of the definition

Clinical Manifestations of Systemic Contact Dermatitis

- baboon syndrome
- previous site of dermatitis(recall reaction)
- previous positive patch tests
- dyshidrotic hand eczema
- flexural dermatitis
- exanthematous rash
- erythroderma
- vasculitis-like lesions

Figure 4 Dermatitis in the antecubital fossae in a nickel-sensitive patient with systemic contact dermatitis

Balsam of Peru

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Allergens likely to cause Systemic Contact Dermatitis

- Metals
  - **Nickel**: vesicular hand eczema
  - Mercury: flexural & gluteal erythematous plaques: baboon syndrome
- Plants and herbals: Compositae, Anacardiaceae, **BOP/ Fragrance**
  - Flare of previous sites of exposure
  - Perioral
  - Eyelid
- Medications

Two most common allergens:
- Nickel
- Balsam of Peru

Nickel

- 10% of population are nickel allergic
- Increasing sensitization in North America
  - Other sources of nickel ACD: cell phones, laptops

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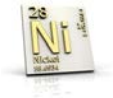
Dermatitis with Scattered Generalized Distribution



Nickel

Estimated SCD following oral nickel in nickel allergic patients

- 1% to 0.3 - 0.6 mg/d (normal diet)
- 10% to 0.55 - 0.89 mg of nickel
- ~ 50% to 2.5 mg nickel

Approximate nickel content of foods

- Soybean: ~ 1 cup=895mcg
- Figs: ~5=85 mcg
- Cocoa: 1 tbsp=147 mcg
- Lentils: ½ cup cooked=61 mcg
- Cashew: ~ 18 nuts=143 mcg
- Raspberry: 56 mcg
- Vegetables: ½ cup canned=40 mcg
- Lobster: 3 oz=30 mcg
- Oat Flakes: 2/3 cup=25 mcg
- Peas Frozen: ½ cup=27 mcg

2 lb. lobster
2 cups soy
1 cup peas
2 tbsp. chocolate
~2.5 mg nickel

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Zug KA, Rietschel RL, Warshaw EM, et al. The value of patch testing patients with a scattered generalized distribution of dermatitis: Retrospective cross-sectional analyses of North American Contact Dermatitis Group data, 2001 to 2004. J Am Acad Dermatol 2008;59:426-431

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Balsam Of Peru

Foods to Avoid in BOP restricted Diet

- **Citrus** fruits: oranges, lemons, grapefruit, tangerines
- Flavoring agents: pastries, bakery goods, candy, gum
- **Spices:** cinnamon, cloves, vanilla, curry, allspice, anise, ginger
- Spicy condiments: **ketchup,** chili sauce, barbecue sauce, chutney,
- Perfumed or flavored tea & tobacco
- Chocolate
- Certain cough medicines & lozenges
- Ice cream
- Cola, spiced soft drinks (Dr Pepper)
- **Tomatoes** & tomato-containing products
- Possible cross reactivity with Compositae (‘‘natural’’ & ‘‘organic’’) containing Sesquiterpene lactones (chamomile, Echinacea)

~ half of patients with (+) PT to MP who followed a low BOP diet had significant improvement of dermatitis

Salam TN, Fowler JF Jr. Balsam-related systemic contact dermatitis J Am Acad Dermatol. 2001 Sep;45(3):377-81
Paulsen E. Contact sensitization from Compositae-containing herbal remedies and cosmetics. Contact Derm 2002;47:189–198.
Paulsen E, Andersen KE. Colophonium and Compositae mix as markers of fragrance allergy: cross-reactivity between fragrance terpenes, colophonium and compositae plant extracts. Contact Derm 2005;53:285–291.

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Other reported causes of SCD

Metals: Cobalt

- Cobalt is the main component of vit B12
- Recall reactions at vit B12 injection sites after oral ingestion of the vitamin

Aspartame

(artificial sweetener in food, medicaments [Montelukast chewable], vitamins)

-SCD in formaldehyde sensitive patients after aspartame ingestion

-Aspartame metabolized to methanol transported to liver (methanol is oxidized formaldehyde)

Methyl Salicylate (Oil of Wintergreen)

(Ben-Gay, Deep-down Pain Relief Rub, Listerine Antiseptic, Sinex Decongestant nasal Spray, Vicks)

- Patients topically sensitized to methyl salicylate may flare when aspirin is ingested

*Paulsen E. Contact sensitization from Compositae-containing herbal remedies and cosmetics. Contact Dermatitis 2002;47:189–98.
**Reider N, Sepp N, Fritsch P, et al. Anaphylaxis to chamomile: clinical features and allergen cross-reactivity. Clin Exp Allergy 2000; 30:1436–43.

Contact Dermatitis in Atopic Dermatitis

Consider CD in AD patients who have:

- Dermatitis that
  - worsens
  - changes distribution
  - fails to improve
  - immediately rebounds
- Atypical distribution/pattern
  - head predominance
  - hand or foot
  - eyelid predominance
  - cheilitis/perioral predominance
- Therapy-resistant hand eczema
- Adult- or adolescent-onset AD w/o childhood eczema
- Severe or widespread dermatitis before initiating systemic immunosuppressant

Consider the following allergens in AD

- Metals (nickel, cobalt, potassium dichromate)
- Fragrances (FM, BOP)
- Preservatives
- Topical emollients, lanolin, corticosteroids, antibiotics, antiseptics
- Patient's products
  - Plants (compositae) Compositae*
  - Herbal medicaments & cosmetics
  - Higher prevalence of (+) PT to compositae in children
- Surfactants (CAPB)
- Rubber accelerators

Tamagawa-Mineoka, R., et al., Contact sensitivity in patients with recalcitrant atopic dermatitis. J Dermatol, 2015. 42(7): p. 720-2.

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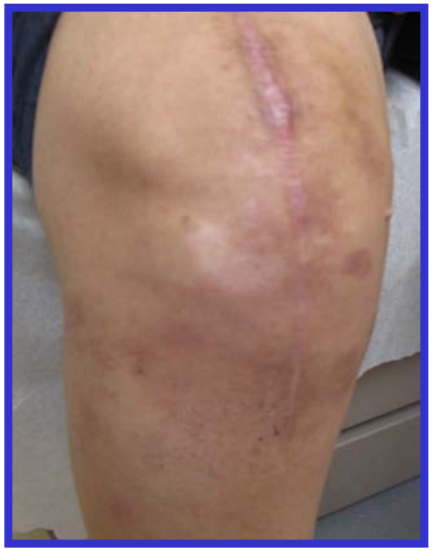
Sensitivity to Biomedical Devices

- >1 million joint replacements/year in the US
- Estimated to reach 4 million/year by 2030
  - Aging of US population
  - Requests to maintain mobility



Reported manifestation of implant allergy

1. Dermatitis
2. Implant failure

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Which subgroups have increased risk of complications with metal implants?

- Unknown… Sensitization to metals increased 6.5% following arthroplasty*

Hip arthroplasty:

- sensitization to nickel, cobalt or chromium
  - 25% in well-functioning implants (>2x general population)**
  - 60% in failed or failing prosthesis (6x general population)**

Total knee arthroplasty:

- metal sensitization rate
  - 20% in pts w/ no implant
  - 48.1% in pts w/ stable implant
  - 59.6% in unstable implant group***

- Available evidence indicates a correlation between metallic orthopaedic implants, development of metal hypersensitivity and implant loosening

Does loosening cause hypersensitivity or……..

……. does hypersensitivity cause loosening?

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* E. Frigerio, P. D. Pigatto, G. Guzzi, and G. Altomare, "Metal sensitivity in patients with orthopaedic implants: a prospective study," Contact Dermatitis, vol. 64, no. 5, pp. 273–279, 2011.
** N. Hallab, "Metal sensitivity in patients with orthopedic implants," Journal of Clinical Rheumatology, vol. 7, no. 4, pp. 215–218, 2001.
*** D. Granchi, E. Cenni, D. Tigani, G. Trisolino, N. Baldini, and A. Giunti, "Sensitivity to implant materials in patients with total knee arthroplasties," Biomaterials, vol. 29, no. 10, pp. 1494–1500, 2008.

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10% of all joint replacements will fail

Causes of Joint Failure:

- Mechanical
- Infection
- Allergy

Contributing factors:

- Obesity
- Cigarette smoking
- Osteoporosis

Allergic Causes of Joint Failure

Metals

- Nickel
- Cobalt
- Chromium
- Titanium (rare)

Bone Cement

- Liquid component:
  - Methyl methacrylate
  - n,n-dimethyl-p-toluidine
  - hydroquinone
- Powder:
  - poly methyl acrylates
  - benzoyl peroxide
- 2-HEMA (hydroxyethyl methacrylate)

Preoperative Patch Testing:

Testing is indicated in patients with

- history of metal reactivity (jewelry, jean snaps, watch bands, belt buckles, necklace etc.)
- Methacrylate's: reactions to gel nails, skin glue (Derma bond), Gorilla Glue
- Reactions to topical antibiotics (Bacitracin, Neosporin, Polymixin)




- ≈70% of patients with pre-operative history of metal reactivity are sensitized to a metal:
  - Nickel
  - Cobalt (30% of Ni allergic are sensitive to Co)
  - Chromium
- Bone cement allergy is rare in this group

Consensus Recommendations for Preimplantation

Allergy Practice Parameters

American Contact Dermatitis Society

Routine preimplant PT not recommended individuals who deny a history of cutaneous reactions to metals and deny previous implant-related adverse events.

Patients with clear self-reported history of metal reactions should be evaluated by PT before device implant
-Self-reported intolerance to jewelry alone is not an adequate screen for cutaneous metal allergy (+ predictive value 59-60%)

Some studies show patients with high suspicion of metal allergy

- **who had pre-operative PT that guided implant selection**
- **have improved outcomes**

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Fonacier L, Bernstein D, Pacheco K, Holness DL, et al. Contact Dermatitis: A Practice Parameter Update – 2015. Journal of Allergy and Clinical Immunology In Practice. Vol 3, No 3 May/June 2015. S1-39
Schalock PC et al Patch Testing for Evaluation of Hypersensitivity to Implanted Metal Devices: A Perspective From the American Contact Dermatitis Society. Dermatitis, Vol 27 ¡ No 5 ¡ September/October, 2016

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Issues to address with a positive Pre-implantation patch test

1. **Which implant/device will give the best outcome (functionality/durability)**
   - **Role of patient's surgeon**
2. **Does a positive PT to metal found in the 'best' device warrant using an inferior device?**
   - **Role of allergist/ dermatologist**
     - **Identify metal/s with positive PT**
     - **Give guidance on safe materials for implantation (i.e. negative reactions with metal screening series)**

Retrospective case–control study prior to total hip replacement
• (+) PT to **metals** and history of metal hypersensitivity had significantly shorter life spans of their implants
• (+) PT to **bone cement** components, none had stable implant at a 10-year endpoint

Schalock PC et al Patch Testing for Evaluation of Hypersensitivity to Implanted Metal Devices: A Perspective From the American Contact Dermatitis Society. Dermatitis, Vol 27 ¡ No 5 ¡ September/October, 2016
Thomas P, Summer B, Sander CA, et al. Intolerance of osteosynthesis material: evidence of dichromate contact allergy with concomitant oligoclonal T-cell infiltrate and TH1-type cytokine expression in the peri-implantar issue. Allergy 2000;55:969Y972

Post Implantation PT:

Patients with no symptoms after implantation do not require PT

- Joint Failure: joint loosening, pain
  - Infection & biomechanical issues have been ruled out
- Dermatitis (above site of implant)
  - beginning weeks to months after implantation
  - resistant to medical therapy

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Thyssen JP et al. Pragmatic approach to the clinical work-up of patients with putative allergic disease to metallic orthopaedic implants before and after surgery. Br J Dermatol. 2011;164(3):473–8.

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Joint Failure: Post Implantation Patch Test

- ~ 10% of patients with joint replacements will fail (pain, swelling, itching/burning, and/or ↓ range of motion)
- More common Causes
  - Infection
  - Biomechanical issues
  - Metallosis – a toxic/necrotic reaction to metal wear particles
  - DVT / hemarthroses

- ~ 50% of patients referred after infection/mechanical causes are ruled out, are sensitized to some component of their joint replacement:
  - ~ 25% to a relevant metal
  - ~ 21% to bone cement

There is increasing evidence to support PT as the next step in evaluating patients as the cause of joint failure when other causes have been ruled out.

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Bone cement components

Common Bone Cement Allergen in Total Joint Arthroplasties	Use
N,N-dimethyl-p-toluidine (DPT)	Reaction initiator
Polymethyl methacrylate (MMA)	Cement Base
Benzoyl Peroxide	Activator
Hydroquinone	MMA Stabilization
Gentamycin	Antibiotic

All manufacturers use similar components

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Thomas P, Schuh A, Eben R, et al. Allergy to bone cement components. Orthopa¨de 2008;37:117–20
Haddad FS, Cobb AG, Bentley G, et al. Hypersensitivity in aseptic loosening of total hip replacements. The role of constituents of bone cement. J Bone Joint Surg Br 1996;78:546–9
Kuehn KD, Ege W, Gopp U. Acrylic bone cements: composition and properties. Orthop Clin North Am 2005;36:17–28

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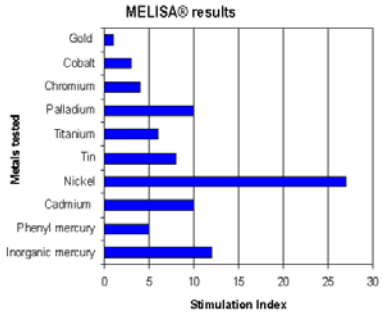
Patch Testing vs Lymphocyte Transformation Test

Practice Parameters:
The clinical relevance of commercially available blood tests to diagnose metal sensitization have not been determined

ACDS:
The LTT is not widely available, not standardized, expensive, subject to variability, may be overly sensitive (false-positive reactions)

- *Measures lymphocyte proliferation* (stimulation index) after 7 days incubation +/- allergen
  - Limited allergens
  - Rapid decay of T cells (rapid transportation)*
- May be useful in questionable cases
  - (-) PT & persistent concerns about metal allergy
  - 54/56 patients with Ti implants, (-) PT & (+) Ti LTT whose systemic symptoms resolved after implant removal



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*(MELISA test: Health Diagnostics and Research Institute, South Amboy, NJ)
Muller K E, Valentine-Thon E. Hypersensitivity to titanium: clinical & laboratory evidence. *Neuro Endocrinol Lett* 2006: 27: 311–313

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Low Contact Allergen Products

Recommendation Prior to Patch Testing

Eliminate most common allergens:

- Fragrance
  - Balsam of Peru
  - Fragrance Mix
  - Fragrance Mix II
- Formaldehyde Releasing Preservatives
  - Formaldehyde
  - Quaternium-15
  - Diazolidinyl Urea
  - Imidazolidinyl Urea
  - Bronopol
  - DMDM Hydantoin
- Non Formaldehyde Preservative
  - MDG/PE (Methyldibromo Glutaronitrile)
- MCI/MI and Methylisothiazolinone
- Lanolin
- Cocamidopropyl Betaine
- Benzophenone-3
- Paraphenylenediamine

- Clinique Stay-Matte Oil-Free Makeup (2019-Mar)
- Clinique blushing blush powder blush
- Bobbi Brown Eye Shadow (2019-Apr)
- Lancôme Color Design Lipstick
- Cover Girl LashBlast Waterproof Volume Mascara
- Mitchum For Men Advanced Gel Antiperspirant & Deodorant, Unscented
- Vanicream Moisturizing skin cream
- Vaniply Ointment/Skin Protectant
- CeraVe Hydrating Cleanser
- Free & Clear shampoo
- Free & Clear Styling and Finishing Hair Spray, Soft Hold/ firm hold
- Free & Clear Hair Styling Gel, For Sensitive Skin
- Banana Boat Simply Protect Baby Sunscreen Spray SPF 50+
- Light Mountain Natural Color The Gray 100% Pure Botanical Hair Color (Henna, Senna and Indigo)

Pre-emptive Avoidance Strategy (P.E.A.S.) in Pediatric ACD

Allergen Avoidance Estimate that 1/3 of children with ACD will potentially benefit from P.E.A.S.	
Neomycin	Formaldehyde
Balsam of Peru	Corticosteroids
Fragrance Mix	MCI/MI
Lanolin	Propylene glycol
Cocamidopropylbetaine	Benzalkonium chloride

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Hill H, Goldenberg A et al, Pre-emptive avoidance Strategy (P.E.A.S.)- addressing allergic contact dermatitis in pediatric population. Jour Expert Review of Clinical Immunology 2016, Vol 12 p 551-561,

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The identification and avoidance of contact with the offending agent(s) is the key to the success of ICD and ACD treatment.

Topical Skin Care Product Databases

	CAMP Contact Allergen Management Program (American Contact Dermatitis Society)	CARD Contact Allergen Replacement Database (MAYO Clinic)
Web Address	www.contactderm.org	www.AllergyFreeSkin.com
Physician	*Requires ACDS Membership* Luz.fonacier@nyulangone.org	*No membership requirements* *Provider portal* *Patient portal* *Web and Smart Device*

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Typical Reimbursement Rates

Visits	CPT Code	Avg. Fee Schedule	Master Fee Schedule (150% Medicare fees)
Initial Consult	**99203 -Non-Referring Provider/Medicare**	**98.67**	**166.00**
Patch Application (2nd Visit)	**95044 (no RVU)**	**5.50 (per allergen) X 80 units= 440.00**	**8.00 X 80 units= 640.00**
Patch Removal (3rd Visit)	**99212 - Office Visit**	**44.98**	**83.00**
Patch Read/Counseling (4th Visit)	**99214- Office Visit**	**106.47**	**191.00**
Total average reimbursement		**690.12**	**1080.00**

- Average reimbursement rates

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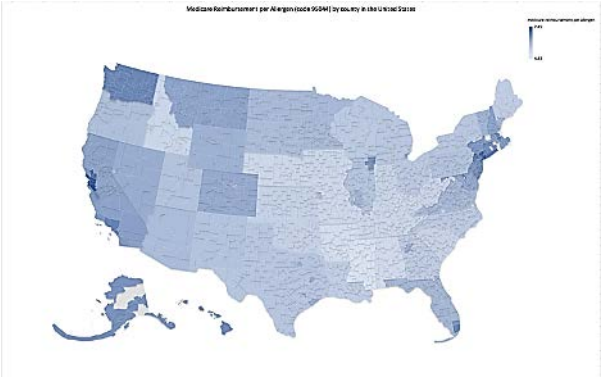
Variables per state…per insurance….

- Medicare reimbursement rates for PT **per unit** of 95044: $4-$8
- Private insurance rates for PT per unit range from around $5-$12
- Medicare PT reimbursement **by county** for the US for 2018
  - Reimbursement per allergen ranges from $4.83 in Mississippi to $7.45 in Santa Clara County, California.
  - The mean reimbursement across all counties is $5.37
- Limits to the **number of tests** that can be done in a year and what insurance limits them?
  - 80 allergens **per day**. Medicare does not limit the amount per year, only per day.
  - There are plans that do limit per year, depending on the employer contract with the insurance company.



Pearls

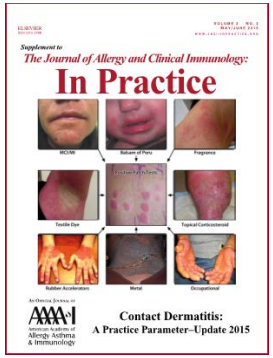
1. Load acrylates, fragrances & allergens in aqueous vehicle immediately before application of PT
2. Systemic antihistamine therapy has no effect on patch test results.
3. Delayed Patch Test readings are common to:
   - metals
   - topical antibiotics
   - topical corticosteroids
5. Testing with MCI/MI mix (3:1 TT) alone will misses ~ 40% of allergy to MI
6. Patch them if you can!

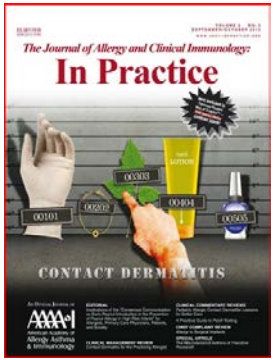
   Relief of symptoms average 143 days sooner on patch tested vs. non patch tested patients

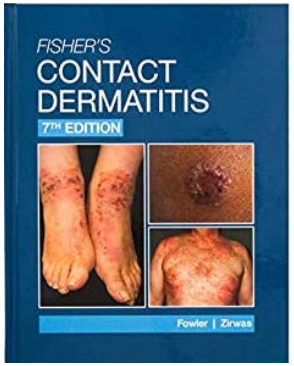
Summary of Pitfalls

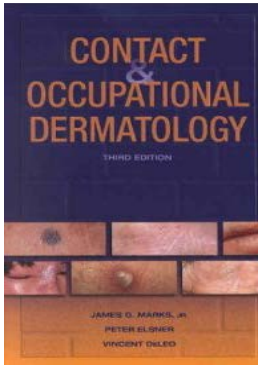
1. Avoid testing patients with acute &/or severe dermatitis
2. Avoid testing patients on systemic corticosteroids
3. Avoid TCS,TCI & UV exposure of test for 5-7 days before PT
4. Fragrances are mild irritant, caution with weak (+) reactions
5. Pustular reaction are common in atopics and to nickel, copper, arsenic & mercury and are false positive reactions

Useful Resources









American Contact Dermatitis Society (www.contactderm.org)

- requires membership

Contact Dermatitis Institute (www.contactdermatitisinstitute.com/mypatchlink.php)

- Patient handouts, webinars

NIH (http://householdproducts.nlm.nih.gov/)

- List of products to avoid

•https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PFSlookup/

•http://www.medicarepaymentandreimbursement.com/2016/08/cpt-code-99243-office-visit.html

•https://www.changehealthcare.com/blog/medical-billing-denials-avoidable/

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Thank You

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