CLINICAL PEARLS FOR ASSESSING AND DIAGNOSING PATIENTS SUSPECTED OF ALLERGIC CONTACT DERMATITIS

David I Bernstein MD
Professor of Medicine and Environmental Health
Division of Allergy and Immunology
University of Cincinnati College of Medicine
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DISCLOSURES

• Consultant - Merck, TEVA, Genentech, Cephalon

• Clinical Investigator
  • NIOSH, NIH
  • TEVA, Merck, Glaxo, Pfizer, Genentech, Novartis, Aztra Zeneca

• Board membership
  • American Board of Allergy Immunology
  • Joint Task Force for Practice Parameters and Contact Dermatitis Workgroup Liaison

• Speaker honoraria
  • Merck
OBJECTIVES

• Identify key factors in clinical history and patch testing in suspected allergic contact dermatitis

• Identify the most frequent contact sensitizers encountered at home and in the workplace

• Discuss the relationship between metal hypersensitivity and prosthetic joint failure
ALLERGIC CONTACT DERMATITIS WORK GROUP MEMBERS

• Luz Fonacier MD, Chair
• David I Bernstein MD, Joint Task Force Liaison
• Karin Pacheco MD, MS
• Linn Hollness MD, NACD??
PARAMETER DRAFT SUMMARY STATEMENTS

CLINICAL HISTORY

• SUMMARY STATEMENT 1: Suspect contact dermatitis in patients with chronic inflammatory changes of the skin, although other eczematous disorders of cutaneous or systemic origin may present similarly.
DIFFERENTIAL DIAGNOSIS – OTHER SKIN DISORDERS

- Irritant contact dermatitis  Patch testing negative
- Atopic dermatitis  Typical distribution, family atopic history
- Seborrheic dermatitis  Scalp, face; areas with sebaceous glands
- Dyshidrotic eczema  Palms, soles, lateral aspects of fingers
- Psoriasis  Plaques
- Dermatitis herpetiformis  Intensely pruritic; papules and vesicles
- Mycoses fungoides  Thin patches, reticulated pigmentation
SUMMARY STATEMENT 14: ACD should always be considered in patients with atopic dermatitis as the two dermatologic conditions often coexist in the same patient.

[Strength of Recommendation: Moderate; C Evidence]
SUMMARY STATEMENT 2: In patients suspected of ACD, patch testing is the gold standard to confirm the diagnosis. (Strength of Recommendation: Moderate; C Evidence)

- Indicated in any patient with acute or chronic, often pruritic, dermatitis
- Moderate sensitivity (76%) and specificity (76%) in establishing the diagnosis
- Nickel has a positive predictive value of 60% vs 12.5-15% of persons with a negative history
CLINICAL EVALUATION

SUMMARY STATEMENT 4: Evaluate patients for both irritant and allergic contact dermatitis, especially in those presenting with hand dermatitis. [Strength of Recommendation: Moderate; C Evidence]
CLINICAL CLUES – LOCATION: HANDS, ARMS

- Irritant dermatitis 25-38%
- Allergic CD in 24-75% depending on exposure or occupation
- Common sensitizers*
  - Quaternium -15 (formaldehyde releaser)
  - Nickel sulfate
  - Fragrances, Balsam of Peru
  - Neomycin, bacitracin
  - Rubber accelerators
    - carbamates, thiurams
    - Latex and neoprene gloves

* North American Contact Dermatitis Group
CLINICAL EVALUATION

SUMMARY STATEMENT 6: In a patient with a facial rash involving the periorbital areas and eyelids, evaluate for ACD caused by components of cosmetics, such as fragrances, because these are the most common sensitizers of the facial skin.

[Strength of Recommendation: Moderate ; C Evidence]
CLINICAL CLUES – LOCATION: FACE AND EYES

- Females, > 40 years
- Facial, eye cosmetics
- Common sensitizers:
  - Nickel, Gold
  - Cobalt (blue eye makeup)
  - Fragrance mixes, Balsam of Peru
  - Thimerasol, neomycin
- Ectopic transfer (e.g., nickel, gold, nail products)
CLINICAL HISTORY – DRAFT STATEMENTS

• The clinician should also consider cosmetics and personal hygiene products as a source of potential allergens in patients with dermatitis occurring in sites other than the site of application.

• Suspect allergy to nail products when the dermatitis present locally at the distal digit or ectopically on the eyelids and face.
CLINICAL EVALUATION

SUMMARY STATEMENT 7: Patients with lip dermatitis (cheilitis) and perioral dermatitis should be evaluated for allergic contact dermatitis.

[Strength of Recommendation: Moderate; C Evidence]
CLINICAL CLUES – LOCATION: LIPS, PERIORAL

- 85% in females
- Most common sensitizers: Fragrance mix, balsam of Peru, nickel sulfate (ectopic transfer)
- Toothpastes, mouthwash, flavors (spearmint, cinnamal)
- Lipstick, lip balms
  - Propolis (bee product)
CLINICAL EVALUATION

SUMMARY STATEMENT 8: The causative associations between allergic contact sensitivity and chronic oral mucosal conditions have not been determined. [Strength of Recommendation: Moderate; C Evidence]

- e.g., burning mouth syndrome, lichenoid tissue reaction, cheilitis, stomatitis, and gingivitis

SUMMARY STATEMENT 9: In the patient presenting with dermatitis involving the scalp and neck, consider patch testing for common causative sensitizers in cosmetics, hair products and jewelry. [Strength of Recommendation: Moderate; C Evidence]
• **Cosmetics, personal use products**  
  (more common in Females)  
  • Fragrance mix, Balsam of Peru  
  • Paraphenylenediamine – azo dye (PPD)  
  • Common sensitizer in hair dyes and “black henna”  
  • X-reactive \( \rightarrow \) parabens, sulfa, benzoic ester anesthetics (benzocaine) PABA sunscreen  
  • Glycerol thioglycolate (perm. wave solutions)  
  • Nail products (ectopic)  
  • Methyl methacrylate  
  • Tosylamide/formaldehyde resin  

**Scalp and Neck**

*Shampoos*  
• Fragrances, isothiazolinones,  
• Formaldehyde releasers (preservatives)  
  • Quart 15, Imidazolidinyl urea  
• Cocamidopropyl betaine  
  • Surfactant from coconut oil
CLINICAL EVALUATION

• SUMMARY STATEMENT 11: Patients with axillary dermatitis should be evaluated for ACD caused by local contact sensitivity to allergens in topically applied products in deodorants and textiles, and also considered as a possible manifestation of systemic contact dermatitis.

[Strength of Recommendation: Moderate; C Evidence]
• Fragrance chemicals in deodorants
  • Hydroxyisohexyl-3-cyclohexene
  • Carboxaldehyde
  • Isoeugenol
  • Cinnamic aldehyde
• Consider Natural botanicals
• Consider textile dyes and finishers!
  • Disperse blue 106, 124 (XR with PPD)
  • Urea formaldehyde – permanent press
• When feet and groin are also involved consider Systemic Contact Dermatitis
• Antiperspirants are rare causes of ACE
SUMMARY STATEMENT 12: Evaluate patients presenting with anogenital dermatitis for possible ACD to antigens contained in topically applied products.

[Strength of Recommendation: Moderate; C Evidence]

- ACD - 44% pts with anogenital dermatitis
- 21% due to irritant contact dermatitis
  - soap, cleansers
- Usual sources - topical medications
  - Cinnamic aldehyde, dibucaine, benzocaine, hydrocortisone-17-butyrate, budesonide
CLINICAL CLUES – LOCATION: FEET

• SUMMARY STATEMENT 13: Consider patch testing to rubber chemicals, adhesives and leather components of patients’ shoes in patients presenting with unexplained chronic dermatitis involving the lower extremities, feet and/or soles. [Strength of Recommendation: Moderate; C Evidence]

Shoe dermatitis: rubber chemicals, adhesives and leather components

• Phenol formaldehyde resin (in adhesives), potassium dichromate, cobalt chloride
• Rubber chemicals
  • carbamates, thiurams, and mercaptobenzothiazole
• Less common → dialkyl thioureas (adhesive)
CLINICAL CLUES – LOCATION: LEGS

Consider patch testing in patients presenting with unexplained chronic dermatitis involving the lower extremities, feet and/or soles who have been exposed to suspected sensitizers.

Topically applied preparations

- Balsam of Peru, fragrance mix I,
- Antibacterials
  - Neomycin, bacitracin
- Corticosteroids 4 classes x-reactivity
- Lanolin
SUMMARY STATEMENT 28: Consider a diagnosis of systemic contact dermatitis (SCD) following systemic exposure (e.g., ingestion, infusion or transcutaneous exposure) to a known contact sensitizer in a patient presenting with generalized dermatitis, as intertriginous and flexural exanthema (Baboon Syndrome), and a flaring at previous cutaneous sites of exposure.
SYSTEMIC ALLERGIC CONTACT DERMATITIS

• Balsam of Peru (*Myroxylon pereireae*) derived from tree bark sap
  • Common contact allergen, blend of 400 chemicals
  • Used in perfumes and flavors including vanilla, cinnamon, citrus flavor
  • Sensitized patients → SCD with ingestion of citrus products, ice cream, cinnamon, chutney, cola, vanilla, curry, ketchup, tomatoes etc.

• Nickel sulfate – ubiquitous in steel devices, jewelry, clothing and food.
  • SCD → ingestion of chocolate, nuts, green beans, peas, canned foods
CLINICAL HISTORY – DRAFT STATEMENTS

• In addition to personal products used by a patient suspected of ACD, the clinician should review the home and workplace for other sources of contact allergen exposure.

• Suspect the diagnosis of photodermatitis to cosmetics when eczema occurs in a light-exposed distribution following the use of a skin care product or cosmetic, including sunscreens. In these cases, photopatch testing must be performed.
PATCH TESTING

• Currently, patch testing is the gold standard for diagnosing ACD.
  • Any patient with dermatitis in whom ACD suspected
• ACD is a significant clinical problem in children. Patch Testing could and should be done and remains the gold standard for the diagnosis of ACD in children.
• In patients suspected of ACD, patch testing should be used to confirm the diagnosis.
  • History alone: Sensitivity 76%; PPV 60%
PATCH TESTING : PARAMETER DRAFT STATEMENTS

• Consider patch test panels tailored to the specific patient’s exposure history to improve the accuracy of the diagnosis

• In addition to using screening patch test panels in evaluating ACD, consider using supplemental allergens, if indicated, to increase the probability of identifying clinically relevant sensitizers.
PATCH TESTING : PARAMETER DRAFT STATEMENTS

• Determine the “relevance” of a positive patch test based on the clinical and exposure history.
  • **Definite relevance** if there is a positive use test with suspected item containing allergen
  • **Probable relevance** if allergen is present and clinical presentation is consistent with exposure
  • **Possible relevance** if skin contact with allergen was likely.
PATCH TESTING

• Patch testing can be performed with either a pre-loaded system such as a thin-layer rapid use epicutaneous testing kit (T.R.U.E. Test™) or antigens loaded individually in chambers. The TRUE Test™ method is widely used consisting of 35 antigens or mixes plus a negative control

Concordance between two methods is only moderate (62-63%)
PATCH TESTING

- Read and interpret patch tests conforming to the scoring system developed by the International Contact Dermatitis Research Group.
- Remove and read patch tests at 48 hours after application. A second reading must be done from 3-7 days after application.
  - Common late reactors: metals, topical CS, antibiotics
PATCH TEST - GRADING

Doubtful, erythema +/-

Erythema, papules Infiltration 2 +

Erythema, papules?

Erythema, vesicles bullous reaction 3 +
PATCH TESTING

• The strength of patch test responses are reduced by treatment with immunosuppressant medications such as systemic corticosteroids, topical corticosteroids, topical calcineurin inhibitors, ultraviolet radiation on the PT site.

  • ↓ with prednisone > 20 mg/day
  • ↓ topical tacrolimus, med/high topical CS
  • Withhold for 5-7 days prior
PATCH TESTING

• Consider the possibilities of false-positive reactions when interpreting patch tests.
  • Usually nonspecific +/- or 1+ readings, “angry back”
  • Poor separation of tests
• Recognize the possibilities of false-negative reactions when interpreting patch tests.
  • Frequency up to 30%
  • Low conc of test allergen, immunosuppressive, UV light
  • Repeat PT if clinical suspicion is high or PT to actual product
SUMMARY STATEMENT 27: Use the repeated open application test (ROAT) to further evaluate a patient suspected of ACD who exhibits doubtful or negative patch test responses to confirm that the patient is reacting to a particular product.

- repeated application of a suspected allergen to the antecubital fossa twice daily for up to 1 to 2 weeks.
THANK YOU
REFERENCES


12. Lazarov A, David M, Abraham D, Trattner A. Comparison of reactivity to allergens using the TRUE Test and IQ chamber system. Contact dermatitis 2007;56:140-5.
# 40 Most Frequent (+) reactions to NACG Allergens 2009-2010

<table>
<thead>
<tr>
<th>Rank</th>
<th>Allergen</th>
<th>NACD %</th>
<th>T.R..U.E Test</th>
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<tbody>
<tr>
<td>1</td>
<td>Nickel Sulfate</td>
<td>15.5</td>
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<tr>
<td>2</td>
<td>Neomycin</td>
<td>8.7</td>
<td>x</td>
</tr>
<tr>
<td>3</td>
<td>Fragrance Mix I</td>
<td>8.5</td>
<td>x</td>
</tr>
<tr>
<td>4</td>
<td>Bacitracin</td>
<td>8.3</td>
<td>x</td>
</tr>
<tr>
<td>5</td>
<td>Balsam of Peru</td>
<td>7.2</td>
<td>x</td>
</tr>
<tr>
<td>6</td>
<td>Cobalt Chloride</td>
<td>6.2</td>
<td>x</td>
</tr>
<tr>
<td>7</td>
<td>Quarternium 15 (Preservative)</td>
<td>5.8</td>
<td>x</td>
</tr>
<tr>
<td>8</td>
<td>Formaldehyde (Preservative)</td>
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<tr>
<td>9</td>
<td>PPD</td>
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<tr>
<td>10</td>
<td>Fragrance Mix II</td>
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<td>Carba Mix</td>
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<tr>
<td>12</td>
<td>Iodopropynyl Butylcarbamate</td>
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<tr>
<td>13</td>
<td>Methyl Dibromo-glutaronitrile/phenoxylethanol</td>
<td>3.8</td>
<td>x</td>
</tr>
<tr>
<td>14</td>
<td>Popylene Glycol</td>
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<td>16</td>
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<tr>
<td>17</td>
<td>Lanolin (Wool Alcohol)</td>
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<td>MCI/MI</td>
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<tr>
<td>19</td>
<td>Potassium Dichromate</td>
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<tr>
<td>20</td>
<td>Cinnamic Aldehyde</td>
<td>2.3</td>
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</tr>
</tbody>
</table>

| 21  | Diazolidinylurea Pet                     | 2.2 | x   |
| 22  | Imidazolidinylurea pet                  | 2.2 | x   |
| 23  | Propolis                                | 2.1 |     |
| 24  | Dimethyldiallylurea Dimethylamine       | 2.0 |     |
| 25  | Hydroxyethylmethacrylate               | 2.0 |     |
| 25  | Tixocortol Pivalate                     | 2.0 | x   |
| 27  | Compositae Mix                         | 1.9 |     |
| 28  | Benzocaine                              | 1.8 | Caine Mix |
| 29  | Oleamidopropyl dimethylamine           | 1.8 |     |
| 30  | Shellac                                 | 1.7 |     |
| 31  | Epoxy Resin                             | 1.6 | x   |
| 32  | P-tert-butylphenol Formaldehyde Resin   | 1.5 | x   |
| 33  | Decyl glucoside                         | 1.5 |     |
| 34  | EthyleneDiamine                         | 1.4 | x   |
| 35  | Cocoamidopropyl betaine                | 1.4 |     |
| 36  | Manjatole                               | 1.4 |     |
| 37  | Ylang Ylang                             | 1.3 |     |
| 38  | Carvone                                 | 1.1 |     |
| 39  | DMDM Hydantoin                          | 1.0 |     |
| 40  | Mixed Diakyl thioureas                  | 1.0 |     |