Challenging Cases and Controversies in Contact Dermatitis

Jennifer Chen, MD
Stanford Hospital and Clinics
Case 1
Case 1

- 37F with pruritic patchy generalized dermatitis x 8 months
- Began on proximal legs, then spread to the trunk and arms, eventually the face
- Had not improved w/ topical corticosteroids
- No meds/supplements
- + FH eczema but no personal history of asthma, allergies, or eczema
Case 1

- Biopsy: Spongiotic dermatitis with eosinophils
- Patch testing: 1+ Nickel
- Diet consisted of heavy amount of seeds/nuts
- Low nickel diet -> clearance over ~1 mo
- On Valentines, had a lot of chocolate and noticed a flare ~ 1-1.5 days later

Again cleared on reinstitution of the diet
Systemic allergic contact dermatitis to nickel
Systemic Allergic Contact Dermatitis

Dermatitis that occurs when a pt sensitized to a contact allergen is exposed to that same allergen or a cross-reacting allergen through a systemic route (transcutaneous, oral, IV, IM, etc)

- Usually occurs within hrs to 2d after exposure
- Systemic symptoms rare

Patch testing is gold standard for diagnosis
Nickel and ACD

- Nickel is the most common cause of ACD in the North America (15-20%)
- Systemic ACD to nickel has been described due to exposure via diet
Nickel and Diet

- Mean [nickel] in typical US diet = 220-350 ug/d
- 1% of nickel-allergic pts will have a cutaneous reaction to 220 ug

Examples
- Chocolate
- Beans/seeds/nuts
- Canned foods
- Soy
- Oatmeal/granola
- Wheat/rye
Systemic ACD to Nickel

Presentations
Systemic ACD to Nickel

Presentations

- Baboon Syndrome
Systemic ACD to Nickel

Presentations

- Baboon Syndrome
- Dermatitis at sites of previous exposure (recall)
Systemic ACD to Nickel

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- Vesicular hand dermatitis
Systemic ACD to Nickel

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- Vesicular hand dermatitis
- Diffuse eczematous eruption
- Erythroderma
Systemic ACD to Nickel

Presentations

- Baboon Syndrome
- Dermatitis at sites of previous exposure (recall)
- Vesicular hand dermatitis
- Diffuse eczematous eruption
- Erythroderma
- Elbow involvement

Dietary Nickel as a Cause of Systemic ACD

- Veien et al. JAAD 1993;29:1002–1007
- 96 of 216 nickel-sensitive pts flared with oral challenge of nickel vs placebo
- 90 agreed to alter diet
- 58 of 90 pts markedly improved or cleared with 4 wks of low nickel diet
- F/u questionnaires: 40 of 55 respondents had long-term improvement w/ continuing diet 1-3 yrs later (mean 1.8 yrs)
Table I. Correlation between the results of diet treatment and the results of patch testing with 5% nickel sulfate in petrolatum

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<td>8 (50%)</td>
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Table II. Factors that aggravated dermatitis on ≥ 3 occasions

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<th>Specific foods</th>
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<td>31</td>
<td>6</td>
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- Jensen et al. Contact Dermatitis 2006;54:79-86
- Meta-analysis of 17 studies evaluating systemic contact dermatitis and oral exposure to nickel
- Excluded studies including pts w/ (+) response to placebo or no placebo testing
- 9 studies were included in the final dose–response analysis
In nickel sensitive pts, dermatitis flares with oral nickel in a dose dep manner.

- 277 of 339 (67 %) nickel sensitive pts cleared or almost cleared on low nickel diet
- 185 of 277 flared with oral nickel challenge vs placebo
- 15 of 185 (8 %) patients who flared with oral nickel challenge reacted to the minimum challenge dose of 110 ug
Treatment: Low Nickel Diet

- Consider if:
  - Patch test positive for nickel allergy
  - Failed usual avoidance measures or has a diet unusually high in nickel content
  - Fitting clinical presentation

- Trial of 2 months

Restrict daily intake of foods high in nickel content
Low-Nickel Diet Scoring System for Systemic Nickel Allergy

Mona Mislankan, BS* and Matthew J. Zirwas, MD†

Background: Consumption of nickel in the diet leads to spongiotic dermatitis in a dose-related fashion in individuals who are allergic to nickel. Dietary modification to reduce nickel intake leads to resolution of this dermatitis.

Objective: This study aims to create an evidence-based, user-friendly diet to assist patients in reducing dietary nickel intake.

Methods: Food and Drug Administration data on the nickel content of foods were combined with serving size information to calculate the upper limit of nickel per serving for a variety of foods. Based on these calculations, a point system was created that allows patients to reduce their nickel intake below the typical threshold for elicitation of the spongiotic dermatitis.

Conclusions: A simplified point-based diet can help patients with dermatitis due to dietary nickel consumption.
Low Nickel Diet: 15 points per day

<table>
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<th>Points</th>
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<tr>
<td>Lettuce</td>
<td>2</td>
</tr>
<tr>
<td>Lima beans</td>
<td>Avoid</td>
</tr>
<tr>
<td>Liver (beef/calf)</td>
<td>1</td>
</tr>
<tr>
<td>Lunch meat (chicken, turkey, or ham)</td>
<td>0</td>
</tr>
<tr>
<td>Lunch meat, salami</td>
<td>1</td>
</tr>
<tr>
<td>Macaroni and cheese</td>
<td>1</td>
</tr>
<tr>
<td>Macaroni salad</td>
<td>1</td>
</tr>
<tr>
<td>Maple syrup</td>
<td>0</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>0</td>
</tr>
<tr>
<td>Meal replacement shake</td>
<td>3</td>
</tr>
<tr>
<td>Meatloaf</td>
<td>1</td>
</tr>
<tr>
<td><strong>Milk shake, chocolate</strong></td>
<td><strong>8</strong></td>
</tr>
<tr>
<td>Milk, chocolate</td>
<td>4</td>
</tr>
<tr>
<td>Milk, white</td>
<td>0</td>
</tr>
<tr>
<td>Muffin, fruit or plain</td>
<td>1</td>
</tr>
<tr>
<td>Mushrooms</td>
<td>0</td>
</tr>
<tr>
<td>Noodles, egg</td>
<td>1</td>
</tr>
<tr>
<td>Oatmeal</td>
<td>9</td>
</tr>
<tr>
<td>Okra</td>
<td>1</td>
</tr>
<tr>
<td>Olive oil</td>
<td>0</td>
</tr>
<tr>
<td>Olives</td>
<td>1</td>
</tr>
<tr>
<td>Onion</td>
<td>1</td>
</tr>
<tr>
<td>Orange</td>
<td>1</td>
</tr>
<tr>
<td>Orange juice</td>
<td>1</td>
</tr>
<tr>
<td>Pancakes</td>
<td>2</td>
</tr>
<tr>
<td>Peach</td>
<td>3</td>
</tr>
</tbody>
</table>

**Refried beans** | **Avoid**

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<tr>
<td>Rice, fried and meatless</td>
<td>3</td>
</tr>
<tr>
<td>Rice, white</td>
<td>1</td>
</tr>
<tr>
<td>Salad dressing</td>
<td>0</td>
</tr>
<tr>
<td>Sausage</td>
<td>1</td>
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<tr>
<td>Sherbet</td>
<td>1</td>
</tr>
<tr>
<td>Shrimp</td>
<td>1</td>
</tr>
<tr>
<td>Soda/pop/cola</td>
<td>0</td>
</tr>
<tr>
<td>Soup, bean, bacon, pork—canned</td>
<td>10</td>
</tr>
<tr>
<td>Soup, chicken noodle, canned</td>
<td>2</td>
</tr>
<tr>
<td>Soup, oriental noodles—ramen</td>
<td>1</td>
</tr>
<tr>
<td>Soup, tomato, canned</td>
<td>4</td>
</tr>
<tr>
<td>Soup, vegetable beef, canned</td>
<td>3</td>
</tr>
<tr>
<td>Sour cream</td>
<td>0</td>
</tr>
<tr>
<td>Spaghetti</td>
<td>1</td>
</tr>
<tr>
<td>Spaghetti with meat sauce</td>
<td>1</td>
</tr>
<tr>
<td>Spinach</td>
<td>2</td>
</tr>
<tr>
<td>Squash, summer</td>
<td>1</td>
</tr>
<tr>
<td>Squash, winter</td>
<td>2</td>
</tr>
<tr>
<td>Steak</td>
<td>0</td>
</tr>
<tr>
<td>Stew—beef and vegetable</td>
<td>3</td>
</tr>
<tr>
<td>Strawberries</td>
<td>2</td>
</tr>
<tr>
<td>Sugar</td>
<td>0</td>
</tr>
<tr>
<td>Sunflower seeds, shelled</td>
<td>Avoid</td>
</tr>
<tr>
<td>Sweet and sour sauce</td>
<td>1</td>
</tr>
<tr>
<td>Sweet potatoes</td>
<td>2</td>
</tr>
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</table>
Low Nickel Diet

- Avoid cooking acidic foods in stainless steel cookware
- Only drink/cook with bottled/distilled water
- Consider stool softener
- Chewable Vitamin C 500 mg tablet w/ meals
- Smoking cessation (Disulfiram)
- Biotin or iron supplements?
Take Home Points: Case 1

- Always evaluate for allergen exposures via the systemic route as well (transcutaneous, oral, IV, IM, etc)
- Consider the low nickel diet in pts with + patch test to nickel who:
  - Failed usual measures of nickel avoidance OR have diet unusually high in nickel content, AND
  - P/w baboon syndrome, vesicular hand dermatitis, generalized dermatitis (esp w/ ELBOW involvement)
Case 2
Case 2

- 57M with 6 month history of erythroderma
- Biopsy showed spong derm
- Failed to clear with pred taper or wet wraps
- Now close to clear on mycophenolate mofetil 1500 mg bid, referred for patch test

What should you do?
Patch testing on immunosuppressants

- Positive reactions have been shown on:
  - Systemic corticosteroids
  - Methotrexate
  - Azathioprine
  - Mycophenolate mofetil
  - Cyclosporine
  - Systemic tacrolimus
  - Biologics

- Data is limited
Patch testing on immunosuppressants

- Multicenter, randomized, double-blind, crossover study
- 24 pts with known nickel allergy
- Patch tested with a nickel sulfate dilution series (aq), 5% nickel sulfate (pet), 2 irritant controls (nonanoic acid and sodium lauryl sulfate)
- Tested twice, during pred 20 daily or placebo
Results of patch testing with nickel dilution series.
- Stronger patch test reactions are more likely to appear, although more weakly than they would have otherwise appeared.
- Weak positives may be missed.
- Doubtful reactions should be carefully considered.
Expert Opinion

Meds less likely to impact patch test results

- Methotrexate (ideally < 0.25 mg/kg/wk)
- Prednisone < 10 mg/day
- Biologic therapy
- Low dose cyclosporine (< 2 mg/kg)
- Azathioprine (dose dependent)
- Mycophenolate mofetil (dose dependent)
- Tacrolimus, systemic (dose dependent)
Expert Opinion

Treatments likely to impact patch test results

- Phototherapy/prolonged UV exposure within the last week
- Topical steroids at patch testing site w/in 3-7d
- Prednisone > 10 mg/day
- High dose cyclosporine (> 2 mg/kg)
- Intramuscular triamcinolone (avoid for 4 weeks)
Approach to Patch Testing Patients on Immunosuppressive Treatments

- Avoid topical immunosuppressants to the patch testing site for at least 3-7 days
- Avoid systemic immunosuppression for 5 half-lives of the drug in question (usually 1 month acceptable)
- When unavoidable, use the minimum dose required
- Carefully consider weak positives/indeterminate reactions
- Consider retesting when off immunosuppression
Case 2

- Dropped his mycophenolate mofetil to 500 mg bid
- Patch testing: 2+ MCI/MI, 1+ MI, ?/1+ multiple personal products containing these
- With avoidance, he cleared completely and was able to be tapered off immunosuppression
Take Home Points: Case 2

- Avoid systemic immunosuppression during patch testing whenever possible
- When unavoidable, try to limit use to the minimum dose required
- Carefully consider doubtful reactions in these patients
- Consider repeat patch testing when off immunosuppression
Case 3 & 4
Case 3

- 52F with a 2 year history of hand/forearm dermatitis
- Failed to improve despite hydrocortisone, triamcinolone, and fluocinonide
- No h/o childhood eczema, allergies, or asthma
Case 4

- 70F with a 10+ year history of hand/foot dermatitis
- Began on the soles
- Failed to improve despite clotrimazole/betamethasone cream, clobetasol ointment, oral terbinafine x 4 weeks
- Also using cetaphil cream rigorously without benefit
- + h/o childhood eczema, allergies
Patch testing

- **Case 3**
  - 2+ tixocortol pivalate

- **Case 4**
  - 1+ propylene glycol
  - 1+ Dr. Scholl’s foam insole
Allergic contact dermatitis to medicaments (corticosteroids)
Medicament Allergy

- Medicament allergy should be suspected in pts w/:
  - Treatment failure
  - Worsening with treatment
  - Initial improvement but drop-off in response
- 0.2-6% corticosteroid
- Patch testing may be challenging
  - Tends to peak late (i.e. Day 7)
  - Finding the right concentration is difficult
  - Reactions may be difficult to interpret
Edge Effect, or Rim Reaction

- High [ ] in center suppresses reaction
- Lower [ ] at edge does not
Corticosteroids

- Class A
- Class B
- Class C
- Class D1
- Class D2
Corticosteroids

- Class A (no modification of C16 or C17)
- Class B (cis/ketotic or dialic on C16-17)
- Class C (methyl group on C16)
- Class D1 (halogenated on C9, methylated on C16, esterified side chain on C17)
- Class D2 (ester on C17)
Corticosteroids – frequency of allergy

- Class A (2.3%)
- Class B (0.9%)
- Class C (0.2%)
- Class D (0.3-0.4%)
<table>
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<tr>
<th>Class</th>
<th>Type</th>
<th>Patch test allergen</th>
<th>Examples</th>
</tr>
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<tr>
<td></td>
<td></td>
<td>Hydrocortisone</td>
<td>Tixocortol pivalate, Prednisone, prednisolone, methylprednisolone, meprednisone, cortisone, hydrocortisone, tixocortol pivalate</td>
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<td></td>
<td></td>
<td>Betamethasone</td>
<td>Desoximetasone, dexamethasone, clocortolone pivalate, rimexolon</td>
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<tr>
<td></td>
<td></td>
<td>D1: Betamethasone dipropionate</td>
<td>D2: Methylprednisolone aceponate</td>
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<td></td>
<td></td>
<td>D1: Clobetasol-17-propionate</td>
<td>D2: Hydrocortisone-17-butyrate, budesonide</td>
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<td></td>
<td></td>
<td>D1: Betamethasone valerate &amp; dipropionate, clobetasol proprionate, aclometasone dipropionate</td>
<td>D2: Hydrocortisone-17-valerate &amp; butyrate</td>
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Approach to Corticosteroid Allergy

- If not having expected response or tests + to just one group, try a steroid from a different group
- If still not improved, then use a class C steroid (desoximetasone for body, clocortolone for face/flexures)
- Up to 10% patients allergic to tixocortol (class A) may have allergy to prednisone – need a class C oral steroid (dexamethasone)
- Patch test to individual agent
Vehicle Allergy

- Formaldehyde releasers (5.6-7%)
- Methylchloroisothiazolinone/methylisothiazolinone (6.4%)
- Lanolin (5.4%)
- Propylene glycol (2.8%)
- Parabens (0.6%)
- Sorbitan sesquioleate
Approach to Vehicle Allergy

- Maintain a high index of suspicion for this
- If True test nonrevealing, consider more extensive testing
- Beware generic substitutions
- ACDS CAMP database is very helpful to limit exposure via medicaments or other sources
Case 3

- Improved with switch to desoximetasone ointment

Case 4

- Stopped cetaphil cream, clobetasol ointment, and clotrimazole/betamethasone cream
- Now on clobetasol compounded in plain petrolatum, new shoes
- Full recovery
Take Home Points: Case 3 & 4

- Suspect medicament allergy when dermatitis fails to improve
- Medicament allergy should also be added to the differential diagnosis for foot dermatitis
- Consider allergy to the vehicle as well as the active ingredient
- Always patch test to medicaments themselves whenever possible
Summary

- Avoid systemic immunosuppression when patch testing, or limit use to minimum dose required.
- Consider repeat patch testing when off immunosuppression.
- Suspect medicament allergy when dermatitis fails to improve.
- Consider allergy to the vehicle as well as the active ingredient.
Thank You