Contact Dermatitis: an Allergic Disease

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Disclosure

- Research and Educational Grants:
  - Novartis-Genentech
  - Alcon
  - Dyax
  - Lev
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- Speaker’s Bureau
  - GlaxoSmithKline
  - Baxter
Objectives:

1. Differentiate different causes of eczema and clues to the diagnosis of contact dermatitis
2. Discuss the relevant allergens in allergic contact dermatitis
3. Demonstrate the proper technique of patch testing and its interpretation
Inflammatory Skin Disorders

**Dermatitis and Eczema**
- Atopic D, Contact D, Seborrheic D, Pruritus, Nummular Eczema, Erythroderma, Lichen Simplex Chronicus/Prurigo Nodularis, Dyshidrosis, Pityriasis Alba

**Papulosquamous disorders**
- Psoriasis
- Parapsoriasis
  - Acute: Pityriasis lichenoides et varioliformis acuta
  - Chronic: Pityriasis Lichenoides Chronica
  - Lymphomatoid Papulosis
- *Pityriasis*
  - *Pityriasis Rosea*
  - *Pityriasis Rubra Pilaris*
- *Lichenoid*
  - Lichen Planus
  - Lichen Nitidus

**Urticaria**

**Erythema Multiforme/Drug Eruption:** SJS, TEN, E Nodosum

**Other Erythemas:** E. Annulare, E Centrifugum, E Marginatum, E Toxicum, Necrolytic Migratory Erythema
Dermatitis of the Eyelid: Guidelines for Diagnosis

Main Risk Factor for the Diagnosis:

- **Allergic Contact Dermatitis:** 4-eyelid involvement
  \( \text{OR} = 3.0; \text{95% CI}, 1.1–8.1 \)

- **Irritant Contact Dermatitis:** Onset of symptoms within 2-6 months from time of exam
  \( \text{OR} = 2.1; \text{95% CI}, 1.1–4.0 \)

- **Atopic Dermatitis:** Onset of symptoms >6 months \( \text{OR} = 4.9 \) & personal history of atopy \( \text{OR}=3.6 \)


Dermatitis of the Eyelid

- **Allergic contact dermatitis: 55-63.5%**
  (as high as 72% if eyelid alone *)
  - 13.4% Fragrances
  - 7.1% Fragrance Mix
  - 6.3% Balsam of Peru
  - 8.2% Gold sodium thiosulfate
    (most common allergen in pure eyelid dermatitis)
  - 6.0% Nickel sulfate
- **Irritant contact dermatitis: 15%**
- **Atopic dermatitis: < 10%**
- **Seborrheic dermatitis: 4%**

Nickel: Contact Allergen of 2008

• 10% of population are nickel allergic
• Increasing incidence of allergic sensitization to nickel in North America
  – New sources of nickel ACD: cell phones
• New insight was offered into the possible genetics of nickel contact allergy
Irritant Contact Dermatitis

- **Primary diagnostic criteria**
  - Macular erythema, hyperkeratosis, or fissuring predominating over vesiculation
  - Glazed, parched, or scalded appearance of the epidermis
  - Healing begin promptly on withdrawal offending agent
  - Patch testing negative

- **Minor objective criteria**
  - Sharp circumscription of the dermatitis
  - Evidence of gravitational influence (dripping effect)
  - Less tendency for dermatitis to spread (than in ACD)
  - Morphologic changes suggest small differences in concentration or contact time producing large differences in skin damage

Localized dermatitis without vesicles
Webs of fingers extending onto the dorsal & ventral surfaces ("apron" pattern), dorsum of hands, palms & ball of thumb

Irritant Contact Dermatitis

Allergic Contact Dermatitis

Often have vesicles
Favor the fingertips, nail folds, dorsum of the hands
Less commonly involve the palms

Hand Eczema
Most Common Irritant Contact Dermatitis

Regional Location of Hand Eczema
– Irritant CD: most common in palmar region
– Allergic CD: more common in dorsal hand & fingers
– Atopic Dermatitis: morphologically distinct involvement of dorsal hand surfaces combined with volar wrist

Pyoderma Gangrenosum

Main Variants

• Classic pyoderma gangrenosum
  – deep ulceration with violaceous border that overhangs the ulcer bed
  – most common on the legs

• Atypical pyoderma gangrenosum
  – Vesiculopustular, "juicy" usually only at the border; erosive or superficially ulcerated
  – often on dorsal surface of the hands, extensor of the forearms, or face
Pyoderma Gangrenosum

- 50% have systemic illnesses that may occur prior to, concurrently or following the diagnosis
- Arthralgias & malaise often present
- Commonly associated diseases
  - inflammatory bowel disease (ulcerative colitis or Crohn’s disease)
  - seronegative or seropositive polyarthritis
  - hematologic disorders (leukemia, preleukemia, monoclonal gammopathies (primarily immunoglobulin A)
  - less common: psoriatic arthritis, osteoarthritis, spondyloarthropathy; hepatitis; SLE
Nummular eczema

- Pruritic
- Plaques of closely set, thin walled vesicles on erythematous base
- Clearly demarcated edge
- Limbs more than trunk
- Variable intermittent course
- ? High incidence of atopy
Contact Dermatitis from Cigarettes

- Occupational ACD in tobacco factory workers
  - Usually on workers’ hands or widespread dermatitis
  - May be due to chemicals in cultivation & processing:
    waxes, paraffins, fatty acids, organic acids, aldehydes, ketones, phenols, paraphenols, ncatechols, & tannins
- Non-occupational ACD
  - dermatitis on 2nd & 3rd digits of hand
  - erythema, edema, scaling on lips
  - macules +/- pigmentation on upper lip

Cigarettes

- Underreported & under recognized cause of ACD
  - ~46 million smokers in the US
  - Nearly 3000 teens/day take up the habit of smoking
- Allergens from filters, paper, tobacco
  - Cocoa Products*
  - Menthol: Mint & peppermint
  - Licorice*
  - Colophony: released from cigarette paper & filters
    - associated with airborne ACD (occupational & non-occupational)
    - can cause asthma
  - Formaldehyde
- Patch Testing is recommended in smokers with dermatitis involving hands, face, & neck**

*main flavor additives in Philip Morris cigarettes

Hypereosinophilic Syndrome

- Skin: Angioedema/urticaria, erythematous, pruritic papules & nodules
- Cardiac disease: major morbidity & mortality
- Neurologic complications: thromboembolic episodes, encephalopathy, peripheral neuropathy
- Respiratory: cough, Eos lung infiltrates
- GI: Eos gastritis, enterocolitis, colitis
Cutaneous T-Cell Lymphoma or Mycosis Fungoides

Stages:

– Patch (atrophic or nonatrophic)
  • Often goes on for many years
  • Patches with thin, wrinkled quality, often with reticulated pigmentation
  • Pruritus varies from minimal or absent to common in premycotic phase & may precede MF by years
  • Often on lower trunk & buttocks
– Plaque
– Tumor
Brachioradial Pruritus

- Sunlight induced chronic episodic pruritus localized to the outer aspect of elbow & adjacent lower & upper arms
- Commoner in fair-skinned people in tropical climates

**Causes:** - probably “solar pruritus”
  - nerve damage from irritation of cutaneous branch of radial nerve or the cervical spine

**Treatment:**
- Sun protection, camphor, menthol, cervical spine manipulation, capsaicin, topical anesthetic

Walcyk PJ *Br J Dermatol* 1986;115:177-80
Bech-Thomjsen N *Acta Derm Venereol (Stockh)* 1995;75:488-9
Dermatophytide

- Secondary distant aseptic lesion
- Criteria
  - Proven focus of dermatophyte infection
  - Positive skin test to group-specific trichophytin antigen
  - Absence of fungi in the id lesion
  - Clearing of id after fungus is eradicated
- Patterns
  - Eczematous vesicles of hands & feet
  - Pityriasis-Rosea like
  - Erysipelas-like
  - Erythroderma
Papulosquamous Disorder

Papules +/- Plaques and scales
(scaly papules and plaques)

- **Psoriasis** (red, scaly lesions)
- **Parapsoriasis** (resembles psoriasis)
  - Large Plaque Parapsoriasis
  - Small Plaque Parapsoriasis
  - Pityriasis Lichenoides
    - Pityriasis lichenoides et varioliformis acuta
    - Pityriasis lichenoides chronica
  - Lymphomatoid papulosis
- **Pityriasis** (flaking or scaling)
  - *Pityriasis* Rosea
  - *Pityriasis* rubra pilaris
- **Lichenoid** (resembles lichen: organisms consisting of a symbiotic association of a fungus)
  - Lichen Planus
  - Lichen Nitidus
Psoriasis

- Plaques typically have dry, thin, silvery-white or micaceous scale
- Removing the scale reveals a smooth, red, glossy membrane with tiny punctate bleeding (Auspitz sign)
Psoriasis

- Plaque psoriasis
- Guttate psoriasis
- Pustular psoriasis
- Inverse psoriasis
- Nail psoriasis
- Erythrodermic psoriasis
Guttate psoriasis

- Abrupt acute eruption of small (< 1 cm) psoriatic lesions
- Typically child or young adult with no history of psoriasis
  - Less commonly, guttate flare occur in preexisting psoriasis
- Primarily the trunk
- Strong association with recent strep infection with serologic evidence* (26-58 %)

Telfer NR; Chalmers RJ; Whale K; Colman G The role of streptococcal infection in the initiation of guttate psoriasis. Arch Dermatol 1992 Jan;128(1):39-42
Parapsoriasis
A Complex Issue

- Resembles Psoriasis (red, scaly)
- Unrelated to pathogenesis, histopathology or treatment

- Large Plaque Parapsoriasis
- Small Plaque Parapsoriasis
- Pityriasis Lichenoides
  - Pityriasis lichenoides et varioliformis acuta
  - Pityriasis lichenoides chronica
- Lymphomatoid papulosis
Parapsoriasis

- Disease processes caused by T-cell–predominant skin infiltrates

- **Large plaque parapsoriasis**
  - ~ 10% progress to CTCL
  - indolent & progresses over years, sometimes decades
  - treatment recommended because it may prevent progression to CTCL

- **Small plaque parapsoriasis**
  - benign; rarely if ever progresses
  - lasts several months to years
  - can spontaneously resolve
Lichenoid skin eruptions

- Subcategory of papulosquamous skin disease
- Scale often subtle; papules tend to remain small & discrete
- Occasionally, confluent plaques may form
Lichen Planus

A disease characterized by "P-words":

- Plentiful
- Pruritic
- Polished
- Purple
- Polygonal
- Planar
- Papules

Long Island, New York
Lichen planus

- Flexor surfaces of upper extremities
- Wickham stria: fine, white lines on papules
- Pruritus common but varies in severity
- > 50% resolve within 6 months
- 85% subside within 18 months
- Other areas of involvement:
  - Mouth: white or gray streaks forming linear or reticular pattern
    - may be asymptomatic, burning or painful
  - Genital
  - Nail plate thinning, grooving, ridging, pterygium
  - Cicatricial alopecia
Eczematous Drug Eruption

- Gold: lichenoid features
  - may progress to erythroderma
- Bleomycin
- Penicillin, chloramphenicol
- Quinine
- β-blocker
- Methyldopa
- Clonidine
SYSTEMIC ALLERGIC CONTACT DERMATITIS

Localized or generalized inflammatory skin disease in contact sensitized individuals when exposed to the hapten orally, transcutaneously, intravenously or by inhalation.
Dermatitis with Scattered Generalized Distribution

• Difficult diagnostic and therapeutic challenge: lacks the characteristic distribution that gives a clue to the etiology

• NACDG data: ~ 15% of the patients patch tested only had scattered generalized dermatitis
  – 49% had a positive patch test deemed at least possibly relevant to their dermatitis
  – The prevalence was higher in patients with a history of atopic dermatitis
  – Two most common allergens:
    • Nickel
    • Balsam of Peru

### Allergens Associated with Food

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>NACD Allergen</td>
<td></td>
</tr>
<tr>
<td>Nickel sulfate 2.5%</td>
<td>38 (48.7%)</td>
</tr>
<tr>
<td>Myroxilon pereirae 25%</td>
<td>20 (25.6%)</td>
</tr>
<tr>
<td>Propylene glycol 30%</td>
<td>5 (6.4%)</td>
</tr>
<tr>
<td>Fragrance mix 12%</td>
<td>4 (5.1%)</td>
</tr>
<tr>
<td>Compositae mix 6%</td>
<td>3 (3.9%)</td>
</tr>
<tr>
<td>Cinnamic aldehyde 1%</td>
<td>2 (2.6%)</td>
</tr>
<tr>
<td>Potassium dichromate 0.25%</td>
<td>2 (2.6%)</td>
</tr>
<tr>
<td>Sesquiterpene lactone mix 0.1%</td>
<td>2 (2.6%)</td>
</tr>
</tbody>
</table>

Food-related allergen: Nickel (most common)

• Top 3 body sites in patients with (+) PT
  – generalized (systemic contact dermatitis)
  – hands (vesicular hand dermatitis)
  – arms (direct physical contact with foods)
• Metal utensils leach nickel esp with acidic foods

*Jensen CS, Menne’ T, Johansen JD. Systemic contact dermatitis after oral exposure to nickel: a review with a modified meta-analysis. Contact Dermatitis 2006;54:79–86.
Dietary Nickel: Most Common Food Related Allergen

- Evidence support the contribution of dietary nickel to vesicular hand eczema
- Meta-analysis of systemic contact dermatitis following oral exposure to nickel estimated reaction in:
  - 1% of nickel allergic patients in a normal diet (0.3 - 0.6 mg/d)
  - 10% to 0.55 - 0.89 mg of nickel *
  - ~ 50% would flare after 2.5 mg nickel
- Case control study of 60 patients found endoscopic bowel inflammation in the oral-sensitive nickel-allergic patients

* Jensen CS, Menné T, Johansen JD. Systemic contact dermatitis after oral exposure to nickel: a review with a modified meta-analysis Contact Dermatitis 2006:54:79–86
Nickel Pyramid

>50 mcg
- Soybean, Boiled ~ 1 cup: 895 mcg
- Cocoa, 1 tbsp: 147 mcg
- Cashew, ~18 nuts: 143 mcg
- Figs ~5: 85 mcg
- Lentils ½ cup cooked: 61 mcg
- Raspberry: 56 mcg

20-50 mcg
- Vegetables, canned ½ cup: 40 mcg
- Lobster 3 oz: 30 mcg
- Peas Frozen, ½ cup: 27 mcg
- Asparagus, 6 spears: 25 mcg
- Oat Flakes 2/3 cup: 25 mcg
- Pistachios, 47 nuts: 23 mcg

<20 mcg
- Strawberries, 7 med: 9 mcg
- Bread wheat, 1 slice: 5 mcg
- Poultry, 3.5 oz: 5 mcg
- Carrots, 8 sticks: 5 mcg
- Apple, 1 med: 5 mcg
- Cheese 1.5 oz: 3 mcg
- Yogurt, 1 cup: 3 mcg
- Mineral water, 8 fl oz: 3 mcg
- Mushroom raw, ½ cup: 2 mcg
- Corn Flakes, 1 cup: 2 mcg
Fragrance: Food-related Allergen

- **Myroxilon pereirae (Balsam of Peru)**
  - One of 5 most prevalent allergens in TT
  - Found in toothpaste, mouthwash, flavors
  - Sensitization to BOP in cosmetics may lead to future systemic ACD flares from foods containing BOP
- **Cinnamic aldehyde**
  - Relatively specific (but not very sensitive) marker for spice allergy
  - Flavoring in gums, mouthwashes, toothpastes
- **Fragrance mix**

All 3 account for 33.3% of food related reactions

Fragrance Systemic Contact Dermatitis

~ 50% of patients with (+) PT to Myroxilon who followed BOP reduction diet had significant improvement of their dermatitis

Foods to Avoid in Balsam-Restricted Diet

• **Citrus** fruits: oranges, lemons, grapefruit, tangerines, marmalade, juices
• Flavoring agents: pastries, bakery goods, candy, chewing gum
• **Spices**: cinnamon, cloves, vanilla, curry, allspice, anise, ginger
• Spicy condiments: ketchup, chili & barbecue sauce, chutney, pickles, pizza
• Perfumed or flavored tea & tobacco
• Chocolate
• Certain cough medicines & lozenges
• Ice cream
• Cola, spiced soft drinks such as Dr Pepper
• **Tomatoes** & tomato-containing products

Mass spectrometry: Tomato peaks at 134 & 180 molecular weight corresponded to cinnamic alcohol & coniferyl alcohol
<table>
<thead>
<tr>
<th>Pt</th>
<th>Medication</th>
<th>Dose*</th>
<th>Reaction</th>
<th>Allergens</th>
<th>Improved</th>
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<tbody>
<tr>
<td>1</td>
<td>Prednisone</td>
<td>10</td>
<td>+++</td>
<td>Balsam of Peru</td>
<td>Yes</td>
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<tr>
<td>2</td>
<td>Pred + cyclosporine</td>
<td>10 / 200</td>
<td>+++</td>
<td>Cobalt chloride neomycin, Nickel</td>
<td>Yes</td>
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<tr>
<td>3</td>
<td>Cyclosporine</td>
<td>200†</td>
<td>+++</td>
<td>Cobalt chloride Carba mix; thiuram mix; tetraethylthiuram</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>Infliximab</td>
<td>5‡</td>
<td>+++</td>
<td>n,n-dialkyl-’diphenyl-4-phenylenediamine; zinc diethyldithiocarbamate</td>
<td>Yes</td>
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<tr>
<td>5</td>
<td>Prednisone</td>
<td>10</td>
<td>++</td>
<td>p-Phenylendiamine, Disperse Orange 3</td>
<td>Yes</td>
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<tr>
<td>6</td>
<td>Prednisone</td>
<td>10</td>
<td>++</td>
<td>Formaldehyde, Grotan BK, benzalkonium chloride</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>Cyclosporine</td>
<td>300§</td>
<td>++</td>
<td>Cinnamyl alcohol</td>
<td>Yes</td>
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<tr>
<td>8</td>
<td>Prednisone</td>
<td>10</td>
<td>+</td>
<td>Benzophenone-4, Grotan BK, cocamide DEA, CAPB, oleamidopropyl dimethylamine, Reactive Black 5, dimethylol dihydroxyethylenurea (aq &amp; FIX NF, modified Fix ECO), melamine formaldehyde</td>
<td>No</td>
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<tr>
<td>9</td>
<td>Prednisone</td>
<td>5</td>
<td>+</td>
<td>Euxyl K400, balsam of Peru, nickel oleamidopropyl dimethylamine, carba mix, potassium DC,</td>
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<tr>
<td>10</td>
<td>Mycophenolate</td>
<td>2000</td>
<td>+</td>
<td>Cobalt, gold, triethanolamine</td>
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<td>Off Mycophenolate</td>
<td>-</td>
<td>++</td>
<td>Formaldehyde</td>
<td>Yes</td>
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<td>+</td>
<td>MCI/MI; diazolidinylurea, DMDM hydantoin, melamine formaldehyde</td>
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<tr>
<td>11</td>
<td>Prednisone</td>
<td>10</td>
<td>?</td>
<td>Fragrance mix, methyl methacrylate</td>
<td>Yes</td>
</tr>
</tbody>
</table>

? = questionable; aq = aqueous; DEA = diethanolamine; DMDM = dimethylol dimethyl; MCI/MI = methylchloroisothiazolinone/methylisothiazolinone; *All meds (mg/d) continued during PT unless otherwise indicated. †D/cd 2 days prior to testing.‡5 mg/kg/d. Patient on infusion q 8 wks; last dose 3 weeks prior to PT. §D/cd the day of PT

## Diagnosis of Contact Dermatitis: Patch Testing to Cosmetics

<table>
<thead>
<tr>
<th>Agent</th>
<th>Test Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leave on cosmetics (make up, perfume, moisturizer, deodorants)</td>
<td>As is</td>
</tr>
<tr>
<td>Wash off cosmetics (soap, shampoo, bubble baths)</td>
<td>1%</td>
</tr>
<tr>
<td>Products with volatile solvents (hairspray, mascara, nail polish)</td>
<td>Dry then as is</td>
</tr>
<tr>
<td>Clothing, shoes, gloves</td>
<td>As is, moisten in saline</td>
</tr>
<tr>
<td>Plants &amp; foods</td>
<td>As is; garlic &amp; onion at 50% dilution</td>
</tr>
</tbody>
</table>

### Use of supplementary allergens/ personal products:
- 16.3% of cosmetic-allergic patients only reacted to a non-NACDG allergen
- ~ 1/3 of allergic contact cheilitis had relevant (+) PT to non-NACDG series, including personal products (especially lip products), food & oral hygiene
Recommendation Prior to Patch Testing  
“Lo.C.A.L. (Low contact allergen) Skin Diet (Zug KA)

Eliminates most common allergens:

- Fragrance
- Formaldehyde Releasing Preservatives
- MCI/MI
- MDG/PE
- Lanolin
- CAPB
- Benzophenone-3

- Cover girl clean fragrance free liquid make-up
- Clinique blushing blush powder blush
- Clinique soft pressed eye shadow
- Max factor vivid impact lip liner-all shades
- Almay hypoallergenic roll-on anti-perspirant/deodorant
- Cerave moisturizing lotion/ vanicream
- Cetaphil gentle skin cleanser
- Free & Clear shampoo
- Free & Clear hair spray - firm hold
TREATMENT OF CONTACT DERMATITIS

• Identify and avoid contact with allergens and irritants
  – Give exposure list (synonyms & sources)
• Alternatives & substitutions if possible
  – Cover nickel plated objects
  – Wash formaldehyde containing garments
  – Gloves & barriers
Acute Contact Dermatitis (wet, oozing lesions)
- Aluminum sulfate & calcium acetate (Domeboro) in clean absorbent cloth 20-30 min as compress 2-3 x a day
- or Oatmeal baths (Aveeno) in extensive areas
- Oral corticosteroid if severe
- Fluorourinated steroids for 1-2 weeks

Chronic contact dermatitis
- Emollients to decrease itching
- Low to medium strength topical cs
- Antihistamines to decrease itching
- UV light
- Cyclosporine
- Topical calcineurin inhibitors
ACDS
Contact Allergen Management Program (CAMP)
Topical Skin Care Product Database

American Contact Dermatitis Society
info@contactderm.org

Allergists who need reference from ACDS member, send CV: Luz Fonacier, MD. Head of Allergy Winthrop University Hospital Professor of Clin Medicine, SUNY at Stony Brook Ifonacier@winthrop.org