What to do When Patch Testing is Negative

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“Patch Test Negative Dermatitis”
Inflammatory skin condition consistent with acute, subacute or chronic dermatitis.

Adequate patch testing failed to show positive allergen or current relevance.

Often dealing with CHRONIC and GENERALIZED dermatitis.

Potential False Negative Results

DISCLOSURES
Celgene: Speaker Bureau

Potential False Negative Results

Testing to Standard Mixes versus Individual Allergens
Patch testing with standard mixes may miss patients allergic to an individual allergen in the mix.

EXAMPLES:
- Fragrance Mix
- MCI/MI
- Thiourea Mix

Potential False Negative Results

Reading Time

Table 1. Comparison of positive patch test results between TRUE Test and neurovascular allergens

<table>
<thead>
<tr>
<th>Allergen</th>
<th>TRUE Test</th>
<th>Neurovascular Allergens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic Mix</td>
<td>88%</td>
<td>90%</td>
</tr>
<tr>
<td>Fragrance Mix</td>
<td>74%</td>
<td>80%</td>
</tr>
<tr>
<td>Thiourea Mix</td>
<td>68%</td>
<td>75%</td>
</tr>
<tr>
<td>Neomycin</td>
<td>57%</td>
<td>65%</td>
</tr>
<tr>
<td>PPD</td>
<td>47%</td>
<td>50%</td>
</tr>
<tr>
<td>Gallates</td>
<td>38%</td>
<td>40%</td>
</tr>
<tr>
<td>Metals</td>
<td>28%</td>
<td>30%</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>18%</td>
<td>20%</td>
</tr>
<tr>
<td>Nonsteroids</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Antimicrobials</td>
<td>4%</td>
<td>6%</td>
</tr>
</tbody>
</table>

SHERETZ 2001
Testing to Non-standardized Allergens

Skin testing to oral medications can be of value in patients with cutaneous adverse drug reactions (CADR) but must be interpreted cautiously.

False positive reactions may be irritant reactions related to additives such as sodium lauryl sulfate or due to low pH.

Sensitivity varies but has been reported to be 50% for patch testing and 65% for intradermal testing in patients with CADR in which a single drug was favored as the cause.

Other Etiologies
- Irritant Contact Dermatitis
- Atopic Dermatitis
- Seborrheic Dermatitis
- Nummular Dermatitis
- Neurodermatitis
- Chronic Eczematous Eruption of the Aged
- Eczematized Psoriasis
- Phytophthosis Rubra Pilaris
- Dermatomyositis
- Non-bullous pemphigoid
- Scabies
- CTCL
- Tinea
- Xerosis
- Drug Reaction
- Urticaria
- Grover’s Disease
- Dermatitis Herpetiformis
- Pruritus

Consider Further Work-Up
- Full review of systems
- Comprehensive exam/lymph node survey
- Test for dermatographism
- Skin biopsy (H&E / DIF)
- CBC with differential
- Thyroid function panel
- Comprehensive metabolic panel
- KOH
- Scabies prep
- HIV
- Stool ova & parasite

Stepwise Dermatitis Management

Recalcitrant severe dermatitis
- Systemic Therapy
- (Corticosteroids, MTX, Mycophenolate mofetil, Ciclosporin, Azathioprine)
- Phototherapy

Mild to moderate dermatitis
- Phototherapy
- Medium potency topical corticosteroids
- Topical calcineurin inhibitors
- Low potency topical corticosteroids
- Topical calcineurin inhibitors
- Skin hydration, exfoliants, irritant avoidance, antihistamines for pruritus

Moderate to severe dermatitis
- BID for 2 weeks
- Low potency TCS or TCI twice a week

Mild to moderate dermatitis
- Rescue Therapy
- Use during acute flares
- Higher potency and increased frequency of application
- Limits set on use

Mild dermatitis
- Suppressing Therapy
- Use on “hot spots” intermittently during quiescent times
- Tissue transglutaminase
- Iron studies
- Age appropriate malignancy screening
- CXR
- SPEP / immunofixation

**Topical Calcineurin Inhibitors (TCI)**

**Agents:**
- Tacrolimus 0.03% or 0.1% ointment
- Pimecrolimus 1% cream

- Inhibit T-cell and dendritic cell activation
- Both have been shown capable of suppressing allergic and irritant contact dermatitis.
- May play a role in both rescue and suppressive regimens.
- Anti-pruritic effects as well as burning dysesthesia with application may be due to neuropeptide release and depletion similar in mechanism to capsaicin.

**Topical PDE-4 Inhibitors**

**Agents:**
- Crisaborole 2% Ointment

- FDA approval for atopic dermatitis
- Anti-inflammatory non-steroidal phosphodiesterase 4 inhibitor

**Antimicrobial Therapy**

**Topical**
- Dilute bleach baths
- Chlorhexidine / Mupirocin
- The combination of a topical antibiotic along with a topical corticosteroid has been shown to be more effective than topical corticosteroids alone in atopic dermatitis.

**Antihistamines**

**FIRST GENERATION H1 ANTAGONISTS**

**Agents:**
- Diphenhydramine / Hydroxyzine

- Often overlooked important adjuvant therapy
- Soporific effect is important therapeutically for restful sleep

**SECOND GENERATION H1 ANTAGONISTS**

**Agents:**
- Cetirizine / Levocetirizine / Loratadine / Desloratadine / Fexofenadine

- Can be used during daytime due to less sedation
- Less effective in controlling pruritus

**Systemic Corticosteroids**

**Clinical Pearls**
- Rule of thumb → Consider if >20% BSA involved or severe facial / genital / hand involvement
- Use caution in patients at risk for volume overload

**Methotrexate**

- Limits lymphocyte proliferation leading to immunosuppressive and anti-inflammatory effects.
- Extensive literature available in management of various types of dermatitis.
- Similar efficacy to azathioprine with more desirable safety profile.
- Monitor for hepatotoxicity.
Cyclosporine

- Systemic calcineurin inhibitor.
- Primary benefit is ability for rapid onset.
- Well established in the literature for the management of severe dermatitis.
- Potential for nephrotoxicity, hypertension, and neoplasia limit long term use.
- Risk of nephrotoxicity increases with doses above 5mg/kg/day, treatment duration greater than 4 months, or increase in creatinine greater than 30% above baseline.

Azathioprine

- Systemic immunosuppressant / purine analog.
- Undergoes a complex metabolism involving the enzyme thiopurine methyl transferase (TPMT).
- Considered second-line therapeutic option for severe atopic dermatitis.
- Steroid sparing agent with slower onset than cyclosporine.
- Potential for myelosuppression, hepatotoxicity, gastrointestinal disturbances, infections, and neoplasia including potential for NMSC and lymphoma.

Mycophenolate Mofetil

- Selectively and noncompetitively inhibits inosine monophosphate dehydrogenase in the de novo purine synthesis pathway.
- More acceptable for chronic use when compared to cyclosporine.
- Dose dependent gastrointestinal side effects.
- Potential for miscarriage and teratogenicity (Mycophenolate REMS).
- Less literature available in management of dermatitis.

Phototherapy (UVA, UVB)

- Narrowband UVB
  - Has been shown experimentally to suppress contact hypersensitivity reactions in mice.
  - Long record of efficacy in management of moderate to severe atopic dermatitis.
- PUVA
  - May be of particular benefit for refractory hand dermatitis.

Apremilast

- Inhibits PDE4 leading to increased levels of cAMP, decreased production of TNF-alpha, and increased levels of IL-10.
- Limited studies available to suggest safety and efficacy in atopic dermatitis.

Dupilumab

- Monoclonal antibody against the IL-4 receptor alpha subunit
- Blocks signaling of IL4 and IL13
- FDA approved for severe adult atopic dermatitis