What to do when patch testing is negative...

**Definitions**

**Patch Testing Scope**

**Other Etiologies**

**Management**

Potential False Negative Results

**T.R.U.E Test versus Expanded Patch Testing**

Potential for false negative reactions – Fragrance mix, balsam of Peru, thiuram, carba mix
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

Reading Time

<table>
<thead>
<tr>
<th>Day</th>
<th>Place Allergens</th>
<th>Photopatch</th>
<th>Remove Allergens</th>
<th>Standard Read</th>
</tr>
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<tbody>
<tr>
<td>0 hr</td>
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<tr>
<td>24 hr</td>
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<td>48 hr</td>
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<td>144 hr</td>
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<tr>
<td>216 hr</td>
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</table>

False Negative Results

Day 1  Day 2  Day 3  Day 5  Day 7  Day 10
0 hr  24 hr  48 hr  96 hr  144 hr  216 hr

Potential False Negative Results

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.

Patch Testing to Drugs

Testing is often performed with 10% dilution

Agents with irritant excipients or low pH may require lower concentrations to avoid irritant reactions.

Example: Aldactone contains spironolactone and SLS. Provokes irritant reactions when tested in pure form. False positive reactions were not seen with testing at 1% in petrolatum.

Patch Testing Scope

Limited screening series have limited value.

Many studies have shown that only about 1/3 of the patients (or less) are fully evaluated by use of a limited patch test screening series.

Targeted Patch Testing

Expanded Patch Testing

Diagnostic Yield

Other Etiologies

- Infantile Contact Dermatitis
- Atopic Dermatitis
- Seborrheic Dermatitis
- Nummular Dermatitis
- Neurodermatitis
- Chronic Eczematous Eruption of the Aged
- Eczematized Poxitids
- Non-bullous (urticarial phase) pemphigoid

- Scabies
- Agrodermatitis
- CTCL
- Hypersensitivity
- Tina
- Xenodermatitis
- Drug Reaction
- Urticaria
- Dermatographism
- 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
- KSHV
- HIV
- Stool ova & parasite
- Bacterial culture
- Tissue transglutaminase
- Iron studies
- Age appropriate malignancy screening
- SIEP / immunofluorescence

Management
- Skin care prescription
- Address multifactorial disease
- Topical emollients
- Soaks & compress therapy (wet wraps)
- Topical anti-itch products
- Antihistamines
- Antimicrobial therapy
- Topical & systemic corticosteroids
- Topical & systemic calcineurin inhibitors
- Phototherapy
- Azathioprine
- Methotrexate
- Mycophenolate mofetil and mycophenolic acid

Stepwise Dermatitis Management
- Resistant severe dermatitis
- Moderate to severe dermatitis
- Mild to moderate dermatitis
- Mild dermatitis

Topical Corticosteroids (TCS)
- Inhibit T-cell activation and leukocyte migration
- Avoid “static” treatment regimen
- Rescue Therapy
  - Use during acute flares
  - Higher potency and increased frequency of application
  - Limits set on use
- Suppressive Therapy
  - Use during acute flares
  - Higher potency and increased frequency of application
  - Limits set on use

Topical Calcineurin Inhibitors (TCI)
- Tocizumab 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.

Antimicrobial Therapy
- 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.

Phosphodiesterase (PDE) Inhibitors
- 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.

Phosphodiesterase (PDE) Inhibitors

Anti-inflammatory cytokines
IL-10

Proinflammatory cytokines
TNF-alpha

Apremilast
Crisaborole

JAK-STAT Inhibitors
- Ruxolitinib, Baricitinib, Tofacitinib, Upadacitinib
- There are 4 members of the JAK family of enzymes: JAK1, JAK2, JAK3, and tyrosine kinase 2 (Tyk2)
- JAK pathway utilized in atopic dermatitis
- Tofacitinib has been shown to reduce inflammation via inhibiting IL-4

IL-31 Inhibitors
- Nemolizumab is a humanized monoclonal antibody to the IL-31 receptor alpha
- IL-31 is a major Th2 pruritogen and activates the JAK/STAT pathway

IL-13 Inhibitors
- Lebrikizumab, Tralokinumab
- IL-13 may decrease loricrin and involucrin thereby decreasing epidermal barrier integrity

Dupilumab
- Inhibits IL-4 & IL-13
- Fully human monoclonal antibody against IL-4 alpha subunit of receptor
- Treatment option for Th2 mediated disease

