What to do when patch testing is negative?

Christen M. Mowad MD
Clinical Professor of Dermatology
Geisinger Medical Center
Danville, PA 17821
cmowad@geisinger.edu
I have no disclosures.
What to do when patch testing is negative

- Is patch testing really negative?
  - False negative
- The patches really are negative
  - What now?
- Is there another diagnosis?
  - Differential diagnosis
- Polling of experts
- Current literature
- Therapeutic options
Patch testing is the gold standard for diagnosing allergic contact dermatitis.
Z HEMA

m-methacrylate

ethylene glycol

dimethacrylate

ethyl acrylate

triethylene glycol

dimethacrylate
Sometimes patch testing is negative….
Sometimes the diagnosis is not ACD….
Patch test referral centers

- Treatment resistant chronic dermatitis sent for patch testing
- Patient frustrated
  - Decreased quality of life
    - Sleep deprived
    - Social issues
    - Work concerns
- Physician frustrated
- Prolonged process
- Challenging diagnostic/management and therapeutic issues
- Multifactorial
Patients referred for expanded patch testing
Often billed as the answer to the problem
Evaluate and consider differential diagnoses
Consider benefit/timing of patch testing
Set expectations
Differential Diagnosis considerations

- Allergic contact dermatitis
- Irritant contact dermatitis
- Psoriasis
- Atopic dermatitis
- Cutaneous T cell lymphoma
- Drug reaction
- Myeloproliferative disease
- Dermatomyositis
- Immunobullous disease
- Scabies
- Tinea
Which of the following may compromise patch test results?

- A. no delayed reading
- B. recent sunburn
- C. antihistamines
- D. oral prednisone
- E. A, B and D
- F. All of the above
Negative patch test results
Considerations.....

* no allergy exists
* did not test to correct allergen
  * expanded allergen series
* improper testing technique
  * no delayed reading
  * immunosuppressants on board
 TRUE Test

* Thin-layer Rapid Use Epicutaneous Test
* FDA approved testing series
* introduced in 1995
* 35 allergens and 1 control
* increased ease of use
* limited and static number of allergens
Standard Allergen Testing

- Any standard tray may be inefficient
- Limitations
- Increased allergens, better yield
- Doesn’t account for patient specifics
  - Occupational
  - Personal exposures
  - Hobbies
  - Environmental issues
Negative patch tests

* Are there really no allergens
  * If only TRUE Test consider more extensive testing
  * 25-33% of allergens missed with TRUE Test only
  * 25% of patients had at least one relevant non-NACDG allergen
Revisit History
Look for other allergen sources

* Ask the questions again
* Consider other possible contacts
  * spouse/significant other
  * child
  * pet
  * someone individual is caring for
* Other sources of allergens
  * Occupation- ? Site visit
  * Hobbies
  * Infrequent exposures
Negative patch test results
Considerations……..

- Was patch testing performed correctly?
  - Allergens active and stored properly
  - Good application/adherence
  - 48 hour occlusion
  - Was a second delayed reading performed?
  - Any immunosuppressives on board?
  - Any recent sunburn or topical steroids?
Two readings necessary
- 27% of dermatologists do 1 reading
- could miss 1/3 of reactions
- helps differentiate irritant from allergic
Possible Delayed Reactors

- disperse blue dyes
- bacitracin
- gold
- corticosteroids
- p-phenylenediamine
- cocamidopropyl betaine
Improper Testing
Other Considerations

- Poor occlusion
  - Hairy back
  - Sweat prevents proper adherence
- Patch testing with active dermatitis
- Steroids - decrease elicitation of contact hypersensitivity
- Other immunosuppressives
- Sunburn - decreases Langerhans cells
* Not a contraindication to patch testing
* Test at lowest possible dose
* ++ or +++ most reliable
* Lose weak relevant reactions
Can still elicit positive patch test
- Azathioprine
- Cyclosporin
- Infliximab
- Adalimumab
- Etanercept
- Methotrexate
- Mycophenolate mofetil
- Tacrolimus

Did not test off immunosuppressives
Unclear effect of suppressing ACD
Patch testing and immunomodulators: expert opinion

Topical steroids
UV
Oral prednisone
Time off oral prednisone
IM prednisone 40 mg
Methotrexate
TNF inhibitors
Azathioprine
Cyclosporine
Mycophenolate mofetil

Avoid for 3-7 days
Avoid for 1 week
Test on 10 mg if necessary
Avoid for 3-5 days
Wait 4 weeks after injection
Little to no effect
Little to no effect
Dose-dependent inhibition
Dose-dependent inhibition
Dose-dependent inhibition

* Local effect of acute low-dose UVB impairs induction of contact hypersensitivity

* Broad spectrum sunscreens protect against UV induced suppression of contact hypersensitivity
Patch testing is negative

* Good news
  * No known allergen/s identified
  * No need to avoid products
* Bad news
  * No diagnosis made
  * No clear path to resolution
  * Additional testing
Paucity of literature
Much of this will be anecdotal
Informal polling of colleagues
Need for research
Formal survey of ACDS conducted
Other studies in progress
What to call Patch test negative dermatitis??

- Endogenous eczema
- Unclassified eczema
- Widespread eczema
- Nonspecific endogenous eczema
- Nonspecific endogenous dermatitis
- Constitutional eczema
- Idiopathic eczema
- Undefined eczema
Differential Diagnosis considerations

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Patch test – negative
Biopsy/DIF
  * not typically helpful- spongiosis
  * Done to rule out other conditions- CTCL/immunobullous/DM etc
Labs to consider
  * CBC with diff
  * Complete metabolic panel
  * Age appropriate screening
  * TSH
  * IgE
  * SPEP
  * Sezary count
  * ANA
  * ?Dust mite
Revisit the patient history

- Past medical history
- Family history
- Work exposure
- Pathology
- Laboratory results
- Symptoms
Avoid irritants- elimination diet
Control itch
Good skin care
  * Emollient creams
  * Mild soaps
  * Short, lukewarm showers
Get rid of loofas
  * ?source of bacteria
Education helpful
Effect of education on quality of life and severity of disease

- Information provided in clinical setting
- Empowers patients and care givers

- 10 studies 2000-2008
  - (8 AD and 2 AD and psoriasis)

- 5 demonstrated improvement in quality of life
- 3 (of 6) demonstrated improvement in severity of disease
Patch test negative dermatitis: Few Studies in the literature

* Unclassified endogenous eczema.
  * Contact Dermatitis 41: 18-21, 1999.

* A clinical and patch test study of adult widespread eczema

* Prognosis of unclassified eczema.

* The value of patch testing patients with a scattered generalized distribution of dermatitis…

* Generalized Dermatitis in Clinical Practice
  * Springer
8% of patch test population- 583
Patch test negative
Intractable eczema referred for patch testing
Further studies performed
45 patients – 34 agreed to further studies
   * 48% male, 62% female
   * Average age 50
   * Average duration 35.7 months
   * 12/34 elevated IgE >100 IU/ml
   * Path
     * 24/26 chronic subacute dermatitis
     * 2/26 urticarial dermatitis
Outcomes two year follow up

1/3 diagnosed with late onset AD
2/3 improved or resolved
  * 25% totally resolved
  * 22% greatly improved
  * 16% improved
  63% improve

* 29% stayed the same
* 10% worse

* 80% of those with high IgE improved
49% with at least one relevant positive allergen
* Patch testing is beneficial
* 16% had at least one non-NACDG allergen
* Most common allergen sources
  * Personal care products 56%
  * Topical medicaments 13%
  * Clothing 8%
  * Jewelry 6%

51% no relevant patch test
Scattered Generalized Distribution of Dermatitis


* 51% with no relevant patch tests

* Diagnosis
  * Other dermatitis 20.4%
    LSC, spongiotic
  * Atopic dermatitis 15.8%
  * Other dermatosis 15.2%
    Nonspongiotic CTD, LP
  * Nummular dermatosis 3.4%
  * Psoriasis 3.3%
  * Irritant 3.1%
Clinical and patch test study of adult widespread eczema


- 108 Widespread eczema
- Men more common
- Older population compared to controls 47.6 years
- ACD 26.9%
- ACD suspected 39.8%
- Unclassified 31.5%
- “Not rare in dermatology practice”
- “Few systemic studies reported”
Prognosis of unclassified eczema

* 655 patients
  * 43.7% allergic contact dermatitis
  * 32.1% unclassified eczema
  * 21.9% other forms of eczema
  * 2.3% atopic dermatitis

* Outcomes 1 year
  * 15% clearance of unclassified eczema
  * 36% improved

* “Not uncommon, should be recognized and further studied”
Adult Onset Atopic Dermatitis

- 9% of patients in CD clinic diagnosed with AD >20
  - Diagnosis- PMH or FH of atopy
  - Elevated IgE >100 IU/ml
  - + prick test
- Women: 65% > men: 38%
- Sites
  - Generalized
  - Hands
  - Face
Treatment

- Skin hydration
- Topical anti-inflammatory
- Anti-pruritic
- Anti-infectious
- Phototherapy
- Systemic therapy
Endogenous Eczema

- Treatment options
  - Emollients
  - Steroids
    - Topical- soak and smear
    - Systemic- rescue
  - Calcineurin inhibitors
  - Phosphodiesterase 4 inhibitor
  - Ultraviolet light
    - UVA1
    - NBUVB
  - Methotrexate
  - Mycophenolate mofetil
  - Cyclosporin
  - Azathioprine
  - Other
Moisturizers should be integral part of AD treatment
- Reduces disease severity
- Decreases need for pharmacologic treatment
- Lessens symptoms: decrease, itch, erythema, fissures
- Apply soon after bathing to improve skin hydration
- Choice is patient dependent (cheap, free of allergens)
**28 patients referred for refractory chronic dermatitis**
- 20 minutes plain water soak
- followed by mid strength topical steroid
- Continue for up to 2 weeks

**Outcomes**
- 17 complete response
- 9 90-100% improvement
- 1 80% improvement
- 1 75% improvement
**First Line Therapy**
- NBUVB
- Mycophenolate
- Methotrexate

**Cyclosporin to clear or rescue**
- Low dose cyclosporin or mycophenolate for maintenance

**Azathioprine- with caution**
- Side effects
- Secondary cancers
Steroids
  * Topical
    * atrophy, striae, telangiectasia, acneiform eruptions
  * Systemic
    * cardiac, GI, bone density, adrenal suppression
Calcineurin inhibitors
  * Topical irritation, black box warning
Phosphodiesterase-4 inhibitor
  * Application site pain, burning stinging
Ultraviolet light
  * skin cancer, availability
Methotrexate
  * liver toxicity
Mycophenolate mofetil
  * Immunosuppression, registry
Cyclosporin
  * Nephrotoxicity, hypertension, immunosuppression
Azathioprine
  * Cytopenia, secondary cancers
Other treatment considerations

- Education
- Bleach baths
- Antibiotics
- Dust mite avoidance
- Antihistamines
- Leukotriene receptor antagonists
- Humanized monoclonal antibodies to IgE
- Interleukin-4 receptor alpha antagonist
Atopics and Skin Flora

- 90% are colonized with staph
- Yeast colonization with malassezia also common
- Treatment considerations
  - Topical/oral antibiotics
    - Decrease inflammation
    - Treat active infection
  - Oral antifungals

Bleach Baths

* Decreases colonization with staph
* 1/4 - 1/2 cup of common liquid bleach (6%) into bath water.
* Mix the bleach in the water
* Creates a solution of diluted bleach (about 0.005%)
* Repeat 2-3 times a week
House Dust mites

- No strong clinical evidence
- Studies show some improvement
- Many recommend
  - allergen-impermeable bedding covers
  - High filtration vacuum cleaner
Evidence lacking in the literature
Insufficient evidence to recommend
Short term sedating antihistamines may help aid sleep
Many dermatologists use them
Increased in AD 43-82%

- Normal IgE does not exclude Atopic dermatitis
- IgE generally not elevated in non-atopic dermatosis
Skin in Atopic Dermatitis

Other treatment considerations

* Increased IgE-bearing Langerhans cells
* Increased leukotrienes produced by proinflammatory cells
Monteleukast

- cysteinyl leukotriene receptor antagonist
- FDA Approved for asthma
- Oral medications dosed daily
- Side effects- well tolerated
  - GI disturbances
  - Insomnia
  - Hypersensitivity
  - Hallucinations
Use in Eczema- off-label

- Inconclusive results
  - Improved sleep
  - Improved dermatitis
  - Improved itch
  - Decreased eosinophil count
  - Decreased disease severity
Omalizumab


- DNA derived recombinant humanized monoclonal antibody specific for Fc-binding domain of IgE
- FDA approved for asthma/chronic idiopathic urticaria
- Dosage based on body weight and pretreatment IgE levels
- Subcutaneous every 2-4 weeks
- Side effects- well tolerated
  - Anaphylaxis, heart disease, headaches, injection site reactions
  - Dizziness, upper respiratory and viral infections
Interleukin-4 receptor alpha antagonist
adult patients with mod-severe atopic dermatitis
Subcutaneous injection
  * 600 mg initial dose, followed by 300 mg every other week
Side effects-
  * Injection site reactions
  * skin irritation, pain
  * Swelling/irritation of the eye
When patch testing is negative..

- Make sure patch testing is really negative
  - Thorough history to make allergen selection
  - Expanded testing
  - Proper technique
- Consider other diagnosis
  - Biopsy and labs as needed
- Review basics of skin care
- Form a treatment plan