Adult Atopic Dermatitis:
To Patch, or not to Patch, that is the Question

Jenny Murase, MD

Palo Alto Foundation Medical Group
University of California, San Francisco

Learning Objectives

This talk details the role of patch testing in differentiating adult atopic dermatitis from allergic contact dermatitis.

1. Review the biological basis for an increased risk of the development of allergic contact dermatitis in patients with lifelong atopic dermatitis.
2. Outline a novel strategy to approach the erythrodermic atopic patient: "Clear, Patch, Avoid, Treat"
3. Detail relevant screening trays when patch testing patients with lifelong atopic dermatitis, and special considerations when patch testing those on systemic therapy.

I believe we are entering a new paradigm where the diagnostic testing for dermatitis is becoming paramount.

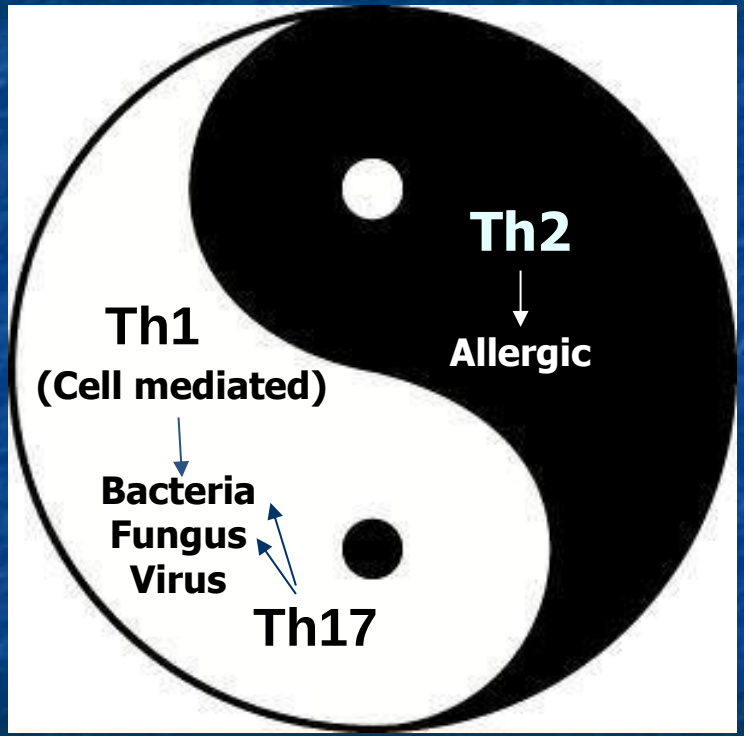
Patch testers are the kings and queens of this diagnostic testing.

https://www.pinterest.com/pin/719309371723512733/

AD Predisposes to ACD Development

- Dysfunctional skin barrier → Increased penetration of chemicals → Increased risk for sensitization
- Exposure from chronic use of emollients and topical anti-inflammatory and antibiotics
- Bacterial colonization activate inflammatory cells involved in contact sensitization
- More prone to ICD which further increases dysfunction of skin barrier

Chen JK, Jacob SE, Nedorost ST, et al. A Pragmatic Approach to Patch Testing Atopic Dermatitis Patients: Clinical Recommendations Based on Expert Consensus Opinion. Dermatitis 2016: 27(4).



Types of Lymphocytes

- Type 1/Th1: Cancer, Intracellular pathogens (B/F/V)
  IFN-gamma
- Type 2/Th2: Parasites (nematodes, mites) and Toxins (venoms)
  IL-4, IL-5, IL-13
- Type 3/Th17: Extracellular pathogens (B/F)
  IL-17, IL-22

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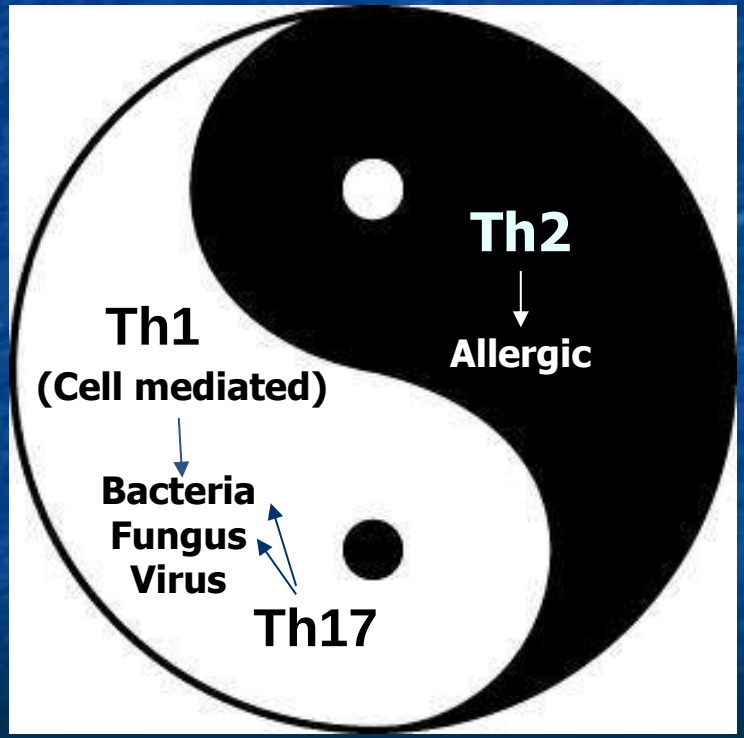
Traditional AD Therapies



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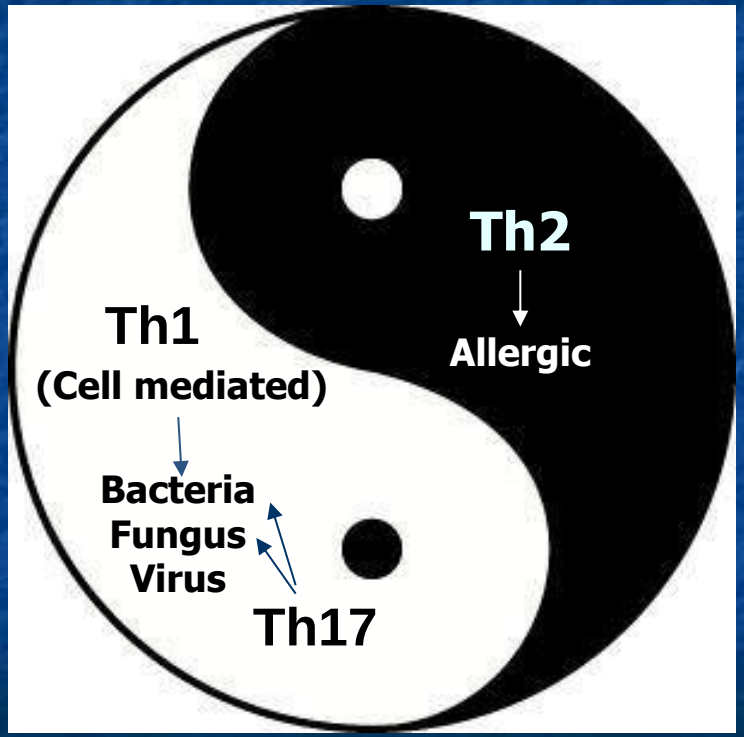
AD Biologics



Reduced rate of bacterial and viral infections

Risk of infection in patients with atopic dermatitis treated with dupilumab: A meta-analysis of randomized controlled trials. Fleming P et al. JAAD 2018 Jan; 78(1): 62-69

https://www.banggood.com/14-Pcs-Adjustable-Speed-Electric-Engraving-Pen-Carve-Carving-Tools-Kit-DIY-Jewelry-Metal-Glass-p-1354685.html?cur_warehouse=CN

Original hypothesis

- Th2 specific immune responses
  Fragrance and rubber dampen
- Th1/Th17
  Nickel and metals unopposed

[Dhingra et al. Molecular profiling of contact dermatitis skin identifies allergen-dependent differences in immune response. J Allergy Clin Immunol 2014; 134:362-372]

Raffi J, Suresh R, Botto N, Murase JE. The Impact of Dupilumab on Patch Testing and the Prevalence of Co-Morbid Allergic Contact Dermatitis in Recalcitrant Atopic Dermatitis: A Retrospective Chart Review. Journal of the American Academy of Dermatology. 2020: 82(1):132-138.

Results: In 125 patch test pairs, only 13 pairs were lost
4 emulsifiers/surfactants, 2 fragrances, 2 metals, 2 sunscreen, 1 topical medication, 1 preservative, 1 resin

Reproducibility of Patch Testing

- Baseline non-reproducibility 5-10% (up to 40%) even in absence of immunosuppression
- Our study: 13/125 lost = 10%
- If remove 11 lost reactions from angry back and immunodeficiency, then non-reproducibility was 1.6% (2/125 lost reactions)

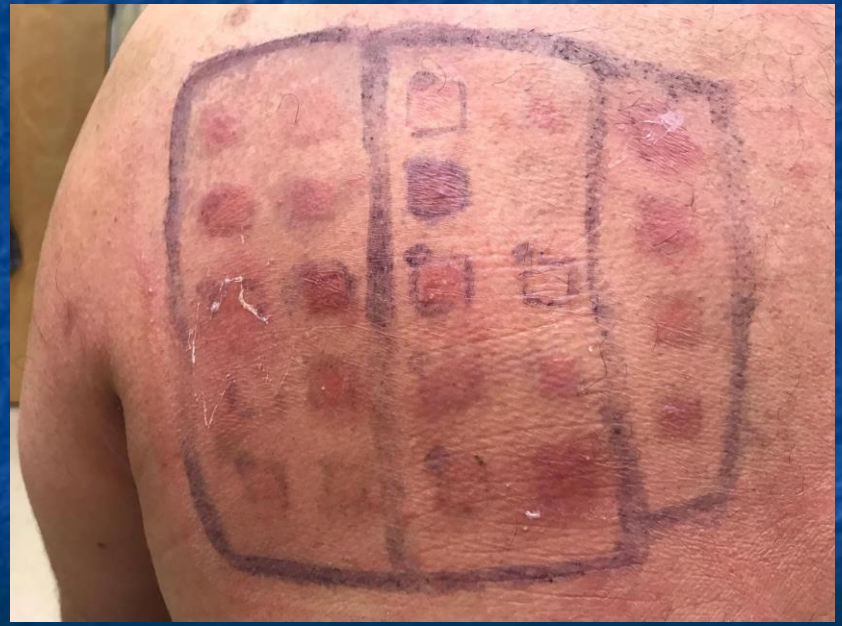
Contact Dermatitis 2004; 50: 304-12. BJD 1982; 107: 461-5.
Contact Dermatitis 1989; 20: 51-56. JAAD 1989; 21(6): 1196-1202.
JAAD 1994; 31(4): 584-91.

Question whether subtle reactions are dampened

- Comment on JAAD 2024 paper by Bocquel
- 36 patients with baseline positive (before and after dupi)
- 24% of patch test reactions lost
- Th2 skewed patch tests are often papular, peak earlier and are weaker than Th1 skewed results

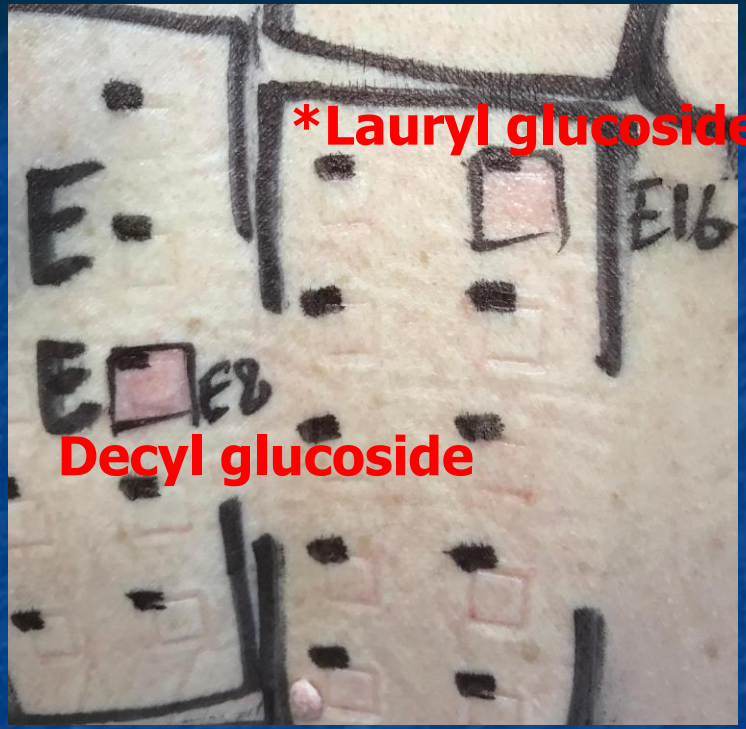
Nedorost S, Wu P, Yu J, Murase JE. To Patch or not to Patch on Dupilumab: That is the Question. Journal of the American Academy of Dermatology. 2025 Apr; 92(4)

Can you patch test on dupilumab?



April 2017: 16 positive rxns at 6 days (NACDS, Metal)
Nov 2018 on dupixent (started Feb 2018): 5 were "lost"
Includes Balsam of Peru/fragrance mix 1 and metals

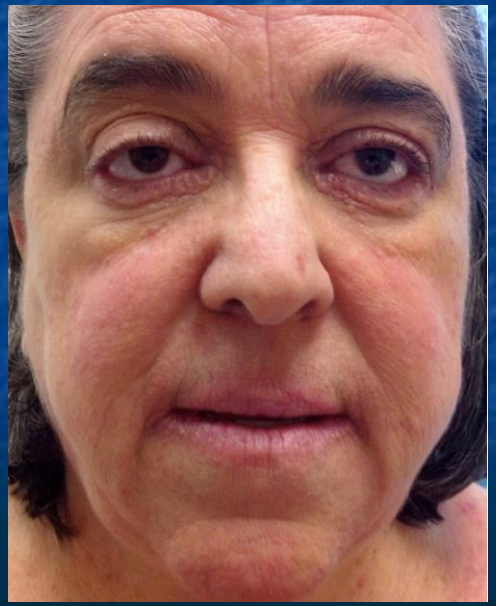
7 months on dupilumab:
reaction to lauryl glucoside
in Free and Clear shampoo



Atopic patients are more allergic to emollients, preservatives, topical anti-inflammatory and antibiotic therapy

Importance of Expanded Series

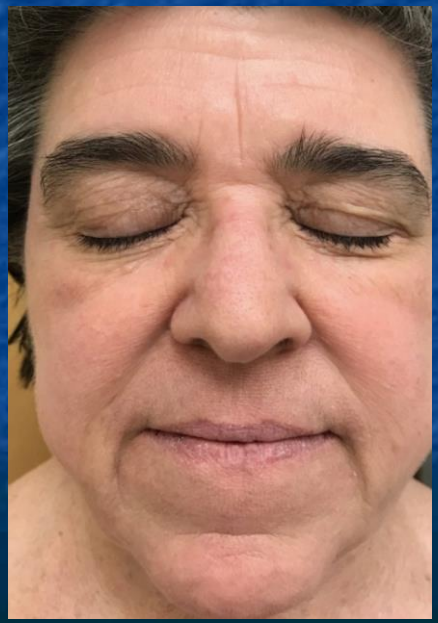
- Suresh R, Murase JE. The Role of Expanded Series Patch Testing in Identifying Causality of Residual Facial Dermatitis Following Initiation of Dupilumab Therapy. Journal of the American Academy of Dermatology Case Reports. 2018: 4(9), 899-904.



6 years prior to D: NACDG, Sunscreen, Corticosteroid

9 months after D: Corticosteroid, Emulsifiers, Eye medicaments, Fragrance, Sunscreen, Cosmetics, patient products

RESULT
Allergy to limonene in Wen shampoo



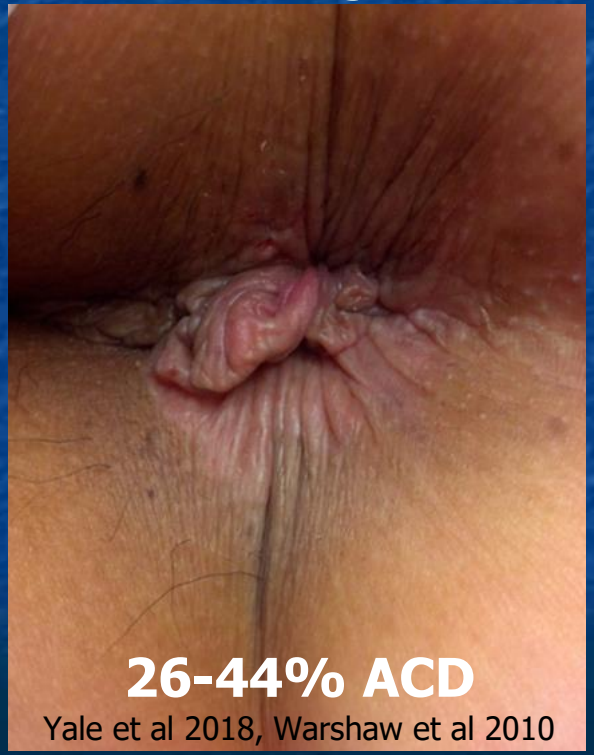
Importance of Expanded Series

Zhu TH, Suresh R, Warshaw E, Scheinman P, Mowad C, Botto N, Brod B, Taylor JS, Atwater AR, Watsky K, Schalock PC, Machler BC, Helms S, Jacob SE, Murase JE. A Review of the Medical Necessity of Comprehensive Patch Testing. Dermatitis 2018: 29(3).

- True test (36): 1/3 allergens missed, only 66% clinical relevant allergens identified (relative to NACDG 70)
- NACDG (70-80): 21-34% of ACD diagnoses are missed without supplemental allergens to NACDG

Location and patterns for ACD…

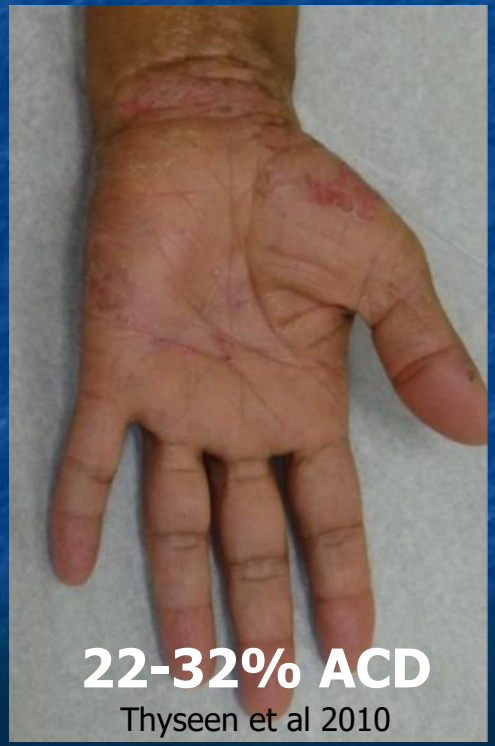
Perianal or genital



26-44% ACD

Yale et al 2018, Warshaw et al 2010

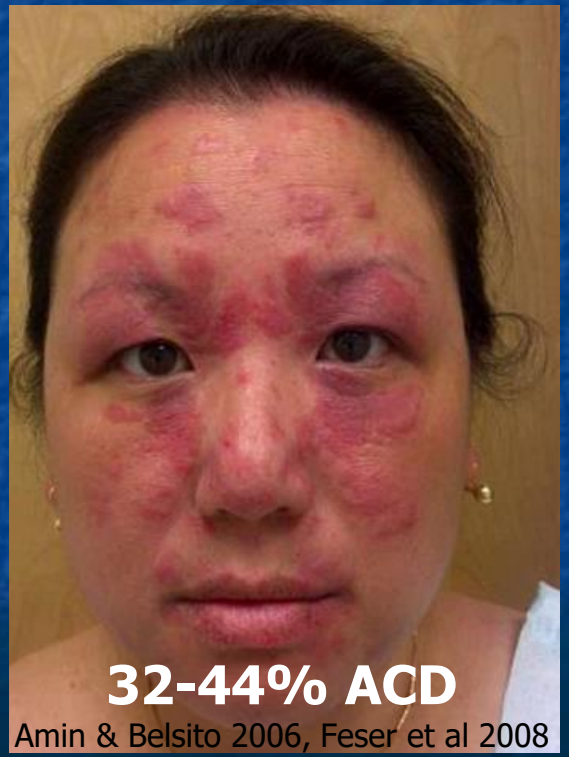
Hands



22-32% ACD

Thyseen et al 2010

Eyelids and face

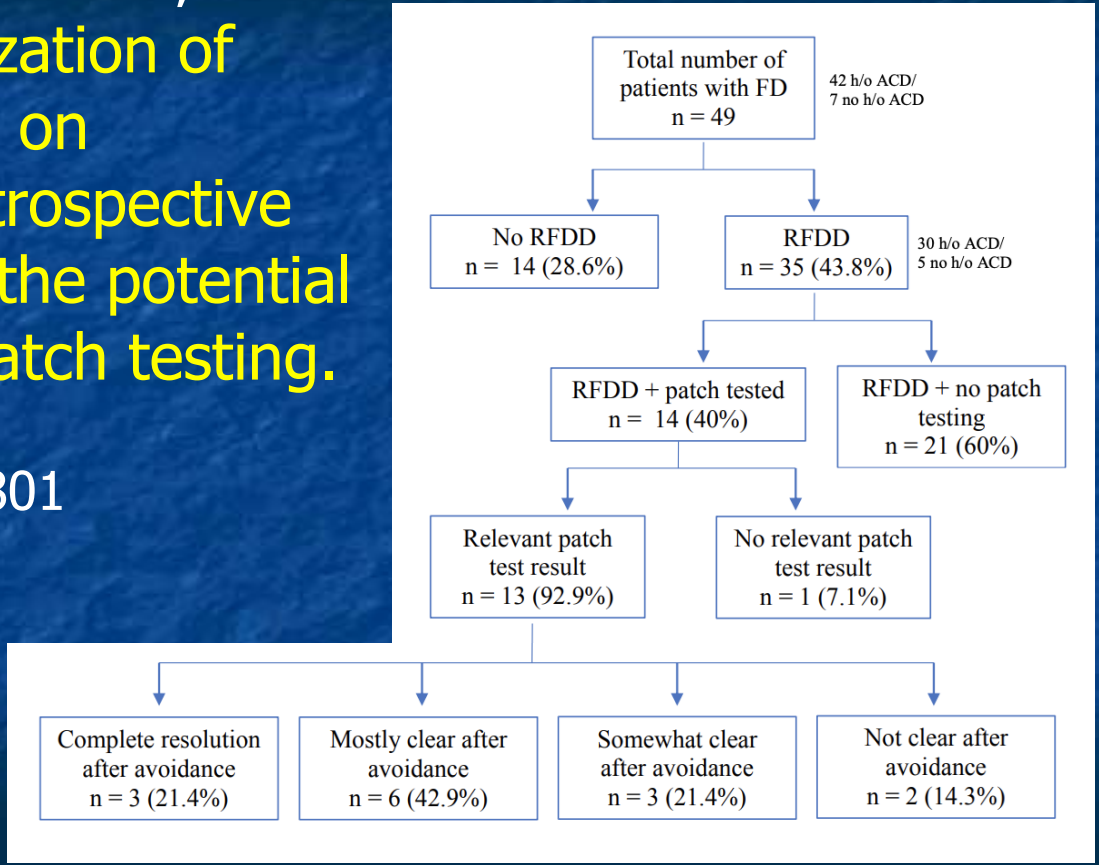


32-44% ACD

Amin & Belsito 2006, Feser et al 2008

Ashbaugh A, Murase EM, Raffi J, Botto N, Murase JE. Characterization of Residual Facial Dermatitis on Dupilumab (RFDD): A retrospective chart review to delineate the potential role of expanded series patch testing. Dermatitis. DOI: 10.1097/DER.0000000000000801

- 80 AD patients
- 80% response @ 3 mo
- 71% (35/49) w/ prior h/o FD had RFDD



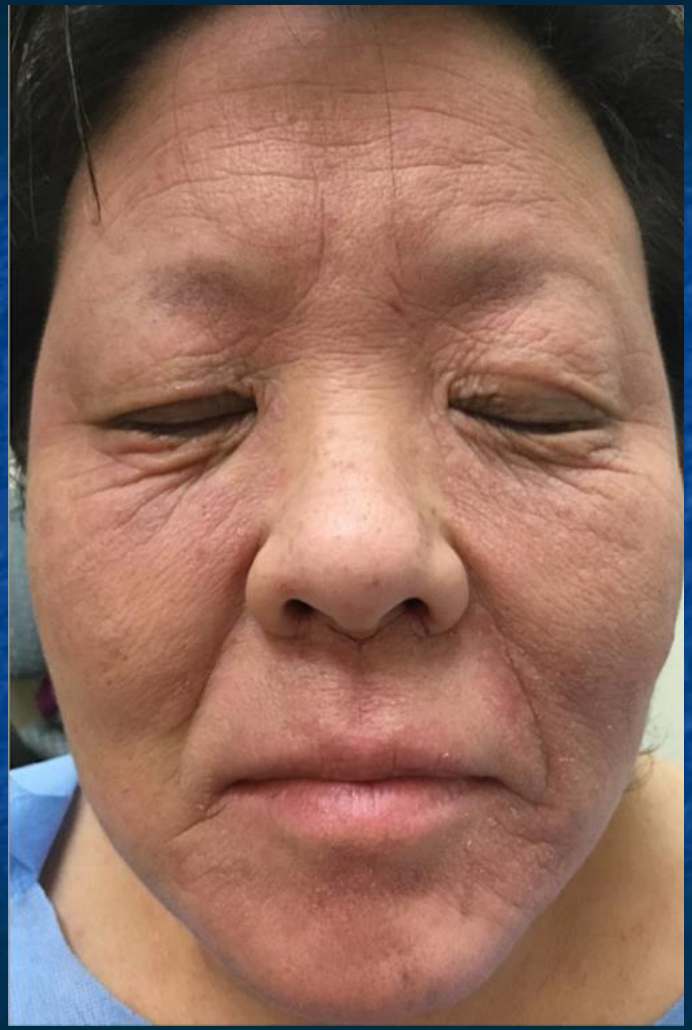
Results

-93% had at least one positive relevant allergen

-50% mostly to completely clear after allergen avoidance [86% at least somewhat helpful]

-50% of positive reactions not on the NACDG Core 80 series (36% emulsifiers/surfactants, 37% fragrances, 12% preservatives)

Category	Number of Allergens	% of Total Positive Reactions
Emulsifiers/Surfactants	15	35.8
Fragrances	12	37.0
Preservatives	7	12.3
Topical steroids & antibiotic agents	4	8.6
Metals	2	3.7
Hairdressing	1	2.5



RESIDUAL HEAD, NECK, HAND →

ACD IS NOT THE EXCEPTION.
IT IS THE RULE.

EXOGENOUS vs. ENDOGENOUS
(ACD) (AD)

http://www.goodskincare.com.au/wp-content/uploads/2016/06/Bellybutton-Psoriasis-300x208.jpg/

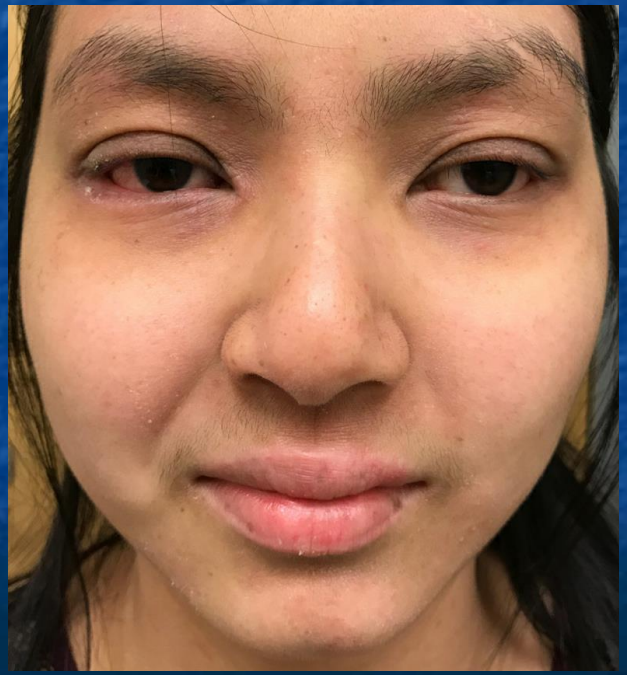
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC281407

Danger in assuming that facial dermatitis is a side effect of dupilumab

June 2017: NACDG, Emulsifier, Corticosteroid negative

11 months after D: Cosmetic and Fragrance, Sunscreen, Cosmetics, Eye, patient products

RESULT
Bcx staph aureus
Allergy to linalool in patient's shampoo



Eyelid Dermatitis on Dupilumab

Raffi J, Suresh R, Berger T, Fishman H, Murase JE. Investigating the Role of Allergic Contact Dermatitis in Residual Ocular Surface Disease on Dupilumab (ROSDD). International Journal of Women's Dermatology. 2019: 5(5), 308-313.

- 14 (29%) had EI on dupi [18 (38%) with a past h/o EI] (EI = eyelid dermatitis, blepharitis, conjunctivitis)
- No cases of dupilumab-associated EI without prior history
- 44% improved EI after patch testing
- Nearly half emulsifier/surfactant; most common personal product was shampoo/facial moisturizer

ROSDD Treatment

Raffi J, Suresh R, Berger T, Fishman H, Murase JE. Non-Steroid Management of Residual Ocular Surface Disease on Dupilumab (ROSDD). International Journal of Women's Dermatology. 2019: 5(5): 383.

IL-4/IL-13 play a role in goblet cell proliferation/mucous secretion (results in tear film instability and dry eye)

Improve meibomian gland dysfunction with antibiotic, anti-inflammatory effects and enhanced tear film production

Omega 3 fatty acid, warm compresses, eyelid hygiene

Treatment	Mechanism in Dry Eye Relief
Lifitegrast 5%	Inhibits T-cell-mediated inflammation
Cyclosporine 0.1%	Anti-inflammatory
Bepotastine 1.5% (azelastine 0.05%, epinastine 0.05%, alcaftadine 0.25%, olopatadine 0.1%)	Blockage of histamine H1 receptors (may aggravate dry eye)
Azithromycin 1%	Antimicrobial, anti-inflammatory, reduced meibomian gland plugging, increased tear stability

Plan that clears the majority of AD

- Calm down skin with soak and smear and bacterial culture/antibiotics (back clear enough to patch test)
- Perform patch testing
  - North American Contact Dermatitis Series
  - External Agents/Emulsifier Tray
  - Fragrance
  - Corticosteroid
  - Personal products
- 2-3 months of allergen avoidance
- Dupilumab or other AD systemic therapy

Clear, Patch Avoid, Treat: CPAT as a Diagnostic and Therapeutic Strategy for Management of Recalcitrant Adult Eczematous Dermatitis.

- 112 patients with recalcitrant eczematous dermatitis

- 66 CPAT (Clear, Patch, Avoid, Treat)
- 17 CTPA (Clear, Treat, Patch, Avoid)
- 9 CPA (Clear, Patch, Avoid)
- 20 CT (Clear, Treat)

Bai H, Murase EM, Botto NB, Murase JE. Clear, Patch Avoid, Treat: CPAT as a Diagnostic and Therapeutic Strategy for Management of Recalcitrant Adult Eczematous Dermatitis.

Diagnostic and Therapeutic Strategy

- CPAT superior to CTPA for patients w/ recalcitrant eczematous dermatitis w/ concomitant ACD
- Faster resolution (12 mos), higher clearance (67% vs. 81%)

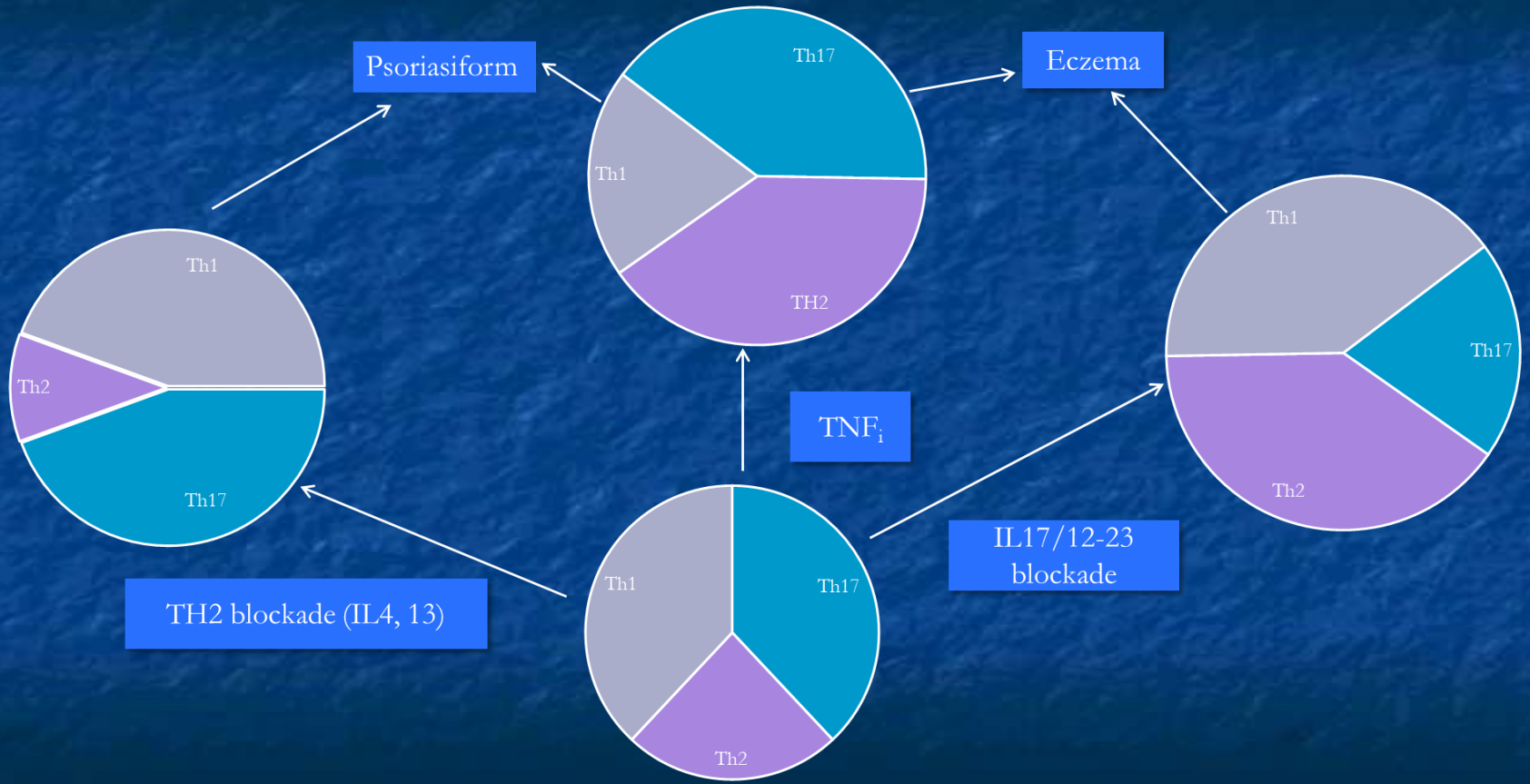
		CPAT (n=66)	CTPA (n=17)	CPA (n=9)	CT (n=20)
Gender	Female	40 (60.6%)	7 (41.2%)	6 (66.7%)	8 (40%)
	Male	26 (39.4%)	10 (58.8%)	3 (33.3%)	12 (60%)
Comorbid allergic contact dermatitis	Female	39 (63.9%)	6 (40%)	6 (66.7%)	0 (0%)
	Male	22 (36.1%)	9 (60%)	3 (33.3%)	0 (0%)

What should you consider in cases of incomplete response to dupilumab?

- 50/233 patients on dupilumab < 80% improvement the first 3-6 mos
- Co-morbid ACD (47)
- Parapsoriasis or psoriasis (3)
- PMLE (8) or cutaneous lupus (4)
- Lymphoma (1)
- Tinea (1)
- Scabies (1)
- Netherton (1)
- Systemic contact dermatitis (1)

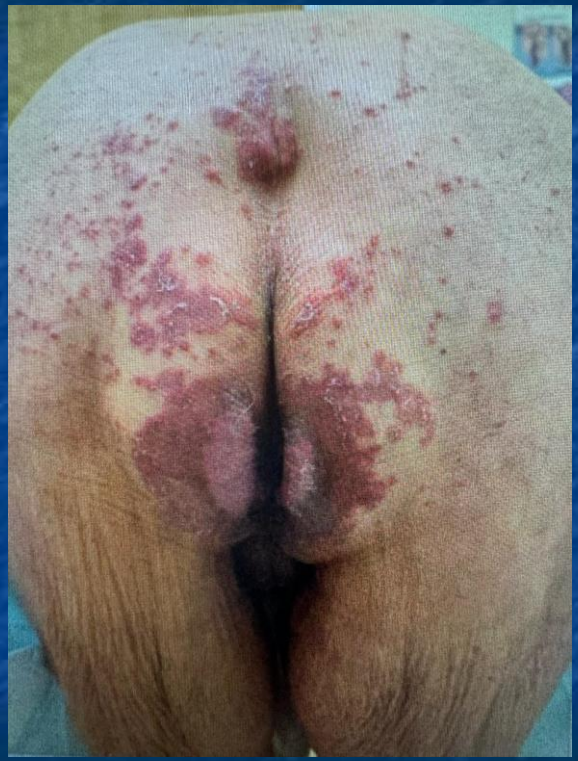
Bai H, Murase EM, Ashbaugh AG, Botto NB, Murase JE. Diagnostic Testing of Eczematous Dermatitis with Incomplete Response to Dupilumab. 2022 Sept; 87(3): 692-695.

Paradoxical Reactions



Dermatographic patient

- 5/21/24 Extended prednisone taper (starting at 60 mg)
- Omalizumab 300 mg started 8/16/24 8/28/24 seen in ER for itch
- Dupilumab 9/6/24 600 mg loading dose (within 2 days developed skin eruption pictured here)
- Nemolizumab 9/16/24 60 mg then 30 mg qmonth
- NRS 0 within 2 weeks maintained for 7 months and no dermatitis



Nemolizumab as a Novel Therapeutic for Pruritus Control Prior to Patch Testing: A Review of Patch Testing on Systemic Modulatory Agents

Eryn Patin, BS[1,2], Emi M. Murase[3], Arianne Shadi Kourosh, MD, MPH[1,4,5], Jenny E. Murase, MD[6,7]

(1) Massachusetts General Hospital, (2) University of Texas Southwestern Medical School,
(3) Department of Genomics, University of California, Davis, (4) Harvard Medical School, (5) Harvard T.H. Chan School of Public Health,
(6) Department of Dermatology, University of California, San Francisco, (7) Department of Dermatology, Palo Alto Foundation Medical Group Department

Massachusetts General Hospital
Founding Member, Mass General Brigham

HARVARD MEDICAL SCHOOL

Objectives

Patch testing (PT) is integral in the diagnosis and management of allergic contact dermatitis (ACD), which often coexists with other forms of dermatitis. Consequently, systemic immunomodulators (SI) may be indicated prior to PT, yet their effects on PT results remain unclear.[1] We aim to summarize the current literature on the use of SI during PT, and introduce a novel treatment option.

Methods

A literature review was conducted using PubMed to identify the effects of SI on PT. Data from 20 patients on nemolizumab for dermatitis-related pruritus was collected for review.

Results

Our review revealed that while effective, prednisone should be discontinued or reduced to ≤ 10mg and intramuscular triamcinolone held ≥ 90 days before PT, as they may interfere with results.[1] JAK1 inhibitors may induce false-negative PT results and mycophenolate mofetil can impair PT readings via dose-dependent inhibition, warranting caution with use (Table 1).[2,3,4] Our preliminary nemolizumab data

References

1. O'Hern K, Chapman MS, Zug KA, Hamann CR. Expert Opinion on Patch Testing While

Results (Continued)

identified a ≥ 4-point improvement in the Numerical Rating Scale (NRS) among all patients within one month of treatment, with 8 patients (40%) reporting complete resolution of symptoms (Table 2).

Table 1: Summary of Effects of Various Treatments on Patch Testing (PT) Results

Treatment	Impact on Patch Testing (PT) results	Notes
Prednisone	Possible interference (especially at doses > 10mg)	Ok to PT on 10mg, but best if able to discontinue. Withdrawl time can take up to 4 weeks.
Intramuscular Triamcinolone	Possible interference	The average withdrawal time is 90 days. It is recommended to wait at least 4 weeks prior to PT following injection.
JAK1 Inhibitors	False-negative PT results possible	Use with extreme caution, lower dose if possible prior to PT.
Mycophenolate Mofetil	Dose-dependent inhibition	Use with extreme caution, lower dose if possible prior to PT.
Nemolizumab	Unlikely to impact PT results based on mechanism of action	IL-31R specific antagonism, unlikely to impact PT results.

Table 2: Summary of dermatitis patients on Nemolizumab (Nemo) -- all underwent patch testing and had pruritus uncontrolled with prior therapy.

Pre-Nemo NRS	Post-Nemo NRS	Itch Response (NRS +/- % improvement)
Hand Dermatitis		
8	1	80% @ D2
Atopic Dermatitis (AD)		
8	4	60% @ D4
10	0	100% @ D3
9	0	100% @ D2
9	3	80% @ D2
7	2	70% @ D15
3	0.5	98% @ D2
4	1.5	60% @ D3
1	0	90% @ D30
9.5	2	80% @ D26
8	0.5	95% @ D5
9	0	100% @ D31
9	0	100% @ D30
9	1	90% @ D30
6	2	65% @ D30
10	0	100% @ D30
Nummular Dermatitis		
8.5	0	100% @ D2
10	4	65% @ D2

Receiving Immunomodulatory Therapy Results of an International Survey Study. *Dermatitis*. 2022;33(4):e51-e53. doi:10.1097/DER.0000000000000837

Discussion & Conclusion

Our results highlight the current lack of pruritus treatments for difficult-to-manage dermatitis that also preserve the validity of PT results. Furthermore, our preliminary results suggest that nemolizumab, a monoclonal antibody targeting the IL-31 receptor (IL-31R), shows promise in managing dermatitis-related pruritus.[5] Given the absence of IL-31R on Th2 lymphocytes, it can be inferred that nemolizumab may serve as a novel agent for managing pruritus in patients prior to PT with likely negligible effects on results (Figure 1).[6]

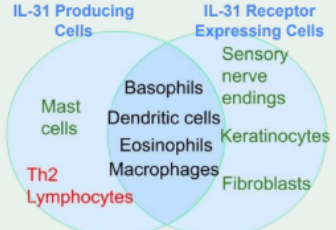


Figure 1: Venn diagram illustrating cell types that produce IL-31 and/or express its receptor, the target of nemolizumab.

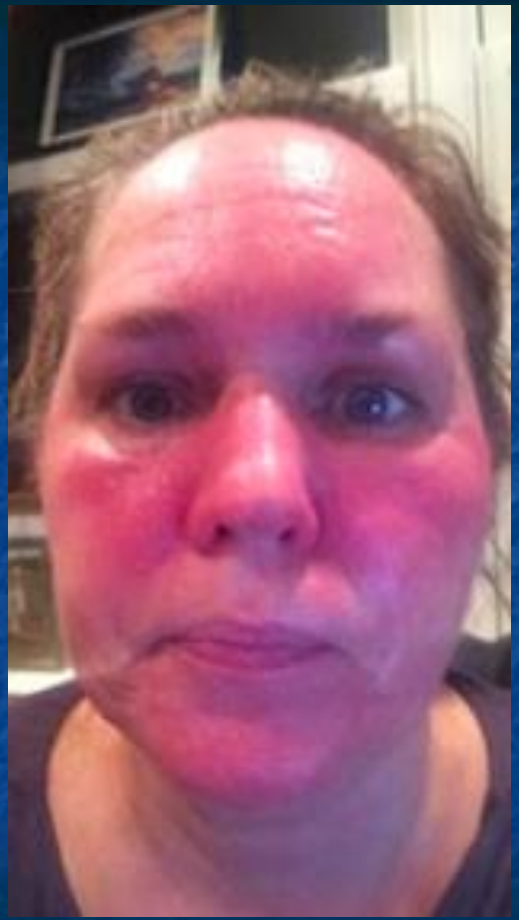
2. Biggs CM, Cordeiro-Santanach A, Prykhozhij SV, et al. Human JAK1 gain of function causes dysregulated myelopoiesis and severe allergic inflammation. *JCI Insight*. 2022;7(24):e150849. Published 2022 Dec 22. doi:10.1172/jci.insight.150849
3.Mainville L, Veillette H, Houle M. Sequential patch testing in a patient treated with dupilumab then with upadacitinib: Differences in patch test results as well as in disease control. *Contact Dermatitis*. 2023;88(5):402-404. doi:10.1111/cod.14278
4. Mufti A, Lu JD, Sachdeva M, et al. Patch Testing During Immunosuppressive Therapy: A Systematic Review. 2021;32(6):365-374. doi: 10.1097/der.0000000000000726
5. Girolomoni G, Mauerli M, Gisondi P. The emerging role of the neuroimmune cytokine interleukin-31 in chronic inflammatory skin diseases. *Ital J Dermatol Venerol*. 2022;157(4):306-312. doi:10.23736/S2784-8671.22.07265-6
6. Nemmer JM, Kuchner M, Datis A, et al. Interleukin-31 Signaling Bridges the Gap Between Immune Cells, the Nervous System and Epithelial Tissues. *Front Med (Lausanne)*. 2021;8:639097. Published 2021 Feb 10. doi:10.3389/fmed.2021.639097

Rapid Clinical Response to Nemolizumab in Dermatologic Diseases Associated with Pruritus and Burning: A Multicenter Case Series

Attribute	Results
Demographics	
Male	19 (27.5%)
Age	Avg = 60.3 yrs (±16.0); Range = 17 - 90
Number of Subjects Having Failed Prior Treatment	
Topical/ Intralesional Steroids	67 (100%)
Antihistamines	66 (98.5%)
Systemic Immunosuppression and Other Biologics	58 (84.1%)

Itching			
Condition	n	% Responders[1]	% Opting to Continue Nemo
Atopic Dermatitis	16	100%	100%
Nummular Dermatitis	2	100%	100%
Hand Dermatitis	1	100%	100%
Dermatographia	17	100%	100%
Neuropathic Itch	4	100%	100%
Subacute Prurigo	1	100%	100%
Immunologic Eruptions of Aging	1	100%	100%
Lymphoma/ Leukemia	3	100%	100%
Scrotal Pruritus	1	100%	100%
Vulvar/ Anal Pruritus	4	100%	100%
Acquired Cutaneous Brachioradial Pruritus	1	0%	0%
Notalgia Paresthetica	2	50%	50%
Scabies	1	100%	100%
Post-scabetic Id Hypersensitivity	1	100%	100%
Lichen Amyloidosis	1	100%	100%
Pernio	1	100%	100%
Granulomatous Dermatitis	2	50%	100%
Burning			
Neuropathic Skin Pain	1	100%	100%
Burning Mouth Syndrome	6	100%	100%
Neurogenic Rosacea	2	100%	100%
Erythromelalgia	1	100%	100%
Adverse Events			
% Experiencing an Adverse Event[2]	7.2%		

Condition	Screening
Immunodeficiency and Leukemia	Complete blood count with manual differential and Total Immunoglobulins (IgG/IgA/IgM)
Hepatic Disease	Comprehensive metabolic panel including BUN/creatinine for renal disease, liver function tests (AST/ALT/Alkaline Phosphate/Bilirubin)
Parathyroid Disease	Calcium
Diabetes	Hemoglobin A1C
Malignancy	Uric acid and LDH
Infectious Diseases associated with Pruritus	HIV, RPR, Hepatitis C Screening
Blood Dyscrasia	Serum electrophoresis or serum immunofixation
Leukemia and Lymphoma	Leukemia/lymphoma blood flow cytometry
Dermatitis Herpetiformis/ Celiac Disease	Anti-endomysial (EMA-IgA)/Anti-tissue transglutaminase (tTG)
Lymphoma	Skin biopsy of primary skin lesions with T-Cell Gene Rearrangement
Hodgkin's Lymphoma	Chest X-Ray



50 years of atopic dermatitis

Therapy
Topical corticosteroid
Antihistamines
Oral steroids
Intramuscular triamcinolone
Omalizumab

Patch test results
Balsam of peru
MCI/MI
Iodopropynyl butyl carbamate
Propolis
(in patient's cosmetics, hair dye, shampoo)

Semaan S, Raffi J, **Murase JE.** Allergic Contact Dermatitis Masquerading as Atopic Dermatitis. International Journal of Women's Dermatology. 2020; 6(4):329-330, doi: https://doi.org/10.1016/j.ijwd.2020.04.005

Take-home points

- AD pts are at higher risk of ACD
- Dupilumab does not appear to affect patch test results but may suppress subtle rxns
- Residual facial, hand, eyelid >90% ACD
- Personal product and expanded series testing
- Clear, Patch, Avoid, Treat (CPAT)
- Broaden your differential diagnosis in cases of incomplete response to anti-IL-4/IL-13