

Atopic Dermatitis And It's Mimics

HEATHER D. VOLKMAN, D.O.
ADULT AND PEDIATRIC DERMATOLOGY

CookChildren's



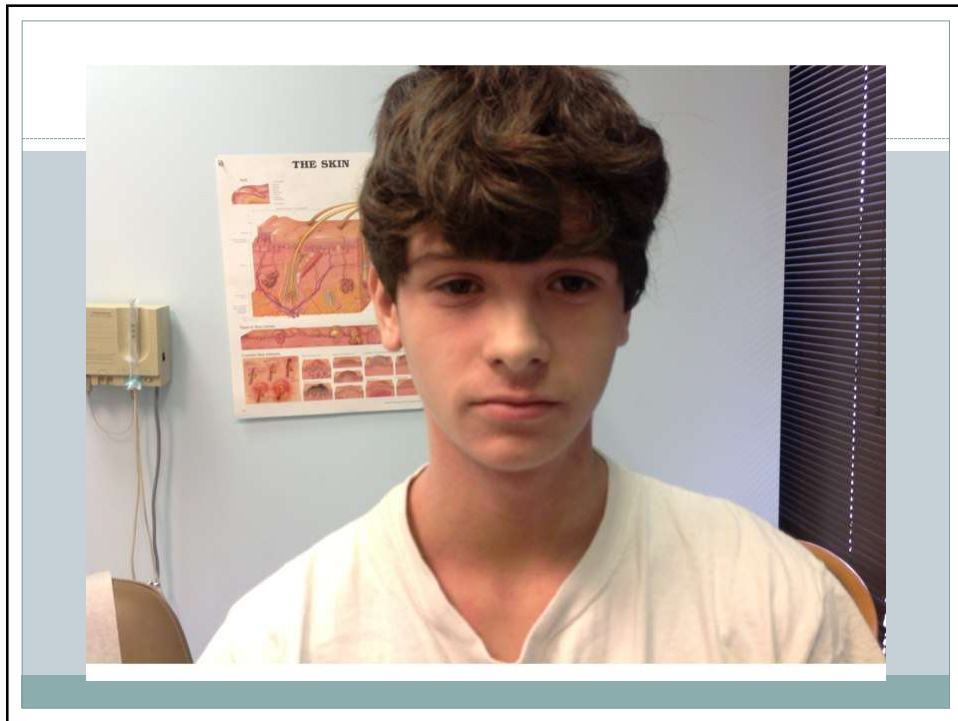
DERMATOLOGY SPECIALISTS
OF FORT WORTH

Objectives

- To understand the etiology/biology of atopic dermatitis
- To discuss other diseases in the differential diagnosis of atopic dermatitis
- To understand the role of atopic dermatitis in asthma, allergic rhinitis, and food allergies
- Discuss current and future treatment options for atopic dermatitis
- To be able to recognize the complications of atopic dermatitis

Case #1





Case #2





Definition of Atopic Dermatitis

- **Age onset**
 - Approximately 2 months of age
 - Adult onset controversial
- **Hanifin and Rajka criteria**
- **Must have**
 - Itching
- **Plus three or more of**
 - Onset under age 2
 - Flexural involvement
 - Personal history of asthma or allergic rhinitis
 - Dry skin

Williams HC.

Epidemiology

- **Prevalence of atopic dermatitis in U.S.**
 - 10-20% of children
- **Higher prevalence**
 - East Coast States, Nevada, Utah, Idaho
 - Metropolitan living
 - Black race
 - Higher education level of parents
 - Smaller families
 - Ethnic groups migrating from a country of low prevalence to high prevalence

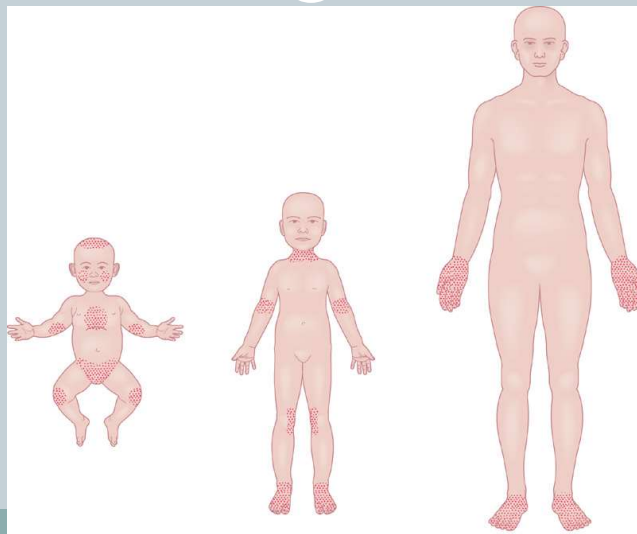
Eichenfield LF, et al., Williams HC

Epidemiology

- **More than 60% start by 2 years old**
- **Remission occurs in approx 65% by age 11**
- **Uncommon late onset form**
- **Adults over 16 y/o**
 - one third of atopic dermatitis patients
- **U.S. National annual costs in 2008**
 - \$3.8 billion dollars

Bieber Th., Williams HC

Age Dependent Distribution of Atopic Derm



Infantile Atopic Dermatitis



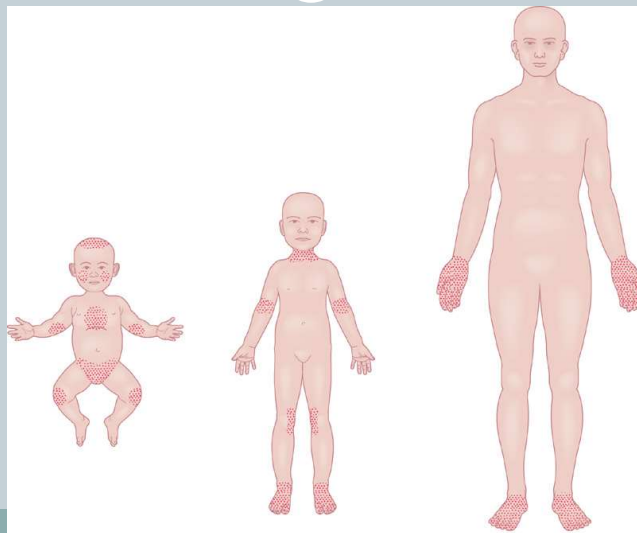
Infantile Atopic Dermatitis



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Age Dependent Distribution of Atopic Derm



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Childhood Atopic Dermatitis



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Associated Features of Atopic Dermatitis



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Keratosis Pilaris



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Pityriasis Alba



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Juvenile Plantar Dermatoses



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Nummular Dermatitis/Eczema



Adult Atopic Dermatitis



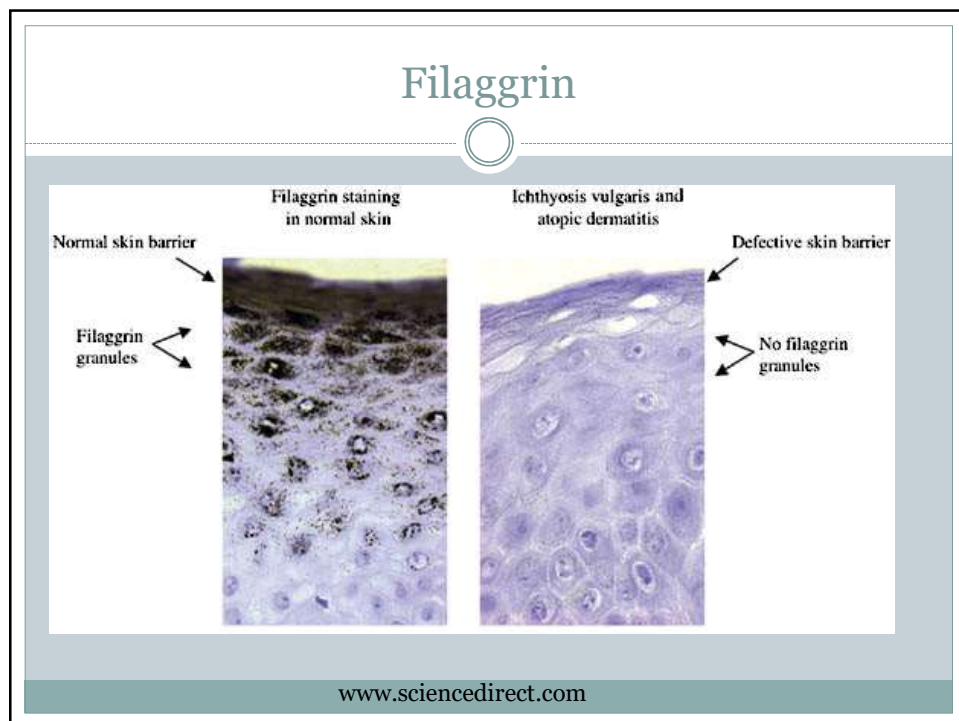
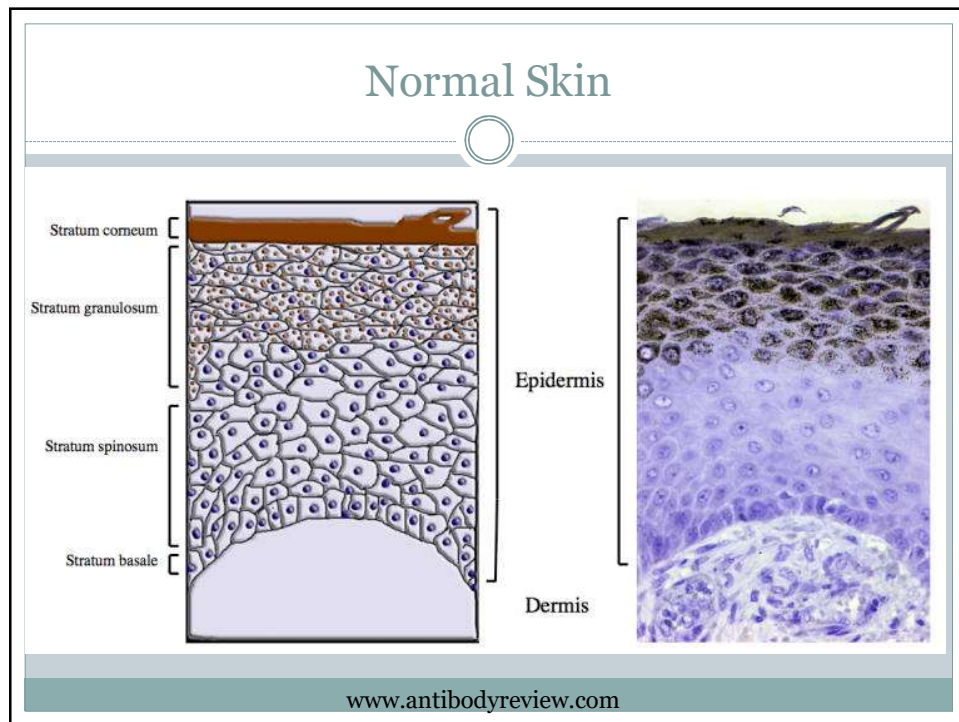
Adult Hand Atopic Dermatitis

- Provoked by loss of ceramides/oils in the skin and increase in the pH
 - Alkaline soaps
 - Other chemicals
 - Ddx: contact dermatitis (ex: leather)
- Treatment
 - Decrease hand washing frequency
 - ✦ Water based sanitizers are better
 - Use gentle soaps
 - Patch testing if indicated
 - Anti-inflammatory treatments
 - ✦ Topicals: topical corticosteroids, crisaborole
 - ✦ Systemic: apremilast, acitretin

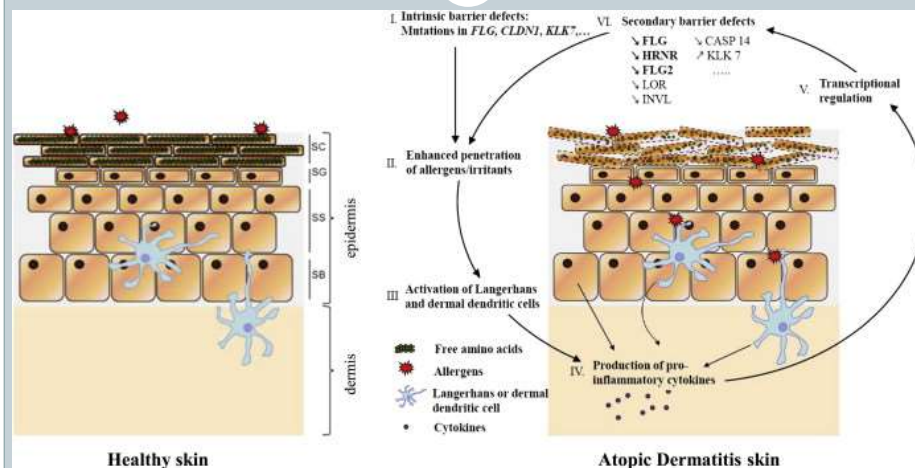
Etiology/Biology of Atopic Dermatitis

- Interplay of the Environment and Genetics
- Epidermal Barrier Function
 - **Filaggrin 2006**
 - Spink 5
 - Decreased expression of corneodesmosin, desmoglein I, desmocollin, TGM-3
 - Activation of epidermal proteases
 - Higher skin pH (ex: soaps) activates proteases and alters lipids and filaggrin of the stratum corneum
- Immune System
 - TLR2, TLR9, IL-4, IL-13, IL-22, IL-25, IL-31, FCER1, FCER1A, FCER1B, FCER1G, TSLP
 - IL-4 and IL-13 suppress filaggrin expression
 - Superantigen induction of cytokines
 - Kallikrein 5 induced by higher skin pH (ex: soaps)
- Gene-Environment Interactions
- IgE-associated (80%) and non-IgE-associated atopic dermatitis

Bieber Th, Eichenfield LF et al, Paller A, Pride HB et al



Role of Barrier Defects and Immune Dysregulation



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Filaggrin

- Encodes profilaggrin, the major component of keratohyaline granules in the epidermal granular layer
- Binds keratins contributing to the protein-lipid cell envelope
- Degraded to release hygroscopic amino acids forming natural moisturizing factor
- Contributes to low surface pH
- Mutations lead to increased severity of atopic dermatitis and environmental allergies

Pride HB et al.

Lipids of the Stratum Corneum

- **Ceramides**
 - Decreased in patients with atopic dermatitis
- **Cholesterol**
 - Recent case reports showing improvement of ichthyosis with topical simvastatin/cholesterol
- **Fatty Acids**
- **Cholesterol Esters**

Paller A, Sajic D et al.

Atopic March

- Loss of barrier function=Sensitization
- Induction of asthma and allergic rhinitis
- Increased transepidermal water loss and penetration of high-molecular wt allergens
 - Dust mite, foods, microbes
- Skin signals ex: thymic-stromal lymphopoietin (TSLP) to GI tract and lungs

Paller A

Role of Environmental Allergens

- Controversial
- Hygiene Hypothesis
 - Switch from previous theories
 - Increasing exposure to allergens early to induce tolerance
 - Past theory of reducing ubiquitous allergens ex: dust mite
- Conflicting data with atopic dermatitis and benefit from allergy immunotherapy
- Frequency of contact allergens in atopic dermatitis
 - 89% of atopic dermatitis positive for atleast 1 contact allergen vs. 66% in non-atopic pts
 - Higher EASI score correlated with higher number of contact allergens
 - Most common contact allergens in atopic derm
 - × Nickel
 - × Balsam of Peru/Fragrance Mix
 - Statistically significant difference between non-atopic pts
 - × Wool alcohols
 - × P-tert-butylphenol formaldehyde resin
 - × Cobalt
 - × Formaldehyde
 - × Colophonium
 - × Potassium dichromate
 - × Neomycin sulfate
 - × Tixocortol-21-pivalate

Williams HC, Cox L et al., Herro EM et al., Pride HB et al.

Contact Dermatitis



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Contact Dermatitis



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Highlights from the National Institute of Allergy and Infectious Disease guidelines

- Sensitization to a food is reflected by positive RAST or skin prick testing and is not the same as food allergy (specific immune response upon food exposure)
- 50-90% of parent/patient presumed food allergies are not allergic in nature
- The introduction of solid foods should not be delayed beyond 4-6 mo of age due to paradoxical increase in food allergies
- Children <5 y/o with atopic dermatitis should be considered for food allergies to milk, egg, peanut, wheat, and soy if:
 - Moderate to severe disease not controlled by conventional tx
 - History of immediate reaction after ingestion of specific food
- Patients should not avoid potentially allergenic foods as a means to control atopic dermatitis

Pride HB et al.

Asthma and Atopic Dermatitis

- U.S. Asthma prevalence: 8.4%
- Increasing prevalence as with atopic dermatitis
- One in three children with atopic dermatitis will develop asthma after the onset of cutaneous disease
- Observation
 - Wheezing often starts before or at the time of onset of atopic dermatitis
 - Questions the atopic march

Williams HC, Cox L et al.

Severity Scale and Quality of Life

- Sleep loss
 - Difficulties initiating and maintaining sleep
- Depression/Anxiety
 - Social functioning
- Time missed from work
- High cost of medications
- ADHD
- Scoring Systems (ex: EASI)
- Atopic Dermatitis Burden Scale (ABS) questionnaire
 - Burden questionnaire for families and children affected by atopic dermatitis

Bieber Th, Meni C et al., Pride HB et al.

Insomnia

- Video of girl scratching?



arndt video.MOV

Atopic Dermatitis Mimics



Seborrheic Dermatitis

Atopic Dermatitis Mimics

- Contact dermatitis secondary to Neosporin



Atopic Dermatitis Mimics



Tinea

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Atopic Dermatitis Mimics



Tinea

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Atopic Dermatitis Mimics



Majocchi's
granuloma

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Atopic Dermatitis Mimics



Scabies

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Atopic Dermatitis Mimics



Scabies

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Atopic Dermatitis Mimics

Langerhans cell histiocytosis



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Atopic Dermatitis Mimics

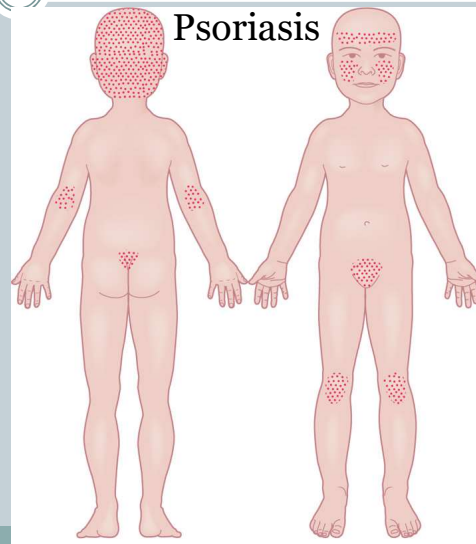
Langerhans cell histiocytosis



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Atopic Dermatitis Mimics

Psoriasis



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Atopic Dermatitis Mimics

Psoriasis



Atopic Dermatitis Mimics

Pityriasis Rubra Pilaris



Atopic Dermatitis Mimics

Acrodermatitis Enteropathica



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Atopic Dermatitis Mimics

- Wiskott-Aldrich Syndrome



Atopic Dermatitis Mimics



Netherton's Syndrome
and other Ichthyoses



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Atopic Dermatitis Mimics

Asteatotic Dermatitis



Atopic Dermatitis Mimics

- Lichen Simplex Chronicus



Atopic Dermatitis Mimics

- Perioral Dermatitis



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Atopic Dermatitis Mimics

- Dermatomyositis



Atopic Dermatitis Mimics

- Subacute Cutaneous Lupus Erythematosus (SCLE)

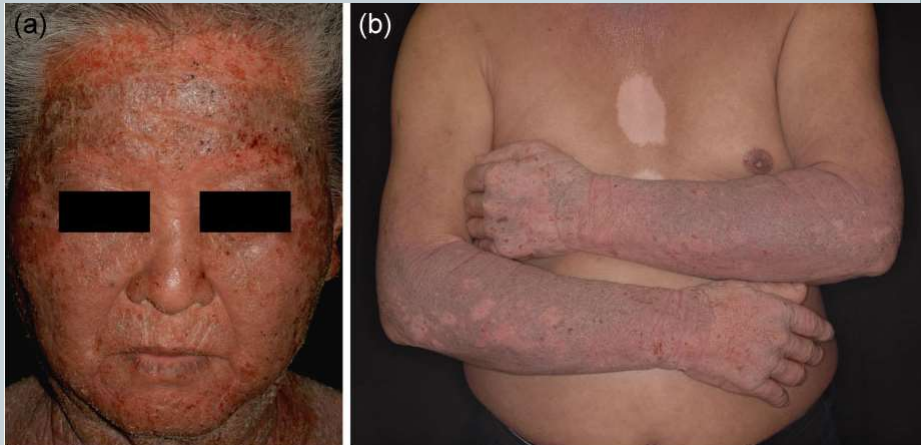


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Atopic Dermatitis Mimics

- Chronic Actinic Dermatitis



Atopic Dermatitis Mimics

- Venous Insufficiency Dermatitis



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Atopic Dermatitis Mimics

- Mycosis Fungoides

Pimpinelli N, et al



Atopic Dermatitis Mimics

- Hypereosinophilic syndrome



Atopic Dermatitis Mimics

- Drug Reactions



Role of Staphylococcus Aureus

- High rates of skin and nares colonization in atopic dermatitis patients
 - Up to 90% of atopic dermatitis patients
 - Role in exacerbation of disease
 - ✦ Correlation between severity of disease and bacterial load
- Lower rates of MRSA in atopic dermatitis than thought
- Etiology
 - Defective epidermal barrier
 - Deficiency of antimicrobial peptides
- Role of superantigens
 - Inhibit T reg cells that normally suppress inflammation
 - Leads to alternatively spliced glucocorticoid receptor preventing corticosteroid binding to T cell

Eichenfield LF et al., Ryan C et al., Huang JT et al., Paller A

Impetigo



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Impetigo



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Secondary Infections



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Secondary Infections



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Role of Sodium Hypochlorite/Bleach

- Need to decrease antibiotic use due to increased community resistant organisms
- Topical antibiotics either not effective or cause irritant contact dermatitis or bad cosmetic look
- Bleach non-toxic to tissues and mucosal surfaces
- Two Studies
 - Bleach baths
 - ✦ 22 children: Blinded, placebo-controlled
 - ✦ Methods: 0.5 cup of 6% bleach to full tub (0.005%) 5-10 minutes twice weekly + intranasal mupirocin BID x 5 days/mo, followed at 4 and 12 weeks
 - ✦ EASI and BSA scores improved from neck down in treatment group, no difference at head and neck
 - ✦ Interestingly, all patients continued to show positive cultures for Staph aureus
 - ✦ Adverse events: one patient initially reported itching
 - ✦ Limitations: 12 week single-center
 - Body wash
 - ✦ 18 children, washed 3 days/week for 12 weeks from neck down, rinse after 1-2 min
 - ✦ Cultures before and at each f/u visit (q2weeks)
 - ✦ Decreasing trend of bacterial counts, statistically significant at 1 month only
 - ✦ No patient required oral abx
 - ✦ IGA score decreased at all time points
 - ✦ Adverse events: stinging and burning, itching
 - ✦ Limitations: non-blinded, no placebo, 12 week open-label, single-center, partially retrospective

Ryan C et al., Huang JT et al.

Molluscum Contagiosum



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Eczema Herpeticum



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First-Line Treatment of Atopic Dermatitis

- **Moisturizers and daily gentle cleansing**
- **Ceramide-based moisturizers**
 - Prevent epidermal water loss and inhibit exogenous peptides
 - Normalize skin pH
 - Steroid-sparing
 - ✦ Several reports shown ceramide based emollients to be equivalent to topical steroids in the treatment of mild to moderate atopic dermatitis
 - ✦ Reduced time to clearance when used in combination with topical steroids
 - Promising studies on synthetic and pseudo-ceramides

Sajic D et al.

First Line Treatment of Atopic Dermatitis

- **Topical Steroids**
 - Within 2-3 days of application shown to:
 - ✦ Decrease epidermal proliferation and differentiation
- **Topical Calcineurin Inhibitors (pimecrolimus/tacrolimus)**
 - Safer on body regions more at risk for steroid atrophy
 - Shown to be more or as effective as topical steroids
 - Limitation: cost
 - Black box warning (2006) for lymphoma and nonmelanoma skin cancer
 - ✦ Results of ongoing long-term studies show no application to humans when topically applied
- **Proactive therapy**
 - Twice weekly treatment with topical tacrolimus or topical steroids resulted in few flares and increased time to next flare when compared to placebo
- **Antihistamines**
 - First-generation to aid in sleeping
- **Avoid systemic corticosteroids due to severe rebounding of disease**

Pride HB et al., Paller A, Tan AU et al.

First Line Treatment of Atopic Dermatitis

- **Crisaborole**
 - Inhibits phosphodiesterase type 4 (PDE4) leading to increased intracellular cAMP and therefore decreased Th2 cytokines
 - Theoretically nice due to lack of atrophy
 - Side effects
 - ✦ Burning/stinging of eroded skin
 - Limit to tougher skin areas when flaring
 - Calm down with a topical steroid before using
 - Mix with Vaseline
 - Counseling patients and families
 - May improve with time

In Office Instructions for Atopic Dermatitis

- **Daily bathing followed by emollients**
 - “Soak and smear”
- **Flares (affected areas)**
 - Use of topical steroids, topical calcineurin inhibitors, or crisaborole BID
- **Maintenance (trouble areas)**
 - Topical medications twice weekly
- **Bleach baths twice weekly**
- **In patients not improving consider:**
 - Infection
 - Compliance
 - ✦ Stealth monitoring through electronic caps
 - ✦ Only 32% of atopic dermatitis patients/parents compliant
 - ✦ Extensive counseling necessary
 - ✦ Regular follow-ups
 - Consider contact dermatitis

Paller A, Tan AU et al.

Role of Probiotics

- Controversial
- Review
 - 21 Articles, 6859 patients
 - Probiotics (10 studies)
 - ✦ Foods composed of live bacteria present in gut microflora
 - ✦ Given to children or mothers in pre- and post-natal periods
 - ✦ Most studies showed decreased development and severity
 - ✦ Conflicting studies
 - Prebiotics (2 studies)
 - ✦ Oligosaccharides that stimulate bacteria growth in colon
 - ✦ Showed lower risk of development but not severity of atopic derm
 - Hydrolyzed or Amino Acid Formulas (5 studies)
 - ✦ Mixed results
 - Fatty Acids (gamma-Linolenic acid)
 - ✦ Favorable trend in AD severity and prevalence reduction

Foolad N et al.

Vitamin D and other Herbal Treatments

- Vitamin D (Huang, et al.)
 - 21 included publications
 - 67% (4/6) reported a significant improvement with supplementation.
 - CONCLUSION: confirmed a link between serum vit D levels and AD severity
 - ✦ Weak evidence was found supporting improvement of AD with supplementation.

Management of Severe Atopic Dermatitis

- **Wet dressing therapy**

- Study at Mayo Clinic over 30 years: total of 218 patients
- Wet dressings
 - ✦ Daily bath
 - ✦ Topical steroids creams (used BID)/emollients (other applications) for total of 5-8 applications/day
 - ✦ Applied every 3 hours for 30-45 min
 - ✦ Cotton flannel clothing over wet gauze and then placement of warm blankets
- Extensive parent education
- 40% not using topical treatments at the time of hospitalization
- Mean duration of hospitalization was 3.61 days
- Over 90% had greater than 50-75% improvement
- Adverse events: some children uncomfortable initially
- Limitations: skilled nursing

Dabade TS et al.

Management of Severe Atopic Dermatitis

- **Phototherapy (narrowband-UVB)**

- Limitations: cost, time away from work

- **Systemic immunosuppressants**

- Cyclosporine
- Azathioprine
- Mycophenolate mofetil
- Methotrexate
- Intravenous immunoglobulin (IVIg)
 - ✦ No comparative studies in pediatric atopic dermatitis between systemic immunomodulators

Paller A, Tan Au et al.

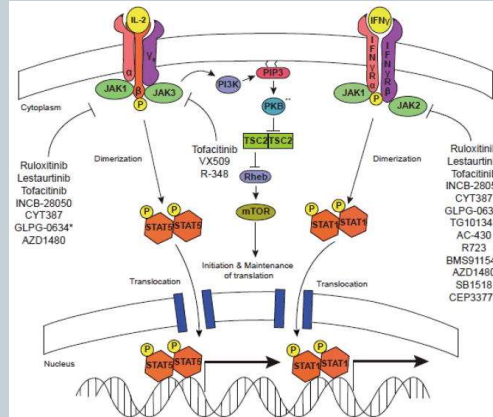
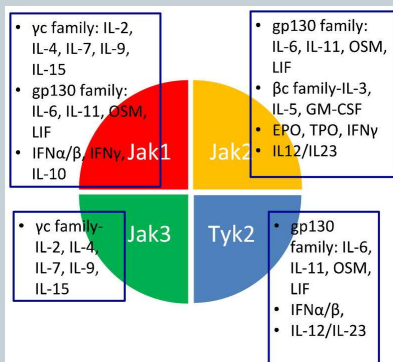
Biologic Therapy for Atopic Dermatitis

• Dupilumab

- Binds and inhibits interleukin(IL)-4 receptor alpha subunit interfering with IL-4 and IL-13 cytokines
- Reduces inflammation and alters immune responses
 - ✦ Side effects
 - Conjunctivitis
 - ✦ Patients need to continue their normal skin barrier routine
 - ✦ Approved for ages 12 and up
 - ✦ Results in a dramatic decrease in baseline inflammation and itching in severe atopic dermatitis
 - Has also been seen to help in chronic contact dermatitis

Biologic Therapy for Atopic Dermatitis

• Janus Kinase (JAK) inhibitors



O'Shea, et al.

Future Biologic Therapy for Atopic Dermatitis

- **Tralokinumab and lebrikizumab**
 - IL-13 specific monoclonal antibodies
 - ✦ Both drugs have completed phase 2 trials in AD patients
- **BMS-981164 and nemolizumab**
 - IL-31 monoclonal antibody and IL31 alpha-receptor (IL-31RA) inhibitor, respectively
 - Phase 1 and 2 trials for pruritus and atopic dermatitis
- **IL-17 antibody secukinumab**
 - phase 2 trial for atopic dermatitis
- **ILV-094**
 - Antibody which targets IL-22
 - Intravenous treatment in a phase 2 trial in adults with moderate-to-severe AD

Patel, et al

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