Papulosquamous, lichenoid, and eczematosus dermatoses

Dermatology Residency of Orlando
AOCD March 2017
Psoriasis
Pathogenesis

- Hyperproliferation disorder, driven by complex cascade of inflammatory mediators
  - Mixed T-helper (Th-1) and Th17 inflammatory disease
  - T cells and cytokines play pivotal role
  - Overexpression of Th1 and Th17 cytokines, along with IL-8 leads to accumulation of neutrophils
    - Main signal for Th1 development- IL12 which promotes IFN-gamma
    - In animals, shifting from Th1 to Th2 improves psoriasis

Main T-helper cell(s) involved?
Th-1 and Th-17
• HLA Cw6 (strongest)
  • HLA B17: early onset
  • HLA B27: psoriatic arthritis
• Drugs that exacerbate psoriasis
  • Withdrawal of systemic corticosteroid
  • Lithium
  • B-blocker
  • Antimalarial
  • Interferon
  • ACEi
  • G-CSF
• Psoriatic arthritis
  • Asymmetrical oligoarthritis (70%)
Pustular Psoriasis

- Generalized (von Zumbusch)
  - Presents initially with malaise and fever
  - Erythematous studded with sterile pustules, initially in intertriginous areas and spread to trunk
  - Risk factors: tapering of oral steroid, infection, hypocalcemia, pregnancy
  - Labs: leukocytosis, hypoalbuminemia, hypocalcemia
Pustular Psoriasis (localized)

• Palmoplantar pustulosis
  • Localized form
  • Tense sterile pustules on palmar/plantar surfaces with yellow-brown macules
  • Maybe associated with SAPHO syndrome
    • Synovitis, Acne (conglobata), Pustulosis, Hyperostosis, Osteitis
    • Inquire about sternoclavicular tenderness and/or back pain

• Acrodermatitis continua of Hallopeau
  • Limited to fingertip or digit
  • Pustules on the fingertips and within nailbed, often with subsequent nail shedding
Small Molecules

- Apremilast (Otezla)
  - PDE-4 inhibitor → increase cAMP
  - Dosage adjustment in severe renal impairment
  - Strong CYP450 inducer
    - e.g. rifampin, phenobarbital, carbamazepine, phenytoin
- Adverse events
  - Diarrhea (first 2 weeks)
  - Nausea
  - Depression (1.3%), weight loss (10%)

**ESTEEM 1 and 2: 16-week efficacy**

- PASI 75 (primary endpoint), PASI 50, and sPGA response at Week 16

- PASI 75
  - PBO (n=262)
  - Apremilast 30 mg bid (n=262)
  - *P<0.0001 vs PBO

- PASI 50
  - PBO (n=262)
  - Apremilast 30 mg bid (n=262)
  - *P<0.0001 vs PBO

- sPGA 0–1
  - PBO (n=262)
  - Apremilast 30 mg bid (n=262)
  - *P<0.0001 vs PBO

+ sPGA: static physician’s global assessment; bid: twice a day; LOCF, last observation carried forward
Small Molecules

- Tofacitinib (Xeljanz)
  - Inhibits JAK1 and 3 > 2
  - JAK-STAT pathway $\rightarrow$ decrease cytokine gene transcription
  - Tofacitinib 10 mg BID was non-inferior to etanercept
  - Increase risk of serious infections including opportunistic infections and malignancy in RA patients

IL-17 inhibitors

• Secukinumab (Cosentyx) / Ixekizumab (Taltz)
  • Human IL-17A antagonist
  • Adverse events
    • Exacerbation of inflammatory bowel diseases
    • Transient and self-limiting neutropenia
    • Mucocutaneous candidiasis

• Brodalumab
  • IL-17 receptor blocker
  • Safety concerns: depression, suicidal ideation, suicide
  • Amgen’s trials were halted
  • Leo & Valeant continue development
  • Future is unclear

<table>
<thead>
<tr>
<th></th>
<th>Ustekinumab</th>
<th>Ixekizumab</th>
<th>Secukinumab</th>
<th>Brodalumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI 75 at 12 weeks</td>
<td>68%</td>
<td>88%</td>
<td>79%</td>
<td>85%</td>
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<tr>
<td>PASI 90 at 12 weeks</td>
<td>38%</td>
<td>69%</td>
<td>56%</td>
<td>70%</td>
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<tr>
<td>PGA ‘clear’ or ‘minimal’ at 12 weeks</td>
<td>65%</td>
<td>85%</td>
<td>65%</td>
<td>75%</td>
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</table>

New Biologics: IL-23 inhibitors

- Guselkumab
- Rizankizumab
- Tildrakizumab

- P35 unique to IL-12. P19 unique to IL-23, Both have P40
Miscellaneous

• Etanercept approved for pediatric moderate to severe plaque PSO (Nov 2016)
  • Age 4 and up
  • not approved for IBD, unlike the other TNF-α inhibitors

• Methotrexate - should not be used concomitantly with TMP/SMX
  • Avoid pregnancy for 3 months

• Acitretin - half-life 2 days but can re-esterify to etretinate, which is highly lipophilic (120 days half-life)
  • Avoid pregnancy for 3 years

• Calcipotriene - inactivated by acidic pH
Contact Dermatitis
Which is the most frequent preservative used in cosmetics?

Parabens

(Uncommonly a cause of ACD)
Which is the most common preservative in cosmetics to cause a positive patch test?

Quaternium 15
### ACDS Allergens of the Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Allergen</th>
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<tbody>
<tr>
<td>2016</td>
<td>Cobalt</td>
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<tr>
<td>2015</td>
<td>Formaldehyde</td>
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<tr>
<td>2014</td>
<td>Benzophenones</td>
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<tr>
<td>2013</td>
<td>Methylisothiazolinone</td>
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<td>2012</td>
<td>Acrylate</td>
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<td>2011</td>
<td>Dimethyl fumarate</td>
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<tr>
<td>2010</td>
<td>Neomycin</td>
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<td>2009</td>
<td>Mixed dialkyl thiourea</td>
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<td>2008</td>
<td>Nickel</td>
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<td>2007</td>
<td>Fragrance</td>
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<tr>
<td>2006</td>
<td>p-Phenylenediamine</td>
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<td>2005</td>
<td>Corticosteroids</td>
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<tr>
<td>2004</td>
<td>Cocamidopropyl betaine</td>
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<tr>
<td>2003</td>
<td>Bacitracin</td>
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<tr>
<td>2002</td>
<td>Thimerosal</td>
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<tr>
<td>2001</td>
<td>Gold</td>
</tr>
<tr>
<td>2000</td>
<td>Disperse Blue Dyes</td>
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</table>
Contact Allergens

• Formaldehyde-releasing preservatives
  • Quaternium-15 - #1 cause
  • 2-Bromo-2-nitropropane-1,3-diol (Bronopol) - #2 culprit
  • Diazolidinyl urea
  • Imidazolidinyl urea
  • DMDM

• Other preservatives
  • Methylisothiazolinone (Kathon CG) – biocidal preservatives added to bubble solutions, baby wipes
  • Methyldibromoglutaronitrite (Euxyl 400) – tissue, toilet paper
  • Thimerosol – mercury-containing compound. Contact lens solution, vaccines
  • Parabens – most common preservative overall, but very low rate of irritancy and allergenicity

• Rubbers
  • Thiram – cross reacts with disulfiram
  • Mercaptobenzothiazole – shoe dermatitis
  • Carba – “bleached rubber syndrome”
  • Mixed diakly thioureas – neoprene rubber, scuba gear

• Metals
  • Nickel – most prevalent allergen (17% worldwide). Beware of technologies containing nickel
    • Dimethylglyoxime test
  • Cobalt – cross-react with nickel
    • Vitamin B12 injection
  • Potassium dichromate – cement, tanned leather

Plant Allergens

• Urushiol
  • Poison ivy, poison oak, poison sumac
  • May cross react with cashew, mango, Japanese lacquer tree, Indian marking nut, gingko
  • Start to appear in a number of personal care products
    • Lip Love Ultimate Lip Rescue
    • Botanic choice cold canker sore relief

• Sesquiterpene lactone
  • Airborne and chronic actinic dermatitis
  • Chrysanthemum, ragweed, sunflower, artichoke, arnica, daisy, marigold
  • May cross react with permethrin
Atopic Dermatitis
Pathogenesis

- **T-helper 2 cells and related cytokines**
  - All stages of the disease
  - IL-4 and IL-13 predominantly
    - IL-4 is also responsible for B cell class switching to IgE

- **T-helper 1 cells and related cytokines**
  - Chronic disease
  - IFN-γ, IL-12

- **T-helper 17 and 22 recently implicated**

**T-helper 2 cytokines?**

IL-4, IL-5, IL-6, IL-10, IL-13
Emerging therapies for AD

• **Crisaborole**
  • Topical PDE-4 inhibitor $\rightarrow$ increase cAMP
  • Mild to moderate AD in adults and children age 2 year and up

• **Dupilumab**
  • $\alpha$ subunit of IL-4R $\rightarrow$ IL-4, IL-13 blockade
  • Adults with moderate to severe AD
  • Headache and nasopharyngitis were more common in Dupilumab group compared to placebo
Atopic dermatitis and ACD

Recent consensus group statement published

• When to patch test:
  • Hand or foot eczema
    • Other very localized distributions
  • Worsens with topical therapy
    • Allergy to topical steroids or propylene glycol
  • Refractory cases
    • May suggest persistent allergenic trigger
  • Adults- or adolescent-onset AD
  • Whenever considering systemic immunosuppressant
    • consider reversible option first

Thank you