Chronic Hand Dermatitis-Handout

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OBJECTIVES-CHRONIC HAND DERMATITIS (CHD)

• Epidemiology
• Overview of etiology
• Presentation-clues to diagnosis
• Treatment/management
Definition: Chronic Hand Dermatitis

• Duration: > 6 weeks, 3mos, 6 mos.
• Mean Duration: 7-11 years.
• Frequency: at least 2 flares/year.
• Multifactorial etiologies and overlapping disease entities.
  • Endogenous and exogenous factors
• Persistent and recurring nature.
• No universal classification and consistent nomenclature.

CARPE CRITERIA:

• Dx duration ≥ 3mos.
• > 3 flares within 12 months.
• Resistant to previous steroid tx.
• No other active severe disease or infection.

Diepgen et al., 2011. JDDG
Definition: Treatment Resistant CHD

- Patients have failed to improve with the use of ultra-potent topical corticosteroids.

Scalone 2015, Ruzicka 2008, Paulden 2010
Severity of Hand Dermatitis

• Mild
• Moderate
• Severe

• Thyssen et al: moderate to severe disease- 30%. Contact Derm 2010, 62; 75-87.
Epidemiology of Chronic Hand Dermatitis

- Chronic hand eczema: 1 yr prevalence of 10%, lifetime prevalence of 15% in the general population.
- Accounts for >80% of occupational dermatitis cases.
- 30% of patients, onset occurs prior to age 20.
- Mean duration > 10 yrs.
- 20% of patients will have ≥ 7 days of sick leave.
- 10% of patients will change their occupation.

Diepgen et al., JDDG 2011
Risk Factors: CHD

- Female > Male
- Risk increases with age
- Nickel allergy
- h/o smoking
- Lower vs higher education
- Lower humidity climates
- Occupation:
  - Nursing, Medical, Service industries
- Respiratory atopy w/out AD
- Genetic predisposition
- AD risk factor in <30 yrs of age

Menne et al., Contact Dermatitis. 2010
Risk Factors: Nickel Allergy

• Ni allergic females –increased risk of hand eczema (Menne)
• 30% of Ni allergy had hand eczema: sig assoc both sexes (Meding)
• 12-16yo Danes: Ni allergy + hand eczema (OR=2.36; CI 95% = 1.39-4.01). (Mortz)
Challenging To Determine Etiology: Chronic Hand Dermatitis

Contact allergy
Irritant exposure
Atopy
Psoriasis
Dyshidrosiform eczema (pompholyx)

Combination of above...
Diagnostic Information: CHD

• History
  • Medical/Risk factors (atopy)*
  • Frequency of flares
  • Exposure to irritants or allergens from occupation or activities
• Physical examination
  • Morphology and Location on hands.
  • Hands and other body sites
  • Nails
• Patch test
  • Helpful in diagnosing allergic contact dermatitis (ACD)
• Skin biopsy
  • Useful?
Distribution of Diagnosis for Hand Eczema

Percentage

<table>
<thead>
<tr>
<th>Condition</th>
<th>Lantinga</th>
<th>Meding</th>
<th>Diepgen</th>
</tr>
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<tbody>
<tr>
<td>ICD</td>
<td>40</td>
<td>45.2</td>
<td>36</td>
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<tr>
<td>ICD + ACD</td>
<td>14.5</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>ACD</td>
<td>18</td>
<td>25.9</td>
<td>16</td>
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<tr>
<td>ICD + Atopic</td>
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<td>30.6</td>
<td>3</td>
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<tr>
<td>Atopic</td>
<td>16</td>
<td>36.1</td>
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<tr>
<td>Hyperkeratotic</td>
<td>45.2</td>
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<tr>
<td>Nummular</td>
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<td></td>
<td>21</td>
</tr>
<tr>
<td>Unclassified</td>
<td></td>
<td></td>
<td>22.4</td>
</tr>
<tr>
<td>Pompholyx</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Fingertip</td>
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<td></td>
<td>7</td>
</tr>
</tbody>
</table>

Meding et al., 1989
Lantinga et al., 1984.
Diepgen et al., 2011
Precursor Lesions for Hand Dermatitis?

![Bar chart showing the percentage of precursor lesions including Erythema, Lichenification, Crusting, Scaling, and Other.]

- Erythema: 91.8%
- Lichenification: 98.8%
- Crusting: 70%
- Scaling: 35%
- Other: 15%
Irritant Contact Hand Dermatitis

- Chronic exposure to soap and water causing subacute eczematous inflammation
- Patients vary in their ability to withstand exposure to irritants
- Healthcare, industrial, mothers
Atopic Hand Dermatitis

• Younger age of onset
• Involves the dorsal hand and fingers
• Dryness, mild erythema and lichenification
• Frequently accompanied by pruritus and pain
• Usually on both hands with involvement of other body area
Psoriasis

• With or without involvement of other body areas.
• Palms and volar aspects of the fingers.
• Less erythema in Hand plaques vs body plaques.
• Hand/nail involvement ↑ joint disease.
Occupational Contact Dermatitis

- **Contact Irritants**
  - Water
  - Soaps and detergents
  - Cleansers
  - Acids/Alkalis
  - Metalworking fluids
  - Solvents
  - Oils/coolants
  - Oxidizing agents
  - Reducing agents
  - Food products
  - Physical factors
  - Degreasers
  - Lubricants

- **Contact Allergens**
  - Biocides
  - Chromate
  - Dyes
  - Epoxy and other resins
  - Essences and fragrances
  - (Meth)acrylates
  - Metal salts (chromates, nickel)
  - Plants and woods
  - Rubber-processing chemicals
  - Germicides
  - Plastic resins
Non-occupational Contact Dermatitis

Contact Irritants
• Household cleaners
• Food products
• Plants
• Water

Contact Allergens
• Fragrance
• Preservatives
• Nickel
Reported ACD-Hand dermatitis

• Lettuce, compositae.
• Spices: garlic, cinnamon, ginger, allspice, clove.
• Hairdressers: most likely: glyceryl monothioglycolate, ammonium persulfate.
• Nail cometicians: acrylates.
• Cement workers: cobalt & chromates

• Woodwork teachers: isothiazolinone, nickel, formaldehyde, colophony
• Painters: nickel, cobalt, isothiazolinones, P-tert-butyphenol formaldehyde.
• Dental workers: epoxy and acrylates.
Top Allergens in Patients with Hand ACD

• Nickel sulfate
• Neomycin sulfate
• Balsam of Peru
• Fragrance mix
• Thimerosal

 • Quaternium-15
 • Formaldehyde
 • Bacitracin
 • Cobalt chloride
 • Carba mix

Protein Contact Dermatitis

- Chronic recurrent dermatitis
- Affects hands, arms and/or fingertips
- May present as chronic paronychia-food handlers
- Rxn may occur within minutes-vesicles, urticarial papules
- 50% associated with atopy
- Fruits, plants, spices, animal proteins, grains, enzymes, cheese, latex

Hand Eczema Management

• Systemic therapies
  • Cyclosporine
  • Methotrexate
  • Azathioprine
  • Mycophenolate mofetil
  • Oral corticosteroids
  • Oral retinoids
  • Biologics

• Phototherapy
  • UVB and excimer laser
  • PUVA

### Treatment: CHD

<table>
<thead>
<tr>
<th>Primary therapy</th>
<th>Secondary therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin protection measures:</td>
<td>Topical agents: Moisturizers, steroids, (soak/smear), calcineurin inhibitors,</td>
</tr>
<tr>
<td></td>
<td>coal tar agents, phototherapy, neurotoxin, Grenz</td>
</tr>
<tr>
<td></td>
<td>Tertiary therapy</td>
</tr>
<tr>
<td></td>
<td>Systemic agents: Methotrexate, cyclosporine, azathioprine, retinoids, oral</td>
</tr>
<tr>
<td></td>
<td>corticosteroids-pulsed.</td>
</tr>
</tbody>
</table>
Treatment: CHD-Soak and Smear Regime

• Soak 20 minutes in pan of water
• Then Smear topical steroid without drying skin
• Possible additions:
  • Tar based emulsion
  • Bath oil
  • Cotton gloves

James et al. Arch Derm., 2005
Treatment CHD: Local Bath PUVA

- 15min soak with 1mg 8-methoxypsoralen.
- Start PUVA at 0.25-0.5J/cm².
- Treat 3x a week.
- Increase dose by 0.25-0.5J/cm² every week.

Cyclosporine vs Betamethasone Dipropionate for CHD

• RCT study w/ Cyclosporine @ 3mg/kg/day vs BDP.
• Enrolled 41 pts, tx resistant for 6 weeks.
• Total disease activity score decrease 57%/58%.
  • no significant difference.

Mycophenolate Mofetil (MMF) for AD

- Severe AD, N=10
- MMF, 1g/d-week 1, then 2g/day for 12 weeks.
- Median Scordad score decreased from 68.3 to 22 (p=0.007).

Diek et al., BJD. 2000
Acitretin for CHD, Hyperkeratotic Varient

- A single-blind placebo-controlled study.
- Treatment of hyperkeratotic HD(eczema keratoticum).
- 14 pts -30mg/day Acitretin, 15-placebo
- Inclusion: hyperkeratotic palms +/- fissures
- Overall score improvement:
  - Acitretin-51%
  - Placebo- 9%

Bexarotene gel 1% for Severe CHD

• Phase I/II open label randomized trial, n=55.
• Stepwise increase in application q2wks: QOD to TID
  • Arm 1: Bexarotene 1%
  • Arm 2: Bexarotene 1% + topical low potency steroid.
  • Arm 3: Bexarotene 1% + topical mid potency steroid.
• Response rate:
  • PGA
  • H-EASI

Breneman et al., Dermatol 2004; 150: 545–53.
Botulinum Toxin for Dyshidrotic HD

• Controlled prospective pilot study with left-right comparison.
• Objective; Is chemical de-innervation of sudoriferic nerves superior to topical corticosteroids?
• Topical corticosteroids + neurotoxin (100units Botox®) to more severely affected hand.
• BTXa decreased itch and sweating.
  • (BTXa inhibits substance P release)
• Mean DASI in (N=6) at week 8:
  • BTXa group changed from 36 to 3
  • Steroid only changed from 28 to 17

Methotrexate for Recalcitrant Palmoplantar Pompholyx

- Pompholyx accounts for 5-20% of HD cases.
- Case series: 5 patients controlled on 12.5-20mg/week of MTX.
- All patients had previously failed topical corticosteroids and were receiving oral steroids when MTX was added.

Kruger JAAD 1999;40;612-14.
Complicated Contact Dermatitis

• 77 yo woman
• Patch tested outside facility. (+) colophony
• Using steroids, develops 12 fingernail onychomycosis.
• Refuses continued steroids, currently failing topical tacrolimus.
• Sent for 2\textsuperscript{nd} opinion.
Future therapies-CHD

• Duplimumab
• Apremilast
• Alitretinoin
• AN2728
Dupilimab

• Fully human monoclonal antibody
• Directed against the shared alpha subunit of IL-4 receptors
• Blocks signaling from both interleukin-4 and interleukin-13
• In Phase III trials for atopic dermatitis

Radin et al., n engl j med.2014
Alitretinoin for Chronic Hand Eczema

• RCT Phase III, double blinded, placebo controlled.
• Dosing 30mg po qd.
• Primary endpoint % clear or almost clear w/ PGA score at week 24;
  • Handel: 40% Alitretinoin vs 15% on placebo
  • Bach: 48% Alitretinoin vs 16.6%
• AE’s: headaches, flushing, nausea, increased TG’s.
CHD: Novel Topicals in Development

- Crisaborole (AN2728) is boron-based PDE4 inhibitors.
- Mechanism:
  - An increase in intracellular cAMP activation of PKA.
  - Phosphorylation and negative regulation of transcription factors of various cytokines.
OPA-15406

• PDE 4 inhibitor, selectivity for 4B
• Phase II RCT for AD dosed at 0.3% and 1.0%
• Clear or almost clear @ week 4:
  • Vehicle 2.7%
  • OPA low dose 14.6%
  • OPA high dose 20.8%
• VAS pruritus scores week1 mean change: 36.4% in 1% arm.

Hanifin et al. Jaad 2016
In Summary

• Consider potential for dual diagnosis for CHD.
• Take complete history on exposures.
• Lifestyle modifications can be helpful.
• Given QOL issues, treatment beyond topical steroids should be considered.