

Nottingham 17 May 2017

Hand eczema

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especially on behalf of ms dr Wianda Christoffers PhD

Disclosure

P.J. Coenraads

More than 10 years ago our department received industry grants to study alitretinoin in hand eczema

More than 6 years ago I received a fee for lecturing on alitretinoin

Hand Eczema Is Common and Multifactorial

Pieter-Jan Coenraads¹

Clinicians agree that hand eczema is multifactorial, although there are many uncertainties regarding causative factors. Atopic dermatitis is assumed to be a major risk factor, whereas the role of allergies is overestimated. Twin studies may shed light on the contribution of other endogenous, possibly genetic factors versus the role of exposure to environmental agents, with the latter being amenable to prevention and intervention.

Journal of Investigative Dermatology (2007) 127, 1568–1570. doi:10.1038/sj.jid.5700781

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Hand Eczema

Pieter-Jan Coenraads, M.D.

EVIDENCE BASED DERMATOLOGY:

Integrating the best external evidence

with

the skills of being a doctor

YOUR SKILLS OF BEING A DOCTOR:

Yes, we believe you have them.....

**THE BEST AVAILABLE
EXTERNAL EVIDENCE
FROM THE LITERATURE:**



**Cochrane
Library**

Cochrane Database of Systematic Reviews

Interventions for hand eczema (Review)

Christoffers WA, Coenraads PJ, Svensson Å, Diepgen TL, Blok JL, Mattered U, Williams HC, Xia J

Christoffers WA, Coenraads PJ, Svensson Å, Diepgen TL, Blok JL, Mattered U, Williams HC, Xia J.

Interventions for hand eczema.

Cochrane Database of Systematic Reviews 2017, Issue 4. Art. No.: CD004055.

DOI: 10.1002/14651858.CD004055.pub2.

www.cochranelibrary.com

Interventions for hand eczema (Review)
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WILEY

Let's have a look.....

Combination of hand-searching and electronic searching in English, German, French, Italian, Dutch language journals from 1977 - 2016

.....trying to find everything on hand-eczema.....

For example:

Martin et al: Resolution of dyshidrotic dermatitis of the hands after treatment with continuous positive airway pressure.
South Med J 2002;95:253-254

HAND ECZEMA INTERVENTION TRIALS IDENTIFIED BETWEEN 1977 - 2015

Total nr of studies identified:	168
Excluded:	83
Assessed for eligibility:	85
Studies included in analysis:	59

Total nr of patients studied: about 5400

Most studies were of relatively short duration

11 studies with duration of 4 months active treatment

Most studies had as comparator no treatment or placebo

About a third had within-participant design (left vs right hand)

Few studies compared two different treatment classes:

- coal tar vs topical steroid
- PUVA (topical) vs X rays
- PUVA (topical) vs UV-B
- Tacrolimus/pimecrolimus vs topical steroid
- Oral cyclosporin vs topical steroid
- Cromoglycate vs diet
- Oral cyclosporin vs oral alitretinoin (discontinued)

Ongoing studies:

13 studies on topical treatment (one on pumpkin ointment)

Four on systemic treatment:

- Alitretinoine vs PUVA (are you contributing ?!)
- Alitretinoin vs cyclosporin
- Alitretinoin vs azathioprine
- Effect of olopatadine on itch

Examples of interventions which may appear odd.
(but at that time there was a rationale):

X rays

Nickel load reduction (diet, chelators)

Diaminodiphenylsulfone (DDS)

Urea

Ranitidine

Pentoxifylline

Iontophoresis

Biofeedback

Vitamins

Fumaric acid (topical)

Evening primrose oil (oral)

Main interventions

UV-phototherapy (UV-B, UV-A, PUVA)

Topical corticosteroids

Oral immunosuppressives

Radiotherapy

Retinoids (oral and topical)

Topical calcineurin inhibitors

Antimicrobial agents (topical)

Guidance from the review:

Many treatments seem effective when compared to placebo.

Note that in most of these studies about 15% of the patients on 'placebo' also improve.

Overall little high-level evidence to make a judgement whether one treatment option should be preferred over the other.

Guidance from the review (2):

Topical corticosteroids:

No clear evidence to recommend a specific type and/or schedule.

Positive tendency towards 3x p week versus 2x per week.

UV-B versus PUVA:

No clear difference.

UV versus topical corticosteroids:

Comparative advantage unknown.

Topical calcineurin inhibitors (tacrolimus, pimecrolimus):

No evidence of advantage over UV or topical corticosteroids.

Positive effect when compared to placebo.

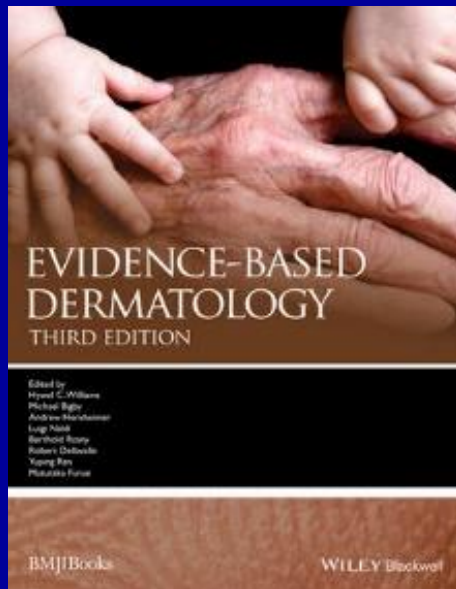
Oral retinoids:

Alitretinoin clearly superior to placebo.

No publications to show comparative advantage over other treatment

Oral immunosuppressants:

One study not showing advantage of cyclosporin over topical corticosteroids



Chapter 22 - Hand eczema

Wietske A. Christoffers et al.

The chapter lists 14 clinical questions

Back to your skills being a doctor

Concise report

CED
Clinical and Experimental Dermatology

Treatment of severe, chronic hand eczema: results from a UK-wide survey

I. L. Smith,¹ S. Brown,¹ J. Nixon,¹ F. C. Cowdell,² S. Ersser,³ C. Fernandez,¹ M. Goodfield,⁴
C. M. Green,⁵ P. Hampton,⁶ J. T. Lear,⁷ C. H. Smith,⁸ L. Sunderland,⁹ S. Tubeuf¹⁰ and
M. Wittmann^{11,12,13}

How heterogeneous is the term “Hand Eczema” ?

A problem with giving guidance for therapies is that we are not yet clear about pathophysiological subtypes.

There are several publications about classifications. Two examples:

Boonstra, Christoffers et al.

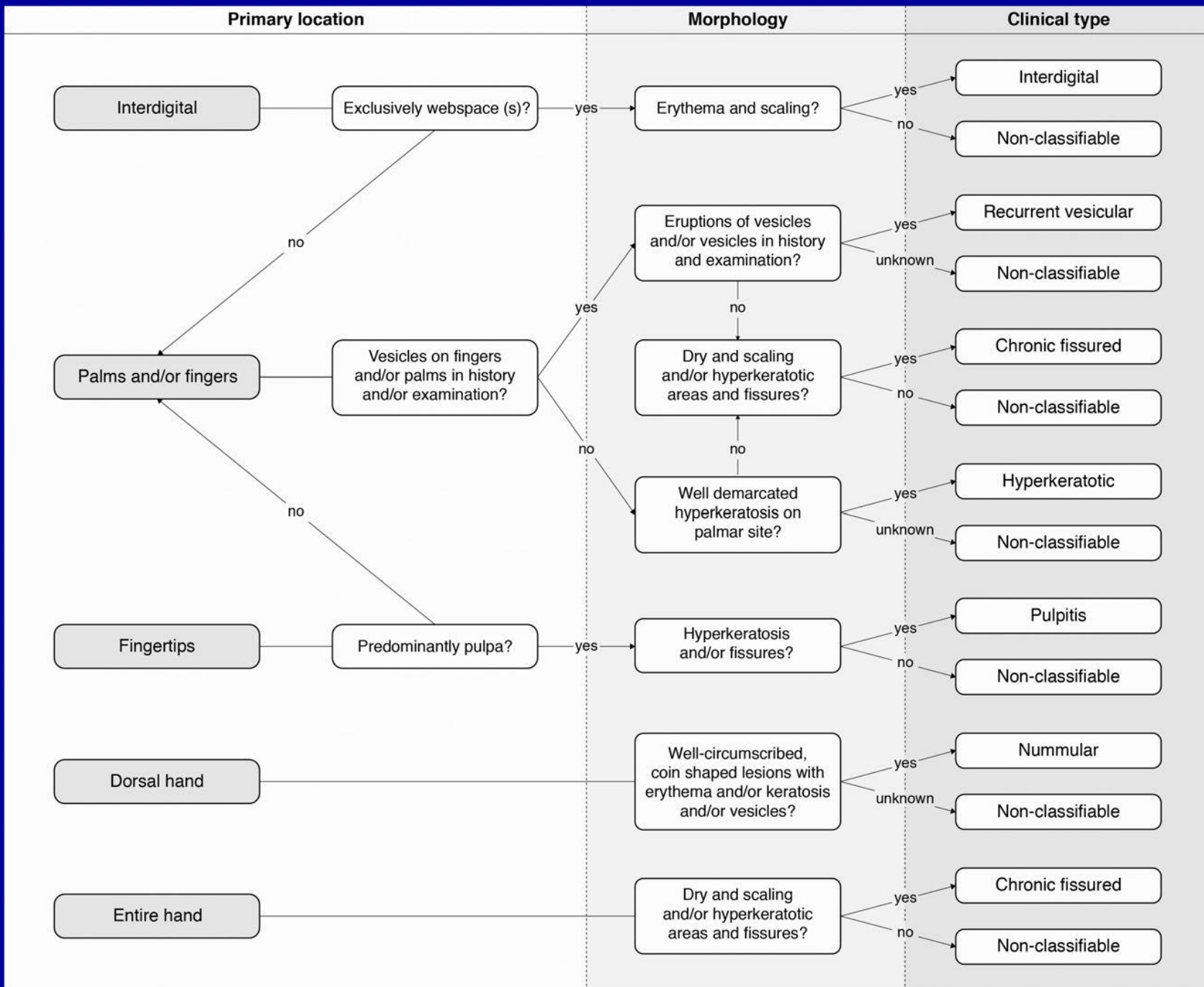
Patch test results of hand eczema patients: relation to clinical types.

J Eur Acad Dermatol Venereol 2015;29:940-7.

Johansen JD et al.

Classification of hand eczema: clinical and aetiological types. Based on the guideline of the Danish Contact Dermatitis Group.

Contact Dermatitis 2011;65:13-21



Clinical subtypes (Boonstra, Christoffers et al 2014)

Recurrent vesicular

Chronic fissured

Hyperkeratotic

Interdigital

Pulpitis

Nummular

Non classifiable

Guidance from the Cochrane review on treatments for sub-types ?

No,
so my ideas are probably as good as yours

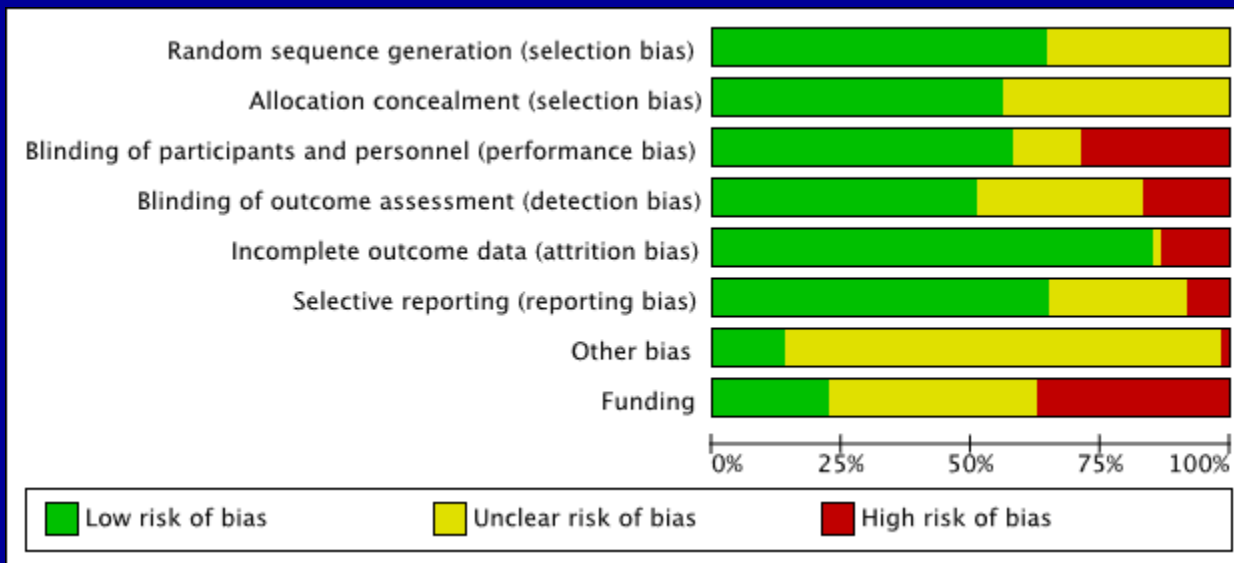
Concise report

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C. M. Green,⁵ P. Hampton,⁶ J. T. Lear,⁷ C. H. Smith,⁸ L. Sunderland,⁹ S. Tubeuf¹⁰ and
M. Wittmann^{11,12,13}

.... and be careful when you are reading a publication



Risk of Bias presented as % across all evaluated Hand Eczema trials

A final note: if everything fails, don't forget the good old coal tar

(only one small trial comparing this with betmethasone)

ORIGINAL ARTICLE

No Increased Risk of Cancer after Coal Tar Treatment in Patients with Psoriasis or Eczema

Judith H.J. Roelofzen^{1,2}, Katja K.H. Aben^{1,3}, Ursula T.H. Oldenhof¹, Pieter-Jan Coenraads⁴, Hans A. Alkemade⁵, Peter C.M. van de Kerkhof², Pieter G.M. van der Valk² and Lambertus A.L.M. Kiemeneij^{1,3,6}

Coal tar is an effective treatment for psoriasis and eczema, but it contains several carcinogenic compounds. Occupational and animal studies have shown an increased risk of cancer after exposure to coal tar. Many dermatologists have abandoned this treatment for safety reasons, although the risk of cancer after coal tar in dermatological practice is unclear. This large cohort study included 13,200 patients with psoriasis and eczema. Information on skin disease and treatment, risk factors, and cancer occurrence was retrieved from medical files, questionnaires, and medical registries. Proportional hazards regression was used to evaluate differences in cancer risk by treatment modality. Patients treated with coal tar were compared with a reference category of patients treated with dermatocorticosteroids (assumed to carry no increased cancer risk). The median exposure to coal tar ointments was 6 months (range 1–300 months). Coal tar did not increase the risk of non-skin malignancies (hazard ratio (HR) 0.92; 95% confidence interval (CI) 0.78–1.09), or the risk of skin cancer (HR 1.09; 95% CI 0.69–1.72). This study has sufficient power to show that coal tar treatment is not associated with an increased risk of cancer. These results indicate that coal tar can be maintained as a safe treatment in dermatological practice.

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Emma Mead, Methodologist

Hywel Williams, Co-ordinating Editor

Backup / reserve

Clinical subtypes (Coenraads NEJM 2012)

Etiologic classification

Irritant contact dermatitis
Atopic hand eczema
Allergic contact dermatitis
Hybrid hand eczema
Protein contact dermatitis

Morphologic classification

Recurrent vesicular
Hyperkeratotic
Chronic fingertip ('pulpitis')
Nummular
Dry fissured

Often a combination of exogenous and endogenous factors

Exogenous factors

- Irritant hand eczema (wet work, food, gloves, oils, etc).
- Allergic hand eczema: Role of chromate and nickel is overestimated (“relevance”).

Endogenous factors

- Constitutional eczema phenotype, with or without atopy.
- Genetic disposition (Laerbek 2007, De Jongh 2008)
- Endogenous (= “I don’t know”)

Patch-testing ?

Our advice: if possible, do it, but be careful with the interpretation of the results.

However

DOI: 10.1111/jdv.12735

JEADV

ORIGINAL ARTICLE

Patch test results of hand eczema patients: relation to clinical types

M.B. Boonstra,[†] W.A. Christoffers,[†] P.J. Coenraads, M.L.A. Schuttelaar*

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*Correspondence: M.L.A. Schuttelaar. E-mail: m.l.a.schuttelaar@umcg.nl

“....subjects with recurrent vesicular hand eczema should be patchtested ... while the need in males with hyperkeratotic palmar eczema may be less imperative”

Genetic factors ?

Genetic factors in nickel allergy evaluated in a population-based female twin sample (*Bryld et al, JID 2004*)

Heritability of hand eczema is not explained by co-morbidity with atopic dermatitis (*Laerbek et al, JID 2007*)

Filaggrin ?

Loss-of-Function polymorphisms in the filaggrin gene are associated with an increased susceptibility to chronic irritant contact dermatitis: a case-control study (*de Jongh et al. Br J Dermatol 2008*)

contested by others.....

Filaggrin null alleles are not associated with hand eczema or contact allergy (*Lerbaek et al. Br J Dermatol 2007*)

The hands in health and disease of individuals with filaggrin loss-of-function mutations: clinical reflections on the hand eczema phenotype (*Kaae et al, Contact Dermatitis 2012*)

Chronic hand eczema: etiology often unclear

- In many patients the original etiology of the disease cannot be established
- Extremely difficult to identify any single causative factor
- There may be an overlap and interaction of causative factors
- The relevance of contact allergens is often not known
- Even when an initial causative agent is avoided, hand eczema often develops into a chronic condition

Predominant sites
of
Atopic Dermatitis (AD)

