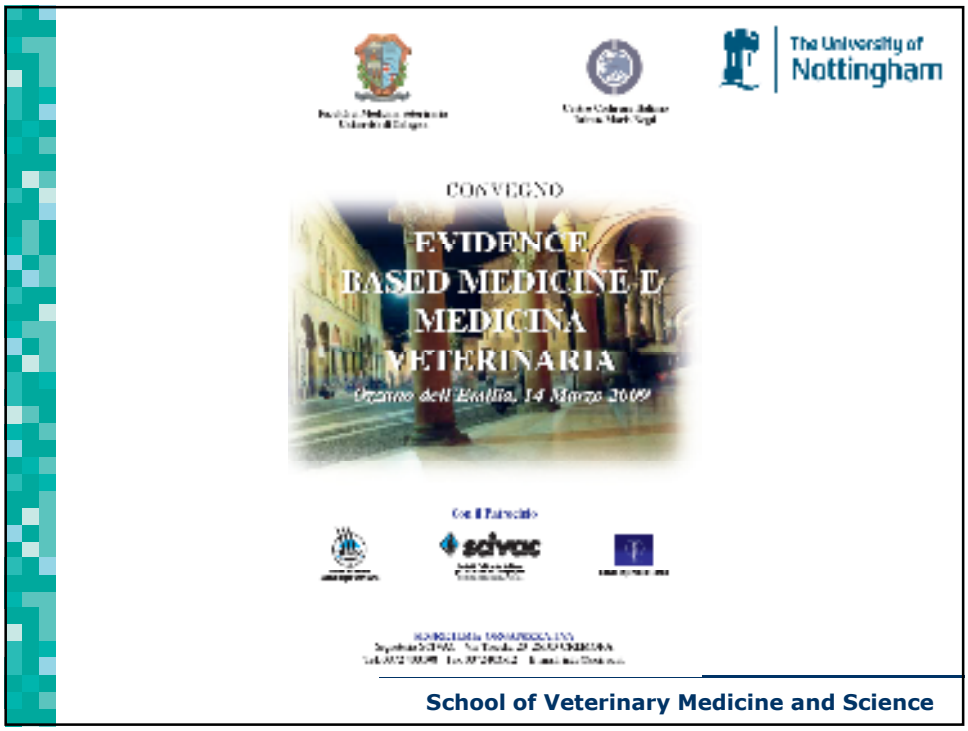
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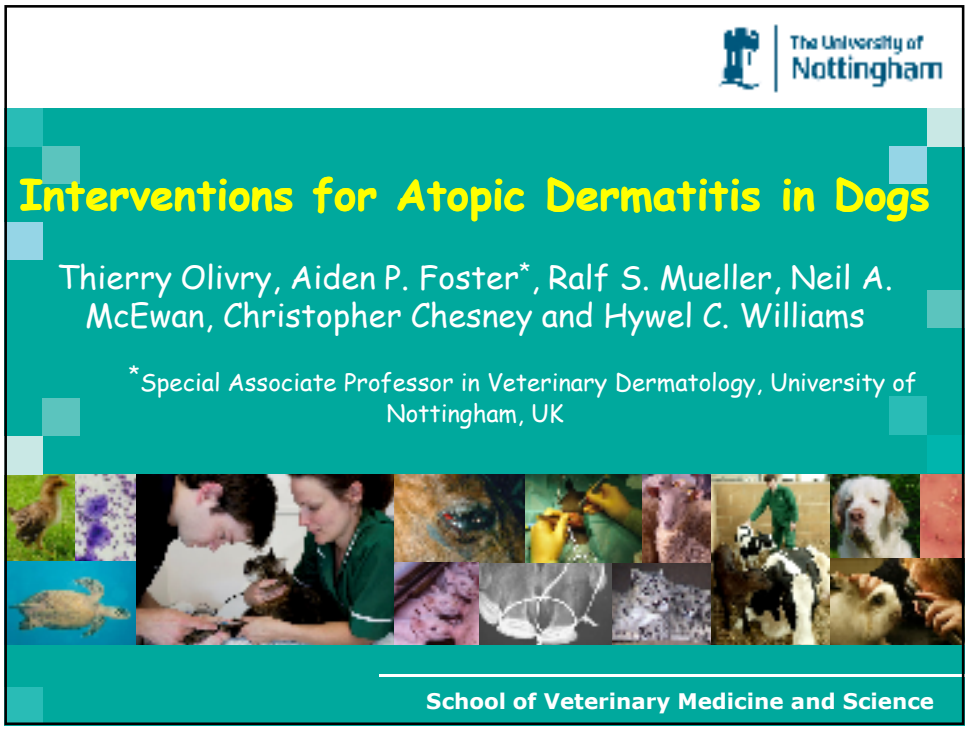
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Interventions for Atopic Dermatitis in Dogs
Thierry Olivry, Aiden P. Foster*, Ralf S. Mueller, Neil A. McEwan, Christopher Chesney and Hywel C. Williams
*Special Associate Professor in Veterinary Dermatology, University of Nottingham, UK
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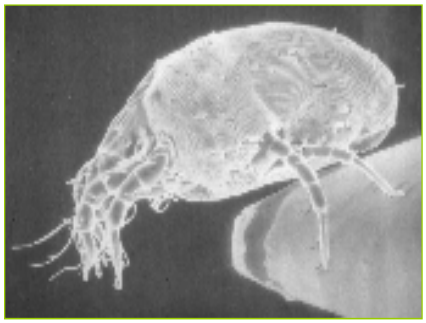
Canine Atopic Dermatitis (CAD)

Epidemiology

- Hypersensitivity reactions to environmental allergens
- IgE antibody-mediated response
- Sensitization may involve percutaneous transport of allergens
- Familial component?
- Prevalence
  - Up to 10% of all dogs?



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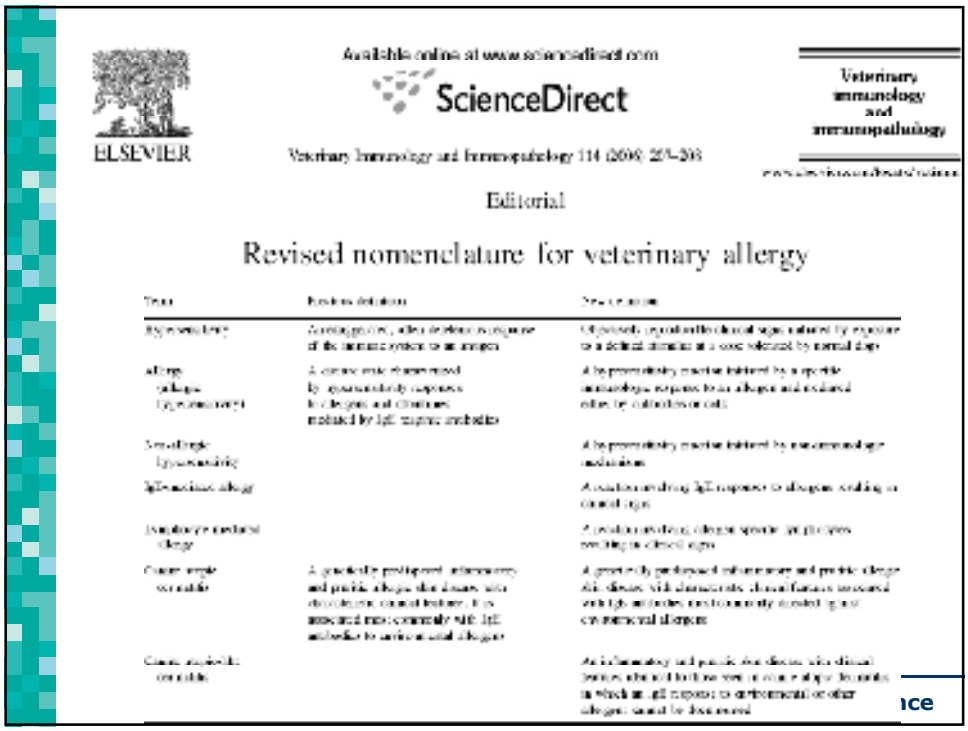

Available online at www.sciencedirect.com

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Veterinary Immunology and Immunopathology 114 (2006) 279–280

Veterinary immunology and immunopathology

www.elsevier.com/locate/vetimm

Editorial

Revised nomenclature for veterinary allergy

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CAD – Clinical diagnosis

- Labrador, Retriever, West Highland white terrier, Boxer and German Shepherd dogs
- Onset of signs occurs most commonly from 1 to 3 years, rare before 6 months and after 6 years of age
- Major sign is pruritus affecting the face (muzzle, eyes, ears), feet, groin and axilla

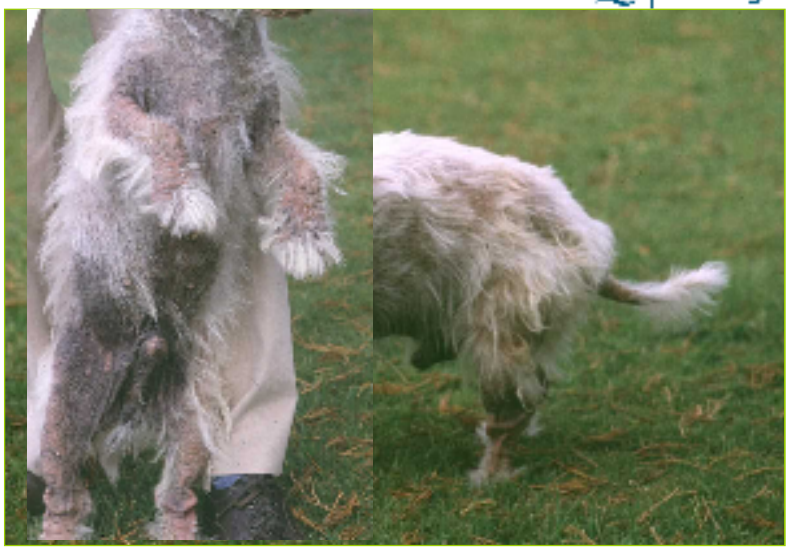
CAD – Clinical diagnosis

- Clinical signs
  - associated with self trauma
  - secondary bacterial and Malassezia infections
  - alopecia, erythema, excoriation, hyperpigmentation and lichenification
- Diagnosis
  - Rule out other conditions that cause pruritus
  - Confirmation by intradermal and / or allergen-specific IgE serology testing

CAD – Clinical diagnosis

Differential Diagnoses:

- Flea bite hypersensitivity
- Sarcoptic mite infestation
- Cutaneous adverse food reaction
- (Demodicosis)
- (Dermatophytosis)



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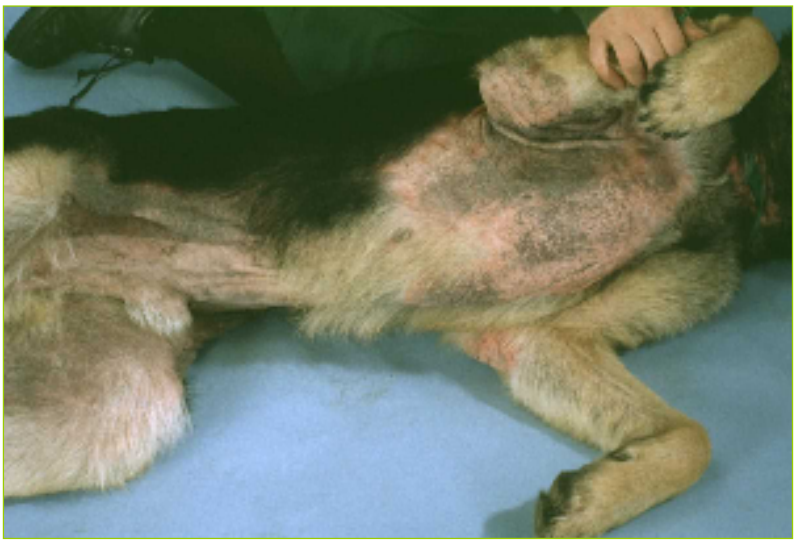

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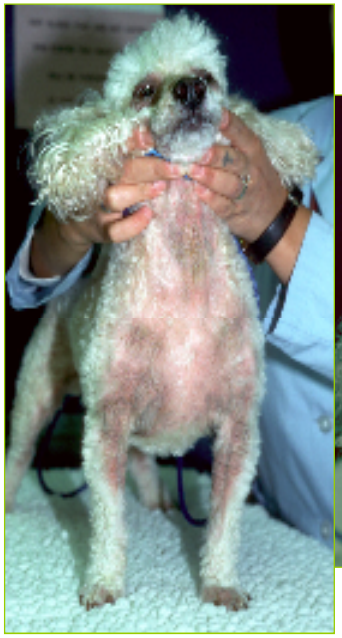

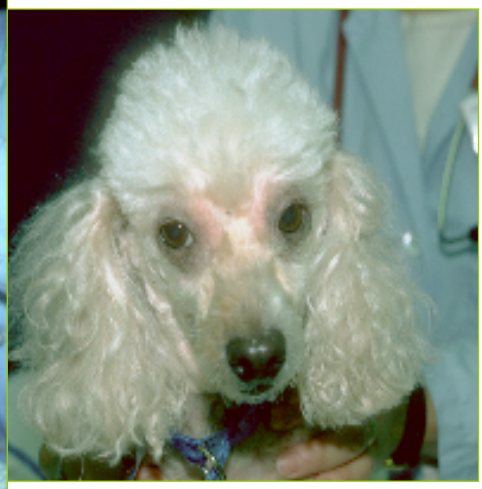

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CAD: Short term Management

- Treat flare factors
  - Fleas
  - Staphylococcal infections
  - Malassezia
- Essential fatty acids
- Anti-histamines
- Bathing
- Glucocorticoids
- Ciclosporin
- Herbal (Chinese)

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Canine Atopic Dermatitis

- Common
- Challenging – financial, emotional, physical
- Environmental allergens – house dust mites
- Allergen-specific immunotherapy
- What is the evidence for efficacy of other interventions?

Interventions for Atopic Dermatitis in Dogs: A Systematic Review of Randomized Controlled Trials

Objectives

- To assess the effects of interventions for treatment of AD in dogs

Search strategy

- Citations were identified from three databases (MEDLINE, ISI/Thomson's Science Citation Index Expanded and CAB Abstracts) from January 2005 to December 2007
  - Unpublished and ongoing trials were identified by posting messages in the veterinary dermatology e-mail lists.
  - Proceedings books from the major veterinary dermatology international congresses were hand searched for relevant citations.

Selection criteria

- Randomized controlled trials (RCTs), published from January 1980 to December 2007
- Efficacy of topical or systemic interventions for treatment or prevention of canine AD
- Studies had to report assessments of either pruritus or skin lesions, or both, during the trials

Data collection & analysis

- Studies were selected and data extracted by two reviewers, with discrepancies resolved by a third arbitrator
- Missing data were requested from study authors of recently published trials
- Design method quality
  - Generation and concealment of randomization
  - Masking of treatment allocation
  - Loss of follow-up
  - Quality of subject selection
  - Comparison of groups at baseline
  - Compliance
- Pooling of results and meta-analyses were performed for studies reporting similar interventions and outcome measures

British Journal of Dermatology 2003; 148: 1154–1160.

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Differences in efficacy between intention-to-treat and per-protocol analyses for patients with psoriasis vulgaris and atopic dermatitis: clinical and pharmacoeconomic implications

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Accepted for publication 28 December 2000

Summary

Background Pharmacoeconomic outcome research is based on three criteria: (i) evaluation of objective therapeutic effects; (ii) quality of life; and (iii) treatment costs. Evaluation of therapeutic effect is mainly based on the results of clinical trials using objective clinical measures, e.g. Psoriasis Area and Severity Index (PASI) (score for psoriasis vulgaris) and the Severity Scoring of Atopic Dermatitis (SCORAD) (score for atopic dermatitis). In most studies only results for a treatment-optimized subpopulation (patients treated according to the protocol) are presented in publications. The relevance of such data for daily routine therapy is doubtful.

Objectives Our purpose was to investigate the expected loss of effectiveness of switching from a clinical trial to daily routine therapy for the synchronous application of narrow-band ultraviolet (UV) B phototherapy (311 nm) and bathing in 10% Dead Sea salt solution (synchronous balneophototherapy) for patients with psoriasis vulgaris and atopic dermatitis.

Methods We conducted a multicentre, uncontrolled observational study of outpatients. To achieve data for 'clinical trial' and 'daily routine' situations, two populations were compared: (i) all patients strictly treated according to the protocol (ATP) with no protocol deviations (data published in clinical trials), and (ii) all patients participating in the study who received active treatment at least once, despite treatment irregularities, non-compliance, early withdrawal or other protocol violations [intention-to-treat-population (ITT), model for 'daily routine'].

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Data collection & analysis

Primary outcome measure

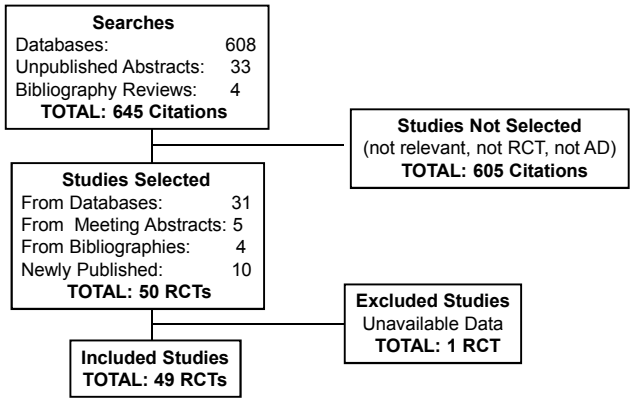
- The proportion of canine participants with at least a good-to-excellent improvement when evaluated on a categorical global assessment scale by
  - either investigators (primary outcome 1a)
  - or dog owners (primary outcome 1b).

Data collection & analysis

Secondary outcome measures

- (a) The percentage of dogs with complete remission of signs, defined by a reduction of 90 per cent or more from
  - baseline investigator-graded lesional (secondary outcome 1a)
  - or owner-rated pruritus scores (secondary outcome 1b).
- (b) The percentage of dogs with a 50 per cent or more reduction from
  - baseline investigator-graded lesional (secondary outcome 2a)
  - or owner-rated pruritus scores (secondary outcome 2b).

Results



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Results: Methodological quality

- Randomization and selection bias
- Blinding of outcome assessment and detection bias
- Handling of losses and attrition bias
- Comparison of groups at baseline
- Used of standardized disease severity scales
- Assessment of compliance

Main results

- 49 RCTs were selected, 2126 dogs enrolled
- Most RCTs were rated with poor or intermediate design
  - quality was higher after 2002 than before
- Some evidence of efficacy of
  - topical tacrolimus (3 RCTs),
  - topical triamcinolone (1 RCT),
  - oral glucocorticoids (5 RCTs),
  - oral ciclosporin (6 RCTs),
  - subcutaneous recombinant gamma-interferon (1 RCT)
  - subcutaneous allergen-specific immunotherapy (3 RCTs)

to decrease pruritus and/or skin lesions of AD in dogs

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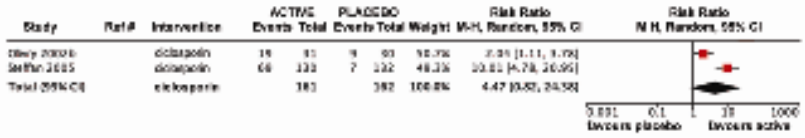
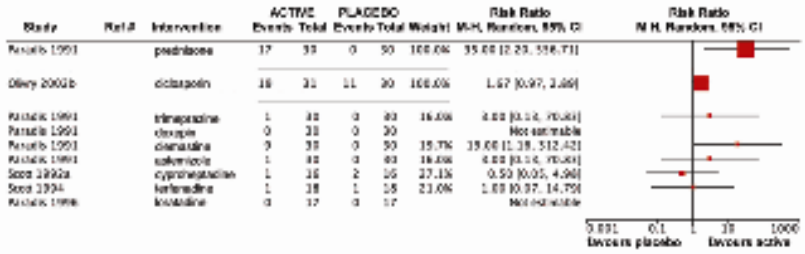
(a) primary outcome measure 1b: "good-to-excellent" response (clinicians)



(b) primary outcome measure 1b: "good-to-excellent" response (owners)



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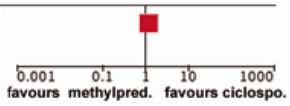
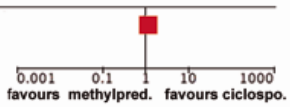
(a) primary outcome measure 1b: "good-to-excellent" response (clinicians)

Study	Ref #	CICLOSPORIN Events	Total	METHYLPREDNISOLONE Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Steffan 2003		85	117	36	59	100.0 %	1.19 [0.94, 1.50]



(b) primary outcome measure 1b: "good-to-excellent" response (owners)

Study	Ref #	CICLOSPORIN Events	Total	METHYLPREDNISOLONE Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Steffan 2003		83	117	34	59	100.0 %	1.23 [0.96, 1.58]



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Main results

- Pooling of data was only considered relevant for two studies of ciclosporin compared to that of placebo
  - Benefit was increased in those dogs given ciclosporin - overall pooled estimate was not statistically significant
    - (risk ratio [RR]: 4.5, 95% confidence interval [CI]: 0.8-24.4 for clinician's assessment of efficacy)
- Oral ciclosporin and oral methylprednisolone appear to have a similar efficacy in reducing skin lesions and pruritus in dogs with AD
  - (RR: 1.2 [0.9-1.5] and 1.2 [1.0-1.6], respectively).
- One high quality RCT with 60 dogs showed that an oral EFA supplement could reduce prednisolone consumption by approximately half

Results - Adverse effects

Glucocorticoids

- 10-81 %
- Rated as mild or moderate
- Polyuria, polydipsia and/or polyphagia
- Vomiting
- Weight gain
- Skin infections

Ciclosporin

- Up to 81
- Most commonly vomiting or diarrhoea/soft stools
- Usually transient, reversible and of mild to moderate severity
- Consistent and clinically relevant changes in routine blood tests were not seen

Discussion

Limitations

- **Participants**
  - Variability of diagnosis of AD
  - Variability of response between ages or breeds
- **Study Design**
- **Outcome Measures**
  - changes in pruritus categorical or visual analogue scales
  - lesional scales (CADESI)
  - global assessment of treatment outcome

Discussion

- **Implications for practice**
- **Implications for research**
  - Insufficient evidence of efficacy vs. evidence of no efficacy
  - Variable disease severity
  - Adequate pharmacological data
  - Adequate power data
  - Common outcome measures
  - Longer term studies

Reviewers ' *conclusions*

- Topical and oral glucocorticoids,
- topical or oral calcineurin inhibitors
- injectable interferon or allergen-specific immunotherapy
  - ***appear* to be effective interventions for treatment of CAD**
- Additional drugs have been tested
  - poor study design or conflicting results
  - ***insufficient* evidence of their efficacy**
- Additional RCTs of high design quality must be performed to remedy previous flaws and to test interventions for prevention of flares of this disease

Acta Derm Venereol 2006; 86: 482–487

SPECIAL REPORT

Conflicts of Interest in Dermatology[1]

Hywel C. WILLIAMS[1], Luigi NALDI[2], Carle PAUL[3], Anders VAHLQUIST[4,5], Sam SCHROTER[6] and Ray JOBLING[7]

[1]Centre of Evidence-Based Dermatology, Nottingham University Hospitals NHS Trust, Nottingham, UK, [2]CSERI Study Centre, Ospedali Riuniti, Bergamo, Italy, [3]Department of Dermatology, Purpan Hospital and Universite Paul Sabatier, Toulouse, France (formerly Clinical Research, Novartis Pharma AG, Basel, Switzerland), [4]Department of Medical Sciences, Uppsala University, Uppsala, Sweden, [5]Editor-in-Chief, Acta Dermato-Venereologica, [6]British Medical Journal, London, UK, and [7]The Psoriasis Association, St John's College, Cambridge, UK

Conflicts of interest exist in dermatology when professional judgement concerning a primary interest, such as research validity, may be influenced by a secondary interest, such as financial gain from a for profit organization. Conflict of interest is a condition and not a behaviour, although there is clear evidence that gifts influence behaviour. Little has been written about conflicts of interest in dermatology. This series of papers raises awareness of the subject by exploring it in greater depth from the perspective of a dermatology researcher, an industry researcher, a dermatology journal editor, a health services researcher and a patient representative. Collectively, they illustrate the many ways in which conflicts can pervade the world of dermatology publications and patient support group activities. *Key words: conflicts of interest;*

on the topic of conflict of interest (COI) in dermatology held at the Spring 2006 European Academy of Dermato-Venereology meeting in Finland. It might strike the reader that the topic of COI was an odd one for a meeting that relies so heavily on sponsorship from the pharmaceutical industry. Nevertheless, the session was well attended and received by a wide range of colleagues from academia, clinical practice and industry. It was clear from the discussion that ensued from the potentially difficult areas surrounding COI in dermatology that some themes relating to COI and dermatology research output needed to be shared more widely amongst the dermatology community through a journal article. This article therefore represents a compilation of these talks, plus an additional contribution about

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Conflict of interest

Consultation and research funding activities

Sources of funding

None declared

Clinical trials: randomised clinical trials (RCTs) and systematic reviews should be reported according to the CONSORT guidelines (www.consort-statement.org)

Acknowledgements

External referees: Peter Hill (content expert), Gerry Neal (consumer)