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DOCTOR OF MEDICINE

Photoallergic contact dermatitis in Europe

Kerr, Alastair

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Alastair Kerr

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Photoallergic Contact Dermatitis in Europe

Alastair Carswell Kerr

Thesis presented for the degree of Doctor of Medicine

The University of Dundee

March 2012

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List of Abbreviations

ACD	allergic contact dermatitis
CAD	chronic actinic dermatitis
CPE	chlorproethazine
CPZ	chlorpromazine
EMCPPTS	European multi-centre photopatch test study
HIC	Health Informatics Centre
ICDRG	International Contact Dermatitis Research Group
INCI	International Nomenclature of Cosmetic Ingredients
IR	irritant reaction
MED	minimal erythematous dose
NSAIDs	nonsteroidal anti-inflammatory drugs
PABA	<i>para</i> -aminobenzoic acid
PACD	photoallergic contact dermatitis
PI	Principal Investigator
PLE	polymorphic light eruption
PPT	photopatch testing
SPF	sun protection factor
TCSA	tetrachlorosalicylanilide
UK	United Kingdom
USA	United States of America
UV	ultraviolet
WSP	white soft paraffin

Acknowledgements

Professor James Ferguson for creating the opportunity for me to undertake this work in such a productive and renowned department. Also for his inspirational guidance and dynamism over the years as my supervisor.

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Alison Bell and Chris Hall in the Health Informatics Centre at the University of Dundee, for the EMCPTS proforma data entry and extraction.

Finally, all the patients and healthy volunteers who consented to participate in all the photopatch testing studies, making these possible.

Declaration

I declare that I am the author of this thesis and have, unless otherwise acknowledged, performed the major part of the work presented. In cases where studies have been undertaken in collaboration, my contribution is described on the following page. I declare that all references cited herein have been consulted by me and that the work has not been previously accepted for a higher degree.

Alastair Carswell Kerr

I certify that Alastair Carswell Kerr has carried out research under my supervision and has fulfilled the conditions of the relevant Ordinance and Regulations for the completion of an MD degree

Professor James Ferguson

Contribution to collaborative studies

I was the primary author of all the studies included in this thesis and wrote the thesis as a whole. A list of relevant publications is provided on page xx, which contains the names of co-authors of collaborative studies. All studies were co-conceived by Professor J. Ferguson and myself. Additionally, for all studies which employed photopatch testing in the Photobiology Unit in Dundee, this was performed by Mrs Lynn Fullerton and her team of skilled technicians. Otherwise, my role in the studies presented in each Chapter, and the contribution of others, is given below.

Chapter 1. Introduction.

My contribution: sole author.

Chapter 2. An occupational outbreak of photoallergy to carprofen.

My contribution: Primary author of the study. Based on parts of an investigative study performed by, and report written by, Dr R.S. Dawe.

Chapter 3. Chlorproethazine: A second photoallergen on the marketplace.

My contribution: Primary author of the study. Laboratory work performed by and co-authored by, Dr J Woods. Investigative idea initially suggested by Dr M-C Marguery.

Chapter 4. A pilot irritancy study of organic ultraviolet absorbers.

My contribution: Primary author of the study. Statistical calculations conducted by Dr R.S.Dawe. Study conducted in collaboration with L'Oreal Research and Development Ltd and Chiltern Early Phase Ltd.

Chapter 5. A survey of the availability of sunscreen absorbers in the UK.

My contribution: Study conducted and authored solely by myself.

Chapter 6. The European multi-centre photopatch test study (EMCPPTS).

My contribution: Primary author of the study. I also undertook all the operative requirements which enabled the project to proceed including protocol refinement, application to regulatory bodies and continual liaison with all collaborative investigators and the Health Informatics Centre. Data input and extraction performed by the Health Informatics Centre team, with data analysis performed by myself. Calibration of UV meters performed by Mrs L Fullerton and Prof H Moseley.

Chapter 7. Conducting the EMCPPTS.

My contribution: sole author.

Chapter 8. A new European Baseline photopatch test series

My contribution: sole author.

Chapter 9. Conclusions and Future Directions.

My contribution: sole author.

List of relevant publications

Relevant peer-reviewed publications are bound in Appendix 4 at the end of the thesis. A list of these publications is given below.

The EMCPPPTS taskforce (Kerr AC first author of group). A European Multi-centre Photopatch Test Study (EMCPPPTS). *Br J Dermatol*, 2012; 166: 1002-9.

Kerr AC. A survey of the availability of sunscreen filters in the U.K. *Clin Exp Dermatol*, 2011; 36: 541-3.

Kerr AC, Becher G, Ibbotson SH, Ferguson J. Action spectrum for etofenamate photoallergic contact dermatitis (Contact Point). *Contact Dermatitis*, 2011; 65: 117-8.

Kerr AC, Ferguson J. Photoallergic contact dermatitis (Review). *Photoderm, Photoimmunol & Photomed*, 2010; 26: 56-69.

Kerr AC, Shareef M, Dawe RS, Ferguson J. Photopatch testing negative in systemic quinine phototoxicity (Brief communication). *Photoderm, Photoimmunol & Photomed*, 2010; 26: 151-2.

Kerr AC, Niklasson B, Dawe RS, Escoffier A-M, Krasteva M, Sanderson B, Ferguson J. A double-blind, randomised assessment of the irritant potential of sunscreen chemical dilutions used in photopatch testing. *Contact Dermatitis*, 2009; 60: 203-9.

Kerr AC, Woods JA, Ferguson J. Photocontact allergic and phototoxic studies of chlorproethazine. *Photoderm, Photoimmunol & Photomed* 2008; 24: 11-15.

Kerr AC, Muller F, Ferguson J, Dawe RS. Occupational carprofen photoallergic contact dermatitis. *Br J Dermatol*, 2008; 159: 1303-8.

Abstract

Photoallergic contact dermatitis (PACD) is a clinical problem that has often been poorly understood and neglected by dermatologists over recent years. This can be partly attributed to its investigation by photopatch testing (PPT) falling between the expertise of photobiologists and contact dermatitis clinicians. One result of this situation was that no European Baseline PPT series had been agreed on. To redress this, the European multi centre photopatch test study (EMCPPTS) was conceived to provide up to date information on which photoallergens are of greatest clinical relevance. Its conduct and results form the core research project of this thesis.

To enable the EMCPPTS to proceed and its results to be viewed in a wider context, the other Chapters of this thesis explore important related aspects of PACD and PPT in Europe. The introduction examines the nature of PACD and PPT and reviews current photoallergens. Then, the investigation of the two photoallergens carprofen and chlorproethazine by PPT is recounted. These studies highlight deficiencies within the current European regulatory system for preventing photoallergens from reaching the marketplace, as well as providing templates for the investigation of new photoallergens in the human environment.

This is followed by a pilot PPT study which provides new information on the optimum non-irritating concentration of the 19 ultraviolet sunscreen absorbers to be used in the EMCPPTS. The issue of attempting to determine the photoallergenic potential of the EMCPPTS agents with respect to exposure patterns is addressed by conducting a sunscreen survey in the UK. The EMCPPTS itself is then detailed, as well as the difficulties that can be encountered when conducting a large clinical study of this nature. The results from the EMCPPTS and other presented studies were shown to be of importance in deciding upon a new European Baseline PPT

series. The process involved in deciding this series, as well as its content are described before overall conclusions and possible future studies in the domain of PACD and PPT are discussed.