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شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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بالرسالة صفحات لم ترد بالاصل

THE MYSTERY OF ALOPECIA AREATA
A CLINICAL - IMMUNO HISTOCHEMICAL AND ULTRASTRUCTURAL STUDY

Thesis

Submitted for Partial Fulfillment of M.D. Degree in Dermatology and Andrology

By

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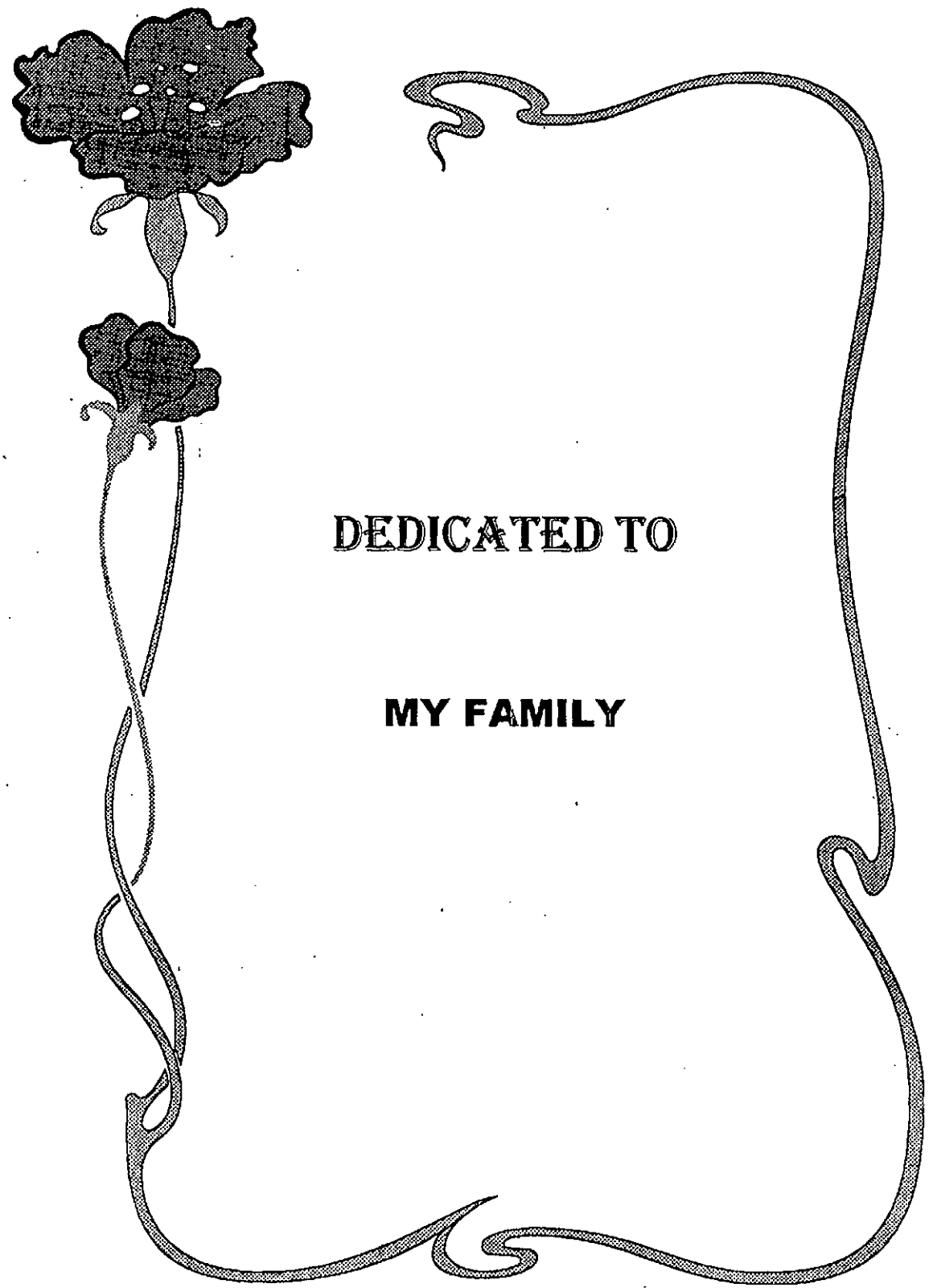

DEDICATED TO

MY FAMILY

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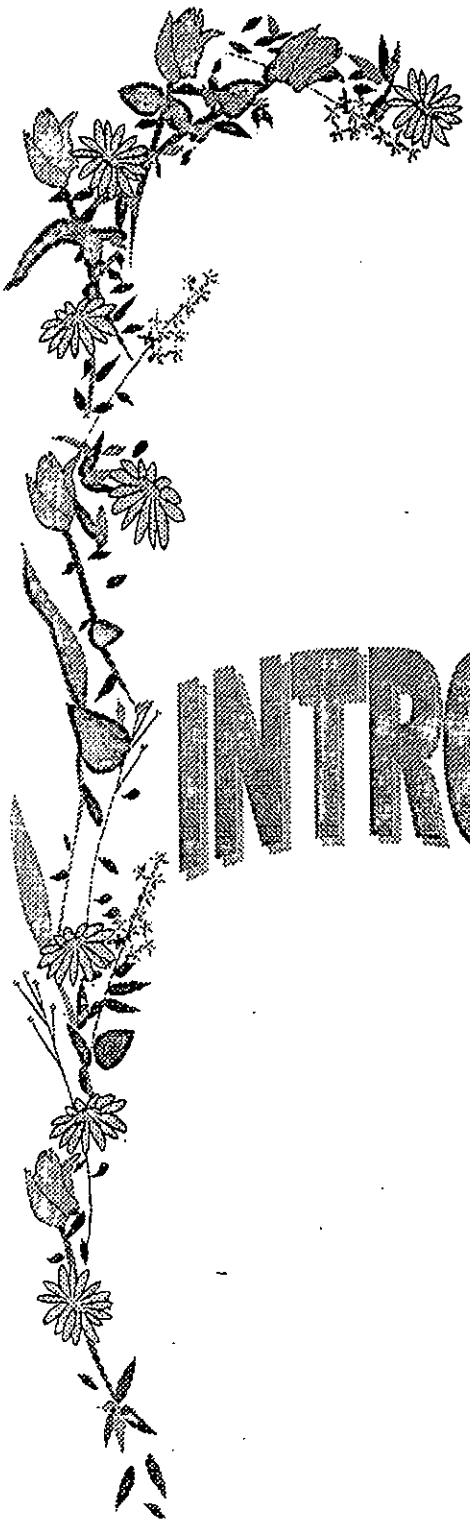
CONTENTS

LIST OF ABBREVIATIONS

AA	Alopecia Areata
ACAM	Adherens junction - specific cell adhesion molecule
APC	Antigen presenting cell
AT	Alopecia totalis
AU	Alopecia universalis
CAMs	Cellular adhesion molecules
$CD1a^{+}$	Langerhans cell marker
CD2	Common differentiation antigen -2
CD3+	Pan T-cell marker
CD4+	T-cell helper/inducer
CD8+	T-cell suppressor/cytotoxic
CLA	Cutaneous lymphocyte associated antigen.
Da	Dalton
DP	Dermal papillae
EGF	Epidermal Growth Factor
ELAM-1	Endothelial leukocyte adhesion molecule -1
Endo CAM	Endothelial cell adhesion molecule.
b-FGF	Basic fibroblast growth factor
HLA	Histocompatibility locus A
ICAM-1	Intercellular adhesion molecule -1
ICAM-2	Intercellular adhesion molecule -2
ICAM-3	Intercellular adhesion molecule -3
IL-1	Interleukin-1
IFN-γ	Interferon - γ
LAA	Localized alopecia areata
LAD	Leukocyte adhesion deficiency disease
LFA-1	Leukocyte function antigen -1
LFA-2	Leukocyte function antigen -2
LFA-3	Leukocyte function antigen -3
Mac-1	Macrophage activation antigen -1
MHC	Major histocompatibility complex antigens.
NCAM	Neural cell adhesion molecule
NgCAM	Neural-glia cell adhesion molecule
NK	Natural killer
PDGF	Platelet drived growth factor
TAG-1	Transient Axonal Gylcoprotein-1
TGF	Transforming growth factor
TNF	Tumor necrosis factor
VCAM-1	Vascular cell adhesion molecule -1
VEGF	Vascular endothelial growth factor
VLA	Very late activation proteins.



INTRODUCTION

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Alopecia areata (AA) is a common disorder that produces a sudden, patchy hair loss, characterized by increased percentage of telogen hair follicles. Although it is a benign disorder, the cosmetic and psychological effects of the disease may be profound *(Baadsgaard, 1991).*

There is increasing evidence that immune/inflammatory cells, such as T-cells, participate in the pathophysiology of several clinically distinct alopecias *(Bystryn and Tamesis, 1991).*

In alopecia areata the mechanisms by which the hair loss is mediated are not understood, but it is well known that AA is associated with a peri- and intrafollicular lymphocytic infiltrate, consisting primarily of CD4+ T-lymphocytes *(Baadsgaard et al., 1987)* and with an aberrant expression of ICAM-1 and HLA-DR molecules on affected hair follicle keratinocytes and papilla cells *(McDonagh et al., 1993).*

The nature of the noxious signal, however, and its anatomical target remain elusive. It has been assumed that an autoimmune process is involved *(Baadsgaard, 1991).*

Apparently the infiltrating T-lymphocytes do not destroy the hair follicle but rather initiate a "switch-off" mechanism of the hair cycle, which is present as long as the lymphocytic infiltrate persists *(Messenger et al., 1986).*

Recently, it has been hypothesized that during the AA-specific immune response T-lymphocytes might mediate their effect through soluble mediators, which arrest the hair cycle in stage IV anagen, and the investigators were able to demonstrate a Th-1 type T-helper cell cytokine pattern in active, untreated AA ***(Hoffmann et al., 1994).***

Other soluble mediators, such as growth factors, have been shown to mediate a rather broad spectrum of biological functions ***(Hoffmann et al., 1996).***

AIM OF THE WORK

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The aim of this study was to identify:

1- By immunohistochemical method, the membrane antigens expressed by cellular infiltrate and follicular keratinocytes in localized AA using CD4, HLA-DR and ICAM-1 monoclonal antibodies and their interrelation and correlation at different stages of the disease.

2- Ultrastructural changes of lesional and non-balding regions of AA scalp to determine the earliest changes at the ultrastructural level that may indicate the primary site of damage in AA hair follicles.

To understand the aetiopathogenesis of AA a brieve review on:

- Cell adhesion molecules.
- The HLA major histocompatibility complex.
- T-cells and cutaneous leukocyte trafficking, is presented.