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CLINICAL, HISTOPATHOLOGICAL, AND HISTOCHEMICAL STUDY OF ACANTHOSIS NIGRICANS

THESIS

Submitted to the Faculty of Medicine Tanta University in Partial Fulfillment for the Requirement of the Master Degree

In

Dermatology and Venereology

By

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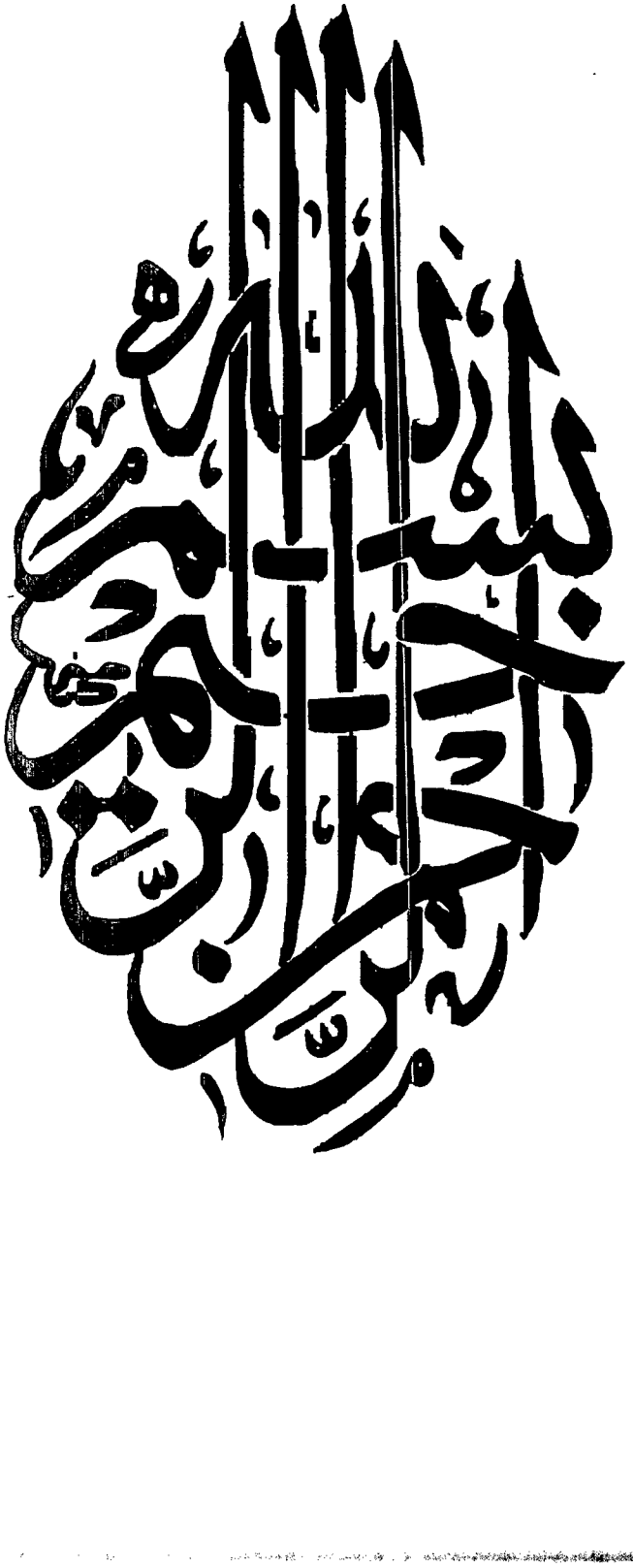
بسم الله الرحمن الرحيم

This work is dedicated

To my Father

To my Husband

To my Brother

And to the

Memory of my lovely Mother

ACKNOWLEDGMENT

To Allah, by Him all things exist. In this work, He has enormously helped me. He offered me what I did not know and which I have to know. Therefore, it was possible to start, continue, and finish this thesis. Hence, if only one is to be thanked, Allah is the first and the last. Then, those offered by Allah to advise and guide have to be thanked.

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List of Abbreviations

AN	: Acanthosis nigricans
IR	: Insulin resistance
DM	: Diabetes mellitus
APUD	: Amine precursor uptake and decarboxylase
ACTH	: Adrenocorticotrophic hormone
B-MSH	: Beta melanocyte stimulating hormone
IGF-I	: Insulin-like growth factor I
HA	: Hyperandrogenism
GH	: Growth hormone
TSH	: Thyroid stimulating hormone
BMI	: Body mass index
Cw-Co_2 Laser	: Continuous-wave carbon dioxide laser
FBS	: Fasting blood sugar
PPBS	: Postprandial blood sugar
DOPA	: 3,4-dihydroxyphenylalanine
TSB	: Total serum bilirubin
SGOT	: Serum glutamic oxalacetic transaminase
SGPT	: Serum glutamic pyruvic transaminase

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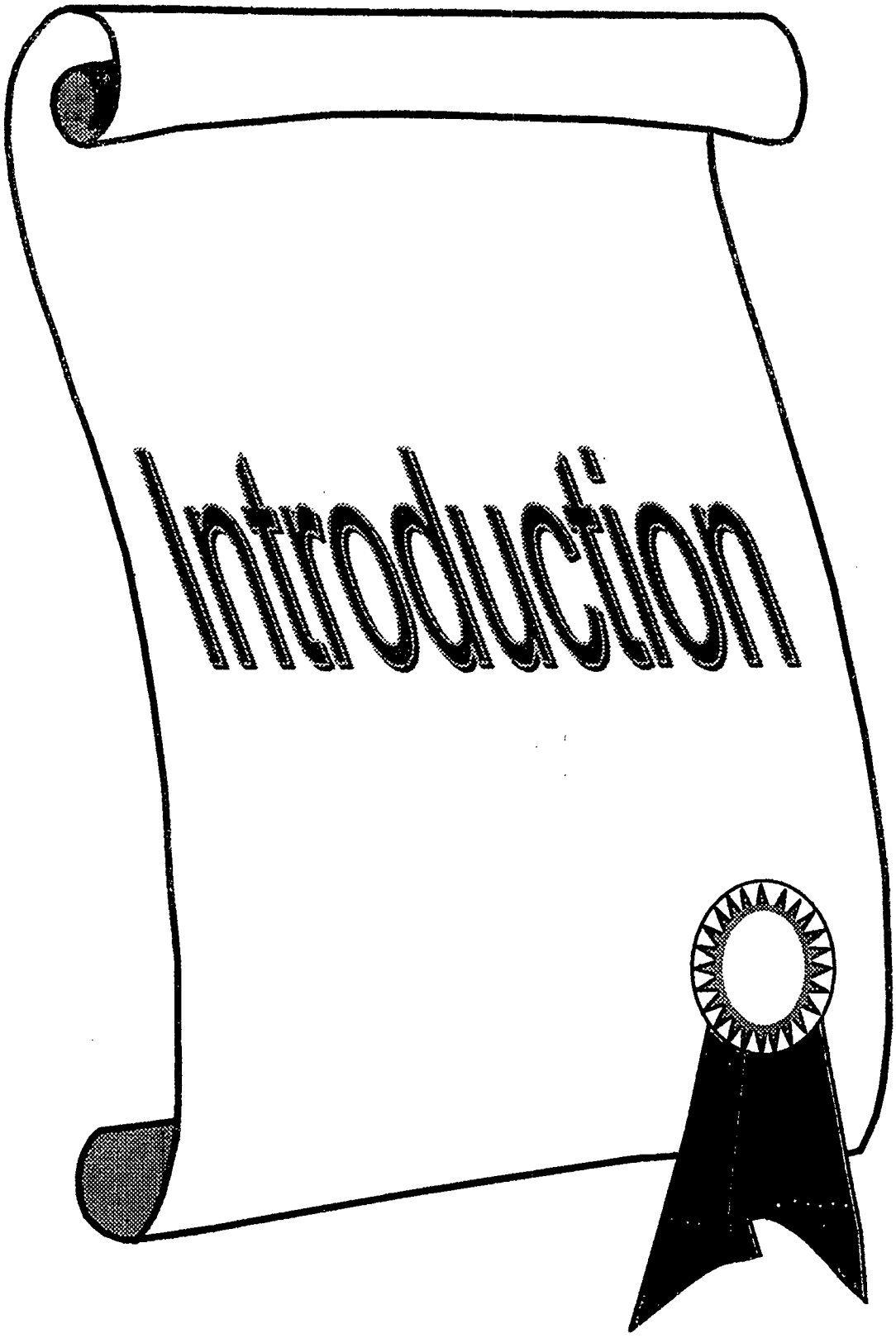
Introduction

ACANTHOSIS NIGRICANS

Acanthosis nigricans (AN) is a symmetric eruption characterized by a hyperpigmented, velvety, mucocutaneous thickening that can occur on any part of the body. It characteristically affects the axillae, nape and sides of the neck, groins, submammary, antecubital and popliteal surfaces, umbilical area as well as the eyelids, vulva, lips, and the buccal, pharyngeal, and laryngeal mucosae.[1]

History

The history of discovery of AN, for the first time, returns back to the nineteenth century when Sigmund Pollitzer in 1889 reported a female patient aged 62 years presented with a hyperpigmented eruption of the mouth, neck, upper extremities, trunk, and genitocrural area.[2] Pollitzer gave the disease the name "acanthosis nigricans" (*acantho,* from the Greek "thorn", which means a sharp pointed outgrowth on a plant, and *nigricans,* from the Latin "becoming black"). Although this patient was originally believed to have an abdominal carcinoma, this could not be confirmed and no autopsy was permitted.[3] Darier used the term *dystrophie papillaire et pigmentaire* to describe similar pigmentation in two patients, one of whom died of an abdominal carcinoma.[4]

By 1909, approximately 50 patients with AN had been described. The

association of AN, in adults, with highly malignant abdominal cancers became clear.[5] Acanthosis nigricans was identified as the foremost cutaneous marker of internal malignancy, and malignant AN was labeled as an obligate paraneoplastic syndrome.[1]

Curth defined the benign and malignant forms of AN and showed that malignant AN is not itself malignant,[6] but rather, it is usually associated with a highly aggressive and rapidly fatal internal malignancy.[7]

Curth divided AN into four types: malignant, benign, syndromic, and pseudoacanthosis nigricans. The last was used to denote skin changes identical to benign AN, but associated with obesity. This term should be abandoned in favor of "obesity-associated AN".[8] The major advance in the understanding of non-malignancy associated AN came in 1976 when Kahn *et al* categorized six patients with AN and marked insulin resistance (IR) into two unusual syndromes; *type A syndrome* with signs of virilization or accelerated early growth with coarse features and *type B syndrome* with signs of an immunologic disease and circulating antibodies to insulin receptors.[9]

Epidemiology

The incidence of AN in an unselected population of 1412 children (Galveston, Texas, USA) was 7.1 %. Regarding sex, the incidence of AN was roughly equal where 52.5% were boys and 47.5% were girls. The prevalence

of AN was 5.7% at age 11, 9.3% at age 12, 6.6% at age 13, 7.1% at age 14, 7.8% at age 15, and 6.5% at age 16.[10] A study of women without diabetes mellitus (DM) found AN only in obese, hirsute, hyperandrogenic women.[11]

The malignant form of AN is far less common, and in one study, only 2 of 12,000 cancer patients were noted in 10 years.[12] Acanthosis nigricans unassociated with malignancy may be present at birth or may occur during puberty or early adulthood, but it can also occur at any age.[13]

Nearly 40% of Native Americans have AN, whereas about 13% of African Americans, 6% of Hispanics, and less than 1% of Caucasians may have the disease.[14] In the familial type, AN seems to be transmitted in an autosomal dominant fashion with variable phenotypic penetrance.[15] In general, black obese persons are more likely to have AN than white obese ones.[1]

However, the exact incidence of AN is unknown and it is unusual even in patients with cancer. Young patients with malignant AN have been described, usually in association with gastric cancer. Malignant AN occurs in both sexes nearly equally and has no apparent racial or geographic predilection.[16]