

## Cutaneous Manifestations of Endocrine Diseases

Walter K.H. Krause

# Cutaneous Manifestations of Endocrine Diseases

With the cooperation of Nathalie Stutz  
Foreword by Serge Jabbour

 Springer

**Em. Prof. Dr. med. Walter K. H. Krause**

Philipps-University Marburg  
University Hospital  
Department of Dermatology  
Deutschhausstr. 9  
35033 Marburg, Germany

With the cooperation of:

Dr. med. Nathalie Stutz  
University Hospital Marburg  
Department of Dermatology  
Germany

ISBN: 978-3-540-88366-1

e-ISBN: 978-3-540-88367-8

DOI: 10.1007/978-3-540-88367-8

Library of Congress Control Number: 2008936138

© 2009 Springer-Verlag Berlin Heidelberg

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permission for use must always be obtained from Springer. Violations are liable to prosecution under the German Copyright Law.

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Product liability: The publishers cannot guarantee the accuracy of any information about dosage and application contained in this book. In every individual case the user must check such information by consulting the relevant literature.

*Cover design:* Frido Steinen-Broo, eStudio Calamar, Spain

Printed on acid-free paper

9 8 7 6 5 4 3 2 1

springer.com

# Foreword

Hormones are known to be essential in regulating physiologic processes in each system of the body, including the skin. Endocrine diseases, through excess or deficiencies of hormones, can result in changes in cutaneous function and morphology and lead to a complex symptomatology. Dermatologists may see some of these skin lesions first, either before the endocrinologist, or even after the internist or specialist has missed the right diagnosis. Because some skin lesions might reflect a life-threatening endocrine or metabolic disorder, identifying the underlying disorder is very important, so that patients can receive corrective rather than symptomatic treatment.

In this textbook, “Cutaneous Manifestations of Endocrine Diseases”, common and rare endocrine disorders are discussed, with major emphasis on skin manifestations and a brief section on aetiopathogenesis, histopathology and treatment. The list of chapters is exhaustive and offers the dermatologist an excellent overview of the skin lesions resulting from dysfunction of the endocrine system, including diabetes mellitus, obesity, hyper and hypothyroidism, pheochromocytoma, Cushing’s, adrenal insufficiency, acromegaly, diabetes insipidus, hyper and hypoparathyroidism, androgen and estrogen excess, pregnancy, and rare syndromes such as carcinoid, glucagonoma, multiple endocrine neoplasia (MEN), autoimmune polyglandular endocrinopathies and other genetic disorders.

Of paramount importance are the chapters on corticosteroids, androgens and estrogens because they constitute the majority of skin-related referrals to dermatologists. Glucocorticoids, either systemic or topical, are commonly used by many physicians to treat a wide variety of medical conditions; long-term use at supraphysiological doses usually induces different cutaneous manifestations, identical to what is seen in endogenous Cushing’s. Androgen excess is one of the most frequent problems in women of reproductive age; the main causative disease being polycystic ovary syndrome. In postmenopausal women, it is estrogen deprivation which leads to skin changes. In men, mostly older than 50 years, gynecomastia is a common problem, although these patients will probably not present to the dermatologist unless there are obvious cutaneous signs such as inflammation.

This special and outstanding book is an excellent educational reference for dermatologists and will help them recognize the endocrinopathies causing the various skin lesions they see on a daily basis to provide their patients with the best treatment.

**Serge Jabbour, MD, FACP, FACE**  
**Associate Professor of Clinical Medicine**  
**Division of Endocrinology, Diabetes & Metabolic Diseases**  
**Jefferson Medical College, Thomas Jefferson University**  
**Philadelphia, PA 19107, USA**

# Preface

Skin lesions are important features of many endocrine diseases. Often skin lesions are the first symptom of the disease and lead to the diagnosis. Their description is thus of relevance for early diagnosis and treatment of endocrine disease for specialists in endocrinology as well as in dermatology. Although several skin manifestations of endocrine diseases are illustrative and well-known already to medical students, e.g. Cushing syndrome or acromegaly, in many other diseases the association with endocrine diseases is less clear and self-evident. Mostly, the features are associated with the physiological effects of the hormones to the skin, for the skin is the target organ for a variety of hormones. In endocrine overproduction, the skin lesions are identical as in over dosage of exogenous hormones. In general, skin lesions do not need a special treatment, but their symptoms vary with the intensity of the endocrine disease.

This book describes the clinical and histological features of skin lesions observed in several endocrine diseases. The illustrations show examples of the clinical and histological features. The source of the illustrations is the photo archive of more than 20,000 clinical pictures of the Department of Dermatology, obtained over more than four decades, and a database of a similar number of histological samples. The chapters are arranged according to the order of endocrine diseases in the leading textbook of endocrinology, William's *Textbook of Endocrinology*, thus illustrating the selection of chapters to endocrinologists and enabling them to find descriptions of skin lesions in the diseases they know. The features themselves are described in the language of dermatologists and dermatohistologists to enable the specialists to associate the features observed with the endocrine aetiology. It is a special concern of this book to consider the current scientific literature in the description of aetiopathogenesis and treatment of the cutaneous diseases and to offer the clinician a tool to manage the diseases.

**Marburg, 2008**

**Walter K.H. Krause**

# Contents

<b>1</b>	<b>Posterior Pituitary Hormone, Diabetes Insipidus</b> .....	1
1.1	Idiopathic Diabetes Insipidus.....	1
1.2	Langerhans Cell Histiocytosis .....	2
	References.....	6
<b>2</b>	<b>Anterior Pituitary Hormones</b> .....	9
2.1	Acromegaly.....	9
2.2	Growth Hormone as a Youth Hormone.....	13
2.3	Pigmentation Disorders.....	13
	References.....	20
<b>3</b>	<b>Thyroid Hormones</b> .....	23
3.1	Myxoedema and Related Disorders.....	24
3.1.1	Myxoedema .....	24
3.1.2	Scleromyxoedema.....	26
3.1.3	Nephrogenic Fibrosing Dermopathy.....	30
3.2	Hyperthyroidism .....	31
	References.....	33
<b>4</b>	<b>Disorders of Calcium Homoeostasis</b> .....	35
4.1	Hypoparathyroidism and Impetigo Herpetiformis.....	36
4.2	Hyperparathyroidism .....	39
4.2.1	General Cutaneous Symptoms.....	39
4.2.2	Calcinosis Cutis .....	39
4.2.3	Calciphylaxis.....	40
	References.....	43
<b>5</b>	<b>Adrenocortical Hormones</b> .....	45
5.1	Addison Disease .....	46
5.2	Cushing Syndrome.....	47
5.3	Drug-Induced Hypercortisolism .....	50
	References.....	56

<b>6</b>	<b>Endocrine Hypertension, Pheochromocytoma</b> .....	59
	References.....	61
<b>7</b>	<b>Androgens</b> .....	63
	7.1 Androgens in the Male.....	64
	7.1.1 Hypogonadism.....	64
	7.1.2 Androgen Deficiency of the Aging Male.....	66
	7.1.3 Acne Fulminans.....	71
	7.2 Androgen Excess in the Female.....	73
	7.2.1 Seborrhoea.....	73
	7.2.2 Acne.....	74
	7.2.3 Hirsutism.....	76
	7.2.4 Androgenetic Alopecia.....	79
	7.3 Dehydroepiandrosterone.....	79
	References.....	83
<b>8</b>	<b>Estrogens</b> .....	87
	8.1 Hyperestrogenism in the Male.....	88
	8.1.1 Gynaecomastia.....	88
	8.1.2 Skin Diseases of the Male Nipple.....	91
	8.2 Estrogens in the Female.....	92
	8.2.1 Climacteric Skin.....	92
	8.2.2 Autoimmune Estrogen Dermatitis.....	97
	8.2.3 Unilateral Nevoid Telangiectasia.....	98
	8.2.4 Melanoma and Estrogens.....	99
	References.....	100
<b>9</b>	<b>Gestagens</b> .....	103
	9.1 Pregnancy Dermatoses.....	104
	9.1.1 Specific Dermatoses of Pregnancy.....	104
	9.1.2 Pigmentation Disorders.....	110
	9.1.3 General Skin Diseases and Striae Gravidarum.....	111
	9.1.4 Pregnancy and Skin Tumours.....	113
	9.2 Autoimmune Progesterone Dermatitis.....	114
	References.....	117
<b>10</b>	<b>Diabetes Mellitus and Glucagonoma</b> .....	121
	10.1 Diabetes Mellitus.....	122
	10.1.1 Diabetic Dermopathy.....	122
	10.1.2 Skin Reaction to Insulin Therapy.....	126
	10.1.3 Necrobiosis Lipoidica Diabeticorum.....	129
	10.1.4 Scleredema Adulorum.....	131
	10.2 Glucagonoma Syndrome.....	133
	References.....	137



---

<b>11 Obesity</b> .....	143
References .....	151
<b>12 Intestinal Hormones</b> .....	155
12.1 Acanthosis Nigricans .....	155
12.2 Carcinoid Syndrome .....	157
References .....	161
<b>13 Polyendocrine Disorders</b> .....	163
13.1 Multiple Endocrine Neoplasias and Lichen Amyloidosis .....	163
13.2 Autoimmune Polyendocrinopathy Syndrome Type I .....	166
References .....	169
<b>14 Genetic Syndromes Including Endocrinopathies</b> .....	173
14.1 NAME Syndrome (Carney Complex) .....	174
14.2 POEMS Syndrome .....	176
14.3 McCune–Albright Syndrome .....	178
14.4 Neurofibromatosis Type 1 .....	180
References .....	185
<b>15 Endocrine Cells of the Skin</b> .....	189
15.1 Merkel Cell Carcinoma .....	189
References .....	194
<b>Index</b> .....	195

# List of Abbreviations

AAS	Anabolic-androgenic steroids
ABCD	Asymmetry – border – colouration – diameter
ACTH	Adrenocorticotrophic hormone
AEP	Atopic eruption of pregnancy
AFA	Acromegaloid facial appearance
AGA	Alopecia androgenetica
AIRE	Autoimmune regulator gene
AN	Acanthosis nigricans
APD	Autoimmune progesterone dermatitis
APS	Autoimmune polyendocrinopathy syndrome
APUD	Amine precursor uptake and decarboxylation system
BPH	Benign prostatic hyperplasia
BRCA	Breast cancer gene
cAMP	Cyclic adenosinmonophosphate
CI	Confidence interval
CK	Cytokeratin
CMC	Chronic mucocutaneous candidiasis
CTGF	Connective tissue growth factor
DHEA-(S)	Dehydroepiandrosterone (sulfate)
DI	Diabetes insipidus
DMSO	Dimethylsulfoxide
EGF	Epithelial growth factor
ER	Estrogen receptor
FGF	Fibroblast growth factors
FPHL	Female pattern hair loss
GH	Growth hormone, somatotropin
GnRH	Gonadotropin releasing hormone
G-protein	Guanine nucleotide-binding proteins
HDL-C	High-density lipoprotein
HHV-8	Herpesvirus 8
HRT	Hormone replacement therapy
ICP	Intrahepatic cholestasis of pregnancy
IDDM	Insulin dependent diabetes mellitus
Ig	Immunoglobulin

---

IGF	Insulin-like growth factors
IHH	Idiopathic hypogonadotropic hypogonadism
IL-2	Interleukin-2
IRS	Insulin-resistance syndrome
LA	Lichen amyloidosis
LCH	Langerhans cell histiocytosis
MC1-R	Melanocortin-1 receptor
MCC	Merkel cell carcinoma
MCV	Merkel cell polyomavirus
MEN	Multiple endocrine neoplasia
MIF	Macrophage migration inhibitory factor
MMAS	Massachusetts Male Aging Study
MMP-1	Matrix metalloproteinases protein 1
MPHL	Male pattern hair loss
MSH	Melanocyte stimulating hormone
NAME	Nevi, atrial myxoma, mucinosis of the skin, endocrine overactivity
NF-1	Neurofibromatosis type I
NFD	Nephrogenic fibrosing dermopathy
NGF	Nerve growth factor
NLD	Necrobiosis lipoidica diabetorum
NME	Necrolytic migratory erythema
PAI-1	Plasminogen activator inhibitor type 1
PAS	Periodic acid Schiff reagents
PCOS	Polycystic ovary syndrome
PEP	Polymorphic eruption of pregnancy
PF	Pruritic folliculitis of pregnancy
PG	Pemphigus gestationis
POEMS	Polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes
POMC	Pro-opiomelanocortin
PRKAR1A	Protein kinase A regulatory subunit-1-alpha gene
PSA	Prostate specific antigen
PTH	Parathyroid hormone
PUPPP	Pruritic urticarial papules and plaques of pregnancy
S(HSI)O2	Sum of haemoglobin saturation
SHBG	Sexual hormone binding globulin
SSSS	Staphylococcal scalded skin syndrome
TEN	Toxic epidermal necrolysis
TGF	Tumour growth factor
TIMP-1	Tissue inhibitor of matrix metalloprotease protein
TK-R	Tyrosine kinase receptor
TNF	Tumour necrosis factor
TSH	Thyroid stimulating hormone
UV	Ultraviolet
VEGF	Vascular endothelial growth factor