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Diagnostics of Endocrine Function in Children and Adolescents
3rd revised and extended edition

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Editor

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114 figures and 88 tables, 2003
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When the first edition of this volume appeared in 1992, it soon became clear that a second edition would follow in order to incorporate the new developments in pediatric endocrinology. The second edition was published in 1996, and further, significant expansions in knowledge have made this new edition necessary. These include the discoveries in molecular genetics which dominated the biosciences in the past decade. It cannot be denied, however, that the prime professional challenges for the physician are to identify clinical symptoms, arrive at a definite diagnosis, and select the most appropriate treatment for each individual patient.

The encouraging response to the first two editions of this book and the readers’ appreciation of its value at various stages of the diagnostic process have led to our decision to adhere to the original format of the chapters, which are a combination of in-depth discussion of the diagnostic process, succinct, practical conclusions, and expert advice deriving from extensive experience. One unique feature of this third edition is that, in light of the wealth of new information and recent discoveries in some fields, most of the contributors offer the readers completely revised chapters. Thus, this edition incorporates several aspects which could not be dealt with previously, such as new information on congenital hyperinsulinaemic states, steroid analysis by GCMS, specific elements in the prematurely born and the neonate, bone development, and the influence of weight changes on the diagnostic process.

This edition also offers improved flow charts which illustrate the differential diagnoses of frequently-encountered disorders that, understandably, continue to be the subject of debate.
It is my sincere hope that the new information, coupled with all of the improvements and revisions, will enhance the value of this book as a guide and reference work in the field of endocrine diagnostics in children and adolescents. I would like to thank all the contributing authors for their co-operation, thoroughness and patience. I am also grateful to Priscilla Herrmann (University Children’s Hospital, Tübingen, Germany) and Thomas Nold (Karger Publishers, Basel, Switzerland) for their support of this project, without which the production of this third edition would not have been possible.

Tübingen, June 2003

Michael B. Ranke
Preface to the Second Edition

The first edition of this volume received a favorable response from readers, who also provided many constructive suggestions for improvements. These and the many new developments in pediatric and adolescent endocrinology have led to a completely revised and expanded second edition. New chapters relating to molecular genetics, imaging methods using radionuclides, sequential hormone measurements, and the measurement and diagnostic relevance of urinary growth hormone have also been added to expand the coverage of areas that were not exhaustively treated in the first edition. An appendix of flow charts illustrating the differential diagnosis of frequently encountered hormonal and metabolic disorders has also been included at the end of the volume to provide physicians with quick guidance on how to deal with complex diagnostic situations.

It is my hope that these revisions will further enhance the value of the book as a practical guide and reference to the diagnosis of endocrine and metabolic disorders in pediatric and adolescent patients. My thanks go to the contributing authors for their collaboration in this project, as well as to Dr. Susan Kentner of Edition J & J for her tireless editorial support, without which the production of this second edition would not have been possible.

Tübingen, July 1996

Michael B. Ranke
Preface to the First Edition

In terms of sheer numbers, hormonal disorders in children and adolescents occupy a significant place in pediatrics. Research in pediatric endocrinology has progressed to the point where it is now possible to arrive at a precise diagnosis of the most important endocrine disorders, classify them exactly according to pathophysiology, and provide treatment based on rational criteria. New molecular genetic techniques have increased our understanding of a variety of pathologic conditions, and the ability to produce hormones biosynthetically has rapidly broadened the spectrum of therapeutic methods at our disposal.

In light of these developments, it seems particularly important for the physician to be able to proceed from the observation of clinical symptoms to the correct diagnosis and the appropriate therapy by following a series of rational diagnostic steps. In most textbooks of pediatrics, methods of diagnosing endocrine disorders in children and adolescents are given little space with no mention of specific details. The objective of this volume is therefore to describe in depth methods for the functional diagnosis of the most important hormonal disorders occurring in pediatric age groups. Special emphasis is placed on evaluating the methods discussed in terms of their clinical relevance. Normal values for hormonal parameters and test results are presented, together with a discussion of methodologic problems and more recent techniques that have not yet become firmly established diagnostic procedures. The intention is to provide a judicious mixture comprising not only knowledge based on long-established diagnostic procedures and confirmed test results, but also reflecting the personal experience of the contributing authors with a variety of newly developed and less well-established test procedures. This combination provides
a picture of the problems associated with functional endocrinologic diagnostics that is at once extremely varied, but always relevant to actual clinical practice.

I thank all the authors for contributing their knowledge and expertise to realize this volume. Special thanks also go to Dr. Susan Kentner, who has guided the publication of the volume with experience and patience.

Tübingen, January 1992

Michael B. Ranke
Before Using This Book

Michael B. Ranke

The pediatrician is frequently confronted with disorders of endocrine function and deviations from normal growth patterns. Diagnosing such conditions often demands detailed knowledge of childhood developmental processes, profound clinical experience, and an understanding of the intricate interaction of metabolic and endocrine factors. At the same time, we are fortunate in having a diverse and well-validated arsenal of diagnostic methods at our disposal.

This volume presents the diagnostic approaches, test procedures, and normative data required to establish diagnoses for a broad spectrum of endocrine disorders. It is hoped that the reader will use this book to obtain reference values for various diagnostic parameters. In this regard, however, it is appropriate to provide a few preliminary words of caution on how to evaluate the information presented in this volume:

(1) The diagnostic approaches outlined here are based on the profound experience of the authors and reflect the state of the art. Nevertheless, other diagnostic paths not discussed in this volume, that are based on different traditions and experience, may also be useful.

(2) Test results may depend on a variety of circumstances related to the individual tested and the test modalities. With regard to the latter, for example, the time of day at which a test is administered may be of particular importance. Specific normative data need to be established for procedures performed at special times during the day owing to circumstances within a particular clinical setting. In special situations, certain requirements (e.g., fasting state) must be fulfilled.

(3) Standard hormone measurements are performed today in many laboratories, and often a multitude of assays are available for the same hormone.
Assay performance and the quality of the results obtained can therefore vary considerably depending on the laboratory and the assay used. Reference data are therefore only valid for the method used and for the laboratory that has established them. The data published in this volume can thus only be taken as guidelines for normative data when different methods are employed.

(4) In general, it is important that those interpreting the results of hormone measurements be familiar with the methods used, the conditions under which they are employed, and the quality of the results obtained with them. If the clinician has no control over the characteristics of a particular assay (e.g., because an outside laboratory is performing it), he or she should obtain the relevant information from the laboratory. In particular, it should be kept in mind that an assay that works well for adults may not be appropriate for children, e.g., because of differences in the relevant range of concentrations or because of other interfering factors specific to the child’s developmental stage.

(5) Each investigator should make an effort to establish normative data with the methodology at his or her disposal. As a minimal requirement, investigators should acquire sufficient experience to develop a ‘feeling’ for the results of a given method in order to be able to judiciously evaluate the figures supplied by the laboratory performing the assay. The latest fashions in methodology may not necessarily serve the needs of either the investigator or the patients – neither do shortcuts imposed by economic considerations. The reader is therefore urged to study not only the tables included in this book, but also the methodological analyses presented by each author in order to gain the critical confidence required to counsel and treat patients.