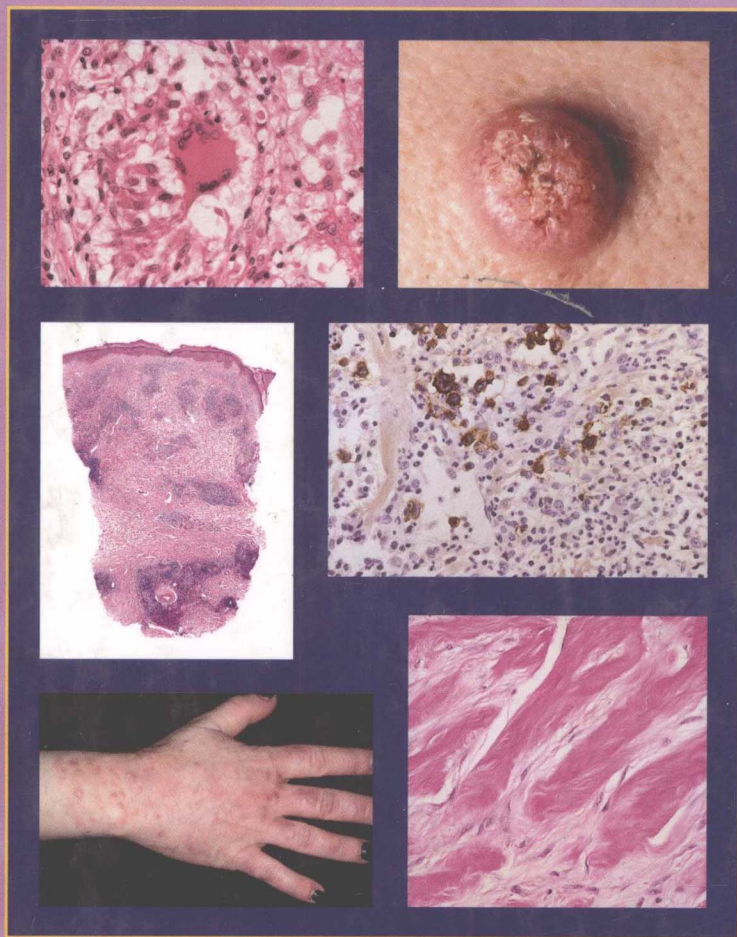


Atlas and Synopsis of

DVD-ROM
Included

Lever's Histopathology of the Skin

SECOND EDITION



David E. Elder
Rosalie Elenitsas
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Health

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Lever's Histopathology of the Skin

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Preface to the Second Edition

In this new edition, we have extensively updated the text, based on review of the recent literature, and also on material from the recently published ninth addition of “Lever’s Histopathology of the Skin”. We have added a more extensive discussion of a score or more diseases that were either not covered, or simply mentioned with little or no elaboration in the first edition. We have added more than 160 new microscopic and clinical images, while aiming to keep this volume reasonably small, manageable, and affordable. We have retained and enhanced the overall organization and format of the book.

Again, we acknowledge our gratitude to authors of all of the present and past editions of “Lever”, and these individuals are listed in the Acknowledgment.

As in the first edition, we would emphasize that this book is not intended to be a comprehensive discussion of all the details of the clinical and histologic features of skin disease. Nevertheless, we have found it to be a useful addition to our armamentarium of reference and teaching dermatopathology texts, particularly as an aid to the understanding of cutaneous reaction patterns and the development of differential diagnoses on the part of trainees, as well as more experienced observers. We hope that our readership will also find it of value in their practices and in their educational activities.

DAVID E. ELDER
PHILADELPHIA, PENNSYLVANIA

Preface to the First Edition

As defined by its title, this volume has been planned and executed as a synopsis and atlas of *Lever's Histopathology of the Skin*. The histopathology of the skin, or dermatopathology, is an important subspecialty discipline of both dermatology and pathology, sharing the language and concepts of each of these major specialties. Comprehensive texts of dermatopathology are typically large and ponderous (both in literary style and in physical weight). These heavy texts serve as excellent references to the literature and provide comprehensive descriptions of a majority of the known classified diseases. However, the knowledge they contain is excessive, in many cases, for readers who may be studying for a nonspecialty board examination, or certainly for residents in the early period of learning their discipline. A more synoptic text can fill this gap by providing information that is selected to provide a framework for future learning, as well as a first step toward the development of basic diagnostic skills in the subject.

The synopsis presented in this book has been literally derived and shortened from the original text published as the eighth edition of *Lever's Histopathology of the Skin* in 1997. Accordingly, we as editors acknowledge a debt of gratitude to the contributors to that edition, who are listed in the Acknowledgments of this book. In a few instances, we have used photomicrographs that were contributed by others to the eighth edition, and in these cases we have specifically acknowledged the contributor in the figure legends. Most of the color photomicrographs in this volume have been painstakingly prepared, to ensure consistency, by Michael Ioffreda. The case material used for these photomicrographs has been taken almost exclusively from cases seen by the Penn Cutaneous Pathology Section of the Department of Dermatology at the Hospital of the University of Pennsylvania, selected by Bennett Johnson, Rosalie Elenitsas, and Michael Ioffreda. Some of the material has been taken from the Course in Dermatopathology offered annually under the direction of Drs. Elenitsas and Johnson. Some additional cases have been identified from the files of the Section of Surgical Pathology at the Hospital of the University of Pennsylvania. Other new material in this volume includes an excellent series of clinical photographs of fine quality derived for the most part from the collections of our father-and-son colleagues, O. Fred Miller and Jeffrey J. Miller. These clinical images, which represent the gross pathology of the diseases, will no doubt be especially useful to those who may not be in regular contact with patients suffering from a large variety of common and uncommon skin diseases.

Traditionally, dermatopathology texts have been organized according to a classification of diseases by a combination of pathophysiologic and clinicopathologic criteria. As discussed in more detail in the Introduction, this approach may serve well as a compendium of multiple disease characteristics, but it does not truly parallel the way in which common reaction patterns may present in histopathological material. These reaction patterns often appear similar in different diseases, which may therefore be difficult or impossible to distinguish from one another in a histology preparation. As a result, the reader of a traditional text will often have difficulty building a histological differential diagnosis because the histological look-alikes are covered in different chapters of the text. In this volume, the subject matter is organized according to the major patterns and cell types that may be involved in the morphological expression of various disease entities in different levels of the skin and subcutaneous tissues. This organization should facilitate an understanding of the way in which different diseases may induce similar reaction patterns in the skin, and should aid in developing a more comprehensive differential diagnosis for a given case.

In selecting the materials to be covered in this volume, we have attempted to provide at least one important example of essentially all of the possible reaction patterns in the skin. For those diseases

considered prototypic of particular reaction patterns, we have provided brief synopses of clinical aspects and histopathology. We have also attempted to illustrate the major entities in the differential diagnosis of the prototypes, usually with an associated text synopsis. In this manner, we have attempted to cover most of the important dermatological diseases (for example, those that might be covered in a board review course for dermatology residents) in one or more sections of the book. Of course, the book is not intended to provide coverage as comprehensive or exhaustive as that in the heavy texts.

This book is directed to all students of dermatopathology, including perhaps some medical students, but in particular pathology and dermatology residents and practicing dermatologists and pathologists. In addition, this book could benefit those family practitioners who do skin biopsies and would like to have a better understanding of the pathology reports that they receive from their laboratories. The particular contributions of this book to the educational experience or diagnostic armamentarium of its readers should include an appreciation for the relationships between clinical and microscopic morphology of the common diseases of the skin, and for the manner in which different diseases may present with similar reaction patterns and thus simulate one another. This should result in an enhanced understanding of the process of differential diagnosis development for unknown skin lesions, and thus in greater diagnostic accuracy.

DAVID ELDER
PHILADELPHIA, PENNSYLVANIA
JUNE 1998

Acknowledgments

This Synopsis has been prepared in part from the eighth and ninth editions of *Lever's Histopathology of the Skin*. Accordingly, we wish to acknowledge the contributors to those editions for their part in the development of the material that we have presented here in a considerably edited form. If any errors are present in this material, however, it is not attributable to these individuals, but to us.

Among the contributors listed alphabetically below, we wish to acknowledge first and foremost the contributions of the founding author of this text, Walter Lever MD, and of his spouse and collaborator, Gundula Schaumberg-Lever, MD

Others to whom we are grateful for assistance in the preparation of this work include many colleagues who have supported our effort, either in the form of helpful discussion, or by the provision of materials used in the book. These include our staff colleagues and the residents and fellows at Penn, Hershey, and Geisinger. Several colleagues have graciously provided materials from their collections to complete our work. These colleagues are acknowledged in the text.

The authors of the previous editions of "Lever" are listed below, as a token of our appreciation for their indispensable contributions.

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Introduction

In this work, it is our goal to provide the reader with an expanded introduction to the concept of diagnosis of cutaneous disease by pattern analysis. This concept was developed by others in a body of work stretching back more than 30 years, and was adapted by us in an introductory form in Chapter 5 of the VIIIth and IXth Editions of Lever's Histopathology of the Skin.

As we stated in those chapters, the diagnosis of disease concerns the ability to classify disorders into categories that predict clinically important attributes such as prognosis, or response to therapy. This permits appropriate interventions to be planned for particular patients. A complete understanding of this process would involve mastery of the stages of disease, the mechanisms of changes in morphology over time, and the molecular, cellular, gross clinical and epidemiological reasons for the differences among diseases. However, in practice, many diseases are successfully diagnosed using only a few of their distinguishing features or "diagnostic attributes".

As there are hundreds of diseases, each having potentially scores of diagnostic attributes, it is evident that an efficient strategy must be employed to enable diagnoses to be considered, dismissed, or retained for further consideration. Observation of an experienced dermatopathologist at work reveals a rapidity of accurate diagnosis that precludes the simultaneous consideration of more than a few variables. The process of diagnosis by an experienced dermatopathologist (as in other fields of medicine) is quite different from that employed by the novice, and is based on the rapid recognition of combinations or patterns of criteria [1,2]. Just as the recognition of an old friend occurs by a process that does not require the serial enumeration of particular facial features, this process of pattern recognition occurs almost instantly, and is based on broad parameters that do not at least initially require detailed evaluation.

In clinical medicine, patterns may present as combinations of symptoms and signs, or even of laboratory values, but in dermatopathology, the most predictive diagnostic patterns are recognized through the scanning lens of the microscope, or even before microscopy, as the microscopist holds the slide up to the light, to evaluate its profile and distribution of colors. Occasionally, a specific diagnosis can be made during this initial stage of pattern recognition, by a process of "gestalt" or instant recognition, but this should be tempered with a subsequent moment of healthy analytical scrutiny. More often, the scanning magnification pattern suggests a small list of possible diagnoses, a "differential diagnosis". Then, features that are more readily recognized at higher magnification may be employed to differentiate among the possibilities. Put in the language of science, the scanning magnification pattern suggests a series of hypotheses, which are then tested by additional observations [1]. The tests may be observations made at higher magnification, the results of special studies such as immunohistochemistry, or external findings such as the clinical appearance of the patient, or the results of laboratory investigations. For example, a broad plaque-like configuration of small blue dots near the dermal-epidermal junction could represent a lichenoid dermatitis, or a lichenoid actinic keratosis. At higher magnification, the blue dots are confirmed to be lymphocytes, and one might seek evidence of parakeratosis, atypical keratinocytes, and plasma cells in the lesion, a combination which would rule out lichen planus and establish a diagnosis of actinic keratosis.

Most diagnoses in dermatopathology are established either by the "gestalt" method, or by the process of hypothesis generation and testing (differential diagnosis and investigation) just described, but in either case the basis of the methods is the identification of simple patterns recognizable with the scanning lens that suggest a manageably short list of differential diagnostic considerations. This *pattern recognition method* was first developed in a series of lectures given in Boston by the late Wallace H. Clark [3], and has been

refined since for inflammatory skin disease by Ackerman [4], for inflammatory and neoplastic skin disease by Mihm [5], and most recently by Murphy [6]. The latter authors have published texts based more or less extensively on the pattern classification.

In the work on which this present Synopsis and Atlas is based, the classification of diseases was organized upon traditional lines, in which diseases were discussed on the basis of pathogenesis (mechanisms) or etiology as well as upon reaction patterns. This classification, in our opinion, has the significant advantage of placing disorders such as infections in a common relationship to one another, facilitating the description of their many common attributes. From a histopathological point of view, however, the novice must learn that some infections, such as syphilis, can resemble disorders as disparate as psoriasis, as lichen planus, as a cutaneous lymphoma, or as a granulomatous dermatitis.

Because there is a limited number of reaction patterns in the skin, morphological simulants of disparate disease processes are common in the skin, as elsewhere. For this reason, classification methods based on patterns and those based on pathogenesis are only loosely compatible with each other. An observer who is studying an unknown case has available only the morphological patterns under consideration. Not until the diagnosis is known can the pathogenesis of the disease be well understood. Thus, it is difficult to use a book based on a pathogenic classification as a guide to the diagnosis of an unknown case. To partially circumvent this problem, this book presents a pattern-based classification of cutaneous pathology based on *location in the skin*, on *reaction patterns*, and where applicable on *cell type*. The classification has been based on original lecture notes prepared by the late Wallace H Clark Jr., MD in 1965 (with permission), and on the published works cited above, especially that of Hood, Kwan, Mihm, and Horn [5]. This book is also closely linked with the “big” Lever, and could in fact be used as a morphology based index to that larger volume.

The classification is presented first in tabular form and is redundant, in that a particular disease entity may appear in several positions in the table, because of the morphological heterogeneity of disease processes, which are often based on evolutionary or involutional morphological changes as a disease waxes and wanes. Within each morphological category, one or more disorders considered to be “prototypic” of that category are described and illustrated. For example, lichen planus is the “prototypic” lichenoid dermatitis. The “prototypic” member of each category is emphasized in the detailed descriptions, because such entities constitute the descriptive standard in a given category, and they are also the standard against which other entities are evaluated. For example, drug eruptions may adopt any of a number of morphologies as reflected by their appearance not only in the lichenoid category but also in the psoriasiform, perivascular, and bullous categories as well as elsewhere. A “naked” epithelioid cell granuloma may suggest sarcoidosis, the prototypic epithelioid cell granuloma, while the presence of lymphocytes and necrosis in addition to granulomas might suggest tuberculosis, plasma cells might suggest syphilis, and neuritis might suggest leprosy.

After discussion of the prototypic entity in each category, a list of differential diagnostic possibilities is presented. The order of presentation of particular entities in any given position in this list reflects the authors’ opinion of the relative frequency of the entities in the list, as encountered in a typical dermatopathology practice. For example, lichenoid drug eruption may be more common than lichen planus in most hospital-based practices. Some of these differential diagnostic possibilities are discussed in more detail because of their importance as diseases in their own right. For example, Spitz nevi are discussed in the section that also contains nodular melanoma, keratoacanthomas are discussed along with squamous cell carcinomas, and so on.

The classification tables may be used as the basis of an algorithmic approach to differential diagnosis, or as a guide to the descriptions in other books, including the VIIIth and IXth edition of Lever’s Histopathology of the Skin, from which this book has been summarized. For example, a lichenoid dermatitis comprised of lymphocytes, could represent lichen planus, graft vs. host disease, or mycosis fungoides, patch/plaque stage, whose descriptions are to be found in Chapters 7, 9, and 31 of the “Big Lever” respectively, but are discussed here in juxtaposition in Section IIIF1. Terms such as “psoriasiform” and “lichenoid” are defined briefly in this book, and illustrated extensively, so that the reader may review more specific criteria for the distinctions among morphological simulants. This system of hypothesis generating and testing should lead not only to more efficiency in the evaluation and diagnosis of an unknown case, but should also facilitate the development of pattern recognition skills as more subtle diagnostic clues are absorbed into the diagnostic repertoire to allow for “tempered gestalt” diagnosis in an increasing percentage of cases.

This book is intended as a guide to differential diagnosis but should not be construed as an infallible diagnostic tool. Diagnosis should be based not only on the diagnostic considerations presented here, but

also on those discussed elsewhere in the literature, all considered in a clinical and epidemiological context appropriate to the individual patient.

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In this Atlas, the cutaneous diseases are listed in morphological categories based on their location in the skin, their architectural patterns, and their cytology. The list of diseases in each morphological category serves as a differential diagnosis for unknown disorders that present with the attributes of that category. The diseases are listed in rough order of their expected frequency in an “average” dermatopathology practice. In this Atlas, representative disorders in each category are briefly described and illustrated. More detailed discussions of most of these and the other lesions in the lists can be found in the parent volume.

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