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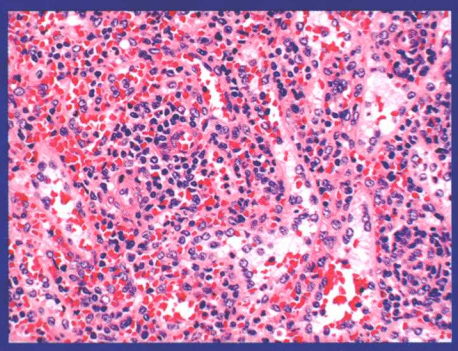
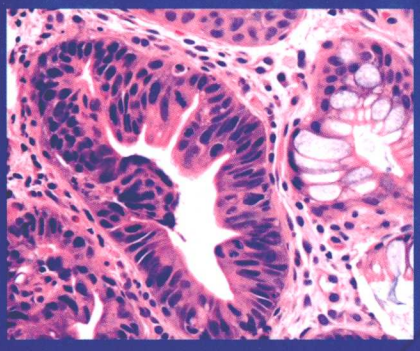
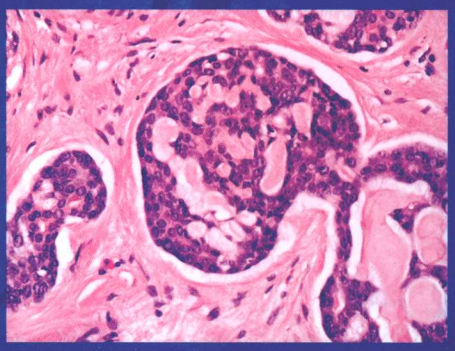
Volume I

STERNBERG'S DIAGNOSTIC SURGICAL PATHOLOGY

6th EDITION

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VOLUME 1

STERNBERG'S Diagnostic Surgical Pathology

SIXTH EDITION

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PREFACE TO THE SIXTH EDITION

The sixth edition of *Sternberg's Diagnostic Surgical Pathology* continues a decades-long effort by the authors and editors to bring thoughtful diagnostic assistance to surgical pathologists at all levels of training and experience. Our goal has always been to emphasize real-life diagnostic problems and pitfalls rather than to simply present "thumbnail sketches" of disease entities. To paraphrase one of our colleagues, "When you already know the diagnosis, almost any pathology textbook will do, but when you really need diagnostic help, this is the textbook you want." The preface to the first edition, reprinted on the next page, sets this tone right from the inception, and we have worked to preserve it in subsequent editions.

As with prior editions, the sixth brings considerable changes in editorship, authorship, and, most importantly, content. The 5 years since the publication of the fifth edition have seen major advances throughout surgical pathology, particularly in immunohistochemistry and molecular pathology. The authors and editors have worked hard to incorporate this new material, including new molecular and immunohistochemical markers for diagnosis and prognosis of neoplasia, improved classification systems for diagnosis and prognosis, the role of pathology in new diagnostic and therapeutic techniques, and the recognition of new entities or variants of entities. Where appropriate, updated World Health Organization terminology has been employed for tumor diagnosis.

Surgical pathology is a visual specialty, and we continue to strive for the best illustrations, all of which have been color balanced by a single individual to bring uniformity to the color illustrations in the text. Reference lists have been considerably updated and, where possible, older references have been eliminated to save space. The editors wish to especially thank the contributing authors, past and present, a veritable "who's who" in surgical pathology for establishing prior editions of this text as a leader in the field and for making the sixth edition the best ever. In addition, we would like to thank the staff of Wolters Kluwer for their unfaltering, enthusiastic support of our text.

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PREFACE TO THE FIRST EDITION

We speak of the loneliness of the long-distance runner, but there may be no one lonelier than a surgical pathologist working solo. Those working in large hospitals have the luxury of being able to consult ad lib with one or more pathologists about a given case, and may even have an associate who is a specialist in the area of difficulty. Easy access to consultation is a prerequisite for accurate diagnosis, and, accordingly, for optimal patient care. It is especially critical in those instances when the busy pathologist has a low level of diagnostic doubt, but this is tempered by the need to sign out the case without consultation because of the press of time. Very difficult cases, those readily recognizable as problem cases, are in a sense less troublesome, as the need for a diagnostic consultation is self-evident. Therefore, knowing when and what one doesn't know is of singular importance.

A pathology reference library is the other information source for the working pathologist. Textbook consultation and human consultation go hand-in-hand. In this text we have attempted to emphasize differential diagnosis of the surgical specimen, and to keep to a minimum discussion of the natural history of disease, treatment and autopsy findings. Although no textbook can take the place of a face-to-face discussion of a diagnostic problem (especially over a multi-headed microscope) between two or more pathologists, we have asked our authors to provide the reader with their reasoning in approaching differential evaluation of a biopsy specimen, thereby giving the flavor of a personal consultation. Moreover, the authors for the various chapters have been chosen based not only upon their recognized knowledge of the specific area, but also upon their skill in written communication. Since surgical pathologic diagnosis is a visual exercise, the book is generously illustrated with color and black-and-white photographs. In addition, the chapter authors have been liberal in their use of references, thereby enhancing the value of their presentations for the reader who wishes additional information.

The Section Editors have worked closely with the chapter authors to ensure that the objectives of the text are met; namely, that it is a treatise on the diagnosis of conditions which confront the surgical pathologist. In summary, the goal of the Editors is that this book will be a working companion, and thereby be accorded a place adjacent to the microscope of the reader.

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†Deceased.

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1 Nonneoplastic Diseases of the Skin

Douglas C. Parker ■ Alvin R. Solomon

Nonneoplastic or inflammatory skin diseases encompass a wide array of pathologic processes ranging from autoimmune to infectious to diseases of unknown etiology. In contrast to neoplastic surgical pathology, the histopathology of inflammatory skin diseases frequently does not exhibit a one-to-one correlation with a single diagnosis and requires correlation with the clinical presentation for a definitive diagnosis. In many instances, the dermatologist is neither looking for nor needs a specific histologic diagnosis. For instance, if the clinical differential diagnosis is between atopic dermatitis and psoriasis, the diagnosis of spongiotic dermatitis conveys the essential information to the clinician and guides appropriate therapy. Although the diagnosis of many inflammatory skin diseases requires correlation with the clinical features, there are critical diagnoses, such as toxic epidermal necrolysis and staphylococcal scalded skin syndrome, which the surgical pathologist may be asked to differentiate.

The most accurate interpretation of the histopathology of inflammatory skin disease is accomplished if the pathologist is cognizant of the clinical differential diagnosis as well as the histopathologic differential diagnosis. The pathologist must insist that an accurate clinical differential diagnosis or impression be submitted in addition to other data such as the age and sex of the patient and the anatomic site of the biopsy. Although dermatopathology specimens should be interpreted objectively, the final interpretation should always be correlated with the clinical findings.

In this chapter, we have divided nonneoplastic skin diseases into various groups based on histopathologic patterns of inflammation (Tables 1.1 and 1.2). This approach is popular because it furnishes a basis for structured learning of these diseases without a prior knowledge of clinical dermatology. Like all classifications, this approach is not perfect, and it falls short at times because of the incredible complexity of the pathologic processes. Few diseases fit exclusively into only one category. Perhaps the best way to use this morphologic approach is to use the metaphor of a framework and superimposed templates. Think of each pattern as the framework and the specific histologic features of each disease as a template. Mentally superimposing the template then results in a modification of the original pattern. For example, in the diagnosis of lichenoid drug reaction, the pattern of lichenoid interface dermatitis is the framework. Superimposing a template of parakeratosis, eosinophils, and plasma cells over the framework leads to the diagnosis of lichenoid drug eruption. Of course, one must learn to recognize the basic patterns for this system to work effectively.

One final important point concerning the histopathologic interpretation of inflammatory skin diseases is that the lesions are dynamic and change is an intrinsic quality. It must be remembered that a biopsy "captures" the histopathology of the lesion at one point in its evolution. Many inflammatory skin diseases may only be readily diagnosed microscopically at certain points within the spectrum of changes. If a lesion is biopsied early or late in its evolution, the microscopic findings may be nondiagnostic.

SPECIMEN PREPARATION

Careful gross processing of skin biopsies is critical for accurate microscopic interpretation. The shave, punch, and elliptical biopsy techniques are most frequently used to obtain skin specimens for microscopic examination.

The elliptical excision is preferred when the disease process involves the deep dermis or subcutis. Superficial fascia can only be obtained reliably with this technique. In our experience, the "bread-loaf" method (sequential serial sectioning) of cutting skin ellipses is best because it is simple, can be performed rapidly, and ensures adequate sampling of the tissue. The skin ellipse is cut perpendicular to the long axis of the specimen at approximately 3-mm intervals. If the cut surface is marked with ink and each tissue slice is embedded in a separate cassette, it is easy to decide which block to recut if additional sections are needed. Some dermatopathologists prefer to section skin ellipses longitudinally in nonneoplastic lesions. For the most part, the choice is a personal one.

The punch biopsy tool is best used to obtain a cylinder of skin that includes the epidermis, dermis, and a small amount of subcutis. Punch biopsies 4 mm in diameter or greater should be bisected before embedding. Smaller punch biopsy specimens are difficult to bisect and should be embedded intact.

The shave or tangential technique (blade parallel to the skin surface) is of limited value for the study of inflammatory skin diseases because only epidermis and superficial dermis are consistently sampled by this method. Shave biopsy specimens should be bisected or trisected if large enough so that a straight edge is available for microtome sectioning. Applying ink to the cut edge with an applicator stick enables the histotechnologist to identify the cut edge.

Ten percent buffered formalin is an excellent general-purpose fixative for skin specimens. Fixation in B5 solution results in the greater preservation of nuclear detail and is especially useful for evaluating lymphocytic infiltrates clinically suspicious for cutaneous lymphoma.

Hematoxylin and eosin (H&E) is the most commonly used routine stain in dermatopathology, but most special stains used

TABLE 1.1 Definitions of Dermatopathology Terms

Term	Definition
Acantholysis	Disruption of intercellular junctions between epidermal keratinocytes, resulting in loss of cohesion and rounding up of the affected cells.
Acanthosis	An increase in the thickness of the stratum spinosum.
Bulla	An intraepidermal or subepidermal blister >0.5 cm. Intraepidermal bullae may be secondary to either spongiosis or acantholysis. Subepidermal bullae can result from disruption of basement membrane components, interface alteration, or dermal edema.
Colloid bodies	Oval to round apoptotic keratinocytes typically found immediately above or below the epidermal basement membrane in interface dermatitis. These are also referred to as *Civatte bodies.*
Dyskeratosis	Abnormal, premature keratinization of keratinocytes. Dyskeratotic keratinocytes have brightly eosinophilic cytoplasm.
Epidermolysis	A distinctive alteration of the granular layer characterized by perinuclear clear spaces, enlarged and irregular keratohyalin granules, and an increase in the thickness of the granular layer. *Acantholysis* and *epidermolysis* are not synonyms; they are different pathologic processes.
Erosion	Partial-thickness loss of the epidermis.
Exocytosis	The presence of inflammatory cells within the epidermis in association with spongiosis.
Hydropic degeneration	See "Vacuolar epidermal interface alteration."
Hyperkeratosis	An increase in the thickness of the stratum corneum. Hyperkeratosis may be either orthokeratotic or parakeratotic. Orthokeratotic hyperkeratosis is an exaggeration of the normal pattern of keratinization (i.e., no nuclei are seen in the stratum corneum). In parakeratotic hyperkeratosis, nuclei are retained in the stratum corneum.
Leukocytoclasis	Karyorrhexis and destruction of neutrophils. It frequently occurs in the setting of neutrophilic vasculitis (i.e., leukocytoclastic vasculitis).
Lichenoid epidermal interface alteration	Destruction of the basal keratinocytes resulting in "remodeling" of the basement membrane zone and associated dyskeratotic keratinocytes. A bandlike lymphocytic inflammatory infiltrate is usually present.
Orthokeratosis	Normal pattern of stratum corneum. Increased in hyperkeratosis.
Papillomatosis	Abnormal elongation of the papillary dermis.
Parakeratosis	Retention of nuclei in the epidermal stratum corneum.
Pseudoepitheliomatous hyperplasia	Acanthosis and hyperplasia of the epidermis in a pattern that mimics squamous cell carcinoma. *Epithelioma* is an archaic term for carcinoma.
Pustule	A subcorneal, intraepidermal, or subepidermal vesicle or bulla filled with neutrophils.
Scale crust	Parakeratotic debris, degenerated inflammatory cells, and fibrinous exudate on the surface of the epidermis.
Spongiosis	Epidermal intercellular edema.
Ulcer	Loss of the entire thickness of the epidermis. The dermis and subcutis may or may not be involved, depending on the depth of the ulcer.
Vacuolar epidermal interface alteration	Destruction of the basal keratinocytes characterized by the presence of intracytoplasmic vacuoles and dyskeratotic keratinocytes. A sparse to mild lymphocytic inflammatory infiltrate is usually present.
Vesicle	A small blister <0.5 cm.

TABLE 1.2 A Few Important Clinical Terms

Term	Definition
Bulla	A large, fluid-filled blister >0.5 cm.
Crust	Fibrinopurulent exudate.
Lichenification	Thickened, rough skin with accentuated skin markings. *Lichenification*, thickening of the skin from chronic rubbing or scratching, is not synonymous with *lichenoid.*
Macule	A flat lesion with change in skin color <1.0 cm.
Nodule	A large, deeply extending papule >1.0 cm.
Papule	A solid elevation of the skin surface <1.0 cm.
Patch	A large flat lesion with change in skin color >1.0 cm.
Plaque	A large, flat-topped papule >1.0 cm.
Scale	Flakes of exfoliated epidermis.
Vesicle	A small, fluid-filled blister <0.5 cm.

in general surgical pathology are also employed. Specific uses of histochemical stains and immunohistochemistry will be discussed along with the diseases in which their use is of value (1–4).

In dermatopathology, it is important to recreate a three-dimensional mental picture of the two-dimensional microscopic sections. In addition, many inflammatory skin diseases are particularly zonal in their microscopic architecture. Therefore, it is frequently helpful to make either step or serial sections from the paraffin block to maximize the yield of information obtainable from the microscopic sections.

Transverse sectioning of punch biopsies from the scalp is frequently used in the diagnosis of alopecia. A detailed discussion of this technique is beyond the scope of this chapter (5–7).

NORMAL HISTOLOGY

The skin comprises three structures: the epidermis, dermis, and subcutis. The superficial fascia marks the deep boundary between the skin and the underlying soft tissues. Regional anatomic variation of the skin is readily apparent if one compares a specimen from the scalp with one from the palm.