

American Journal of Dermatopathology:

April 2002 - Volume 24 - Issue 2 - pp 169-179

Book Reviews

Neoplasms With Follicular Differentiation, 2nd edition

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Neoplasms With Follicular Differentiation, 2nd edition. Bernard Ackerman, Vijaya B. Reddy, and H. Peter Soyer. New York: Ardor Scribendi, 2001, 1,109 pages, \$225.00

Some books are to be tasted, others to be swallowed, and some few to be chewed and digested. - Sir Francis Bacon (1561–1626), *Essays, Of Studies*

To elaborate Bacon's idea: some books entertain, some serve to teach, some serve as a reference, some should be read from cover to cover, and some facilitate contemplation of one's purpose in life. The second edition of *Neoplasms with Follicular Differentiation*, written by Drs. A. Bernard Ackerman, Vijaya B. Reddy, and H. Peter Soyer, is all these things: it is interesting to read; it deals with history, facts, and abstract conclusions; it is exhaustive; it has a message obtained best by reading all of it; and one can learn about philosophy (and contemplate one's own philosophy) by reading it.

AIM

Ackerman and his coauthors state their hopes for the book in their preface:

Articles and chapters that concern follicular neoplasms in general are available, and we commend them to readers. It is accurate to state, however, that virtually every attempt to make lucid the subject of follicular neoplasms has failed because of two severely limiting factors: incomprehensible terminology and illogical classification. In undertaking the second edition of this monograph, as was the case in the first edition, we sought to overcome those hazards by endeavoring to make each proliferation with follicular differentiation diagnosable, definable, and understandable to every reader who seeks to learn about them... (p. IX).

Their aim for this book, identical to that of the first edition, is stated succinctly:

The aim of this book is to provide a method, based on an algorithmic system for histopathologic diagnosis, for specific accurate diagnosis of proliferations with follicular differentiation... (p. 3).

STRUCTURE AND CONTENT

The book is part of the series entitled *Ackerman's Histologic Diagnosis of Neoplastic Skin Diseases: A Method by Pattern Analysis*, which began in 1990 with the publication of *Neoplasms with Eccrine Differentiation* by Drs. Pascual Abenozza and Ackerman. This was followed in 1993 by the first edition of *Neoplasms with Follicular Differentiation*, written by Drs. Ackerman, Pierre A. De Viragh, and Nidhi Chongchitnant. Drs. Charles Steffan and Ackerman produced the third book in the series, *Neoplasms with Sebaceous Differentiation*, in 1994. Drs. Luis Requena, Hiromaro Kiryu, and Ackerman wrote the final book in the series, *Neoplasms with Apocrine Differentiation*, in 1998. This second edition of *Neoplasms with Follicular Differentiation* is the first of the second series of these books.

Ardor Scribendi published the second edition in March 2001; it sells for \$225.00. It contains 1,109 pages (actually 1,140 when the color atlases are counted) in an 8.5-in × 11-in format and weighs 8 lb (compared to the 5-lb first edition). It contains 25 chapters as well as a preface. Two color atlases are present: the first is located in Chapter 5 and covers lesions with all types of follicular differentiation, and the second is located in Chapter 23 and covers the spectrum of trichoblastic (basal cell) carcinoma clinically and histologically. There is a 12-page glossary after Chapter 25. Finally, there is a 19-page index that closes the book.

Compared to the first edition, the second edition has significant physical changes. It contains an additional 464 pages. There are an almost equal number of text pages in the second edition (221.9 in the second edition compared to 226.7 in the first edition); however, the text layout has a two-column format in the second edition, whereas the first edition had a single-column format. The font is slightly smaller in the second edition; thus, I suspect there is actually more text in the new edition. The percentage of text to total pages is 19.5% in the second edition compared to 33.5% in the first edition.

There are 207 additional figures "as stated" in the new edition, making a total of 574 figures. This corresponds to an additional 751 separate high-quality photographs (1,829 total), mostly in black and white, except for the two color atlases that contain 236 photographs on 59 plates (the first edition contained a single color atlas with 15 plates and 60 photographs). Compared to the first edition, there has been a reduction in the number of photographs in chapters dealing with the specific proliferations, except for the chapters on trichoblastoma and trichoblastic carcinoma, both of which are expanded considerably. There are 39 drawings and 25 tables in the second edition, corresponding to an equal number of drawings and 2 more tables than in the first edition. There are 250 additional references in the second edition, making a total of 549, versus a total of 299 in the first edition. The glossary of the new edition defines 78 terms, which is 1 less than the first edition (the term *adenoid cystic* is omitted).

One somewhat subtle change between the first and second editions is how the text relates to the figures. In the first edition, the text in every chapter referenced every figure and table. This is not the case in the second edition. Although Chapters 1 through 5 and Chapter 7 do relate text to figures, the remaining Chapter 6 and Chapters 8 through 25 do not, with rare exception. The text obviously

parallels the figures but does not actually refer to them (except for specific and unusual reasons). The most obvious examples of this are Chapters 22 and 23 on trichoblastoma and trichoblastic carcinoma, in which each neoplastic pattern is discussed in the text and then followed by an atlas of black and white photographs with explanatory notes for each photograph or group of them. For the most part, this is not distracting; I actually found it less distracting than losing my train of thought by being led to a figure from a number in the text. My sense is that there is more continuity in the study of a particular chapter by referring to the atlas in toto rather than moving back and forth from text to figures. In this regard, this book is actually two parallel books: one in text and the other in photographs.

The first seven chapters address the authors' approach to the subject matter as they lay the philosophic and historical groundwork for the particular proliferations addressed in Chapters 8 through 25. They categorize the types of proliferations as malformations, cysts, hamartomas, hyperplasias, and neoplasms (benign and malignant).

There are numerous changes in structure, content, or both, between the first and second editions; the authors acknowledge a few of these, and I synopsise the major changes and additions here, with the exception of Chapters 1 through 3 and Chapters 5, 8, 9, 11, 13, 20, and 21 in the second edition, which are almost identical to their respective chapters in the first edition.

Chapter 4: Anatomic, Histologic, and Biologic Aspects

The chapter on anatomic, histologic and biologic aspects is much the same as in the first edition. The title has been shortened: "of Hair Follicles and Hairs" has been removed. The section on "Anatomic Features and Functions of Hair" has been moved from the introduction to later in the chapter. There are syntax and specific word changes throughout. There is a slightly updated position on the "bulge-activation hypothesis (p. 36). The order of the "Matrical Differentiation" section has changed, now beginning with the inner sheath (p. 52), to hair (p. 54), to outer sheath (p. 55). In the first edition, the progression was from outer sheath, to inner sheath, to hair. In addition, the inclusion of the outer sheath in the section on matrical differentiation seems out of place, because the authors state that:

It must be stressed, too, that the outer sheath is not a product of matrical differentiation, but an extension downward from the isthmus of cells situated at the periphery of the new germ (p. 55).

The figures are mostly the same, albeit in somewhat different order than in the first edition.

Chapter 6: Critique of Current Classifications

The chapter on critique of current classifications of proliferations with follicular differentiation has been changed and simplifies the authors' prior critique in the first edition. In essence, most of the text was deleted and replaced with tables of prior classifications of neoplasms with follicular differentiation. This new critique includes classifications that span 1987 to 1998, deleting Dr. Headington's 1976 classification, retaining the remainder of classifications, and adding the classifications of Drs. Mehregan and his colleagues (1995), Weedon (1997), Elder and his colleagues (1997), Wick and his colleagues (1998), and Maize and colleagues (1988), which I wrote. I believe this critique is much easier to compare from classification to classification than the one in the first edition. Ackerman and his coauthors expose the differences in all the schemes and add their parenthetical comments after each entry. This was clarifying for me, having written one of the chapters they criticize, because it helped me to understand their areas of disagreement with my writing and where I should concentrate my efforts to understand some of the differences in how I had conceptualized these lesions compared to them.

Chapter 7: The Authors' Classification

Although similar in format to the first edition, a direct comparison of the chapter on the authors' classification of proliferations with follicular differentiation in the first and second editions shows in the illustrations how the structure of the book has changed. Hair follicle nevus and trichofolliculoma are now included together (Chapter 10), whereas they appeared as two chapters in the first edition. Folliculosebaceous cystic hamartoma is given a separate chapter (Chapter 12) but was referred to only in comparison to fibrous papule in the first edition. The chapter on trichoblastoma (Chapter 22) has integrated the classic trichoepithelioma (now termed *cribriform trichoblastoma*) and desmoplastic trichoepithelioma (now termed *columnar trichoblastoma*) from the first edition. No longer are these considered in separate chapters. Basal cell carcinoma has now been drawn fully within the fold of adnexal neoplasms and has been termed *trichoblastic carcinoma* (Chapter 23), whereas it was designated as basal cell carcinoma with "follicular differentiation" in the first edition and covered only a small part of the spectrum of those neoplasms. Finally, proliferating tricholemmal cystic squamous cell carcinoma (Chapter 25) is no longer considered a follicular neoplasm, has been dropped from the classification altogether, and is included only as a historical point of reference.

Chapter 10: Trichofolliculoma

The chapter on trichofolliculoma incorporates the concept of trichofolliculoma fully with the concept of hair follicle nevus, combining the separate chapters of the first edition in one unified concept and chapter in the second edition. Whatever doubts about these two concepts that were present in the first edition have been removed in the second edition and for good reason. The authors show convincingly that lesions under each concept are merely two different expressions of the same condition; they are synonyms, but the authors favor the term *trichofolliculoma* to cover both. They also mention briefly a relatively recent addition to the literature that elaborates even further why the variations in this spectrum of lesions exist; it is because the vellus follicles of a trichofolliculoma cycle just as do normal hair follicles. Ackerman and his coauthors separate "sebaceous trichofolliculoma" from classic presentations of trichofolliculoma, because the former lacks vellus follicles that radiate from a central epithelial lining of one or more dilated infundibula. They now classify that condition under "folliculo-sebaceous cystic hamartoma" and take a firm stand on its position, which is a change

from the first edition. Their position then was that the nosologic position of sebaceous trichofolliculoma was unknown.

Chapter 12: Folliculo-Sebaceous Cystic Hamartoma

The chapter on folliculosebaceous cystic hamartoma is a new addition in the second edition; however, much of the writing is not new. It was presented first in 1994, with similar content and illustration, in *Neoplasms with Sebaceous Differentiation* by Drs. Steffan and Ackerman. The reasons for including it in this edition are as follows:

Because folliculo-sebaceous cystic hamartoma is fundamentally follicular (it has features within it of other follicular hamartomas, such as fibrous papule commonly and trichofolliculoma rarely), we have devoted Chapter Twelve in this second edition to it (p. xiii).

Chapter 14: Fibrofolliculoma/Trichodiscoma

The chapter on fibrofolliculoma/trichodiscoma remains much the same as in the first edition, with minor editing of the text and photographs. It is interesting to note that Drs. Steffan and Ackerman, in Chapter 10 of their 1994 book on sebaceous neoplasms, elaborate in some depth about these lesions and their presence in the Birt-Hogg-Dubé syndrome. In that work, much more historic detail was given, even to the point of reprinting photographs from the original articles. I recommend the 1994 chapter as a supplement to this one.

Chapter 15: Induction of Follicles

Some 19 photographs have been pared from the chapter on induction of follicles, but the content is similar to that of the first edition. A few historical references are included in the second edition; this provides a richer context for the evolution of knowledge of this phenomenon. References to follicular induction in nevus sebaceus have been removed from the text but not from the figure captions. The reasons for this are not stated, and it seems somewhat puzzling why these references were removed.

Chapter 16: Tricholemmoma

The chapter on tricholemmoma has been placed before the chapter on inverted follicular keratosis in the second edition. In contrast to my prior understanding (and misunderstanding) of the position of Ackerman and his coauthors on the concept of tricholemmoma, they do not believe that all tricholemmomas are verrucae vulgares, just most of them, especially in their common clinical presentation as small verrucous papules on the face, notably in the context of Cowden disease. Of course, there is evidence to back this up today, which was not discovered until 1997, when examples of tricholemmoma were found by means of the polymerase chain reaction technique to harbor human papillomavirus (Chapter 16, Reference 16, 291) ⁽¹⁾. As an interesting sidelight to this, Ackerman and his coauthors advocate that a neoplastic form of tricholemmoma is a valid concept when it occurs in a nevus sebaceus but that the authentic neoplasms are rare (p. 272). In Figure 16-9, however, the example shown is labeled “trichoblastoma with tricholemmal differentiation in a nevus sebaceus.” This same series of figures was labeled “authentic tricholemmoma in a nevus sebaceus” in the first edition (Fig. 17-8). Thus, it appears that the authors have changed their minds about the fundamental nature of the lesion in question in the figure from the first edition to the second edition. I believe it would have been useful, as well as clarifying, for the authors to have shown what they considered to be an authentic example of tricholemmoma within a nevus sebaceus in the second edition.

Chapter 17: Inverted Follicular Keratosis

The chapter on inverted follicular keratosis is now placed after the chapter on tricholemmoma (Chapter 16), whereas, in the first edition, the chapter on inverted follicular keratosis preceded it. Although the content and photographs are similar to those of the first edition, there needs to be a point of clarification about the reports of human papillomavirus in these lesions. Ackerman and his coauthors state:

Furthermore, a consensus regarding the origin, differentiation, and pathogenesis of inverted follicular keratosis has yet to be reached, despite the fact that it has now been shown by polymerase chain reaction to be caused by human papillomavirus (pp. 293–4).

This is incorrect. There is no article cited about human papillomavirus in inverted follicular keratosis. The article to which Ackerman and his colleagues refer is one by Rohwedder et al. ⁽¹⁾, which they cited in the previous chapter on tricholemmoma (Chapter 16, Reference 16, 291). Ackerman and his coauthors also cite this same article in the chapter on inverted follicular keratosis (Reference 19, p. 309); however, that article addresses only tricholemmoma and not inverted follicular keratosis. Ackerman and his coauthors omitted a reference that was cited in the chapter on inverted follicular keratosis in the first edition, one by K. Hori ⁽²⁾ that specifically addressed inverted follicular keratosis. Human papillomavirus was identified in it not by the polymerase chain reaction but by an immunoperoxidase technique. The only investigation of inverted follicular keratosis with the polymerase chain reaction to date is that of Shih et al. ⁽³⁾. These investigators found no evidence of human papillomavirus in a single case of inverted follicular keratosis.

Chapter 18: Tumor of Follicular Infundibulum

The chapter on tumor of follicular infundibulum has been moved to the “front” of the benign follicular neoplasms in contrast to the first edition, where it was presented at the end of them. I like this presentation better because it is a logical progression from superficial to deep in the follicle. There is some paring of the photographs, but the text is similar to that of the first edition.

Chapter 19: Pilar Sheath Acanthoma

In the chapter on pilar sheath acanthoma, Ackerman and his coauthors present the largest series of these lesions to date (21 cases), a fact that is lost in the attempt of anyone to find them by means of a Medline search. The text is, with minor editing, unchanged, whereas the number of photographs is decreased compared to the first edition.

Chapter 22: Trichoblastoma

The chapter on trichoblastoma is much longer in the second edition because it integrates trichoepithelioma and desmoplastic trichoepithelioma as types or species of trichoblastoma (the genus), whereas they were treated in separate chapters in the first edition, although trichoepithelioma was considered to be a synonym of trichoblastoma even then. Moreover, it updates and expands the concept of "adamantinoid trichoblastoma," their preferred synonym for cutaneous lymphadenoma, including its entire updated history. Even if one considers all three chapters from the first edition, an additional 34 new figures "as stated" and 101 new photographs are included in the second edition.

Perhaps in no other article or book in the history of dermatopathology has this concept been elaborated more lucidly than in both editions of *Neoplasms with Follicular Differentiation*. Before the first edition, only a smattering of articles addressed neoplasms of the hair and follicle germ at all. In fact, only scattered reports followed Dr. Headington's review in 1976 ⁽⁴⁾, perhaps because the concept was poorly understood and needed elaboration or because authors interested in adnexal neoplasms were not familiar with or did not understand Dr. Headington's ideas. For instance, when my associates and I wrote the article on "immature trichoepithelioma" ⁽⁵⁾, there was precious little in the literature that had illustrated these neoplasms in a systematic way. Despite my ignorance (at the time) of Dr. Headington's paper, once Dr. Zaim pointed it out in his letter to the editor ⁽⁶⁾, I still could not relate the neoplasms we described to those of Dr. Headington; I could not make the connection. Even to this day, some 13 years later, I cannot. My oversight notwithstanding, we were part of the movement to bring attention to these neoplasms, which had been largely unrecognized from 1962 until 1988.

The culmination of the concept can be found in Chapter 18 of the first edition of *Neoplasms with Follicular Differentiation* and in Chapter 22 of the second edition.

In addition to the inclusion of conventional trichoepithelioma and desmoplastic trichoepithelioma fully within the realm of trichoblastoma, Ackerman and his coauthors organize the material somewhat differently compared to the first edition. Instead of discussing the subtypes altogether, they are now separated in sections of each morphologic type, with each followed by an extensive atlas, to wit:

1a. Large nodular

1b. Small nodular (a synonym for "immature trichoepithelioma," which the authors believe to be incorrect terminology, as well as "cutaneous lymphadenoma," for which the authors prefer the term *adamantinoid trichoblastoma*)

2. Retiform (giant solitary trichoblastoma)

3. Cribriform (conventional trichoepithelioma)

4. Racemiform (unconventional trichoepithelioma)

5. Columnar (desmoplastic trichoepithelioma)

The major addition to this list is the columnar type (desmoplastic trichoepithelioma). Ackerman and his colleagues have taken a different position on desmoplastic trichoepithelioma from the first edition to the second edition. In the first edition, they said of it:

Is desmoplastic trichoepithelioma an authentic trichoepithelioma? It is not. A true trichoepithelioma shows follicular differentiation only (rarely subtle sebaceous differentiation) and then mostly in the form of germs and primitive papillae, i.e., limited differentiation. Desmoplastic trichoepithelioma, however, shows follicular differentiation in concert commonly with sebaceous differentiation and uncommonly with tubular differentiation and presumably is apocrine, and hardly ever in the form of germs and papillae (pp. 597, 599).

In the second edition, they say of it:

Is desmoplastic trichoepithelioma truly a trichoepithelioma? Although it is very different in many ways from conventional trichoepithelioma, desmoplastic trichoepithelioma, like conventional trichoepithelioma, is a trichoblastoma because it is a benign neoplasm made up mostly of follicular germinative cells. In short desmoplastic trichoepithelioma is just as much a trichoblastoma as are trichoepitheliomatous trichoblastoma and adamantinoid trichoblastoma, just as morpheiform basal cell carcinoma is as much a trichoblastoma (sic) carcinoma as are fibroepitheliomatous trichoblastic carcinoma and infundibulocystic trichoblastic carcinoma. Ours is a unifying concept of trichoblastoma and of trichoblastic carcinoma (p. 619).

It is somewhat mysterious why the authors changed their minds about the nature of desmoplastic trichoepithelioma. Perhaps they now believe that they overemphasized the elements of sebaceous and ductal differentiation in these neoplasms. Perhaps the striking morphologic differences between the classic trichoepithelioma (their cribriform trichoblastoma) and desmoplastic trichoepithelioma (their columnar trichoblastoma) precluded them from expanding their thinking in a wider context to include desmoplastic trichoepithelioma as an authentic type of trichoblastoma in the first edition. Perhaps, and most likely, they considered trichoepithelioma and trichoblastoma as synonymous terms such that they never considered the classic trichoepithelioma (cribriform

trichoblastoma) to be a species of trichoblastoma rather than a cogenus. This would also explain why they now accept the cribriform (classic) pattern and the columnar (desmoplastic) patterns as part of the same conceptual spectrum under the heading of trichoblastoma. Thus, what was not completely clear until the second edition is the authors' position that "trichoblastoma" is the genus and that the five species are nodular, retiform, cribriform, racemiform, and columnar.

Chapter 23: Trichoblastic Carcinoma (Basal Cell Carcinoma)

Like the climax of a great novel, where the major conflicts come in focus in preparation for resolution, trichoblastic carcinoma (basal cell carcinoma) holds a similar place and purpose in this book. Whereas most classifications of adnexal neoplasms relegate this spectrum of neoplasms to a footnote, Ackerman and his coauthors have made it the centerpiece of the book, developing the concept of it more fully than any other treatise extant.

Just for sheer length alone, it is impressive at 381 pages, some 327 more than its treatment in the first edition, and could have been a stand-alone book. Furthermore, the 696 separate photographs in the second edition far exceed the mere 113 in the first edition.

Although the first edition emphasized "follicular differentiation" in basal cell carcinoma (trichoblastic carcinoma), the second edition takes a different stand; its position is that this malignant neoplasm *is* follicular with minimal to some degree of advanced differentiation from the germ toward specific follicular structures in some cases.

Ackerman and his colleagues open the chapter with a critique of prior classifications of basal cell carcinoma in major textbooks from 1972 to 1998, a total of 21. It is an interesting, if not humbling, experience to read this in one sitting, because it is obvious that there are inconsistencies in nomenclature from author(s) to author(s) (of whom I am one). Ackerman and his coauthors unceremoniously extirpate these inconsistencies in each classification, offering the following conclusion:

As must now be apparent, there is no agreed-on classification of basal-cell carcinoma. Parenthetically, there also is no unanimity about the essential nature of that carcinoma (p. 636).

What is the essential nature of basal cell carcinoma identified by conventional microscopy? According to Ackerman and his colleagues, it is a carcinoma composed of abnormal cells of the "folliculo-sebaceous-apocrine germ," or, to be brief, the follicular germ or trichoblast. Thus, it is a trichoblastic carcinoma (footnote, p. 636).

This position on trichoblastic carcinoma is followed by verbatim accounts of 20 prior classifications by conventional microscopy. In none of these accounts do the respective authors state explicitly that basal cell carcinoma is similar to the follicular germ. It should also be noted, for completeness, that other than neoplasms designated "basal-cell carcinoma with follicular differentiation" in the first edition of *Neoplasms with Follicular Differentiation*, nodular basal cell carcinoma was considered undifferentiated by Ackerman and his coauthors, to wit:

The overwhelming majority of basal-cell carcinomas are nodular in type and nearly always are undifferentiated as we judge them by criteria derived from study by conventional microscopy...We acknowledge that basal-cell carcinomas of all types are comprised mostly of neoplastic follicular germinative cells, but neither origin from nor composition of follicular germinative cells is synonymous with follicular differentiation (pp. 605, 607).

In the second edition, this position has changed as Ackerman and his colleagues proceed to state their five clinicopathologic types of trichoblastic carcinoma:

Nodular

Superficial

Morpheiform

Fibroepithelial

Infundibulocystic

This simple classification is followed by an in-depth discussion of each variant. Within each discussion, an atlas of figures runs in parallel. Those readers who are inclined toward understanding concepts through historical elaboration should find these sections absorbing and thought provoking.

For reasons made clear in the text (p. 948), the infundibulocystic type of trichoblastic carcinoma is the one most closely associated with the senior author of this book. It is also the nidus for his thinking about the entire spectrum of trichoblastic carcinoma belonging within the realm of follicular neoplasia and thus its inclusion in toto in this book. In the exchange of ideas with Dr. Rosai that resulted from the publication of the first paper reporting infundibulocystic trichoblastic carcinoma ([7](#)), Ackerman and his colleagues came to agree with Dr. Rosai's assertion ([8](#)) that:

...most basal carcinomas (like many other cutaneous and noncutaneous neoplasms) differentiate in the direction of embryonal rather than adult structures (p. 949).

The chapter concludes with discussions of basosquamous carcinoma and metatypical basal cell carcinoma (p. 982), metastatic basal cell carcinoma (p. 986), and nevoid basal cell carcinoma syndrome (p. 995).

Ackerman and his coauthors regard basosquamous carcinoma as a variant of basal cell carcinoma *or* squamous cell carcinoma *or* a collision of both rather than as a mixture fundamentally of basal cell carcinoma *and* squamous cell carcinoma. They regard the term as confusing and unnecessary, one that should be abandoned.

Metastatic basal cell carcinoma is exceedingly uncommon. Ackerman and his coauthors aver that it hardly, if ever, occurs and that most reported cases of it are really not metastases of an authentic basal cell carcinoma but metastases of carcinomas that can mimic basal cell carcinoma such as squamous cell carcinoma, sebaceous carcinoma, and neuroendocrine carcinoma. This point is well taken after reading their detailed review of the literature and their thesis that there is minimal objective documentation of the phenomenon.

A comprehensive historical review of nevoid basal cell carcinoma syndrome highlights the fact that this is a complex, autosomal dominant, genetic syndrome that contains authentic basal cell carcinomas, mostly of the nodular type. Nevertheless, indubitable examples of superficial and infundibulocystic basal cell carcinoma have been documented in the syndrome as well as rare examples of the fibroepithelial and morpheiform types. Although it is impossible to identify with certainty whether a patient has this syndrome based on the morphology of a particular trichoblastic carcinoma, one histologic clue may have significance according to Ackerman and his coauthors, to wit:

If, in tissue sections from a biopsy specimen, a histopathologist observes numerous discrete infundibulocystic basal-cell carcinomas in continuity with contiguous infundibula, the person almost certainly has a genetically conditioned syndrome, usually nevoid basal-cell carcinoma syndrome (p. 1001).

Chapter 24: Matrical Carcinoma

There are minor updates in the text of the chapter on matrical carcinoma, although a significant number of photographs have been added. Additional commentary has been added to the initial sections on the historical review, and the references have been updated.

Ackerman and his colleagues review the major reports of matrical carcinoma and emphasize that many purported cases of matrical carcinoma are not authentic carcinomas but pilomatricomas, concluding that:

...the silhouette of matrical carcinoma is that of a malignant neoplasm, and the nuclear characteristics of the neoplastic cells are those associated commonly with malignant neoplasms in general. Only the presence of "shadow cells" qualifies the malignant neoplasm as a matrical carcinoma, and without those distinctive cornified cells, a diagnosis of matrical carcinoma cannot be made with confidence (p. 1011).

Chapter 25: Proliferating Tricholemmal Cystic Squamous Cell Carcinoma

In a major departure from his previous viewpoint (Chapter 24, first edition), the senior author now regards these neoplasms as carcinomas rather than benign neoplasms. He states:

Although difficulty in distinguishing proliferating tricholemmal cyst from squamous-cell carcinoma has been mentioned episodically, the truly malignant nature of that so-called cyst has not until now been appreciated (p. 1039).

Furthermore, Ackerman and his coauthors no longer consider these neoplasms to be follicular in their differentiation, to wit:

This chapter [Chapter 25] does not really belong in a book about neoplasms with follicular differentiation, because the squamous-cell carcinoma under consideration here does not truly differentiate toward tricholemmal sheath; the epithelium of the carcinoma simply resembles the outer sheath at the isthmus and of a follicle well advanced in catagen. The neoplasm is included in this volume because it has been designated, incorrectly, *proliferating tricholemmal cyst*, in times past and in current articles and chapters in books (p. 1037).

In short, they regard this class of lesions as neither tricholemmal nor a cyst but as a specific type of squamous cell carcinoma, despite the fact that they persist in using a name that explicitly states both, probably to allow for a historical bridge.

Much of the new viewpoint was elaborated originally in a journal article from 1998 ⁽²⁾. In that article, and now in this chapter, the authors add considerably more depth in their historical perspective compared to what is found in the first edition. Their interpretation, now through a different conceptual filter, takes a new position on the literature, namely, that the neoplasms reported previously were all carcinomas, even in publications whose authors regarded them as benign, including the reports cowritten by the senior author of this book. This new position is bolstered further, and with compelling objectivity, by the fact that six patients recounted from the literature suffered metastatic carcinoma and death from these neoplasms, whereas five others had documented metastases.

Another interesting facet to this is that Ackerman and his coauthors regard these neoplasms as arising *de novo* in contrast with the views of many that they arise within a tricholemmal (i.e., isthmic-catagen) cyst or that they progress from a cyst to a carcinoma in a multistep process. In this vein, Figures 7 through 9 from the first edition have been removed from the second edition. In Figures 8 and 9 from the first edition, the portions of the respective lesions arranged in interconnected nests of squamous cells are present in the context of what appears to be an isthmic-catagen cyst. I assume that Ackerman and his coauthors would now regard the entire structure, including the simple cystic elements, as part of a carcinoma, but because these figures were not included in the new edition, this is speculation on my part.

Is there a benign analogue to the neoplasm the authors now consider a malignant one? Yes, it is a proliferating tricholemmal cystic acanthoma, based on their experience with a single case and depicted in Figure 1 (p. 1042). Is the benign analogue considered follicular? The authors do not state this explicitly in the text, but Figure 1 indicates that they consider it a variant of an isthmic-catagen cyst.

QUESTIONS AND COMMENTS ADDRESSED TO THE AUTHORS ABOUT THE SECOND EDITION**Follicular Neoplasms?**

Should not this book be entitled *Neoplasms of the Hair and Follicle* (predominantly the follicle)?

In Chapter 2, page 10, "Terminologic Considerations," Ackerman and his coauthors state the following:

In virtually all writings about hair and hair follicles, the terms *pilar*, *tricho*, and *follicular* are used interchangeably; yet the three surely are not synonyms. The word *pilar* comes from the Latin word *pilus*, which means "hair," and *tricho* derives from the Greek word for "hair." In short, *pilar* and *tricho* are synonyms for hair, and *hair* is equivalent to *hair shaft*. In contrast, the word *follicle* originates from Latin *folliculus*, which means "a tiny leather sac." A hair follicle consists of the entire epithelial structure that manufactures and houses a hair. In exceptional instances, the terms *pilo-*, *tricho-*, and *pilar* are used correctly (e.g., pilo-erector muscle and trichostasis spinulosa). In most instances, however, they are used incorrectly, particularly when *pilo-* and *pilar* are invoked where *folliculo-* and *follicular* are really intended (pp. 10–11).

After this statement is a list of terms that the authors regard as examples of inappropriate uses of the *pilar* or *hair*, when the term should be *follicular* or *folliculo*. Pilomatricoma is cited as one example (p. 11) in which the differentiation is toward the follicle and the hair and which they believe is really a folliculomatricoma.

I take no issue whatever with their use of and reference to the prefixes *tricho*, *pilo*, and *folliculo*. The *Oxford English Dictionary* (second edition) also lists similar definitions and applications of these terms. I take issue, however, with the statement that because "a hair follicle consists of the entire epithelial structure that manufactures and houses a hair," the cellular components that ultimately become the cornified hair filament should be grouped together as if they were follicular, when they are, in fact, the hair itself. The hair is housed or ensheathed by the follicle (the "little sac"); it is not synonymous with the follicle, and the proliferations differentiated toward it should not be considered follicular but *pilar* or *tricho*. Thus, the neoplasm termed *pilomatricoma* is differentiated predominantly toward the part of the matrix containing zones that do not always appear to be differentiated specifically toward the hair or the follicle, but it always contains zones differentiated toward the supramatrical zone of a bulb, and thus the hair itself. Similarly, hamartomas such as trichofolliculoma contain both hair and its follicle (plus perifollicular sheath) and are not differentiated solely toward the follicle. Perhaps, in this context, Ackerman and his coauthors are just foreshortening the use of the terms *hair* and *follicle* by using only the term *follicle* for simplicity. Perhaps Drs. Ackerman, Reddy, Soyer, or all three would be willing to clarify this position in their rebuttal of this review.

Undifferentiated but Identifiable?

I have never been able to grasp the position that a proliferation can be considered undifferentiated yet be classified as something specific. It makes no sense to me. The authors approach this issue as follows:

By using repeatable and reliable criteria, specific, accurate diagnosis of benign and malignant epithelial and nonepithelial neoplasms may be made histopathologically, except for those that are undifferentiated. There are even exceptions to that exception. For example, some trichoblastomas, trichoblastic carcinomas of nodular type, and neuroendocrine carcinomas are undifferentiated, but each may be diagnosed with confidence at scanning magnification by virtue of particular characteristics (pp. 6–7).

There is a contradiction in this statement. If the neoplasms mentioned here have "particular characteristics" such that they can "be diagnosed with confidence at scanning magnification," they are differentiated rather than undifferentiated. An undifferentiated neoplasm cannot be identified with certainty; that is precisely why it is considered undifferentiated. I would appreciate the authors' clarification of this point.

The Function of a Follicle: Manufacture of a Hair in Anagen?

In Chapter 4, the authors state that:

The *raison d'être* of a follicle, namely, manufacture of a hair during anagen, is a responsibility that falls to the lower segment alone (p. 29).

I view this in a different way. Because the matrix is responsible for the production of the hair and the inner sheaths as well as the cuticles of both, the follicle does not manufacture the hair, because it is produced by the same type of cell that produces the hair, but rather ensheaths it.

Subjectivity Versus Objectivity

Dr. Ackerman has stated in several publications, including this one, that a diagnosis is "so subjective." I have a different point of view about this and want to challenge him and his colleagues about that issue in relation to the nature of classification. In Chapter 7, the authors conclude with the following statement regarding the classification of follicular neoplasms:

One caveat hardly needs mentioning because it is truistic—all classifications based on morphology and biology are imperfect because they are so subjective, formulated as they are by the brain of man (p. 107).

I believe that it *does* need mentioning. The *Oxford English Dictionary* (second edition) defines the term *truism* as "a self-evident truth, esp[ecially] one of slight importance; a statement so obviously true as not to require discussion." Thus, Ackerman and his

colleagues believe it is self-evident that biologic classifications such as neoplasms of hair and follicles are inherently, by their nature, imperfect *because* they are formed by a human method, one requiring man's brain, and that they require no discussion.

The reasoning they imply but do not state explicitly is as follows: man's brain is involved in the formulation; therefore, the formulation must be imperfect and subjective, because, after all, a human subject (an observer) is required, and no two are alike. Because no two are alike, no one can know what is the "perfect" classification.

If knowledge is subjective, how can Dr. Ackerman and his colleagues even make or imply such a statement? Would that statement not also be subjective, thus refuting their entire proposition? Why, furthermore, is a *human* method of classification *inherently* imperfect? Imperfect compared to what? Plato's world of perfect forms? Are we human beings just prisoners in Plato's cave, unable to grasp the "true" reality and formulate valid concepts of things in reality?

No, human beings *are* capable of objectivity and of knowledge.

We human beings, through each individual observer, perceive the same reality directly, with our senses. A subject is required (a human being), but the *process* is not subjective. One cannot make up just any conclusion and hope "somehow" that it explains what occurs in reality or that reality conforms to one's wishes just because one wants it that way.

An objective method is, in essence, the object as perceived and integrated conceptually by the mind of a man (the subject) by the process of induction in harmony with the laws of logic, communicated in words, formulas, and illustrations. Words and their precise definitions, as Dr. Ackerman well knows and has defended on numerous occasions, are an essential tool of objective communication. They are a bridge between one person's observations and his objective way of communicating those findings to himself and others. Objectivity claims that man is neither infallible nor omniscient but that he is capable of learning truth from facts provided that his conclusions explain, in conceptual terms, the nature of the facts he observes. This process allows one to discover and correct his errors by the same process.

Perfect is defined by the *Oxford English Dictionary* (second edition) as "in the state proper to anything when completed; complete; having all the essential elements, qualities, or characteristics; not deficient in any particular." Thus, it is not appropriate to apply the concept of "perfect" to a classification scheme in a scientific context (a biologic classification in this case). Nevertheless, one can be perfect in how he uses the method of discovery and classification, in essence, the faculty of reason. Using reason does not mean that the observer has to know more than he can possibly know or that he is never going to make errors. No one is omniscient or infallible; human perfection cannot be held to such an impossible, in fact mystical, standard of error-free classification.

Every proper scientific classification is an objective work in progress, because that is the nature of scientific inquiry and classification. When new observations are made or new conceptualizations are formed, they must be tested against what is known or presumed known. A better proof always has the ability to replace a poorer one. This occurs precisely because objectivity has such epistemological power and requires such disciplined thought that when an objective position is made well, it is laid before the entire scientific community, explaining and clarifying the vagaries of the past so that each person can understand what is true and why (this book, by the way, is an excellent example of the process.).

Even with the unknown and with error, our understanding of the biology of many lesions is certainly good enough, even when we disagree on certain points, to allow each of us who practice dermatopathology the good fortune of being benefactors of human life.

Follicular Cysts: Where Are They?

Surely Ackerman and his coauthors are not ignorant of follicular cysts, but it is not clear why they are not elaborated in the book with the exception of one specific type of follicular cyst discussed in Chapter 9, "dilated pore," and briefly in Chapter 25 in reference to "proliferating tricholemmal cystic acanthoma." It would seem reasonable to include infundibular and isthmic-catagen cysts as well other than just a brief mention of them, without illustration, in Chapter 4 (pp. 36, 40).

Tricholemmoma as a Hyperplasia Versus a Neoplasm?

In Chapter 16, Ackerman and his coauthors summarize their position on tricholemmoma after reviewing statements made about it by Dr. Headington, who, together with Dr. French, originated the concept:

In our judgment, none of these six statements made by Headington is correct and, moreover, none is incompatible with the idea that what he named "tricholemmoma" is verruca vulgaris, and, in actuality, that is our interpretation of it (p. 290).

It is now been shown unequivocally by polymerase chain reaction technology that human papillomavirus is present in some tricholemmomas, thus corroborating the position of Ackerman and his colleagues that many if not most tricholemmomas are morphologic expressions of viral changes in the infundibulum of a follicle (p. 272). This being the case, why does tricholemmoma now deserve its own chapter in this book? Should it not be relegated to a footnote or perhaps included within a chapter entitled "Follicular Hyperplasias Caused by Viral Agents"? Furthermore, if there is truly a neoplasm that should be considered under this name, should it not be classified under its own heading in the section on neoplasms? As an aside, a similar question could be raised for inverted follicular keratosis.

Tumors of Follicular Infundibulum and Pilar Sheath Acanthoma: Should They Be Renamed?

I agree with Ackerman and his coauthors that tumor of follicular infundibulum is a neoplasm differentiated principally toward the isthmus, although, in the past, I was not convinced that it was neoplastic. That aside, I agree that it is misnamed. Pilar sheath

acanthoma, a neoplasm differentiated mostly toward the infundibulum and isthmus and arranged in lobules, seems to have been given a name that overreaches its usual presentation, even though minor components of the follicle other than the infundibulum and isthmus are present within it. I am somewhat surprised that Ackerman his colleagues have not made an attempt to propose different names for these neoplasms, ones that better reflect their specific differentiation or, in the case of tumor of follicular infundibulum, correct its erroneous appellation. I believe that tumor of follicular infundibulum should be termed *isthmicoma* and that pilar sheath acanthoma should be termed *lobular infundibuloisthmicoma* to reflect their principal patterns of differentiation, which are both reproducible and repeatable from case to case. How do the authors regard this issue?

Proliferating Tricholemmal Cystic Squamous Cell Carcinoma: Not Differentiated Toward the Tricholemmal Sheath in Catagen?

The authors state that:

This chapter does not really belong in a book about neoplasms with follicular differentiation, because the squamous-cell carcinoma under consideration does not truly differentiate toward tricholemmal sheath; the epithelium of the carcinoma simply resembles the outer sheath at the isthmus and of a follicle well advanced in catagen (p. 1037).

I simply cannot understand what is meant by "...the squamous-cell carcinoma under consideration does not truly differentiate toward tricholemmal sheath; the epithelium of the carcinoma simply resembles the outer sheath at the isthmus and of a follicle well advanced in catagen." What is the distinction between the terms *resemble* and *differentiate* in this context?

The *Oxford English Dictionary* (second edition) defines the term *resemble* as "to be like, to have likeness or similarity to, to have some feature or property in common with (another person or thing)."

It defines *differentiate* as "to make different in the process of growth or development; to make unlike by modification, esp[ecially] for a special function or purpose; to specialize (chiefly used in pass[ive])."

This definition is similar, in essence, to Ackerman and coauthors' definition of *differentiation* in the glossary.

Thus, the distinction between "resemble" and "differentiate" is that resemblance emphasizes *similarity* of an attribute or attributes of entities (i.e., specific examples) that are compared directly, whereas differentiation stresses *differences* between the entities examined, usually in the context of the development of a structure from a generalized one to a specific one. Both of these terms are used by means of comparison to a standard, typically structures in control skin. Nevertheless, what are seemingly two antithetical points, resemblance and differentiation, actually refer to different aspects of the same issue in this particular context: how does what one observes compare with an aspect of cornification seen in a follicle in catagen? With respect to resemblance, the cornification resembles that seen at the level of the isthmus in advanced catagen, and it is differentiated presumably from a germ and toward the isthmus in catagen.

Thus, I do not understand Ackerman and coauthors' point in all this. Specifically, I do not understand the meaning of their comment:

Neither can it be said that proliferating tricholemmal cystic squamous-cell carcinoma differentiates toward the tricholemmal sheath, because a squamous-cell carcinoma already is fully differentiated; unlike trichoblastic (basal-cell) carcinoma which may show authentic tricholemmal differentiation, squamous-cell carcinoma cannot and does not do that (p. 1074).

I believe the lesions in question are differentiated toward the isthmus of a follicle in advanced catagen; they resemble it, and they are similar to it (just as an isthmic-catagen cyst is differentiated toward the same even though it is not a neoplasm). It is true, of course, that no one knows the origin of these carcinomas, but that can be said of many if not all neoplasms. I believe that this issue needs to be clarified further by the authors, either to point out my error in thinking, to agree with my argument, or to elaborate more on their meaning so that I can understand their argument fully.

DOES THE BOOK ACCOMPLISH THE AIMS STATED BY THE AUTHORS?

Drs. Ackerman, Reddy, and Soyer succeed in accomplishing the aims they set forth early in their work by presenting an algorithmic structure, but there are a few issues that need to be addressed.

The *Oxford English Dictionary* (second edition) defines *algorithm* as "a step-by-step procedure for reaching a clinical decision or diagnosis, often set out in the form of a flow chart, in which the answer to each question determines the next question to be asked."

Thus, in the context of a histologic diagnosis, it should begin with concretes (i.e., perceptual findings under a conventional microscope) and should lead the observer to a set of findings that, when they occur together, results in the formulation of a diagnosis.

This goal is accomplished in part by the authors' algorithm; however, one has to decide whether the lesion is benign or malignant at the main branch point. Thus, the authors must assume that the reader brings some degree of diagnostic ability to the material. That aside, within each branch point (i.e., benign or malignant), the reader can find a lead to the diagnosis if he knows the morphology of the different parts of a hair and its follicle, which he can learn in extensive and precise detail in Chapters 3 and 4. That accomplished, the chapters provide an impressive historical and clinicopathologic pathway to one's understanding of all the lesions presented.

The algorithm on pages 116 and 117 is succinct and easy to follow, if not somewhat skeletal in structure. It would have been useful to have this algorithm on the inside covers, both front and back, so that the reader could find a specific chapter more easily when needed. Inclusion of chapters and page numbers in the algorithm would also have been useful.

IS THE BOOK LIKELY TO INTEREST THE READERSHIP OF THE *American Journal of Dermatopathology*?

Yes.

My comments come as no surprise to readers of the first edition of this work, but to those who have not had the pleasure and the intellectual challenge of reading the first edition, the second edition greatly surpassed my expectations. This is not only “must” reading for anyone serious about cutaneous pathology, but it also has wide implications for general pathology and for how a book should be conceived and structured.

I cannot overemphasize this point. Although most books in pathology, including those about cutaneous pathology, are boring, this book is not. It is interesting, absorbing, and compelling. The writing is clear, concise, and consistent. The terms are defined and explained further in the text; there are also interesting footnotes filled with unexpected and welcomed explanation.

I believe the secret of why it is so good is that Ackerman and his coauthors lay a framework that allows the reader to be drawn easily toward the subject matter. Most texts of pathology do not do this; furthermore, if it is done at all, it is only in a cursory way. This book regards every subject in a historical context, including many exact quotes from the authors of the original papers, which are set aside in the text for easy identification, thus greatly enriching the experience of the reader and eliminating the reader's need to stop reading to check the cited reference against the text. Over the 4 months I spent working on this review, I was always eager to read and reread passages, hoping to find some new insight, which happened with regularity, as I thought about each section and looked forward to the next.

Moreover, the photography is outstanding; it is so good that it stands on its own merits, not requiring the text in many sections (although the text greatly enhances the message). It is comparable to the best photography ever produced in a book of pathology, period.

Despite Ackerman and his colleagues' belief that their classification is imperfect and that it is subjective, I want to congratulate them on producing it with a perfect method: reason. It is the most objective and lucidly stated classification to date. Whatever my disagreements with it, I have learned a great deal from reading it, as will other dermatopathologists who make a concerted effort to spend time thinking seriously about the information contained in its pages. I know I will be referring to it for years to come.

REFERENCES

1. Rohwedder A, Keminer O, Hendricks C, et al. Detection of HPV DNA in trichilemmomas by polymerase chain reaction. *J Med Virol* 1997; 51:119–25.
2. Hori K. Inverted follicular keratosis and papillomavirus infection. *Am J Dermatopathol* 1991; 13:145–51.
3. Shih CC, Yu HS, Tung YC, et al. Inverted follicular keratosis. *Kohsiung J Med Sci* 2001; 17:50–4.
4. Headington JT. Tumors of the hair follicle. A review. *Am J Pathol* 1976; 85:479–514.
5. Long SA, Hurt MA, Santa Cruz DJ. Immature trichoepithelioma: report of six cases. *J Cutan Pathol* 1988; 15:353–8.
6. Zaim MT. “Immature” trichoepithelioma. *J Cutan Pathol* 1989; 16:287–9.
7. Tozawa T, Ackerman AB. Basal cell carcinoma with follicular differentiation. *Am J Dermatopathol* 1987; 9:474–82.
8. Rosai J. Basal cell carcinoma with follicular differentiation [Letter]. *Am J Dermatopathol* 1989; 11:479–81.
9. Mones J, Ackerman AB. Proliferating trichilemmal cyst is squamous-cell carcinoma. *Dermatopathol Pract Concept* 1998; 4:295–310.

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American Journal of Dermatopathology:

April 2002 - Volume 24 - Issue 2 - pp 179-181

Book Reviews

Neoplasms With Follicular Differentiation, 2nd edition.: Reply to Book Review

Ackerman, A. Bernard M.D.

To the Editor

I first read Mark Hurt's unconventional review of *Neoplasms with Follicular Differentiation* on October 22, when it was forwarded to me by the editorial office of this journal with an invitation to reply, and I sent him these lines by post immediately.

I have just returned from Japan and, perforce, this letter to you must be brief. I want to thank you, profusely, for your extraordinarily instructive review of our book about *Neoplasms with Follicular Differentiation*; I only wish that I had shown you the manuscript *before* it became bound as a book! In short, I cannot thank you enough for contributing to the education of

A. Bernard Ackerman, M.D.,

who looks forward to preparing responses to your thoughtful questions.

Now, having had the opportunity to peruse Mark's critique again, I am even more impressed by and grateful for his reasoned, reflective, and comprehensive assessment of our work. Would that every reviewer brought to the task the sense of responsibility and purpose, the directness and sensitivity, the profundity, and the graciousness of Mark Hurt. His review is entirely *ad rem* and not at all *ad hominem*.

Let me begin by making certain comments in response to remarks made by Dr. Hurt in the course of his review and, having done that, attempt to give meaningful answers to the questions he put to me.

1. “. . .the inclusion of outer sheath in the matrical differentiation section seems out of place . . .” *Comment:* I have come to think that the cells that reside in the germ that sits at the base of the isthmus at the end of telogen quickly go from being made up of germinative cells to being composed of matrical cells, which, as they descend along a fibrous track early in anagen, mature at the periphery to cells of the outer sheath, in the center of cells of the hair, and in between to cells of the inner sheath. In short, I now believe that matrical cells in a follicular bulb differentiate along three lines, to wit, outer sheath, inner sheath, and hair.

2. “References to follicular induction in nevus sebaceus have been removed from the text . . .” *Comment:* It is my current thinking that unlike the situation in dermatofibroma, for example, in which mesenchymal cells may induce follicles, or a part of them, the rudimentary follicles in nevus sebaceus are integral components of the hamartoma and do not represent “induction.”

3. “Thus, it appears that the authors have changed their minds about the fundamental nature of the lesion in question . . .” *Comment:* In my judgment, every papule designated, conventionally,

“tricholemmoma” and conceived, universally, to be a neoplasm of the outer sheath (as Headington and French contended at the outset) really is a largely involuted verruca vulgaris, that is, a hyperplasia (as a consequence of infection by human papillomavirus) of infundibular epithelium with differentiation toward the outer sheath at the bulb. In contrast is the rare benign neoplasm with tricholemmal differentiation that sometimes appears in a nevus sebaceus. The silhouette of it, unlike that of stereotypic “tricholemmoma,” is not that of a mostly resolved wart.

4. “This is incorrect. There is no article cited about human papillomavirus in inverted follicular keratosis.” *Comment:* Dr. Hurt is not completely correct. He is right about the references that we cited, but he seems to have overlooked an article by Soyer et al. (1) in which the authors write as follows: “Furthermore, numerous whorls of keratinocytes (so-called squamous eddies) were present within the squamous areas of the hyperplastic epithelium of the [verrucous] cyst, morphologically reminiscent of inverted follicular keratosis . . . In all 5 cases of verrucous cysts, HPV-specific DNA sequences were detected [by polymerase chain reaction].” In short, I am as confident about the human papillomavirus cause of “inverted follicular keratosis” as I was of “tricholemmoma”; almost everyone who has written about the subject has commented on the “overlap” of the two conditions morphologically. The reason, in my view, is that those lesions situated usually on a face are one and the same, namely, a verruca vulgaris in denouement.

5. “Should not this book be entitled *Neoplasms of the Hair and Follicle* (predominantly the follicle)?” *Comment:* The hair consists wholly of corneocytes, which are dead cells, and a neoplasm consists in some measure, usually large, of viable cells. Therefore, there can be no neoplasm of hair alone.

6. “The hair is housed or ensheathed by the follicle (the ‘little sac’); it is not synonymous with the follicle . . .” *Comment:* The hair is an integral part of the follicle, being the product of maturation of matrical cells present in the center of a follicular bulb and at the base of it. The hair is “ensheathed” by the inner sheath, which, in turn, is enveloped by the outer sheath at the bulb and stem. Neoplasms with follicular differentiation may possess morphologic attributes, like those of any part of a hair follicle, from matrical cells in the bulb (as are encountered in pilomatricoma, with the “pilo” part being manifested as “shadow cells” that represent a flawed attempt at differentiation toward hair shaft and the “matricoma” part being expressed as matrical cells that have capability to differentiate not only toward hair itself but toward inner and outer sheaths) to isthmic cells (as they are found in tumor of follicular infundibulum and in pilar sheath acanthoma). In brief, the follicle consists of epithelium that extends from the base of the bulb to the base of the infundibulum (the constituent parts being the bulb, stem, and isthmus); the hair being as much a part of the follicle as are the inner sheath and the outer sheath. Parenthetically, the infundibulum is not outer sheath but rather infundibular epidermis in contrast to surface epidermis.

7. “Undifferentiated but Identifiable?” *Comment:* Were a cutaneous neoplasm to consist only of matrical cells, germinative cells, or neuroendocrine cells, it would be undifferentiated, that is, the cells are not modified further to a specific form such as any structure that resembles that in normal embryonic or mature tissue; nonetheless, each of those three aforementioned neoplasms is identifiable for what it is in sections of tissue stained by hematoxylin and eosin, namely, as matricoma, trichoblastoma, and Merkel cell carcinoma, respectively, and by virtue of both silhouettes and cytopathologic attributes.

8. “. . . the follicle does not manufacture the hair . . .” *Comment:* The matrical cells in the center of the bulb of a follicle mature to become hair. For that reason, it may be intuited that the

purpose of a follicle is to produce a hair.

9. "Subjectivity Versus Objectivity" *Comment*: The definition I use for "subjectivity" can be found in the most recent edition of Langenscheidt's *New College Merriam-Webster English Dictionary* and reads as follows: "*subjective* . . . characteristic of or belonging to reality as perceived rather than as independent of mind." I also endorse the definition in the same dictionary of the word "objectivity," which is set forth thus: "*objective* . . . of, relating to, or being an object, phenomenon, or condition in the realm of sensible experience independent of individual thought and perceptible to all observers." All classifications predicated on morphology are subjective, and that is why in the realm of books and/or chapters of books devoted to the subject of neoplasms with follicular differentiation, no two of the more than score of them are in synchrony with one another. That is why the "accepted" classification of lymphomas changes radically every 5 years. That also is why when "experts" in interpretation of findings in sections of tissue are recruited for a panel such as the 1991 "Workshop Without Walls" concerning melanocytic neoplasia, which preceded the Consensus Development Conference at the National Institutes of Health that concerned dysplastic nevus (about which there was no consensus), there *always* is no concordance in diagnosis, even when the changes are reputed to be "classic." When the findings in those sections are vexing, chaos reigns, and that is true of "experts" in histopathologic diagnosis of conditions in every organ. Last, it should be noted that Dr. Hurt refers repeatedly to "biology" in his discussion of "subjectivity" and "objectivity," whereas I am addressing matters of morphology only. In sum, I continue to contend that what we histopathologists do professionally is 100% subjective, with claims to the contrary being expected because interpretation of the matter is subjective.

10. "Follicular Cysts: Where Are They?" *Comment*: In my judgment, there is but a single authentic follicular cyst, to wit, the one that we designate "isthmic-catagen cyst" and that everyone else calls tricholemmal cyst, pilar cyst, or wen. Because we name all cysts in skin according to the normal epithelial structure that the lining of the cyst resembles most closely, the cyst in point is called isthmic-catagen, because its lining looks like the isthmus of a normal follicle and the outer sheath of a normal follicle well advanced in catagen, with those two epithelia being indistinguishable from one another. An "infundibular cyst" is not follicular; it is epidermal, because the infundibulum is an invagination of epidermis. If a third edition of *Neoplasms with Follicular Differentiation* is undertaken by my colleagues and/or others, it is reasonable for them to include in it a discussion of "isthmic-catagen cyst" as Dr. Hurt advises.

11. "Tricholemmoma as a Hyperplasia Versus a Neoplasm?" *Comment*: This subject has been dealt with already. In brief, that which is called "tricholemmoma" truly is an infection by human papillomavirus, an involuting wart, and a hyperplasia because it fulfills the definition of hyperplasia in classic pathology, that is, a proliferation of cells that involutes when the stimulus responsible for it (in this instance, a virus) is withdrawn or disappears. The rare benign follicular neoplasm that shows signs of tricholemmal differentiation at the bulb does not resemble at all a wart histopathologically unlike, the situation for conventional "tricholemmoma." As a parenthetical comment, a rare expression of trichoblastic (basal cell) carcinoma exhibits tricholemmal differentiation at the bulb.

12. "Tumors of Follicular Infundibulum and Pilar Sheath Acanthoma: Should They Be Renamed?" *Comment*: Only if one renames all neoplasms with follicular differentiation and virtually every disease of the skin. For practical purposes, all the terms are misnomers, with some of the most egregious being pyogenic granuloma, adenoma sebaceum, mycosis fungoides, tumor of follicular infundibulum, sebaceous trichofolliculoma, and proliferating tricholemmal cyst.

13. "Proliferating Tricholemmal Cystic Squamous Cell Carcinoma; Not Differentiated Toward the Tricholemmal Sheath in Catagen?" *Comment*: I must have been under the influence of a Mickey Finn when I asserted that this malignant neoplasm was a squamous cell carcinoma. Despite the bolus of corneocytes contained within the cystic neoplasm, the actual nature of it, as Dr. Hurt correctly avers, is follicular, that is, outer sheath; in actuality, it is a proliferating tricholemmal cystic carcinoma. Moreover, I have come to think that the carcinoma originates in a preexisting isthmic-catagen (tricholemmal) cyst. I plan to acknowledge these changes in my thinking in the second issue for 2002 of *Dermatopathology: Practical and Conceptual* and to give proper credit to Dr. Hurt for nudging me in the proper direction. Dr. Hurt also points out, rightly, that on more than one occasion, ". . . it appears that the authors have changed their minds . . ." If one is engaged fervently in a discipline that is as subjective as dermatopathology, how could one not, from time to time, be compelled to change one's mind—and that is one of the reasons why one undertakes a next edition!

Thanks once again to Dr. Hurt.

A. Bernard Ackerman, M.D.

REFERENCES

1. Soyer HP, Schadendorf D, Cerroni L, et al. Verrucous cysts: histopathologic characterization and molecular detection of human papillomavirus-specific DNA *J Cutan Pathol* 1993; 20:411–7.

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