THE ARTICLE PUBLISHED BY SKVARA ET AL. IN THIS ISSUE OF THE ARCHIVES FOCUSES ON THE LIMITATIONS OF DERMOSCOPY IN THE DIAGNOSIS OF VERY EARLY AND MAINLY FEATURELESS MELANOMAS. THE AUTHORS REPORT THAT BASELINE DERMOSCOPIC PATTERNS OF 262 MELANOCYTIC NEVI DID NOT DIFFER FROM THOSE OF 63 MELANOMAS OBSERVED BY DIGITAL DERMOSCOPY AND FINALLY EXCISED BECAUSE OF CHANGES OVER TIME. THE AUTHORS WISELY FORESEE THAT THIS BASICALLY FEATURELESS OR “FEATURE-POOR” GROUP OF MELANOMAS WILL BE USED BY BOTH SIDES IN THE DIGITAL DERMOSCOPY CONTROVERSY: PROONENTS WILL CITE THEM AS EVIDENCE THAT FOLLOW-UP WITH DIGITAL DERMOSCOPY IS NECESSARY; OPPONENTS POINT TO THEM AS EVIDENCE THAT DERMOSCOPY IS UNNECESSARY AND THAT EVERY CLINICALLY SUSPICIOUS LESION MUST BE EXCISED. THE AUTHORS ACKNOWLEDGE THE STRENGTHS AND LIMITATIONS OF BOTH VIEWS, BUT THE QUESTION REMAINS WHETHER DERMOSCOPICALLY FEATURELESS OR FEATURE-POOR LESIONS WARRANT EXCISION.

See also page 155

Interestingly, the authors do not discuss at all the validity of the histopathologic diagnosis of the 325 melanocytic skin lesions sampled in their study. They just state that histopathologic examination of the 325 lesions identified 262 melanocytic nevi and 63 melanomas. They later assert that the histologic report is regarded as the gold diagnostic standard in our field, and usually our scientific journals will not accept a manuscript on dermoscopy that includes lesions for which the diagnosis has not been proven histologically. We are bewildered and perplexed by the certainty with which Skvara et al seem to accept histopathologic diagnosis as the gold standard without mentioning the limitations and intrinsic difficulties of its application to melanocytic skin lesions.1,2

THE BENIGN/MALIGNANT THRESHOLD IN PATHOLOGIC EVALUATION

The boundary between benignity and malignancy is not as sharp as our mental categories would like it to be. Also, limitations to histopathologic diagnoses are subjective as well as objective. Both of these facts were well recognized already in 1962 by Rambo,3 who stated that pathologists are physicians and human beings. They . . . traditionally have been regarded to be more scientific than many of their colleagues. A mystic perversion of this assumption prevails among those clinicians who believe that the pathologist, given only a piece of the patient’s tissue, has all the other ingredients necessary to produce a statement of absolute truth at the end of his report. More dangerous to mankind is a pathologist with the same concept.

Remarkably, subsequent literature has not dealt adequately with this important issue. It is difficult to find admissions that expert pathologists sometimes have great difficulties in recognizing, for example, the threshold separating carcinoma in situ or melanoma in situ from atypia or dysplasia. Subjective limitations in diagnostic histopathology have been addressed by few studies of interobserver agreement. In 1992, Schnitt and Connolly4 studied the interobserver reproducibility in the diagnosis of ductal proliferative breast lesions using standardized criteria and concluded that a 33% rate of disagreement at the benign/malignant threshold was “encouraging.” Rosai,5 in the last edition of Rosai and Ackerman’s Surgical Pathology, underlines that some follicular and papillary neoplasms of the thyroid show “questionable” histopathologic features, and he introduces terms such as follicular tumor of uncertain malignant potential and well-differentiated tumor of uncertain malignant potential in the current diagnostic practice. It is quite surprising that in the molecular medicine era, the diagnostic accuracy of histopathologic analysis is recognized to be lower than expected and desired.

In the field of dermatopathology, the subjective and objective diagnostic limitations are even more pronounced. In a 1996 study of 95 pigmented skin lesions, Cook et al.1 reported a poor concordance among dermatopathologists in distinguishing severe dysplasia in the junctional component of melanocytic proliferation from melanoma in situ. Since melanoma in situ and severe dysplasia cannot be distinguished by objective measurements, and since their clinical management is the same, the panel suggests that attempts to distinguish them in diagnostic reports should be discontinued and that they both be referred to as melanocytic intraepidermal neoplasia or MIN. However, despite an extensive debate over this article in The Lancet, MIN terminology has been rejected by both the pathology and the dermatology communities.7,8

The differential diagnosis between Spitz nevus and spitzoid melanoma is one of the best known dilemmas in dermatopathology. Perhaps 6% to 8% of spitzoid neoplasms show highly conflicting histopathologic characteristics that disarm the histopathologist.9 The introduction of the term malignant Spitz nevus further underlines the diagnostic difficulties encountered in these neo-

©2005 American Medical Association. All rights reserved.
plasms because it refers to histopathologically benign cases that metastasize to lymph nodes. This occurrence clearly proves the inadequacy of the histopathologic criteria in predicting the biological behavior of some lesions.

The scarcity of literature on the histopathologic validity of melanoma diagnosis may be explained in part by methodologic problems and by the fact that only pathologists currently have the competence to challenge their own diagnostic monopoly, something they are obviously reluctant to do. In this context we cite the legendary comments of Foucar10:

[Like the surgical monopoly on therapeutic decisions, the pathology monopoly on nosology has become dysfunctional. Pathologists’ inability to move beyond their benign vs malignant paradigm should result in loss of their terminology monopoly.]

Today we are on the edge of a period of radical change in histopathology: DNA and RNA can be analyzed by advanced technologies, even from archival paraffin-embedded materials, allowing us to make substantial diagnostic advances.11 The new biological techniques evolving within histopathology will certainly allow pathologists to refine the benign/malignant threshold and thus establish a more functional approach to identifying risk. Sharply defined categories will soon replace the currently fanciful indicators of distinction between benign and malignant.10

**Figure.** Pigmented lesion situated on the lower leg of a 49-year-old woman. A, Clinical image; B, dermoscopic image; C and D, histopathologic images.

**CORRELATION OF CLINICAL AND DERMOSCOPIC FINDINGS WITH HISTOPATHOLOGIC ANALYSIS**

Dermoscopic images and clinical findings take on new relevance when used by pathologists to perform clinico-pathologic correlation. Currently, the gross sampling techniques used to obtain skin biopsy specimens are probably an underestimated source of diagnostic errors. In a pilot study on dermoscopic-pathologic teleconsultation, Ferrara et al12 compared dermoscopic and histopathologic features and found that 1 in 12 cases had probably been underdiagnosed by the histopathologists because of a poor gross sampling technique. We believe that by applying dermoscopy and a standardized gross pathology protocol to the diagnosis of pigmented skin lesions, a more precise clinicopathologic correlation can be achieved between relevant dermoscopic features and cutaneous pathologic findings.13 Focusing the histopathologists’ attention to a suspect area, sometimes even very small, has been shown to improve the diagnostic accuracy of histopathologic analysis.14 Braun et al15 recently suggested performing a 1-mm micropunch biopsy in dermoscopically determined relevant parts of a pigmented skin lesion to better correlate dermoscopic findings with the underlying histopathologic ones.
In our estimation, the conceptual and practical link between dermoscopy and histopathology is strong. In 2002, Ferrara and colleagues\textsuperscript{16} demonstrated in a study of 107 equivocal melanocytic lesions that a diagnostic discrepancy among formally trained dermatoscopists seemed to predict a diagnostic disagreement among histopathologists. These data lend increasing importance to establishing a dialogue between dermatoscopists and histopathologists who will probably experience similar diagnostic troubles on a given case.

**AN ANECDOTAL OBSERVATION**

We know that progress in medicine is based on evidence and not on anecdotal observations. Sometimes, however, a straightforward and simple observation tells the story well, and in this context we exhibit the clinical, dermoscopic, and histopathologic images from a pigmented lesion situated on the lower leg of a 49-year-old woman (Figure, A and B). This lesion was diagnosed histopathologically "most probably as regressive melanocytic nevus" (Figure, C and D). According to the referring pathologists, who had not seen the clinical and dermoscopic images, the differential diagnoses included "a regressive lichen planus–like keratosis and less likely a regressive melanoma." The reader might come up with his or her own opinion about the diagnosis of this pigmented lesion, but in our estimation, it is a clear-cut example of regressive melanoma.

**ILLUSION OF CERTAINTY AND LIFE GOES ON**

In 1979, Ackerman\textsuperscript{17} wrote

Dermatopathologists, like pathologists in general, are often asked by clinicians whether, on the basis of the histologic findings, a particular neoplasm is benign or malignant. The question seems simple enough, but an answer as simple is often too simple.

In 2000, Cerroni\textsuperscript{18} reflected on the human urge to classify in pursuit of certainty: "the dichotomy 'benign vs. malignant' is only one of the many faces of the human struggle in search of certainty." Cerroni summarized his philosophy in these words: "Wisdom lies in understanding our limitations: wisdom lies in understanding that certainty is an illusion."\textsuperscript{18}

Histopathology, as every other purely morphologic method, is limited by methodologic drawbacks and sometimes by practitioners' personal limitations. Today we are on the edge of a new biology in histopathology, and one can foresee that our beloved classic morphology will soon be replaced by new technologies. In the meantime, a combined morphologic approach linking dermoscopy and histopathology might be helpful for pathologists to come to more reliable diagnostic conclusions for patients and their physicians.

**Financial Disclosure:** None.

**Correspondence:** Dr Soyer, Department of Dermatology, Medical University of Graz, Auenbruggerplatz 8, A-8036 Graz, Austria (peter.soyer@meduni-graz.at).

**REFERENCES**