Diagnosis! (Not Prognosis, Not Potential, Not Risk)

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■ *Melanocytic tumor of uncertain malignant potential (MELTUMP). A phrase coined by David Elder and used by him, his coworkers, and followers of them for diagnosis of a "category" that "is comprised of melanocytic proliferations that form tumors in the dermis and are therefore potentially capable of metastasis." For Elder et al, "examples of such lesions may include atypical Spitz nevi, deep penetrating nevi, possible nevoid melanomas, or cellular blue nevi, where because of increased mitotic activity or cytologic atypia, a diagnosis of invasive or tumorigenic melanoma cannot be ruled out." Because MELTUMP is as unfathomable and as unuseful as superficial atypical melanocytic proliferation of uncertain significance, another acronym spawned by Elder et al, it is best discarded now before a foothold is gained in the lexicon of general pathology and dermatopathology.*

Ackerman AB, Elish D, Shami S. *"Spitz's Nevus": Reassessment Critical, Revision Radical*. New York, NY: Ardor Scribendi, 2007.

One never stops learning from a great teacher, the kind of teacher that *was* Bernie Ackerman. Even after his death recently, his words continue to guide, challenge, and inspire.

When Dr. Sangüeza asked me to consider writing a small article for this *Festschrift* for Bernie, I was at first reluctant because I could draw readily neither on a topic that was close to Bernie nor on which I thought I could communicate in a short piece; yet, after a day of thinking, I decided on a topic that Bernie and I discussed many times and which was somewhat difficult for me to understand initially but which later I have come to champion, at least on a local level. After thinking seriously about it over a period of several years, I will now attempt to lay out the issue and suggest a course of action for colleagues. The idea, however, was Bernie's, not mine. What was the idea? It was that a dermatopathologist's *primary responsibility* is to the diagnosis, *not* the prognosis, *nor* the potential, *nor* the risk.

Pathologists and dermatopathologists have rendered diagnoses for well more than 100 years by means of observations on tissue sections stained with hematoxylin and eosin identified with aid of a light microscope. In that span of time, no one has *ever* rendered specifically a prognosis, a potential, or a risk, although all have been advocated aplenty.

Diagnosis, "the art or act of identifying a disease,"[1] literally "across knowing" or "through knowing", is a concept that refers to the identification of a specific disease that the observer accomplishes by evaluating criteria and understanding that certain *essential* criteria are present in a given case for the purpose of effecting a given treatment (or no treatment). For one to establish a diagnosis, one must "know through" a set of criteria that are derived *inductively* from the observation of actual patients (including their biopsies) to determine which criteria matter—in fact, which are fundamental—and which do not. These criteria are then applied *deductively* to new cases to identify new examples of the same type or class of diagnosis. The inductive, then deductive, process directs (in fact refines) one to the *fundamentals* of the diagnosis.

Knowledge is derived from observation and conceptualization of facts in nature; these facts are integrated into concepts by a process of thought, and the concepts are, in turn, applied to instances of observation of new facts to understand concepts even better. Because this process is neither automatic nor infallible, it can take some time to understand *which* criteria are valid for a given diagnosis and whether the diagnosis itself is valid. This applies to the establishment of the knowledge of a disease in general but is also applied to an individual's personal knowledge of an already established disease. In the latter case, one must evaluate facts, judge whether certain criteria are present, and conclude that the weight of evidence supports a diagnosis, does not support it, or one does not have enough evidence to establish it in a given case.

In contrast, a *prognosis* refers to "the act or art of foretelling the course of a disease."[2] Furthermore, a *potential* refers to "existing in possibility: having the capacity or a strong possibility for development into a state of actuality."[3] A *risk* is "something that creates or suggests a hazard or adverse chance: a dangerous element or factor."[4]

Now consider the following phrases:

- Melanocytic Tumor of Uncertain Malignant Potential (MELTUMP)

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- Superficial Atypical Melanocytic Proliferation of Uncertain Significance (SAMPUS)
- Neoplasm with low risk
- Neoplasm with high risk

By the very nature of these phrases, the proponents of them admit openly that they do not know the diagnosis; yet, they advocate using these phrases in pathology reports instead of specific diagnoses or admitting forthrightly that they do not know the diagnosis, in fact, making new diagnostic categories that all state varying degrees of uncertainty as if they were on equal status with certainty.

This approach is flawed from the outset. *Certainty* is a concept that refers to the identification of facts that, taken together, mean something specific, given a context of knowledge in a given discipline in a given timeframe in which the knowledge was discovered. *Uncertainty* exists in one's mind when criteria are not fully sufficient to establish the nature of what is being considered. For one to claim that *nothing* is certain is also flawed because certainty is a presupposition of such a statement, making it an invalid assertion producing an infinite regress. A diagnosis is a statement of certainty. Anything else is a qualification, a statement of uncertainty that should not be elevated in a diagnosis line other than to admit the uncertainty.

But let us not confuse the issue of things as they exist in nature *versus* what one knows about them. Because the former, things in nature, exist apart from one's knowledge of them, one must make considerable intellectual effort to understand the natural history of a disease, including neoplastic disease. It is therefore tempting to accept the premise that all diseases exist on a spectrum and that the terms "benign" and "malignant" should be relegated to the dustbin of history to be replaced with the terms "low risk", "high risk" and various "risks" between those two extremes.[5] Worse yet is the proposition that the spectrum consists of benign neoplasms "transforming" into malignant ones, which is a sure sign of a mind out of focus.

The very nature of the arguments against using the dichotomy of "benign" versus "malignant" requires that those polar terms be accepted for the truth they convey about neoplasms, despite the fact that they do indeed exist on a spectrum of histological findings and clinical outcomes. For instance, there are neoplasms with a "low" histological grade, such as well-differentiated squamous carcinomas that no one today would be willing, on moral grounds, to perform the experiment to determine the biologic spectrum of those outcomes, which might have been allowed to play out in earlier times. Even the actinic (solar) keratosis, which is a form of superficial squamous carcinoma, is not really believed to be benign by anyone anymore; it, moreover, does not go untreated even by those who claim it to be benign by calling it "precancer." They know better. It is not merely a matter of fear of a lawsuit, it is the fact that the lesions are a rudimentary expression of squamous carcinoma, and, as a rule, will become the bigger lesions of squamous carcinoma if given enough time unchecked by the scalpel, cryotherapy, or chemical agents.

The example of melanocytic nevi existing as a continuous spectrum to melanoma is, in my opinion, the most notorious example of illogical thinking that exists in the field of dermatopathology. Yes, it is true that some melanocytic nevi can mimic melanomas morphologically, and, yes, it is true that the opposite occurs. It is even true that some melanocytic nevi occur in conjunction with melanomas and can be diagnosed as such. It is *not* true, however, that melanocytic nevi "convert" or "transform" into melanomas or that the natural history of a melanocytic nevus is to become a melanoma. If this were true, one would need no concept of melanocytic nevus; *all* melanocytic neoplasms would be melanomas (which they are not!).

The most problematic area of diagnosis of cutaneous neoplasms is with a small subset of melanocytic neoplasms. As Bernie indicated in the initial quotation in this essay, an entire lexicon has been constructed by various authors to attempt to name, in equivocal terms, melanocytic lesions that are difficult to diagnose, some of which are melanocytic nevi and some melanomas. It is tempting to believe that lower grade histological features somehow correlate to better outcomes, but even a single case of metastatic melanoma causing the death of a patient in such a case is enough to refute that position altogether (and it *is* false; some "low-grade" melanocytic lesions *do* metastasize and they *are* melanomas). The H&E characterizations of such lesions can get us only to the realization that they are different morphologically from the classically definable melanocytic nevi or melanomas that serve as contrasts; this fact does not *negate* the problem of benign versus malignant in melanocytic neoplasia but serves, rather, as an *example* of the problem. It shows clearly that some melanocytic lesions are difficult to diagnose and that criteria for a specific diagnosis still needs refinement by H&E, immunohistochemistry, genomic studies, or combinations of these if a diagnosis is ever to be established with certainty. This realization still leaves the problem of uncertainty of diagnoses of some neoplasms, a problem that will likely elude even the most advanced technology when studying biologic systems.

What something *is,* determines the range of what it *does*, which is nothing more than the law of causality applied to the practice of dermatopathology. Stated another way: diagnosis implies potential, prognosis, *and* risk because one cannot identify the diagnostic criteria without first having had the opportunity to observe a range of outcomes and learn to identify fundamental criteria observable from those outcomes.

Dermatopathologists do not have direct access, as a rule, to the biologic outcomes of a given neoplasm in daily practice; what they offer in its place is a diagnosis, which is an integration of the gross, histologic, immunohistoloigic, and molecular characteristics of a neoplasm compared to similar neoplasms that have been studied and reported formally in journals or textbooks or understood from one's own practice. In fact, not all of those extended techniques are necessary to establish many a diagnosis. Many, if not most, are established definitively only by the H&E coupled with a well-trained mind.

What should be done? How should certainty and uncertainty be handled in pathology reports? I advocate that a diagnosis is the *only* valid way to frame a pathology report. A potential is not a valid designation, neither are prognostic terms valid in this context, nor is risk. One cannot with certainly, for instance, determine how a melanoma will affect a given patient based on the thickness of it.[6] A statement of prognosis or potential or risk has no meaning in this context. Only a diagnosis is meaningful because it determines immediately what must be done: excision.

If a specific diagnosis cannot be made, it must be indicated clearly in the report, and it must be stated why a specific diagnosis cannot be made in a given case. "I don't know," without an explanation, will satisfy neither the clinician's inquiry nor the patient's needs.

Yet, even when the diagnosis of malignancy *is* known with certainty in a given case, it implies only a *range* of outcomes. Because the nature of a diagnosis in dermatopathology is the identification of a set of morphologic criteria, a specific diagnosis stands for a range of outcomes of lesions of similar structure morphologically. It is simply not possible in a given case to determine a specific outcome on that basis; that problem is addressed properly by clinical experience and by statistical methods based on a large number of cases of a similar type so that rational treatments can be effected by clinicians and oncologists. The knowledge and science of prognosis *is dependent*, however, on establishing a *diagnosis* in any given case and that order cannot be reversed in any useful, meaningful way. It is time that dermatopathologists stand proudly to defend the process of diagnosis because it is the anteroom to the understanding of the proper treatment of the patient.

If Bernie were alive, I believe he would agree with me that dermatopathologists need to dedicate themselves fully to establishing diagnostic criteria and learning how to define and apply them in given cases, especially cases where there tends to be a range of disagreement among reviewers. Here is the way he phrased it in response to a question about criteria that was posed by my associate, Sarah N. Walsh, MD, regarding his textbook on Spitz's nevus:

Dr. Walsh asks properly how it is possible to identify with confidence a lesion challenging diagnostically as either a Spitz's nevus or a melanoma when a metastasis has not become evident. The answer for me is application of criteria histopathologic that actually work. A Spitz's nevus is no more a melanoma than a donkey is a horse. Even "identical twins" are not identical! One simply has to know what to look for to distinguish between them—and when one knows the distinction can be made with repeatability. It is not necessary to see a donkey run in order to differentiate it from a horse, and it is not necessary to wait for a metastasis to determine that a neoplasm is a melanoma and not a Spitz's nevus. In fact, many a patient with a rather thick melanoma lives in harmony with that malignant neoplasm, sometimes even with metastases of it that are only identified postmortem, for decades and dies from a cause entirely unrelated. Nothing pertinent to history should have any influence on interpretation of findings in sections of tissue, those being the sole considerations in rendering a diagnosis with specificity. In sum, although a metastasis seals a diagnosis of melanoma, absence of metastasis proves nothing and, in the analysis ultimate, diagnosis morphologic turns wholly on assessment of changes morphologic. Parenthetically, in the majority vast of instances, a melanoma is as different histopathologically from a Spitz's nevus as a giraffe is from a chimpanzee.[7]

In sum and in short: Diagnosis! (*not* prognosis, *not* potential, *not* risk).

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